

Fibrotic Interstitial Lung Diseases: CAR/CSTR Practice Guidelines for HRCT Diagnosis

Canadian Association of

Radiologists Journal

1–18

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DOI: 10.1177/08465371261486850

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Abstract

Fibrotic interstitial lung diseases (fILD) are a heterogeneous group of chronic diseases that require clinical, radiological and pathological correlation for diagnosis and management. In this setting, the role of radiologists is to define the ILD pattern using high-resolution CT (HRCT). These practice guidelines, developed by the Canadian Society of Thoracic Radiology (CSTR) and the Canadian Association of Radiologists (CAR), provide evidence-informed recommendations to assist practicing radiologists in standardizing HRCT acquisition and pattern recognition in fILD. Based on an integration of current evidence and expert consensus, it outlines core knowledge for identifying features of fibrosis and ancillary radiological findings that assist on pattern identification, providing a practical framework to imaging diagnosis. The document includes multidisciplinary correlation for the diagnosis of most common fibrotic ILDs and an updated review of specific clinical diagnoses relevant to the radiology practice.

Résumé

Les pneumopathies interstitielles fibrosantes (PIF) constituent un groupe hétérogène de maladies chroniques nécessitant une corrélation clinique, radiologique et pathologique aux fins de diagnostic et de prise en charge. Dans ce contexte, le rôle des radiologistes consiste à définir le profil de la PIF à l'aide de la tomodensitométrie haute résolution (TDM-HR). Ces lignes directrices de pratique, élaborées par la Société canadienne de radiologie thoracique (CSTR) et l'Association canadienne des radiologistes (CAR), formulent des recommandations éclairées par les données probantes afin d'aider les radiologistes praticiens à standardiser l'acquisition d'images par TDM-HR et la reconnaissance des profils dans les PIF. S'appuyant sur une synthèse des données probantes actuelles et sur un consensus d'experts, ce document présente les connaissances fondamentales permettant d'identifier les caractéristiques de la fibrose et les résultats radiologiques accessoires qui facilitent l'identification des profils, en proposant un cadre pratique pour le diagnostic par imagerie. Le document comprend une corrélation multidisciplinaire pour le diagnostic des PIF les plus courantes ainsi qu'une revue actualisée des diagnostics cliniques spécifiques pertinents pour la pratique de la radiologie.

Keywords

fibrotic interstitial lung disease, high-resolution computed tomography, interstitial lung disease, usual interstitial pneumonia, nonspecific interstitial pneumonia, practice guideline

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Introduction

Fibrotic interstitial lung diseases (fILD) encompass several chronic conditions characterized by variable degrees of inflammation and fibrosis, resulting in restrictive lung physiology and respiratory symptoms. Clinical course and prognosis vary depending on the etiology, and pattern on high-resolution CT (HRCT) and histology, ranging from slowly progressive disease to inexorable progression and respiratory failure. Fibrotic ILD may be idiopathic or secondary to a variety of causes such as autoimmune disease, environmental, and drug exposure; it can be sporadic or associated with a familial history.¹⁻⁴ Treatment options include immunosuppressants and anti-fibrotic agents that are indicated depending on etiology and clinical evolution. A diagnosis of fibrotic ILD can be achieved only after assessment and integration of clinical, radiological, and at times pathological data. Multidisciplinary discussion (MDD) including respirologists, radiologists, and pathologists with expertise in ILD is considered the reference standard for diagnosis.

HRCT of the chest plays a key role in the assessment of patients with fILD. HRCT patterns of fibrotic ILD correlate with the probability of a specific diagnosis,^{2,4} inform management and correlate with prognosis.^{5,6} The central role of radiology in the diagnosis and management of fILD emphasizes the importance of knowledge of current guidelines definitions and nomenclature. The objective of this document, endorsed

by the Canadian Association of Radiologists (CAR) and the Canadian Society of Thoracic Radiology (CSTR), is to assist practicing radiologists in the HRCT interpretation of fILD. It is not intended to replace existing guidelines that are the cornerstone of ILD diagnosis. Rather, this document outlines the core knowledge necessary for diagnosing fILD and provides a concise and pragmatic integration of current guidelines, scientific evidence, and evidence-informed expert opinion, aiming to improve and standardize HRCT interpretation in fILD.

Technical Recommendations for HRCT in Fibrotic ILD

The imaging diagnosis of fILD requires HRCT of the chest with specific parameters that ensure high imaging quality at the lowest possible radiation dose.^{7,8} Following well-established technical parameters, the CSTR issued a simplified HRCT protocol that can be easily used in clinical practice, summarized in Table 1.⁹

Patients are scanned in the supine position with one breath-hold at end inspiration. Expiratory scans should be routinely performed as part of the initial assessment of ILD but are generally not required at follow up imaging, unless deemed necessary to reassess a particular finding. HRCT scans should be obtained without intravenous contrast. If contrast is required, for example to diagnose pulmonary embolism, contrast-enhanced CT should

Table 1. HRCT Protocol—CSTR Recommendation.⁹

Image series	Technical parameters	Window settings	Indication
Inspiratory (supine scan, without IV contrast)	Volumetric acquisition One breath hold, end inspiration Axial contiguous 1-1.25 mm High frequency algorithm Standard dose MPR (coronal and sagittal)*	Lung kernel Window level: -600 to -700 HU Window widths: 1000 to 1500 HU	All baseline studies All follow-up studies
Expiratory* (supine scan)	Axial 1-1.25 mm slice thickness Contiguous or 1-2 cm intervals High frequency algorithm (consider low or very low dose)	Lung kernel Window level: -600 to -700 HU Window widths: 1000 to 1500 HU	All baseline studies Follow-up studies if expiratory imaging not done previously, and if the ILD pattern remains uncertain
Prone imaging** (inspiratory)	Axial 1-1.25 mm slice thickness contiguous or at regular intervals End inspiration High frequency algorithm	Lung kernel Window level: -600 to -700 HU Window widths: 1000 to 1500 HU	Not required routinely Assessment of questionable abnormalities in the dependent lungs
Mediastinal windows	Axial 2.5-5 mm slice thickness Contiguous	Soft tissue kernel Window level: 40 to 60 HU Window widths: 350 to 450 HU	All baseline studies All follow-up studies
Multiplanar reformats: maximum intensity projection (MIP)	8 mm thick, contiguous reconstruction	Lung kernel Window level: -600 to -700 HU Window widths: 1000 to 1500 HU	Optional for baseline studies and follow-up studies Useful for nodule detection

Note. *Important to ensure if adequate expiratory scan by assessing anterior bowing of the posterior tracheal wall.

**Useful in selected cases to distinguish interstitial lung disease from dependent atelectasis. Review of prior imaging (including CT abdomen) with lung bases can determine whether prone imaging is needed.

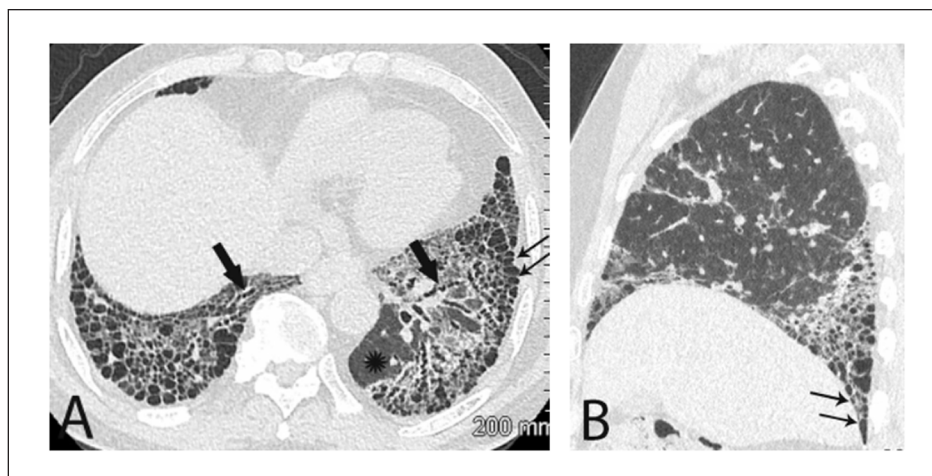


Figure 1. UIP (usual interstitial pneumonia) pattern—83-year-old man with clinical diagnosis of IPF. (A) Axial HRCT image shows findings of fibrosis, including reticulations, traction bronchiectasis and bronchiolectasis (arrows) in a subpleural, dorsal and lower lung distribution. Cystic spaces with well-defined walls in the immediate subpleural lung are consistent with honeycombing (thin arrows). Note the areas of relative normal lung parenchyma within the areas of fibrosis (asterix) reflecting temporal heterogeneity. (B) The subpleural and dorsal distribution and the involvement of the extreme costophrenic sulci, expected for the diagnosis of UIP pattern, are best appreciated on sagittal reformats (thin arrows).

be preceded by a non-contrast HRCT scan.^{7,8} Prone HRCT scan is not routinely recommended and should be reserved to cases where dependent opacities are identified and it is unclear whether these represent subtle interstitial changes versus dependent atelectasis. This may have particular relevance in patients with scleroderma and asbestos exposure.

