



IMAGES OF ILD

High Resolution Computed
Tomography (HRCT)

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HRCT — METHODS

In high resolution computed tomography (HRCT), thin sections of <1.5 mm width are acquired and reconstructed with a high spatial frequency algorithm, allowing the visualisation of submillimetre structures and detection of discrete abnormalities as small as 0.3 mm at the level of the secondary pulmonary lobule.^{1,2}

HRCT offers two different techniques:¹⁻³

SPACED AXIAL HRCT

- ▶ Thin sections (1-2 cm intervals) from the lung apices to the bases
- ▶ Sufficient to detect abnormalities in diffuse lung diseases
- ▶ Low radiation dose vs volumetric imaging

VOLUMETRIC HRCT (MULTIDETECTOR ROW CT)

- ▶ Allows assessment of the entire lung^{1,3}
- ▶ Easier and better interpretation by performing coronal and sagittal reformations
- ▶ Greater radiation dose vs axial imaging^{1,3}

BASIC LUNG ANATOMY

The **secondary lobule** is the basic functional unit of the lung. Understanding its anatomy is key to interpreting the imaging results of interstitial lung diseases (ILDs) and is based on the type of secondary-lobule involvement.¹

- \emptyset = 1-2.5 cm with up to a dozen acini
- Supplied by 1x terminal bronchiole & 1x pulmonary artery branch
- Surrounded by lobular septum – pulmonary veins + **lymphatics**

These surrounding septa are very thin and only a few of them will be seen under healthy conditions.¹

The lymphatic system comprises two parts:²

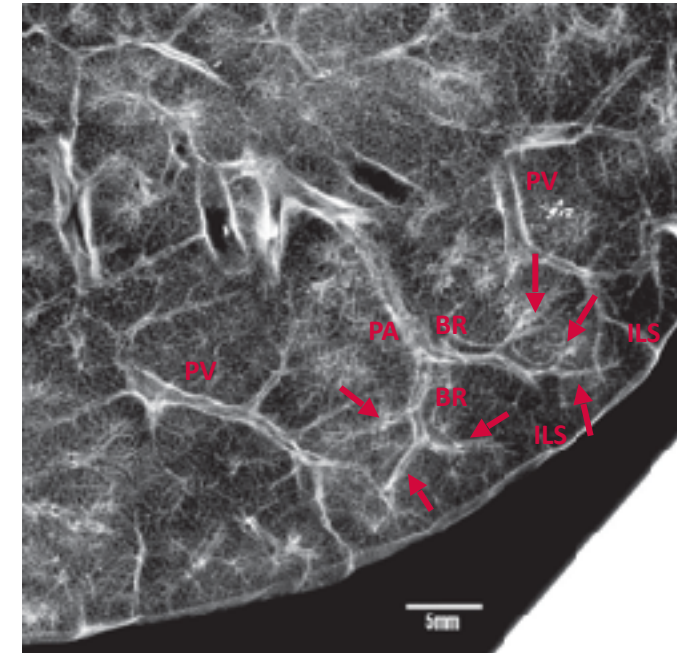
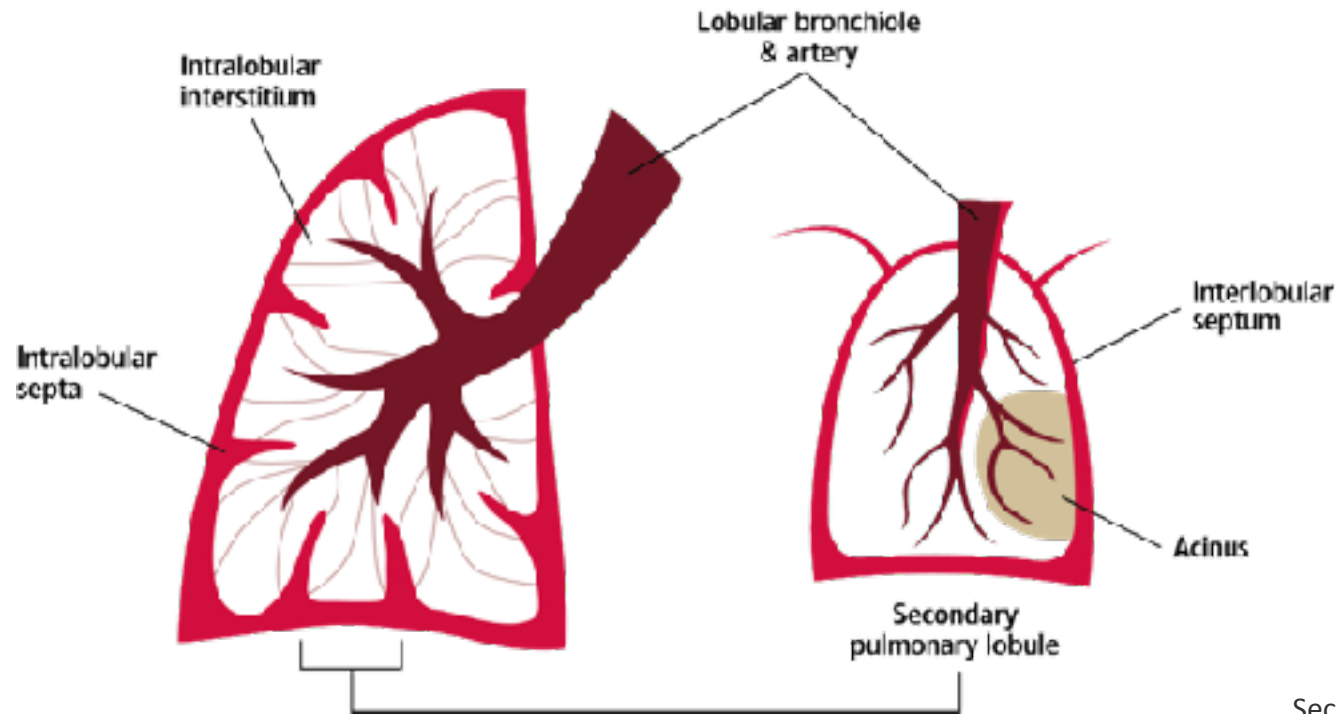
A CENTRAL NETWORK (CENTRIOBULAR AREA):

- ▶ Runs along the bronchovascular bundle towards the centre of the lobule

A PERIPHERAL NETWORK (PERILYMPHATIC AREA):

- ▶ Located within the interlobular septa and along the pleural linings

BASIC LUNG ANATOMY^{1,2}



Secondary pulmonary lobule: Reid's definition. Contact radiograph of the inflated fixed lung specimen showing the branching terminal bronchioles (arrows). These terminal bronchioles arise at intervals of 1 to 2 mm. The bar represents 5 mm.²

Figure from Takahashi M, et al. *Int J Chron Obstruct Pulmon Dis.* 2008;3(2):193–204.