Consistent window settings are essential in the interpretation of HRCT of the chest. Variations in window parameters can have a substantial impact in the appearances of the lung parenchyma and in the detection of abnormalities. More important than specific window width and levels is the consistent use of the same window settings in all patients. This helps radiologists to develop personal parameters of what is normal and abnormal and is particularly important when comparing different exams from the same patient. Sagittal and coronal reconstructions with thin sections can provide useful information in selected cases, particularly regarding distribution of the disease. Soft tissue kernel/low frequency filter reconstructions are required and may reveal mediastinal or pleural findings that may support specific fILD diagnoses, such as pleural plaques and esophageal dilatation.

HRCT Findings in Fibrotic ILD

Defining Features of Interstitial Fibrosis

The defining HRCT features of interstitial fibrosis are reticulations, traction bronchiectasis and bronchiolectasis, honeycombing, and architectural distortion. Early fibrosis may manifest with fewer and subtler findings.

Reticulation or reticular opacities are caused by thickening of the intralobular and interlobular interstitium by inflammation and fibrosis, manifesting on HRCT as intralobular linear opacities (reticulations) and irregular septal thickening,

respectively (Figure 1).¹⁰ *Reticulations* are one of the earliest signs of fibrosis on HRCT and may progress from fine to coarse with disease progression. To represent fibrosis, reticulations must be associated with lung distortion, best seen on CT as traction bronchiolectasis/bronchiectasis. Reticulations can cause irregular interfaces between the lung and adjacent vessels, bronchi and pleura, the so-called *interface sign*.^{8,10}

Traction bronchiectasis and bronchiolectasis refer to dilatation and distortion of the small airways by surrounding fibrosis, thus typically seen within areas of reticulation. Traction bronchiolectasis implies dilatation of peripheral bronchioles whereas traction bronchiectasis refers to dilated and tortuous segmental and subsegmental bronchi, often with thickened walls (Figure 1).^{8,10} The branching and irregular tubular appearance of traction bronchiectasis and bronchiolectasis are helpful in the distinction from honeycombing, and this can be better appreciated in multiplanar reformats.¹¹

Honeycombing refers to cystic spaces with well-defined walls usually ranging from 3 to 10mm (but that can be several millimeters in diameter).^{10,11} The presence of three cysts in a row, in a single or in multiple layers,¹⁰ allows a diagnosis of honeycombing in the presence of other findings of interstitial fibrosis.⁸ Distribution along the immediate subpleural lung is required (Figure 1). Honeycombing can usually be differentiated from subpleural (paraseptal) emphysema by its association with other findings of fibrosis, preferential involvement of the lower rather than the upper lobes, and cysts that usually measure <10mm and have thick walls, as compared to paraseptal emphysema that tends to be larger with thin walls. However, differentiation can be challenging in individual cases, particularly when they coexist, being difficult to ascertain where one starts and the other begins.^{10,11} Studies of CT-pathological correlation have demonstrated that the conceptual separation of

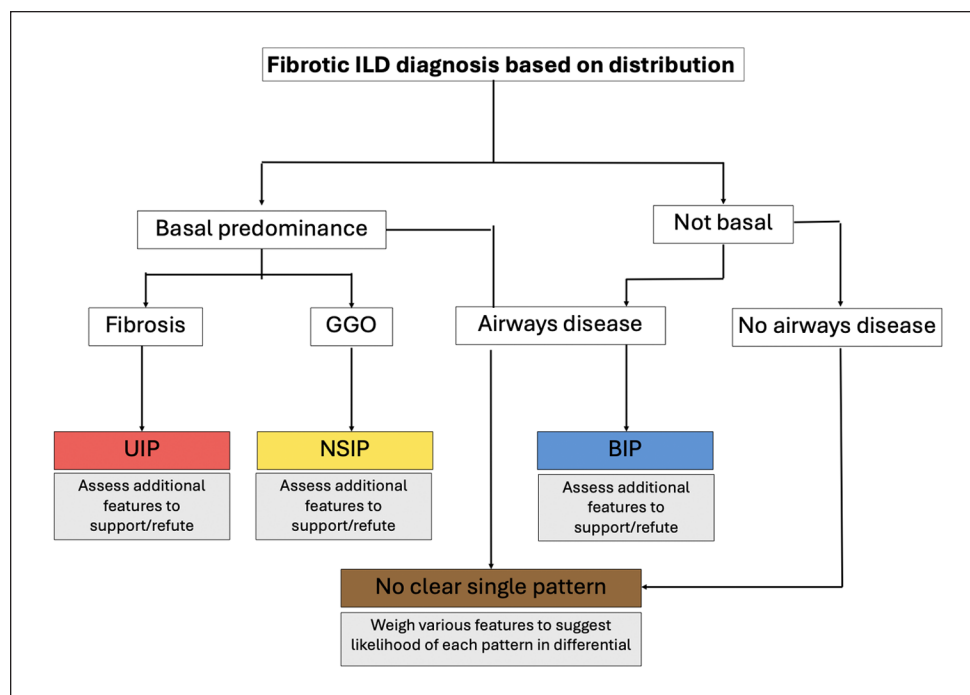


Figure 2. Fibrotic ILD diagnosis based on disease distribution.

honeycombing and traction bronchiolectasis may be deceiving. Honeycombing seen on HRCT may reflect actual pathological honeycombing or traction bronchiolectasis seen tangentially.^{4,12,13} Pathologically, traction bronchiolectasis and honeycombing are part of a continuum of lung fibrosis and remodeling, reflecting a spectrum of fibrosis severity. Nonetheless, the diagnosis of honeycombing on HRCT is important and may predict response to pharmacotherapy and prognosis.^{2,5} In a recent study, the extent of traction bronchiectasis and honeycombing were independently associated with worse prognosis regardless of ILD subtype (Figures 2 and 3).⁵

Ancillary HRCT Features in Fibrotic ILD

HRCT features of fibrosis are often accompanied by ancillary findings that may reflect pathological changes seen in specific ILD patterns. The presence and distribution of these ancillary findings, integrated with the distribution of fibrosis, are essential in the identification of HRCT patterns.

Ground-glass opacities (GGO), defined as increased attenuation of the lung parenchyma without obscuration of underlying vessels and bronchi,¹⁰ are common in ILD. In these patients, GGO occurring away from areas of fibrosis often reflects active interstitial inflammation with increased likelihood to respond to anti-inflammatory therapy, whereas GGO superimposed on traction bronchiectasis/bronchiolectasis or honeycombing usually represents irreversible microscopic fibrosis below the resolution of HRCT (Figure 4A).¹⁴⁻¹⁶ However, the radiological-pathological correlation of GGO and inflammation in fILD is not perfect and based on limited data. GGO with

fine reticulations but with no traction bronchiectasis or honeycombing represents a nonspecific feature that may reflect inflammation or fibrosis.¹⁷ In patients with acute clinical change, patchy or diffuse GGO unrelated to fibrotic areas is most suggestive of a transient process such as infection, pulmonary edema, hemorrhage, or acute exacerbation of fILD. In these cases, determining a specific diagnosis may be difficult. The distribution of abnormalities, temporal evolution, and correlation with acute symptoms are helpful in the differential.

Attention must be paid to proper technique and potential pitfalls in the identification of GGO. HRCT thin-collimation, sharp reconstruction algorithm, full inspiration, and appropriate and consistent window settings are required to confidently diagnose GGO.⁸ Motion artifacts and suboptimal inspiration can result in areas of high attenuation that may lead to misdiagnosis.¹⁴ Anterior bulging of the posterior wall of the trachea and flattening of the azygoesophageal recess indicates that the scan was obtained during expiration. Assessment of the large airways may also be helpful to determine if GGO is artifactual: if the air in the trachea and main bronchi appears hazy and gray rather than black, the increased lung attenuation is likely artifactual rather than pathological.⁸ In addition, increased attenuation can be seen in the dependent portions of the lungs and must be differentiated from early fibrosis. In these cases, prone CT may be required.

Mosaic attenuation describes an inhomogeneous appearance of the lungs caused by differences in attenuation. It can be a combination of normal lung (higher attenuation) and areas of decreased (lower) attenuation, as seen with decreased perfusion, or may be a combination of normal

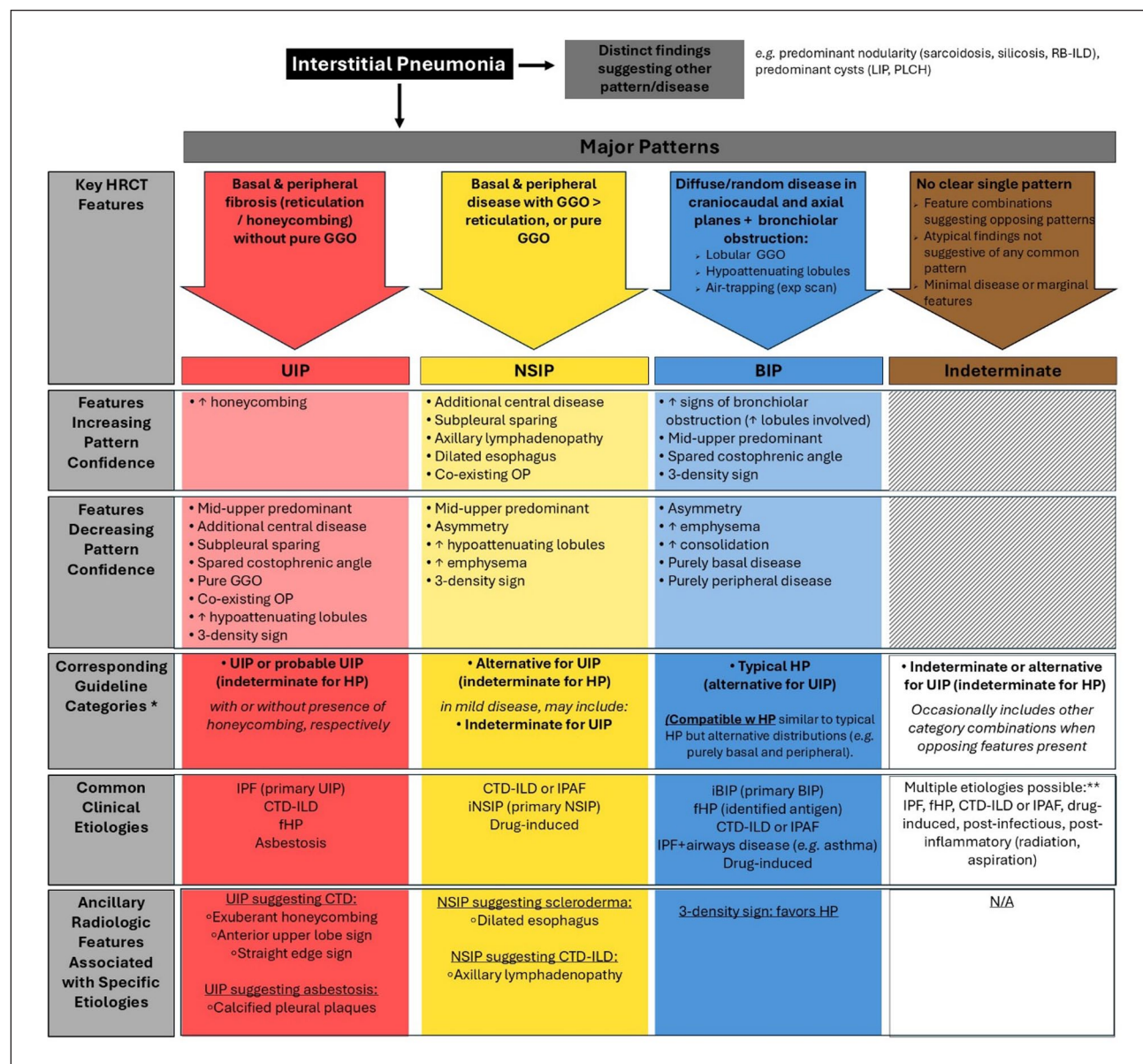


Figure 3. Major patterns for fibrotic ILD diagnosis.

Note. *2022 IPF/PPF guidelines⁴ and 2020 HP guidelines³ (in brackets).

**Minimal disease may evolve to UIP or NSIP patterns.

lung (lower attenuation) and GGO (higher attenuation), as seen in infiltration of the interstitium or airspaces. The term can be applied when the cause of inhomogeneous attenuation is unclear.^{8,10}

Mosaic perfusion refers specifically to a mosaic attenuation caused by regional differences in lung perfusion.^{10,18} Vessels within the areas of decreased attenuation may be smaller relative to vessels of similar order in the denser lung, a feature that when present helps in the distinction with mosaic attenuation caused by GGO, where vessels of similar order have similar sizes in the abnormal and normal lung. Of note, the descriptor “perfusion” in this setting does

not necessarily imply a primary vascular disease. Mosaic perfusion can be caused by vascular pathologies such as chronic thromboembolic disease, but it is more commonly related to reflex vasoconstriction driven by areas of hypoventilation in small airways diseases. Areas of hypoattenuating lung with lobular distribution are a reliable finding of small airway disease and bronchiolar obstruction (Figure 5).^{3,18}

Air-trapping is defined as focal areas of gas retention seen as regional areas of low attenuation on expiratory CT (Figure 5C). Mosaic attenuation and air-trapping are distinct CT findings that should not be applied interchangeably, with the term air-trapping being reserved to expiratory images.^{10,18}

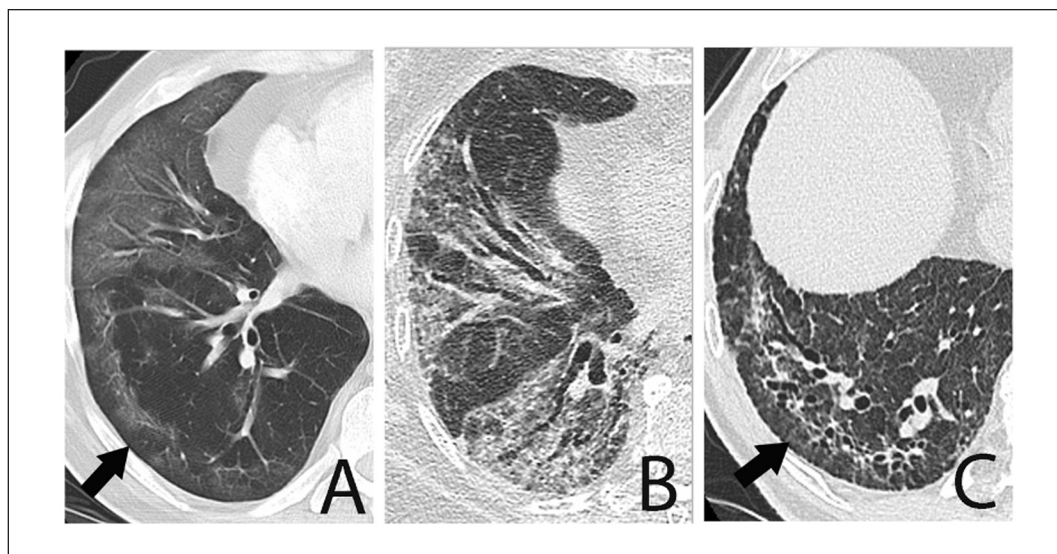


Figure 4. NSIP (nonspecific interstitial pneumonia) pattern. HRCT scans in three different patients show variable degrees of ground-glass opacities and fibrosis in a predominant lower lobe distribution. (A) 64-year-old man with mixed connective tissue disease. There are ground-glass opacities and fine reticulations with very mild traction bronchiectasis. The presence of subpleural sparing, seen as relatively normal subpleural lung (arrow), is one of the best imaging predictors of the NSIP pattern. Note the central (peribronchovascular) distribution in the right middle lobe (B) 71-year-old woman with inflammatory myositis. There is fibrosis with coarser reticulations and traction bronchiectasis, and mild ground-glass opacities. The peribronchovascular distribution and central bronchiectasis in the right middle lobe are characteristic for NSIP. (C) 77-year-old-man with dermatomyositis. There is more severe fibrosis and traction bronchiectasis without ground-glass opacities. The presence of subpleural sparing (arrow) supports the diagnosis of an NSIP pattern.

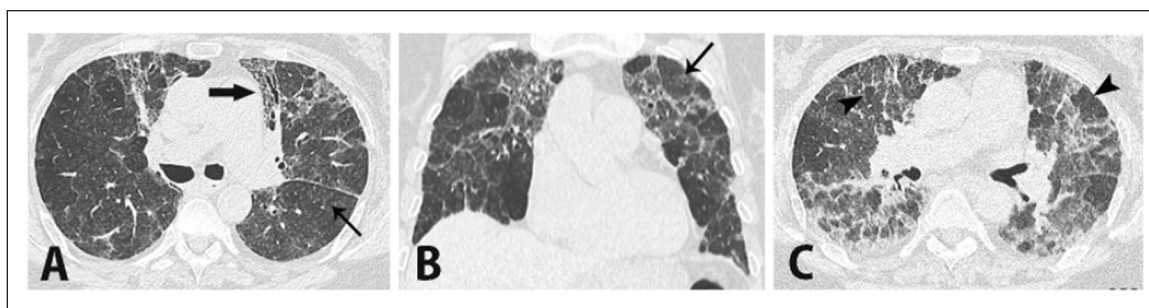


Figure 5. BIP (bronchiolocentric interstitial pneumonia) pattern. 64-year-old man with clinical diagnosis of fibrotic hypersensitivity pneumonitis. Inspiratory HRCT images with axial (A) and coronal (B) reformats show features of fibrosis (arrow) and bronchiolar obstruction presenting with the three-density sign, a combination of well-demarcated normal lung, ground-glass opacities, and decreased attenuation. Centrilobular ill-defined ground-glass nodules are present (thin arrows), reflecting bronchiolar and peribronchiolar inflammation that leads to airway obstruction. The disease has a random distribution in the axial plane (central and peripheral fibrosis) as well as in the craniocaudal plane. Expiratory HRCT scan (C), shows well defined areas of low-attenuation reflecting air-trapping (arrowheads).

The *three-density or three attenuation sign* (previously called the head-cheese sign) is defined as a combination of well-demarcated normal lung, GGO (high attenuation), and decreased attenuation (hypoperfusion) seen in inspiratory scans (Figure 5).^{3,10,18}

Centrilobular nodules with ground-glass attenuation may also be a manifestation of chronic small airways disease (Figure 5).^{3,18} In the setting of ILD, these centrilobular nodules reflect bronchiolar and peribronchiolar inflammation on

histology, which lead to airway obstruction, hypoventilation, and reflex hypoperfusion.