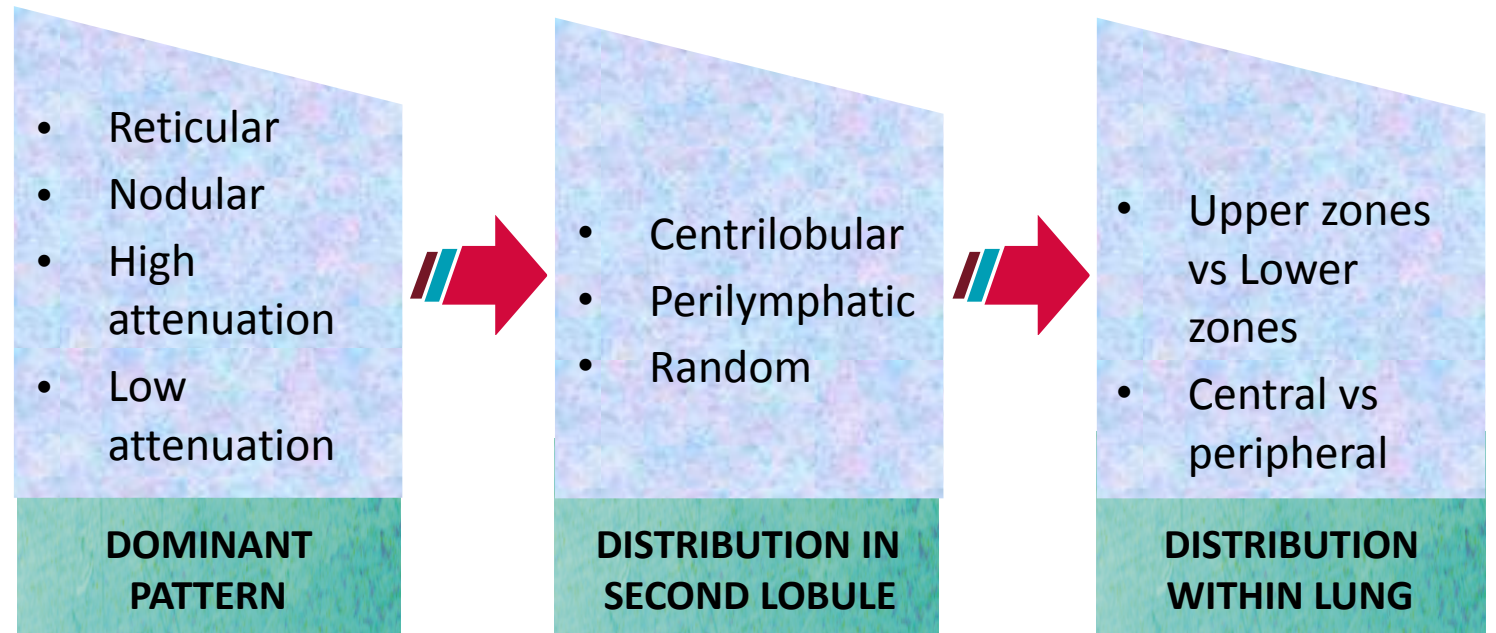
1. Smithuis R, et al. The Radiology Assistant: Lung - HRCT Basic Interpretation. *Radiologyassistant.nl*. Available from: <http://www.radiologyassistant.nl/en/p42d94cd0c326b/lung-hrct-basic-interpretation.html#i456353497daa9>. Accessed June 10, 2019.

2. Takahashi M, et al. *Int J Chron Obstruct Pulmon Dis.* 2008;3(2):193–204.

HRCT INTERPRETATION

For a structured interpretation of HRCT images, the following aspects should be looked at carefully¹:

- ▶ Dominant HRCT features
- ▶ Feature location within the secondary lung lobule
- ▶ Predominant distribution within the lung



For any diagnosis, all morphological findings from HRCT must always be combined with the patient's history and additional clinical findings (e.g. pleural fluid, traction bronchiectasis).

HRCT FEATURES IN ILDs

HRCT scans show diverse features which, individually or in combination, can indicate the presence of a certain type of disease.

In diagnosing ILDs, there are 4 general indicators for the presence of pathological abnormalities which are important to the interpretation of HRCT scans¹:

1

Reticular opacities

2

Nodules

3

Increased lung opacity (high attenuation)

4

Decreased lung opacity (low attenuation)

Further consideration of potential co-occurrence/overlap of features, additional findings and the distribution of abnormalities in the axial and coronal planes can help narrow the differential diagnosis.²

1. RETICULAR ABNORMALITIES

INTERLOBULAR SEPTAL THICKENING

Reticular opacities seen in HRCT are a result of the thickening of the interlobular septa or fibrosis (honeycombing).¹

Definition: the thickening of the intralobular interstitium by fluid, fibrous tissue, or infiltration by cells. It can have a smooth, nodular or irregular appearance.¹

Visualisation of numerous septa, which are normally about 0.1 mm thick, indicates an abnormal condition.¹⁻³

Differential diagnosis of interlobular septal thickening as the predominant abnormality²

Smooth	Nodular	Irregular
Pulmonary oedema	Sarcoid	Fibrosis (IPF, HP, sarcoid, etc.)
Lymphangitic spread of tumor	Lymphangitic spread of tumor	
Erdheim-Chester disease (Non-Langerhans cell histiocytosis)	Lymphoproliferative disease	