Pulmonary ossification, reflecting metaplastic bone formation and presenting as small high-density (calcified) nodules, occurs in approximately 20% of patients with pulmonary fibrosis, most commonly in IPF.^{8,19}

Consolidation, defined as homogeneous increased attenuation with obscuration of the underlying vessels and bronchi,¹⁰ is often a manifestation of an acute transient process in patients with fILD. Less commonly, extensive confluent



Figure 6. NSIP with OP (organizing pneumonia) overlap. 44-year-old female with anti-synthetase syndrome. Axial HRCT scans demonstrate consolidations with OP pattern superimposed to otherwise typical features of NSIP, including fibrosis in a peribronchovascular distribution as seen in the right middle lobe. Note the well-demarcated elongated consolidations with peribronchovascular distribution (arrows) and the reversed halo sign (thin arrow), features characteristic of OP.

interstitial thickening and dense fibrosis may manifest with consolidation on CT. Consolidation with elongated or curvilinear peribronchovascular distribution is suggestive of organizing pneumonia (OP; Figure 6).^{10,20} OP can be a reaction to a transient process such as infection and drug toxicity, or can be related to the underlying ILD, a pattern of injury commonly seen in autoimmune or connective-tissue diseases (CTD).^{21,22}

Disease Distribution

Assessment of distribution of abnormalities on HRCT is key in the differential diagnosis of fILD, as most fILD show preferential or specific distributions in the lungs.²³

In the axial plane, *peripheral* or *subpleural* abnormalities affect the periphery (outer one-third) of the lungs and may or may not touch the pleura (Figure 1). *Central*, *bronchocentric*, or *peribronchovascular* are synonymous terms describing a distribution characterized by involvement of the inner-two thirds of the lungs, surrounding the central bronchi and vessels in the axial interstitium (Figure 4). Fibrotic ILD may exhibit axial distributions that are predominantly peripheral, central, or a combination of both. In cases where the disease has no clear peripheral or central predominance, the distribution may be described as *diffuse in the axial plane* (Figure 5).

Subpleural sparing refers to an area of relative normal appearance of the immediate subpleural lung (within 1 cm or less from the pleura), typically in the dorsal regions of the lungs (Figure 4).^{10,24,25}

A *posterior or dorsal predominance* is common in fILD, often associated with lower lobe predominance. Posterior distribution as well as involvement of the *extreme costophrenic sulci* just above the diaphragm, are best appreciated on sagittal and coronal reformats (Figures 1 and 7). *Anterior predominance* of abnormalities is relatively uncommon in fILD, but it is well described as sequela of diffuse

alveolar damage (DAD)/acute respiratory distress syndrome (ARDS).

For the assessment of *craniocaudal* distribution, the relative extent and severity of the abnormalities is compared in the mid-upper and lower lung zones. Diseases with no craniocaudal predominance and relative uniform distribution are described as *diffuse*. Diseases with multifocal or patchy distribution and no preferred craniocaudal or axial distribution, are described as *random*. Coronal reformats can be useful to determine the craniocaudal distribution in challenging cases.

Fibrotic ILD often has a *bilateral* and relative *symmetrical* distribution but asymmetric involvement is occasionally seen and does not necessarily preclude a specific pattern.

Typical HRCT Patterns of Fibrotic ILD

Characterizing the HRCT pattern is a critical initial step in the diagnosis of fILD. Using established criteria, combinations of HRCT features are categorized into specific fILD patterns that, when combined with clinical data, correlate with the probability of a specific disease etiology.¹⁻⁴ These HRCT patterns also inform management, with extents of inflammatory or fibrotic features sometimes influencing the choice of immunosuppressant and/or antifibrotic treatments. Importantly, the extent and severity of fibrosis on HRCT correlate with prognosis.^{3,5,6} Specific HRCT patterns correlate with and serve as surrogates for pathological patterns, giving them substantial weight during MDD. However, it is essential to emphasize that an HRCT pattern alone does not constitute a clinical diagnosis. MDD remains the reference standard for diagnosing fILD, integrating clinical, radiological, and—when available—pathological findings. The radiologist's role is to accurately describe and define the HRCT pattern. In this section, typical HRCT patterns of fILD are described.

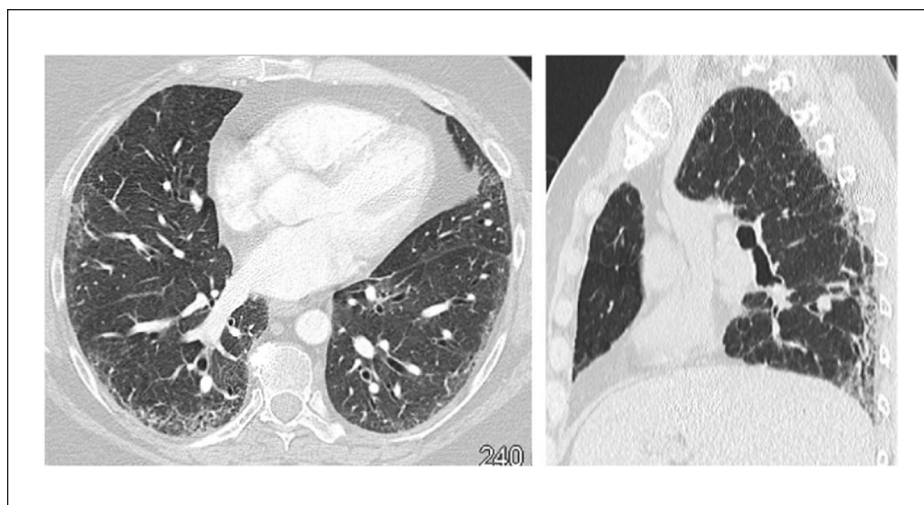


Figure 7. Probable UIP pattern. 67-year-old man heavy smoker presenting with shortness of breath and restrictive physiology. Axial and sagittal HRCT scans show mild fibrosis with reticulation and traction bronchiectasis in the peripheral and dorsal aspects of the lower lobes. Note the involvement of the posterior costophrenic sulcus in the sagittal reformat. The appearance and distribution are similar to UIP however there is no honeycombing. The absence of subpleural sparing helps in differentiating from the NSIP pattern. The patient was diagnosed with IPF after multidisciplinary discussion.

Usual Interstitial Pneumonia (UIP) Pattern

UIP is the most common fibrotic ILD pattern and the one generally with the worst prognosis.^{1,2,6} Guideline-defined UIP pattern on HRCT is based on the presence of fibrosis in a predominantly subpleural, dorsal, and basal or lower lung distribution, in the absence of features that suggest an alternative diagnosis, such as nodules, consolidation, pure GGO or extensive admixed GGO, mosaic perfusion, or air-trapping.^{2,4} These abnormalities are thought to necessarily involve the extreme costophrenic sulci (Figure 1), with experts considering absence of involvement indicative of a non-UIP diagnosis. Presence of upper lung reticulation is not uncommon and has been shown to be an independent predictor of UIP. However, when present, the burden of disease is milder than in the lower lobes.^{6,25,26}

Areas of fibrosis interspaced with areas of normal lung (spatial heterogeneity) are seen in most cases of UIP. Reticulation causing irregular pleural, vascular, and bronchial interfaces (interface sign) is common, as well as architectural distortion in more advanced cases. The presence of honeycombing is required for the identification of a UIP pattern according to current guidelines and correlates with a high likelihood of UIP on histology in the appropriate population (i.e., individuals without antigen exposure or a clinical diagnosis of CTD).^{2,4}

The term *probable UIP* is used to describe similar findings except without honeycombing, and is associated with a slightly lower, yet still high (70%-89%) probability of histological UIP in selected patients without alternative explanation for the fILD.^{2,4} Probable UIP may manifest with mild changes of fibrosis and reticulation in the dorsal lungs; in these cases, the absence of subpleural sparing helps in

differentiating from NSIP (Figure 7).^{24,25} Merging UIP and probable UIP into a single category has been suggested in view of their radiological and clinical similarities and the high confidence of UIP on histology; nonetheless, they remain in separate in current guidelines.^{2,4} UIP and probable UIP patterns on HRCT are sufficient to indicate a clinical diagnosis of IPF without biopsy if other potential causes are excluded.⁴

Nonspecific Interstitial Pneumonia (NSIP) Pattern

NSIP pattern is defined by bilateral, symmetric, and lower zone predominant ground-glass opacities, fine reticulation, and traction bronchiectasis/bronchiolectasis. NSIP is almost invariably basal predominant. In the axial plane, a peribronchovascular distribution is characteristic and helps in the differentiation from UIP that has a subpleural distribution.^{17,24,25,27} Peribronchovascular distribution may occur either in isolation or most commonly with a combination of central and peripheral disease (Figure 4).²⁴ A distinct peribronchovascular distribution in the right middle lobe immediately above the diaphragm has been described as characteristic for NSIP.^{25,28} Subpleural sparing is one of the best predictors of NSIP;^{24,25} in a large cohort, it was seen in 47% of patients and correlated with a better outcomes.²⁵ The lack of subpleural sparing however does not exclude NSIP.⁴

In mild NSIP, ground-glass predominates and may occur in the absence of reticulation or fibrosis, evolving to a more reticular appearance with traction bronchiectasis and bronchiolectasis as the disease progresses (Figure 4).^{24,27} Honeycombing is rare but may be present, complicating differentiation with UIP pattern.^{1,25,27} Although the severity of fibrosis may vary considerably, the terms “non-fibrotic NSIP” and “fibrotic NSIP” have no formal imaging definition and

have shown limited correlation with cellular, mixed and fibrotic NSIP described on pathology.^{17,29} Substantial mosaic perfusion and air-trapping, emphysema, asymmetry, or the presence of the 3-density sign on HRCT are features that make NSIP less likely and should lead to consideration of other patterns.

NSIP with organizing pneumonia (OP) overlap refers to findings of OP, characterized by consolidations and/or ground-glass opacities, superimposed to otherwise typical features of NSIP (Figure 6).^{20,21} The proportion of OP and NSIP varies with the stage and severity of the process. Areas of OP may either resolve or progress to fibrosis. NSIP with OP overlap is a radiological and pathological pattern typically associated with CTD-ILD, particularly inflammatory myositis.^{22,30,31}

Bronchiolocentric Interstitial Pneumonia (BIP) Pattern (Formerly Fibrotic Hypersensitivity Pneumonitis Pattern)

The presence of interstitial fibrosis along with features of bronchiolar obstruction are considered distinctive for the diagnosis of bronchiolocentric interstitial pneumonia (BIP), traditionally referred as *HP pattern*.^{3,25,32} The small airways disease is caused by bronchiolar and peribronchiolar inflammation and/or fibrosis leading to obstruction, hypoventilation, and reflex hypoperfusion. Historically felt to be related to inhaled antigens, the BIP pattern of injury can be seen in diseases other than HP, notably CTD-ILD (particularly rheumatoid arthritis), aspiration, other inhalational diseases, and drug-associated ILD.^{23,33} Thus to better reflect the differential diagnoses of these airway-centered process, the recent ATS/ERS update on interstitial pneumonias has recommended the term *BIP pattern* to replace the term *HP pattern* seen on imaging and histology, and that the latter term be reserved for the multidisciplinary diagnosis of HP (i.e., secondary BIP due to an identified inhaled antigen).³⁴ The term BIP prevents confusion between *pattern* and *clinical diagnosis*, akin to the classification of other interstitial pneumonias (i.e., UIP pattern and IPF).^{2,4}

The clinical, imaging, and histological features of BIP have not been fully characterized and derive from the HP literature.³⁴ Based on current evidence and expert opinion, the present document describes a diagnostic approach to BIP similar to the 2020 HP guidelines,³ applying the term “BIP (HP)” in reference to existing literature while encouraging adoption of the term BIP over the traditional “HP pattern.”^{3,32,34} Histologically, BIP (HP) presents with variable degrees of inflammation and fibrosis and can be classified as non-fibrotic (or cellular) and fibrotic. The radiological features in cases of histologically confirmed BIP require further investigation.³⁴ Extrapolating from the HP literature, a fibrotic BIP pattern manifests on HRCT with features of fibrosis and bronchiolar obstruction, including ground-glass and mosaic attenuation in the inspiratory view, typically hypoattenuating lobules, and lobular air-trapping on expiratory views. The

three-density sign in inspiratory images has high specificity for distinguishing BIP (HP) from UIP and NSIP patterns.^{3,25,32} Interstitial fibrosis presents with fine or coarse reticulations, alone or with traction bronchiectasis/bronchiolectasis, with or without honeycombing, and often within areas of ground-glass attenuation. The distribution of BIP (HP) varies, being more commonly randomly distributed in the craniocaudal plane with both peripheral and central involvement.^{3,25,32,34}

Pleuroparenchymal Fibroelastosis (PPFE). PPFE is a rare fibrotic ILD pattern characterized by progressive apical and upper lobe-predominant fibrosis involving the pleura and subpleural lung. PPFE can be idiopathic or secondary to an identifiable cause, including CTD, lung or hematopoietic stem cell transplantation, medications, radiation therapy, recurrent infections, and occupational.^{30,35} PPFE may co-exist with other patterns of fILD such as UIP, NSIP, or BIP.³⁵

PPFE is characterized by upper lobe predominance of dense, irregular subpleural thickening or nodular consolidation and reticulation, often associated with traction bronchiectasis and upper lobe volume loss (Figure 8).³⁵ Diagnostic criteria for PPFE have been proposed and can be helpful to radiologists.^{30,36} In many cases of PPFE, there is concurrent lower lobe involvement, most commonly with UIP or probable UIP patterns.^{1,35} PPFE must be differentiated from apical scarring, a common incidental finding in older patients, that tends to be more regular and restricted to the uppermost aspect of the apices.³⁷ The most reliable distinguishing feature is the progression over time seen in PPFE, in contrast to the long term stability in apical scarring. Differentiation with end-stage sarcoidosis relies on the peribronchovascular and perihilar distribution of the latter, the absence of substantial subpleural thickening or consolidations and in some cases the presence of perilymphatic nodules and central progressive massive fibrosis. Spontaneous and recurrent pneumothorax is common in PPFE and may help in the differentiation.³⁵

Integration of Current Imaging Guidelines

Fibrotic ILD are a heterogeneous group of diseases that can present with similar clinical and imaging manifestations. Identification of a specific HRCT ILD pattern can be challenging. Current multidisciplinary evidence-based guidelines for IPF and HP help to address this issue by defining HRCT categories that correlate with radiologists' confidence and likelihood of a pathological and clinical diagnosis.^{2,4,32} The proposed HRCT patterns have different specificities for various diagnoses and are used to guide further investigations and treatment. Existing guidelines have been written in relative isolation of one another, and there are no evidence-based guidelines for NSIP and other fibrotic ILDs. This section provides practical recommendations for integration and application of available guidelines in daily

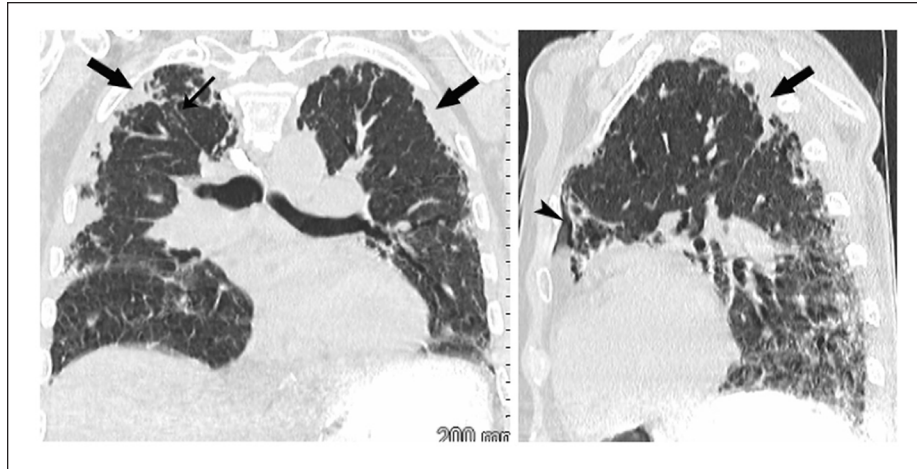


Figure 8. Pleuroparenchymal fibroelastosis (PPFE). Coronal and sagittal HRCT reformats in an 81-year-old man shows bilateral upper lobe irregular subpleural thickening, some with wedge-shaped appearance (arrows), along with traction bronchiectasis (thin arrow) and architectural distortion. Interstitial fibrosis with UIP pattern is present in the lower lobes, better demonstrated in the sagittal view. Note the presence of a small pneumothorax, a common finding in patients with PPFE (arrowhead).

practice and proposes a systematic approach to the imaging diagnosis of fibrotic ILDs.

Traditionally, the initial approach for an unknown case of fILD is centered on identifying or refuting the presence of a UIP pattern, and differentiating UIP from non-UIP patterns.^{2,4} In practice, a comprehensive approach that considers multiple key patterns simultaneously is helpful, with attention to features that suggest alternative diagnoses (notably NSIP and BIP), other specific, or indeterminate patterns. Assessment of disease distribution is a valuable first step (Figure 2), followed by a detailed assessment of findings that may refine the level of confidence for a specific HRCT pattern (Figure 3).²³

For the differential diagnosis of most common fILD patterns (UIP, NSIP, and BIP), the cranio-caudal distribution is assessed, with particular attention to whether the disease is basal-predominant or not. In the presence of basal-predominant and peripheral disease (without signs of bronchiolar obstruction), UIP and NSIP must be differentiated. Assessment of the relative proportion of fibrosis versus ground-glass may be helpful. In a large study assessing HRCT pattern recognition, the presence of any pure GGO or >10% lung volume affected by GGO admixed with fibrosis suggested against UIP, with specificity of approximately 80%; the presence of any honeycombing was a reasonable indicator of UIP and suggested against NSIP pattern with specificity of around 80% for both.²³ However, these criteria are imperfect, and advanced fibrotic NSIP may be difficult to differentiate from UIP, mainly due to traction bronchiectasis that may be indistinguishable from honeycombing.^{11,24}

Distribution of the findings in the axial plane can be very helpful. A UIP or probable UIP pattern requires a peripheral distribution of fibrosis, whereas presence of peribronchovascular component, in isolation or along with peripheral

disease, strongly favors NSIP over UIP, particularly in the presence of subpleural sparing.^{4,23,25,38} Subpleural sparing can occasionally be seen in HP.⁴ A dilated esophagus, axillary nodal enlargement, and co-existing consolidation with organizing pneumonia appearance also support a NSIP diagnosis. Distribution of fibrosis in the periphery and dorsal aspects of the lower lobes are diagnostic for a UIP or probable UIP pattern in the absence of any findings that suggest an alternative diagnosis, such as GGO, mosaic perfusion, consolidation, nodules, and peribronchovascular disease. Sparing, or relatively more mild involvement, of the costophrenic sulci weighs against a UIP diagnosis.^{2,4} When present, asymmetry of the findings favors UIP over other patterns.