1. RETICULAR ABNORMALITIES

INTERLOBULAR SEPTAL THICKENING



..... Regular septal lines → Septal thickening

Septal thickening forming polygons in the lung parenchyma

1. RETICULAR ABNORMALITIES

HONEYCOMBING

Used to describe the end stage of diseases that cause **diffuse fibrotic destruction**, which are irreversible and have a poor prognosis.¹

If present, HRCT shows thick-walled clustered cystic air spaces ($\emptyset = 0.3-1.0$ cm), which are distributed subpleurally and basally.¹

These cysts resemble a honeycomb in cross-section; a feature typically accompanied by other signs of fibrosis, e.g. traction bronchiectasis.^{2,3}

For a differential diagnosis it is also important to consider pulmonary emphysema, which can mimic honeycombing.

CLINICAL AND HISTOPATHOLOGICAL CORRELATIONS²:

- ▶ Idiopathic pulmonary fibrosis
- ▶ Collagen vascular diseases
- ▶ Hypersensitivity pneumonitis
- ▶ Fibrosing sarcoidosis (stage IV)
- ▶ Nonspecific interstitial pneumonia
- ▶ Drug-induced lung disease
- ▶ Asbestosis

1. RETICULAR ABNORMALITIES

HONEYCOMBING



→ Honeycombing

73-year old man with usual interstitial pneumonia
– Subpleural honeycombing forming several layers of cysts

1. RETICULAR ABNORMALITIES

TRACTION BRONCHIECTASIS

Definition: an abnormal dilatation of the bronchial tree occurring due to interstitial fibrosis.

The bronchus is pulled apart by the traction of surrounding parenchymal fibrosis.¹

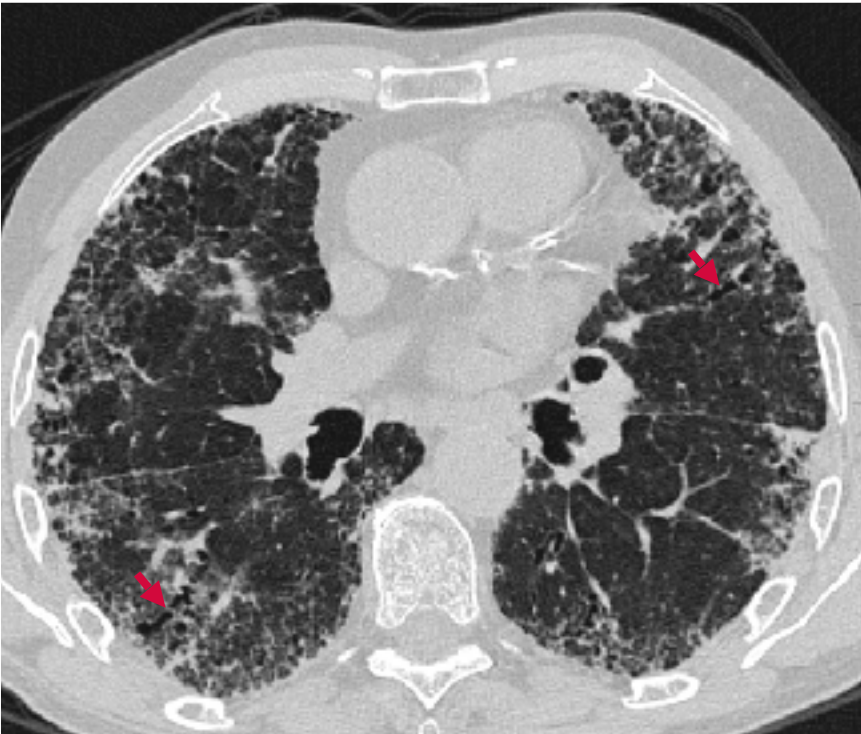
It can arise from several underlying causes which result in lung fibrosis.^{2,3}

CLINICAL AND HISTOPATHOLOGICAL CORRELATIONS²:

- ▶ Specific for fibrosis, especially in the presence of honeycombing

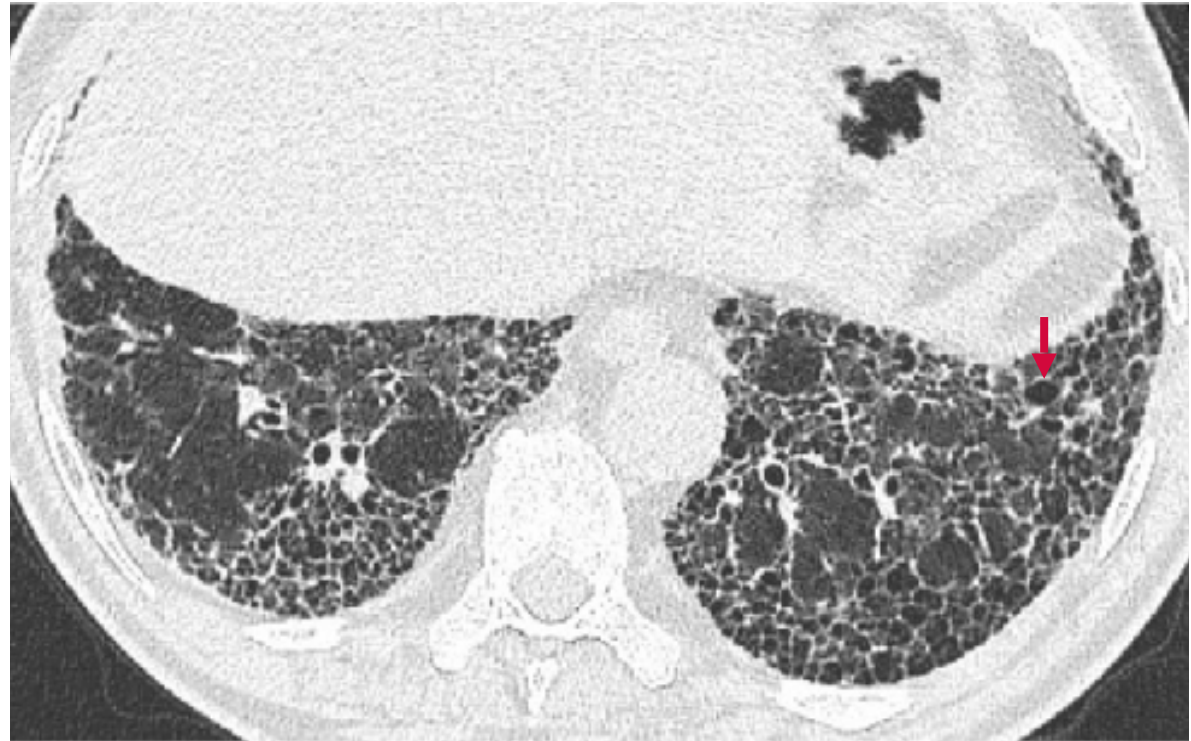
1. RETICULAR ABNORMALITIES

TRACTION BRONCHIECTASIS



→ Traction bronchiectasis

72-year old man with usual interstitial pneumonia
– HRCT shows traction bronchiectasis



→ Traction bronchiectasis

73-year old man with usual interstitial pneumonia
– HRCT shows traction bronchiectasis

2. NODULES

The distribution of nodules within the secondary lobule is essential for the accurate diagnosis of the nodular pattern. Nodules can be distributed in three different ways¹:

- ▶ Perilymphatic
- ▶ Centrilobular
- ▶ Random



▶ Micronodules

Coal worker's pneumoconiosis

- Extensive micronodulation with a perilymphatic distribution. Micronodules have an apical and posterior predominance

2. NODULES

PERILYMPHATIC¹⁻³

- ▶ Present in the interlobular septa, pleural surfaces, and the bronchovascular sheath
- ▶ Most commonly seen in sarcoidosis or neoplasms

CENTRIOLOBULAR¹⁻³

- ▶ Present **only** in the centrilobular region
- ▶ Spaced 5-10 mm from the pleura and ≥ 1 cm in size
- ▶ Not necessarily central in the secondary lobules, but the **pleural surfaces are spared**
- ▶ Can appear in rosettes or be diffuse
- ▶ Not necessarily disease-related

Possible association:
subacute hypersensitivity pneumonitis,
respiratory bronchiolitis interstitial lung disease
(RB-ILD)

RANDOM³

- ▶ Randomly distributed relative to structures of the secondary lobule throughout the lung parenchyma
- ▶ Possible association: haematogenous metastases, miliary tuberculosis, miliary fungal infections, or Langerhans cell histiocytosis (early nodular stage)

1. Elicker B, et al. *J Bras Pneumol*. 2008;34(9):715-744.

2. Webb WR. *Radiology*. 2006;239(2):322-338.

3. Smithuis R, et al. The Radiology Assistant: Lung - HRCT Basic Interpretation. *Radiologyassistant.nl*. Available from: <http://www.radiologyassistant.nl/en/p42d94cd0c326b/lung-hrct-basic-interpretation.html#i456353497daa9>. Accessed June 10, 2019.

2. NODULES

CENTRILOBULAR NODULES – “TREE-IN-BUD” SIGN

“Tree-in-bud” opacities with a branching structure, represent an impacted centrilobular bronchus dilated by pus, mucus or fluid.

Almost always associate with inflammation due to pulmonary infections.

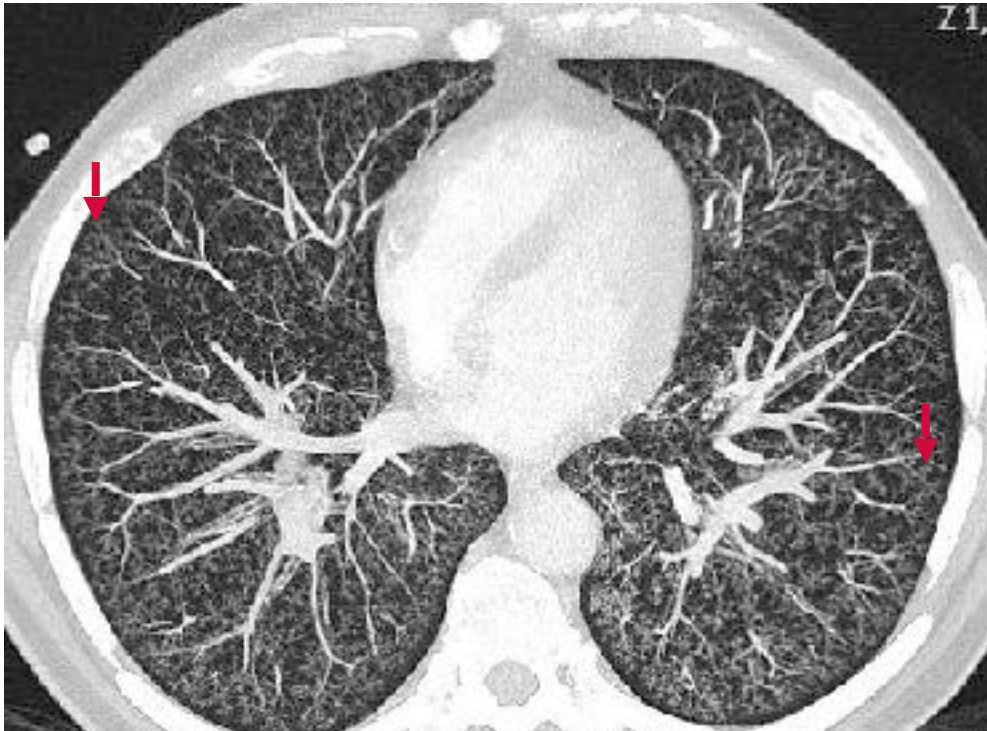
The identification of **Y-/V-shaped structures** on HRCT for narrowing the differential diagnosis.^{1,2}