Clinical profiles immediately available at the time of imaging interpretation may be helpful, with an NSIP pattern being favored over UIP in females of younger age (<60 years), in contrast to elderly men.^{2,38,39} This can be particularly helpful in mild basal predominant fibrosis with no honeycombing and without features of bronchiolar obstruction, where the differential is a probable UIP pattern versus NSIP. In this context, recognition of the relative rarity of idiopathic NSIP is beneficial. Adjustment of pretest likelihood improves diagnostic performance, with MDD as a reference standard. The temporal evolution of the disease may also be helpful when prior remote imaging is available. NSIP tends to progress slowly when compared to UIP, and an NSIP pattern may be more evident early in the disease, progressing to a pattern more consistent with UIP as disease advances.^{4,24}

Bronchiolar abnormalities and findings of small airways disease are the defining feature of BIP.³⁴ On inspiratory CT, the most specific indicators of BIP pattern are widespread hypoattenuating or ground-glass lobules, especially when they coexist to form the three-density sign. In one study,

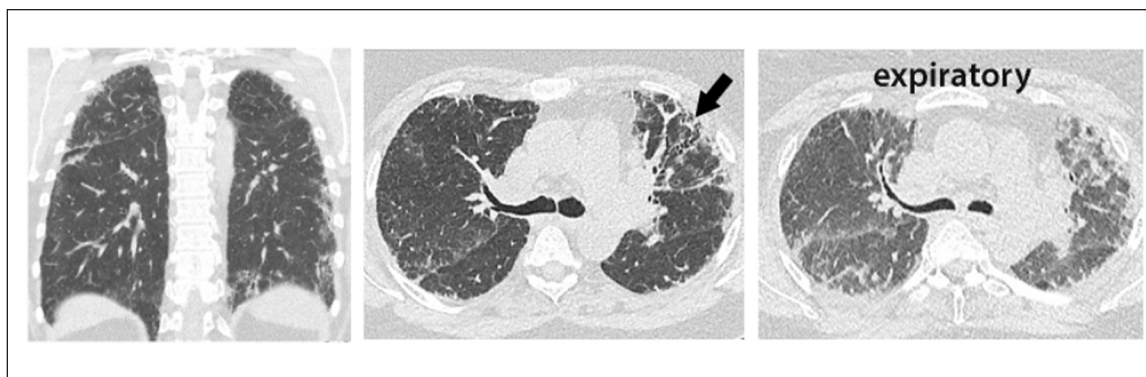


Figure 9. Fibrotic ILD with indeterminate pattern. HRCT images in a 64-year-old female shows interstitial fibrosis with random distribution in the axial and craniocaudal planes. There is both central and peripheral fibrosis (arrow), and involvement of all pulmonary zones demonstrated in the coronal reformat. While the distribution may suggest hypersensitivity pneumonitis, there are no features of bronchiolar obstruction, such as mosaic perfusion, hypoattenuation lobules or air-trapping in the expiratory acquisition.

hypoattenuating lobules affecting $\geq 10\%$ and $\geq 20\%$ of the lungs had specificities of 79% and 94%, respectively for the diagnosis of fHP.²³ Similarly, increasing lobules and extent of air trapping seen on expiratory scan increases confidence in identifying a BIP pattern. Although differentiation between UIP and BIP patterns is made primarily by the presence of features of bronchiolar obstruction, this may be challenging and distribution of the disease offers additional important clues. Mid-to-upper lung predominance weighs against UIP and the sparing or lessening of disease at the extreme costophrenic sulci suggests a non-UIP diagnosis, and specifically a BIP pattern. Peribronchial disease is common in BIP, in contrast to UIP. The ATS/ERS/JRS/ALAT guideline-defined criteria for “*typical HP pattern*” and “*compatible with HP pattern*” relies on distribution of the findings to assess the degree of certainty for a HP clinical diagnosis.³ The *typical HP pattern* requires a mid-upper predominant or diffuse distribution in the craniocaudal axis and similarly diffuse, or both peripheral and peribronchial distribution on the axial plane. Other variant distributions, including basal predominant disease, are permitted for “*compatible with HP pattern*.”

Basal and peripheral fibrotic ILD with signs of bronchiolar obstruction is a particularly challenging imaging pattern, possessing intermediate features between UIP and NSIP with respect to distribution and BIP with respect to features of small airways disease. According to the HP guidelines,^{3,32} this could be categorized as “compatible with fHP” based on less characteristic distribution although this category is much less specific for any specific fILD diagnosis. A recent study assessing radiological diagnoses of the “compatible with fHP” category showed this to be a non-specific designation, with expert radiologists variably identifying cases as BIP (HP) (35%), NSIP (26%), UIP (9%), or no confident pattern (29%).³³ This study additionally showed that the “compatible with HP” pattern had low specificity for any

single disease etiology in MDD, and it was most seen in CTD-ILD (48%), as compared to fHP (22% of cases), reflecting airways involvement and bronchiolar obstruction known to occur in CTD. For these reasons, we advise caution in the use of this category, with awareness that a “compatible with fHP” diagnosis based on the 2020 guidelines has a poor association with fHP as a clinical diagnosis after MDD. Features of small airways disease may also be present in patients with otherwise typical features of UIP pattern in IPF, both more common in elderly smokers.¹³ Ultimately, in cases of lower-lobe predominant fibrosis with features of bronchiolar obstruction, integration of other imaging features may help to guide the radiologist toward UIP, NSIP or BIP, or may support classification as indeterminate when no confident pattern can be identified.

Cases with no specific HRCT pattern are categorized as indeterminate for UIP (and guideline-defined indeterminate for HP) and may occur for different reasons. This includes cases with mid-upper lung fibrosis in the absence of features of small airways disease, or basal-predominant disease with areas of hypoattenuating lung on inspiratory imaging (mosaic attenuation) but without definitive features of bronchiolar obstruction (e.g., 3-density sign and air-trapping on expiratory imaging; Figure 9).^{3,4} Subtle basal and peripheral disease that cannot be confidently identified as early UIP or NSIP due to its mild extent has been often categorized in practice as indeterminate by many ILD experts, although not explicitly included in the definition of indeterminate pattern in the latest 2022 IPF/PPF guidelines.⁴ It is important to note that these findings should still involve $\geq 5\%$ of the *total lung* or should otherwise be accompanied by clinical symptoms or abnormalities on pulmonary function testing (PFT) in order to qualify as ILD,⁴⁰ as distinguished from interstitial lung abnormality (ILA), as discussed in the ILA section below. In any case, these cases generally require longitudinal follow-up.

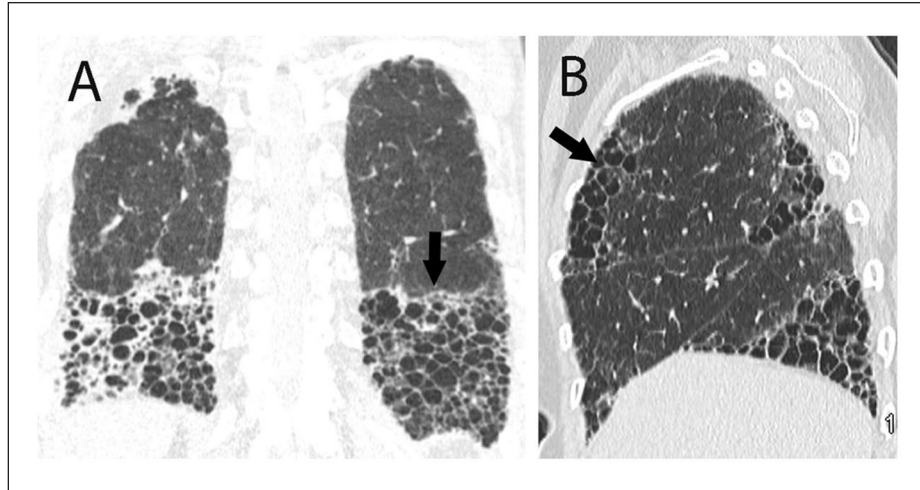


Figure 10. Connective-tissue disease (CTD)—related UIP pattern. HRCT scans in two different patients with rheumatoid arthritis show fibrotic ILD with UIP pattern. The presence of exuberant honeycombing in the lower lobes, the sharp demarcation between the lower lobe fibrosis and the normal lung, the so called “straight-edge sign” (A, arrow), and localized anterior upper lobe fibrosis, the so called “anterior upper lobe sign” (B, arrow) are features suggestive of UIP secondary to CTD.

Multidisciplinary Diagnosis

HRCT patterns have variable correlation with distinct ILD subtypes and need to be integrated with available clinical and pathological data for a multidisciplinary diagnosis.