TREE-IN-BUD STRUCTURES ARE SEEN IN^{2,3}:

- ▶ Bronchiectasis
- ▶ Infectious bronchiolitis
- ▶ **Uncommon** in emphysema, respiratory bronchiolitis, bronchiolitis obliterans, or hypersensitivity pneumonitis

2. NODULES

CENTRIOLOBULAR NODULES - “TREE-IN-BUD” SIGN



→ Tree-in-bud sign

Infectious bronchiolitis (MIP reformation)

– Axial MIP image shows tree-in-bud pattern in a bilateral distribution

3. HIGH ATTENUATION

An opacification on HRCT:

- Obscuration of underlying vasculature in **consolidations**

OR

- Present without obscuration – **ground-glass opacities**¹

Both can be associated with active/reversible lung disease

- Ground-glass opacity can be seen **more often in predominant fibrosis**¹

A differential diagnosis should be based on symptom duration or acute vs chronic disease, respectively¹

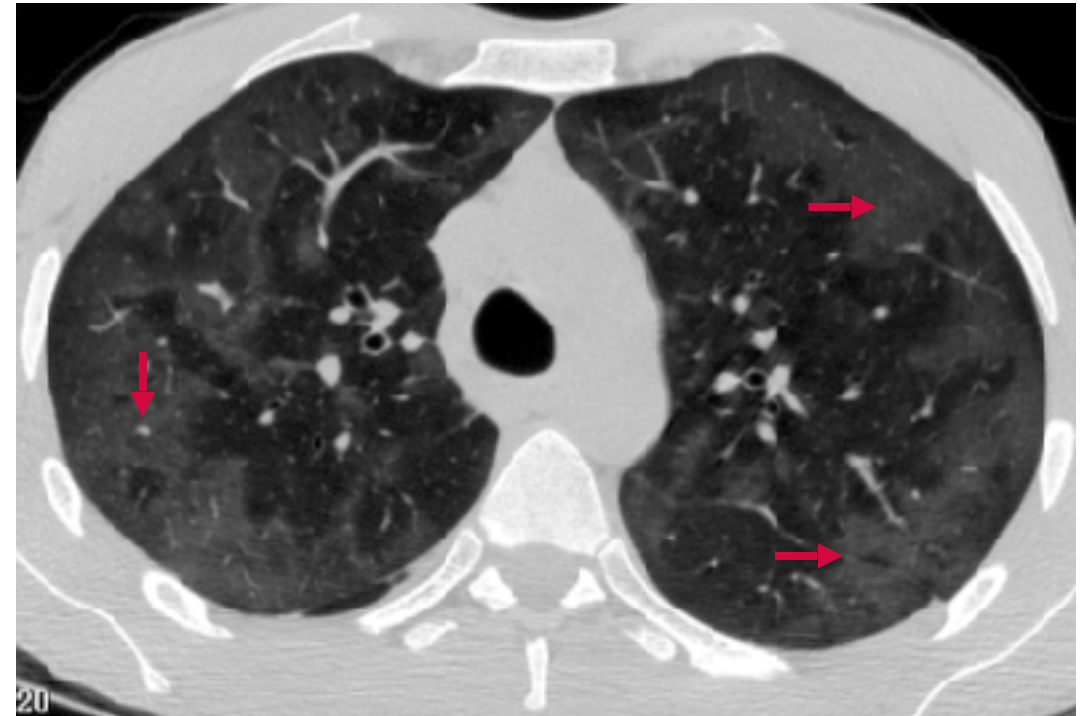
3. HIGH ATTENUATION

GROUND-GLASS OPACITIES

Ground-glass opacification **does not obscure** underlying vasculature and can be caused by various abnormalities¹⁻³:

- ▶ Air space disease - filling of the alveolar spaces with pus, oedema, haemorrhage, inflammation or tumour cells
- ▶ ILD - thickening of the interstitium or alveolar walls below the spatial resolution of HRCT as seen in fibrosis
- ▶ A combination of the above

These opacities are **non-specific** and can also be due to the limitations of HRCT resolution.²



→ Ground-glass opacity

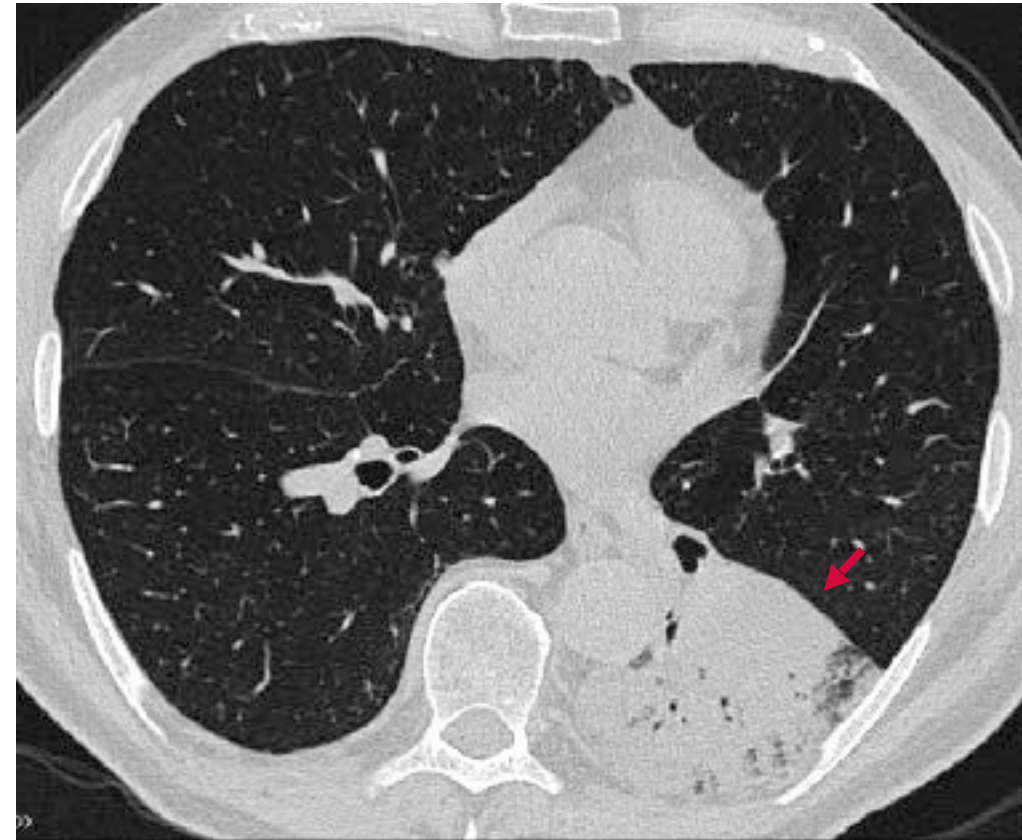
Pneumocystis jirovecii pneumonia in a patient with HIV