UIP or probable UIP patterns correlate with UIP on histology in more than 90% and 70% of cases respectively.^{4,26} In the correct clinical context, notably elderly men with a smoking history and no identifiable cause (CTD, environmental exposure, asbestosis and drug toxicity), UIP or probable UIP HRCT patterns almost invariably reflect clinical IPF and a confident diagnosis can be made without need for biopsy confirmation.⁴

A UIP pattern in the setting of CTD is most common in rheumatoid arthritis (RA).⁴¹ Although often indistinguishable from UIP seen in IPF, certain ancillary HRCT findings favor CTD. These include exuberant honeycombing (honeycomb cysts accounting for most of the fibrotic changes), sharp demarcation of lower lobe predominant fibrosis in coronal images (straight-edge sign) and localized anterior upper lobe fibrosis with concomitant lower lobe predominant disease (anterior upper lobe sign; Figure 10).⁴² Anterior upper lobe fibrosis with posterior sparing in a UIP pattern has been shown to have a 25% sensitivity and 87% specificity in differentiating UIP of CTD from that of IPF. Concomitant airways involvement is well-described in CTD-ILD, particularly RA,^{41,43} manifesting on CT with a combination of interstitial fibrosis that may be UIP-like pattern, but with superimposed mosaic perfusion and expiratory air-trapping that defines BIP. The presence of osseous erosions in the sternoclavicular and acromioclavicular joints on CT are additional ancillary findings helpful in the diagnosis of UIP seen in RA. Asbestosis can manifest with a

UIP pattern, and bilateral pleural plaques in a bilateral and symmetric distribution indicate the diagnosis.

A NSIP pattern most commonly correlates with a clinical diagnosis of CTD.^{27,34} The term CTD-ILD refers to the occurrence of fILD in any form of CTD. CTD-ILD is more common in systemic sclerosis, inflammatory myositis, and mixed connective tissue disease, but all CTD are at increased risk of developing fILD and this can be the first and only manifestation of the disease.⁴⁴⁻⁴⁶ An NSIP pattern on CT should prompt investigation for CTD if not yet diagnosed. In the presence of NSIP with OP overlap, dermatomyositis and anti-synthetase syndrome should be excluded with specific serology. However, CTD-ILD may present with any of the defined HRCT patterns or may have atypical appearances.^{46,47}

Interstitial pneumonia with autoimmune features (IPAF) describes patients with ILD who exhibit clinical, serologic, or morphologic features suggestive of an underlying autoimmune process but do not meet established criteria for a defined CTD.²¹ An NSIP pattern on HRCT constitutes one of the morphologic manifestations supporting a diagnosis of IPAF. However, IPAF is not a radiological diagnosis and should only be made in multidisciplinary evaluation, following integration of clinical and serologic data.^{21,45}

In cases with an NSIP pattern on HRCT and no clinical evidence of CTD or IPAF, correlation with histological NSIP is inconsistent and a variety of histological patterns may be encountered. Thus in these relatively rare cases, which without histology, are often given a clinical-radiologic diagnosis of “idiopathic” NSIP, lung biopsy can be especially helpful for clinical diagnosis and guiding management.

Of note, the term systemic autoimmune rheumatic diseases (SARD) has been recently proposed by the rheumatology

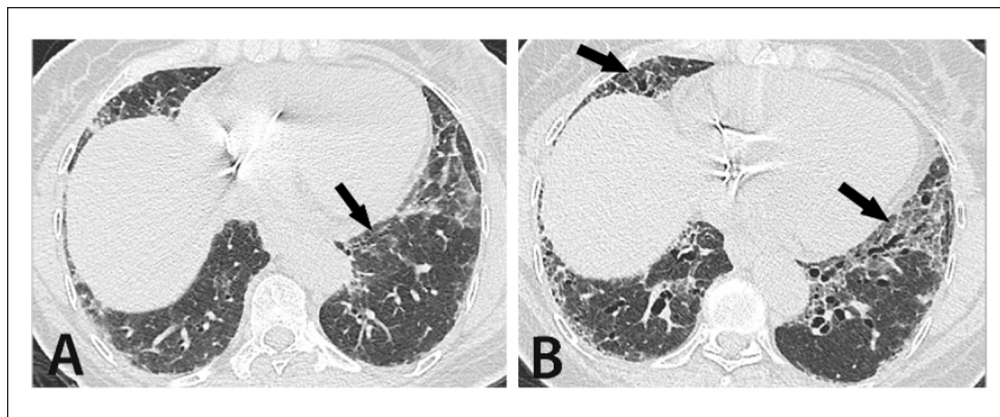


Figure 11. Progressive pulmonary fibrosis (PPF). 68-year-old male with Sjogren's syndrome and NSIP. (A) Axial HRCT scan performed at baseline shows fine reticulations and ground-glass opacities with mild traction bronchiolectasis (arrow). Patient was started on immunosuppression. (B) One year later, there was physiological decline on pulmonary function test and repeat HRCT scan shows progression of ground-glass opacities to reticulation, new and coarser reticulations, and worsened extent and severity of traction bronchiolectasis, as seen in the right middle lobe and lingula (arrows), consistent with radiological progression of fibrosis. A diagnosis of PPF was made and the patient was started on anti-fibrotic therapy.

community to replace CTD and has been increasingly adopted.^{45,47} In the current guidelines, we continue to use the term CTD as it remains uncertain whether SARD will replace CTD in the imaging and pathology fields, and in accordance with recent ILD literature.¹⁹

A BIP pattern (guideline-defined “typical for fHP” pattern³), with mid-upper lung predominance and diffuse axial involvement has been shown to be relatively specific (65% of cases) for fibrotic HP when an inciting antigen is identified.^{33,48} A significant minority of these cases represent CTD-ILD or IPAF. Otherwise, these cases may be deemed idiopathic, or what has been described as “fHP without an identified inciting antigen.”³⁴ The term “idiopathic BIP” has been recently proposed for the latter but not yet formally adopted in the literature.^{19,34}

Cases with an indeterminate pattern on HRCT can be challenging to diagnose and often benefit most from expert MDD and additional investigation, including surgical lung biopsy. Importantly, a pattern “indeterminate for UIP” by guideline criteria does not exclude a clinical diagnosis of IPF. Although this category is associated with a lower probability of UIP on histology compared to UIP or probable UIP patterns, a substantial proportion of cases, approximately 50%, demonstrate UIP on biopsy and ultimately receive a multidisciplinary diagnosis of IPF.^{2,4}

Unclassifiable ILD refers to cases where a confident diagnosis is not achieved even after comprehensive multidisciplinary discussion.¹ Unclassifiable ILD is not a radiological diagnosis, and the term should not be used in isolation from clinical findings.¹⁹ Importantly, it is not to be considered synonymous with an “indeterminate pattern” on imaging. A case may be deemed unclassifiable due to inadequate clinical, radiological, or pathological information at time of assessment, major discordance between clinical, radiological or pathological findings, or unusual variants of ILD not recognized in

current guidelines.⁴⁹ Unclassifiable ILD may be a temporary diagnosis that changes after further information is obtained. If truly unclassifiable after comprehensive assessment, management is based on the most probable MDD diagnosis and expected disease behavior based on available information.¹

Specific Clinical Scenarios

Progressive Pulmonary Fibrosis (PPF)

PPF is defined as progression of fibrosis in any fILD other than IPF, irrespective of the primary ILD pattern. A diagnosis of PPF does not replace the baseline ILD diagnosis, it rather indicates a worse behavior and may inform management and prognosis. The definition is important because patients with PPF can receive the anti-fibrotic drug nintedanib, otherwise reserved to IPF patients, if standard management failed (immunosuppressants, antigen remediation or observation).⁴

The current diagnosis of PPF requires evidence of progression in two of the three domains: worsening of respiratory symptoms, worsening PFT, or CT evidence of progressive fibrosis, occurring within the past year and with no alternative explanation.⁴ Radiological evidence of progressive fibrosis is based on visual assessment on HRCT for one or more of the following: increased extent or severity of traction bronchiolectasis and bronchiolectasis; new ground-glass opacity with traction bronchiolectasis; new fine reticulation; increased extent or increased coarseness of reticular abnormality; new or increased honeycombing (including size and number of cysts) and increased lobar volume loss. It may include progression of ground-glass opacities to reticulation and of reticulation to honeycombing (Figure 11). New or worsening ground-glass opacities without traction bronchiolectasis may reflect progressive fibrosis however should be assessed with caution and

differentiated from transient causes. Acute exacerbation of ILD is not included in the definition of PPF. Radiological identification of progression requires meticulous assessment with careful side-by-side comparison of longitudinal HRCT images at the same levels, visually adjusted for changes in lung volumes between scans, and with attention to confounding differences in imaging acquisition that may influence interpretation (e.g., slice thickness, kernel reconstruction, intravenous contrast). Use of bronchovascular structures as landmarks to ensure accurate slice by slice comparison is useful when comparing CT scans.

HRCT is particularly useful for the diagnosis of early PPF, in contrast with PFT that may have lower sensitivity for detection of mild progression.⁴ The optimal interval for follow-up HRCT to diagnose progressive fibrosis is uncertain. In practice, repeat HRCT is indicated when there is clinical suspicion of progression.

Acute Exacerbation of ILD (AE-ILD)

In a small but significant number of patients with fILD, episodes of acute exacerbation occur and negatively affect survival. Acute exacerbation (AE) is more common in IPF but can occur in any other fILD, including CTD-ILD, IPAF, fHP, and unclassifiable.⁵⁰ It can be triggered by external insults such as surgery, invasive procedures, infection, and aspiration, but often have no identifiable cause. Mortality is relatively high and recurrent episodes of AE have been described.⁵⁰⁻⁵²

AE should be suspected in patients with acute respiratory failure and imaging showing new ground-glass opacities or consolidations on a background of fibrosis. Imaging and pathological findings reflect acute lung injury that may manifest with OP or diffuse alveolar damage (Figure 12).⁵²⁻⁵⁴

Distinguishing ground-glass opacities caused by AE from chronic ground-glass as part of fibrosis, as often seen in NSIP, can be difficult in the absence of prior CT or a known ILD diagnosis. In these cases, follow up imaging will assist in the differentiation, showing rapid changes in AE. Infection, pulmonary edema, or other treatable causes must be excluded.