– Heterogeneous distribution of ground-glass opacity giving the appearance of mosaic pattern

3. HIGH ATTENUATION

CONSOLIDATION

- ▶ The presence of opacification that obscures the underlying vasculature, which indicates air space disease or fibrotic changes.¹
- ▶ Consolidation distribution is important for a successful differential diagnosis:
 - Peripheral or subpleural distribution: cryptogenic organising pneumonia, chronic eosinophilic pneumonia, atypical pulmonary oedema, Churg-Strauss syndrome, drug reactions, pulmonary contusion, pulmonary infarct, or sarcoidosis.²



→ Consolidation of the left low lobe

Invasive mucinous adenocarcinoma

- Chronically evolving pulmonary consolidation (>8 weeks) that is retractile with air bronchogram

1. Smithuis R, et al. The Radiology Assistant: Lung - HRCT Basic Interpretation. *Radiologyassistant.nl*. Available from: <http://www.radiologyassistant.nl/en/p42d94cd0c326b/lung-hrct-basic-interpretation.html#i456353497daa9>. Accessed June 10, 2019.

2. Gotway MB, et al. *Radiol Clin North Am*. 2005;43(3):513-542,viii.

4. LOW ATTENUATION

ABNORMALLY LOW ATTENUATION ON HRCT CAN BE CAUSED BY¹:

- ▶ Emphysema
- ▶ Cystic diseases (lymphangioleiomyomatosis, lymphoid Interstitial pneumonia, Langerhans cell histiocytosis)
- ▶ Bronchiectasis, honeycombing



▶ Low attenuation micronodules

Respiratory bronchiolitis in smoker

– Poorly defined and low attenuation micronodules within the upper lobes in an active smoker

4. LOW ATTENUATION

EMPHYSEMA

An abnormal, irreversible enlargement of the distal air spaces which is accompanied by destruction of their parenchymal walls resulting in areas of low attenuation on HRCT.^{1,2}

Classification of lung emphysema:

- ▶ Centrilobular (upper lobe, centrilobular origin portion of the lobule)
- ▶ Panlobular (lower lobe, diffuse distribution, affects the whole secondary lobule)
- ▶ Paraseptal (upper lobe, subpleural and interlobar distribution, can resemble honeycomb changes)

4. LOW ATTENUATION

CYSTIC DISEASES

Pulmonary cysts – circumscribed and radiolucent lesions with a thin wall (<3 mm thick), often caused by fibrotic changes resulting in honeycombing.

Diameter ranges from several mm to several cm. Adjacent cysts share the wall, a finding not seen in other cystic lung diseases^{1,2}:

- ▶ Lymphangiomyomatosis
- ▶ Langerhans cell histiocytosis
- ▶ Lymphocytic interstitial pneumonia
- ▶ Pneumatocoles



▶ Irregular pulmonary cysts

Langerhans cell histiocytosis

- Sagittal reformation in a 58-year-old patient who was a former smoker and developed Langerhans cell histiocytosis. HRCT shows large cysts with bizarre shapes

1. Elicker B, et al. *J Bras Pneumol*. 2008;34(9):715-744.

2. Gotway MB, et al. *Radiol Clin North Am*. 2005;43(3):513-542,viii.

4. LOW ATTENUATION

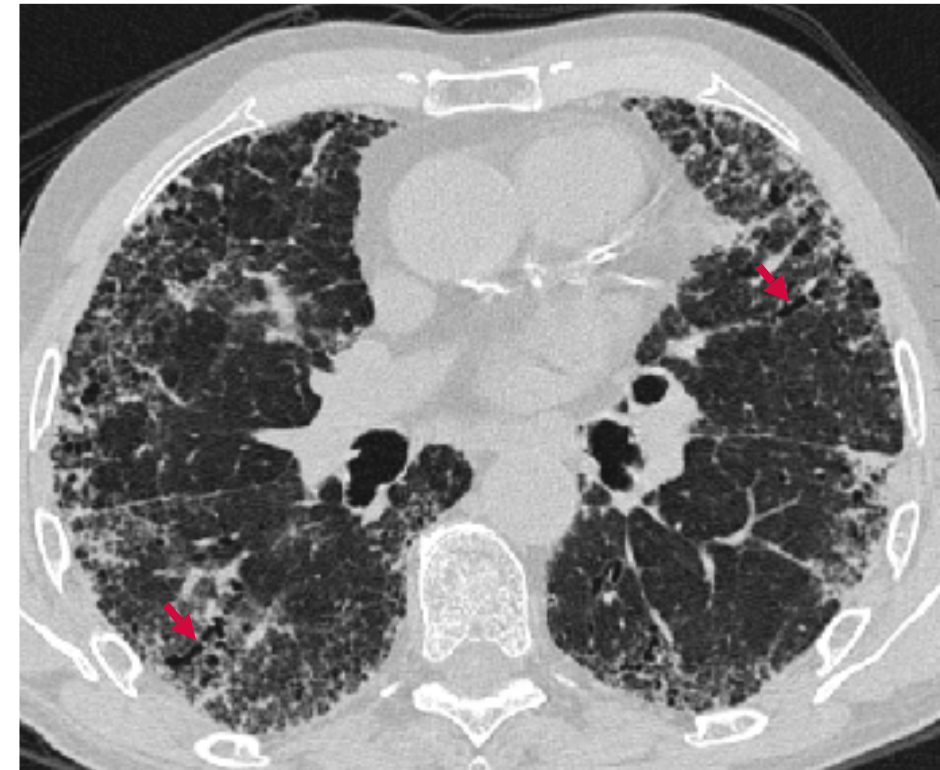
BRONCHIECTASIS

An abnormal, **irreversible bronchial dilatation** – often a result of prior infections, chronic bronchitis, COPD, asthma and cystic fibrosis.^{1,2}