Importantly, diagnosis of a HRCT pattern in cases not yet diagnosed, or assessment of progression of fibrosis in patients with known fILD, should be reserved for patients with no acute respiratory symptoms and no clinical evidence of acute exacerbation. Superimposed acute findings may obscure radiologic features relevant for accurate pattern definition, potentially leading to misdiagnosis.

Familial Pulmonary Fibrosis

Familial pulmonary fibrosis (FPF) is defined as any ILD affecting at least two first or second-degree family members. FPF has been linked to specific genetic variants, notably telomere-related and surfactant-related genes and MUC5B polymorphisms.^{55,56} Telomere variants are characterized by early cellular senescence (short telomere syndrome) and may be associated with extrathoracic abnormalities such as liver

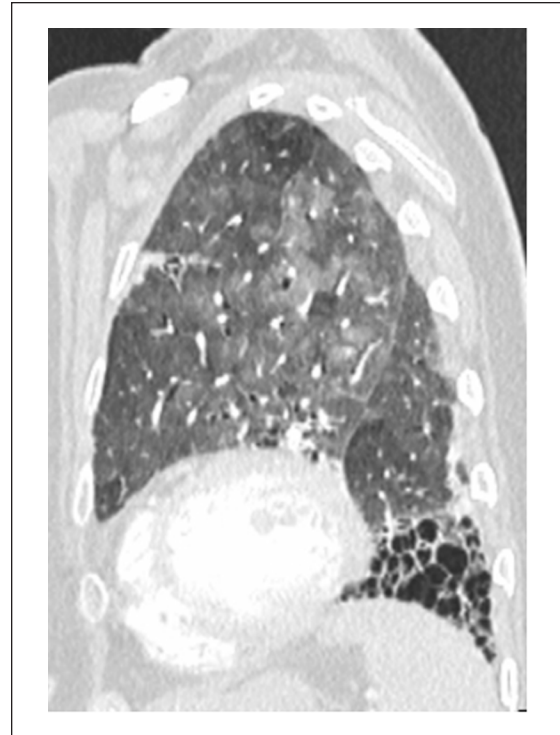


Figure 12. Acute exacerbation of fibrotic ILD. 82-year-old patient with known IPF presenting with acute worsening of respiratory symptoms that rapidly evolved to respiratory failure. HRCT sagittal reformat shows lower lobe dorsal fibrosis with honeycombing, compatible with UIP pattern and extensive ground-glass opacities in the remainder of the lungs consistent with diffuse alveolar damage. Pulmonary infection was excluded clinically.

cirrhosis, bone marrow diseases, and significant early gray hair (before the age of 30). Relatives of patients with IPF have a 10-fold increased risk of developing fILD. Genetic predisposition is however not limited to IPF and can lead to progressive forms of pulmonary fibrosis including CTD-ILD, IPAF, fHP and unclassifiable ILD. Importantly, FPF may have atypical and discordant features on pathology and radiology, and often cannot be categorized in any specific ILD diagnosis (unclassifiable ILD).⁵⁶⁻⁵⁸ Patients with FPF are usually younger and have a higher likelihood of PPF with limited survival independent of the disease entity. Consensus guidelines for FPF are not yet available but a recent evidence-based statement provides information about the genetic diagnosis, clinical management, treatment and screening of patients with FPF and their relatives.⁵⁶

Combined Pulmonary Fibrosis and Emphysema (CPFE)

Pulmonary emphysema is common in patients with fILD, notably IPF. In patients with a combination of emphysema and fibrosis on CT and distinct physiological changes, the term CPFE has been used. The 2022 ATS/ERS/JRS/ALAT Research Statement proposed a CT emphysema extent of

$\geq 15\%$ of lung involvement for the diagnosis of CPFE. The extent and severity of fILD has clinical relevance but a minimal threshold on CT has not been defined for CPFE.⁵⁹ CPFE is not a specific ILD subtype and any fILD with concurrent emphysema can be labelled CPFE. In a recent study of a large cohort of patients with fibrotic ILD, the prevalence of CPFE was 20% for IPF and 7% in non-IPF cases.⁶⁰ CT emphysema extent of $\geq 20\%$ was associated with worse outcomes whereas emphysema subtype (centrilobular, paraseptal or panlobular) did not affect outcome. In another study, ILD CT pattern was associated with the rate of fibrosis progression in CPFE, being worse in radiological UIP (UIP/probable UIP) than in an NSIP pattern.⁶¹

CPFE is characterized by relatively preserved lung volume and airflow rates on spirometry and severe reduction of DLCO (diffusion lung capacity for carbon monoxide).⁵⁹ This pseudonormalization of lung volumes is caused by the counteracting effects of emphysema (airway obstruction and increased lung volume) and fibrosis (decreased volume but increased airflow relative to lung volume) that may lead to underestimation of functional impairment by spirometry alone. DLCO is a better reflection of lung function in such cases. Patients with CPFE exhibit more severe hypoxemia, especially on exertion, and have increased risk of pulmonary hypertension and lung cancer.^{59,62} HRCT may show fibrosis in the lower lobes and isolated emphysema in the upper lobes or a pattern of admixed fibrosis and emphysema; the latter may complicate assessment of severity of fibrosis and presence of honeycombing.^{59,62}

Interstitial Lung Abnormalities (ILA)

A consensus statement on ILA was first published in 2020 by the Fleischner Society.⁶³ In 2025, a document published by the ATS updated the initial definition of ILA, providing evidence-based guidance for diagnosis and management.⁴⁰ ILA is defined as the presence of non-dependent bilateral opacities on CT (that may include ground-glass, reticulation, architectural distortion, traction bronchiectasis and/or honeycombing), involving $\geq 5\%$ of any lung zone (but $< 5\%$ total lung volume) by visual estimate, in the absence of clinical symptoms or physiologic abnormalities. The six lung zones are defined as right and left upper, mid, and lower zones, separated at the levels of the inferior aortic arch and right inferior pulmonary vein.

The updated guidelines remove the prior requirement that ILA be incidentally detected, allowing the term to be applied more broadly, including in patients undergoing evaluation for suspected ILD or screening of high-risk populations (e.g., underlying CTD), provided that criteria for ILD are otherwise not met. In this framework, ILA captures cases with limited radiologic involvement without accompanying clinical or physiologic impairment. By contrast, ILD is defined by the presence of symptoms or physiologic abnormalities

attributable to ILD and/or more extensive radiologic involvement. On imaging, ILD rather than ILA should be identified when fibrotic abnormalities involve $\geq 5\%$ of total lung volume, when there is progression of fibrosis on serial CT, or when a clear ILD pattern is identified (e.g., UIP, NSIP, or BIP). In otherwise mild cases meeting the threshold of $\geq 5\%$ of total lung volume involvement, imaging findings may overlap with or be described as an indeterminate pattern, as previously discussed.

The current statement maintains the initially proposed ILA subcategories that correlate with risk of progression: nonsubpleural, subpleural non-fibrotic and subpleural fibrotic. Subpleural fibrotic ILA, in contrast to non-fibrotic subcategories, is the most concerning and defined by the presence of architectural distortion, traction bronchiectasis and/or honeycombing, whereas nonfibrotic forms present with ground-glass and/or reticulations. CT findings excluded from ILA definition are dependent atelectasis, linear scarring, nonemphysematous cysts, PPFE, centrilobular nodularity and unilateral disease.

In the presence of ILA, radiologists should recommend clinical assessment and baseline PFT, and counselling for risk reduction (i.e., smoking cessation). If a specific ILD diagnosis is ultimately not apparent after clinical evaluation, ILA suspected on radiology is confirmed and HRCT is indicated. In patients with higher risk for ILD and for subpleural ILAs, HRCT can be performed in 12 months, otherwise it can be performed in 2 to 3 years, interval guided by individual risk factors as determined by the referring clinician.⁴⁰

Conclusion

Fibrotic ILD are a heterogeneous group of diseases with distinct etiology and prognosis that may present with overlapping clinical and imaging manifestations. The diagnosis of ILD requires integration of clinical, radiological and pathological findings. In this context, the definition of the HRCT pattern of ILD is central and informs subsequent diagnostic investigations and management, according to multidisciplinary guidelines. In the evolving realms of ILD, it is acknowledged that contentious issues and areas of uncertainty remain. Whereas much progress has been achieved in the standardization of fILD definition and management in the last decades, further changes may be expected. The pivotal role of radiology in the diagnosis of ILD emphasizes the importance of continued education and up-to-date knowledge. The goal of the CSTR guidelines is to assist radiologists in this endeavor, including future updates.

Acknowledgments

The authors would like to thank the members of the Canadian Association of Radiologists who took time to provide their feedback and peer review during the drafting of these guidelines.

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Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Declaration of Conflicting Interests

The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: The following relationships are disclosed for transparency: Dr. Souza has received honoraria from Boehringer Ingelheim and AstraZeneca, and unrestricted educational grants from Boehringer Ingelheim. Dr. Hague has received speaker fees and honoraria from Boehringer Ingelheim and consulting fees from VIDA Diagnostics. Dr. McInnis has received honoraria from Boehringer Ingelheim, AstraZeneca, and Sanofi. Dr. Marinescu has received speaking and consultancy fees from Boehringer Ingelheim.

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