Consider a combination of the following additional findings for differentiating the causes:

- ▶ “Signet-ring sign” reflecting bronchial dilatation
- ▶ Bronchial wall thickening
- ▶ Lack of tapering
- ▶ Mucus retention in the bronchial lumen
- ▶ Air trapping

NB: Bronchiectasis must be discriminated from traction bronchiectasis, which is a result of fibrosis.



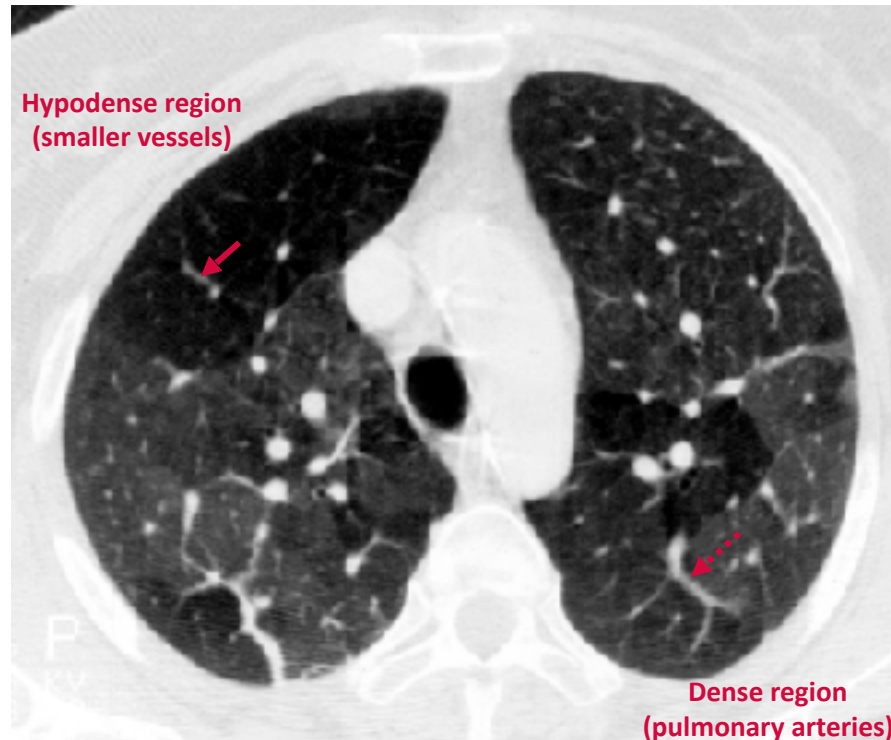
→ Traction bronchiectasis

72-year old man with usual interstitial pneumonia - HRCT shows traction bronchiectasis

MOSAIC ATTENUATION

Regions of differing attenuation appearing as patchy areas of **black** and **white** lung on HRCT: corresponding to **affected** and **non-affected** lung areas, respectively:

- A result of alterations in lung parenchymal perfusion that creates **hyperperfused** and **hypoperfused** lung areas.¹⁻³



.....▶ Pulmonary arteries —▶ Small-sized blood vessels

Chronic thromboembolic PAH

The hypodense regions of the lung contain smaller vessels, the number of which decrease while the size of the pulmonary arteries in dense regions increases corresponding to a redistribution of vascular flow to these perfused regions.

A CT scan with injection of contrast agent synchronized to opacification of the pulmonary arteries, must confirm chronic thrombosis of the pulmonary arteries

UNDERLYING CONDITIONS^{1,2}:

Low attenuation

- ▶ Obstructive small airways disease (e.g. bronchiectasis, cystic fibrosis, constrictive bronchiolitis)
- ▶ Occlusive vascular disease (e.g. chronic pulmonary embolism)

High attenuation

- ▶ Parenchymal disease represents ground-glass opacity

RECOGNITION OF IIP PATTERNS ON HRCT

Idiopathic interstitial pneumonias are defined as an entity of interstitial lung diseases of unknown cause.

Specific morphological patterns are associated characteristic HRCT features, which are **unique** for each of the entities included in the group of IIPs classified by the ATS/ERS.¹⁻³ (see table)

MORPHOLOGICAL PATTERN	HRCT FEATURES	DISTRIBUTION ON CT
UIP	Reticular opacities, honeycombing, traction bronchiectasis, focal ground-glass opacity	Peripheral, Subpleural Basal, Lower lung zones
NSIP	Ground-glass opacities, irregular linear or reticular opacities, micronodules, consolidation, microcystic honeycombing	Peripheral
COP	Airspace consolidation, mild bronchial dilatation, ground-glass opacity, large nodules (rare)	Peripheral Peribronchial
RB-ILD	Centrilobular nodules, patchy ground-glass opacities, bronchial wall thickening	Diffuse or upper lung predominance
DIP	Ground-glass opacities, irregular linear or reticular opacities, occasionally cysts	Lower lung zones Peripheral predominance
LIP	Ground-glass opacities, perivascular cysts, septal thickening, centrilobular nodules	Basilar predominance or diffuse
AIP	Exudative phase shows ground-glass opacities, airspace consolidation, organising phase shows bronchial dilatation, architectural distortion	Diffuse

Table adapted from Mueller-Mang 2007¹ and ATS/ERS 2002³

DIAGNOSIS OF ILDs OF UNKNOWN CAUSE: UIP

Usual interstitial pneumonia (**UIP**) – the typical histological and CT patterns occurring in idiopathic pulmonary fibrosis (**IPF**)¹

UIP is **required** for the diagnosis of IPF, when other known causes/features **inconsistent with UIP** can be **ruled out**^{1,2}

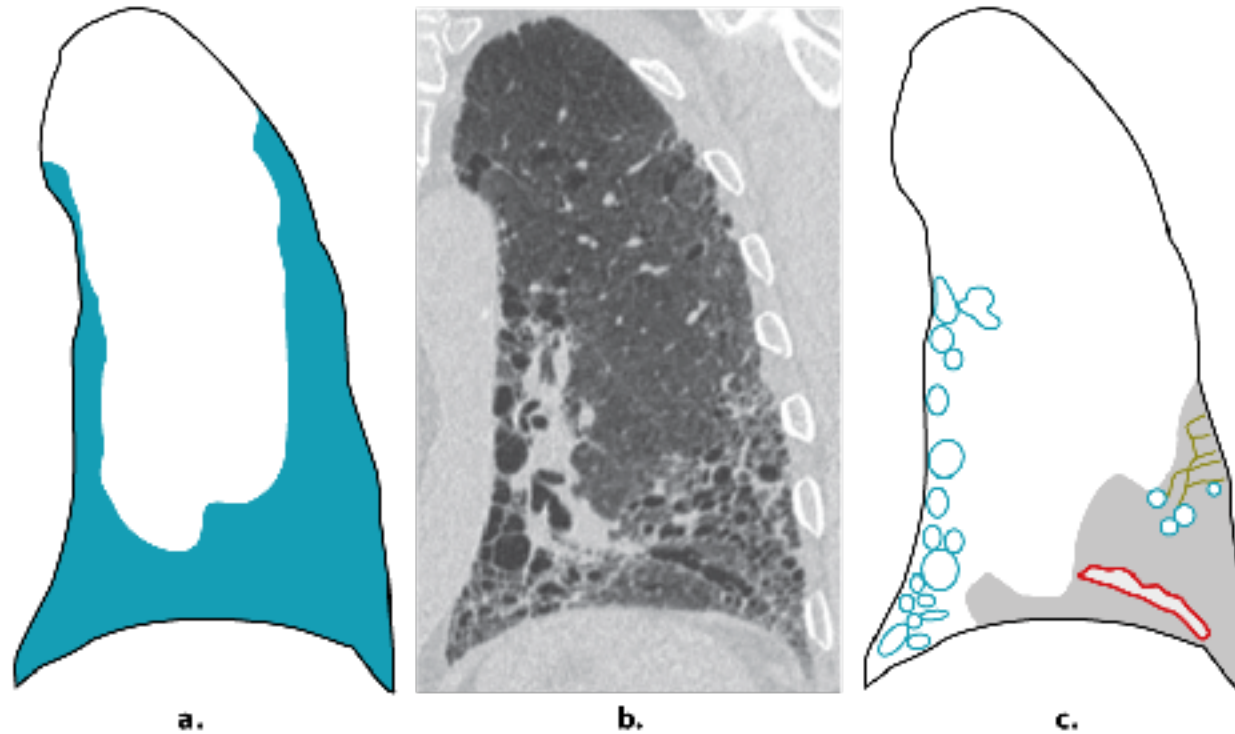
The most predominant HRCT features in cases of IPF²:

- Reticular changes – **honeycombing**, traction bronchiectasis
- Disease most extensive in the **lower lobes**
- **Peripheral distribution**

Honeycombing on HRCT is **paramount** for diagnosis, but its identification can be challenging²:

- Conditions that mimic honeycombing (e.g. **emphysema**, **traction bronchiectasis**)

DISTRIBUTION AND CT PATTERN OF UIP



Distribution **(a)**, CT image **(b)**, and CT pattern **(c)** of **UIP**.
The distribution is subpleural with an apicobasal gradient (blue area in **a**). CT shows honeycombing (blue areas in **c**), reticular opacities (green areas in **c**), traction bronchiectasis (red area in **c**), and focal ground-glass opacity (grey area in **c**).

Figure adapted from Mueller-Mang 2007¹

HRCT CRITERIA FOR UIP PATTERN¹

UIP PATTERN¹

- ▶ **Subpleural and basal** predominant; **distribution** is often **heterogeneous***
- ▶ **Honeycombing** with or without peripheral traction bronchiectasis or bronchiolectasis[†]

PROBABLE UIP PATTERN¹

- ▶ Subpleural and basal predominant; distribution is often heterogeneous
- ▶ Reticular pattern with peripheral traction bronchiectasis or bronchiolectasis
- ▶ May have mild GGO

INDETERMINATE FOR UIP¹

- ▶ Subpleural and basal predominant
- ▶ Subtle reticulation; may have mild GGO or distortion (“early UIP pattern”)
- ▶ CT features and/or distribution of lung fibrosis that do not suggest any specific aetiology (“truly indeterminate for UIP”)

*Variants of distribution: occasionally diffuse, may be asymmetrical.

[†]Superimposed CT features: mild GGO, reticular pattern, pulmonary ossification.

CT, computed tomography; CTD, connective tissue disease; GGO, ground-glass opacity; HRCT, high-resolution computed tomography; IPF, idiopathic pulmonary fibrosis; RA, rheumatoid arthritis; UIP, usual interstitial pneumonia.

DIFFERENTIATING BETWEEN UIP AND NSIP

Although less common than UIP, non-specific idiopathic pneumonia (**NSIP**) is the **most frequent differential diagnosis** of UIP. On HRCT the patterns of both conditions overlap considerably, complicating the diagnosis^{1,2}

Some distinct imaging features **favour** the diagnosis of **NSIP** over UIP^{1,2}:

- **Homogeneous** lung involvement **without** obvious apico-basal gradient
- Extensive **ground-glass abnormalities** without progressing to honeycombing areas
- **Finer reticular pattern**
- **Micronodules**

A **lung biopsy** is a necessary measure for clarification to distinguish UIP and NSIP in addition to CT¹

DIFFERENTIATING BETWEEN UIP AND NSIP^{1,2}



Adapted from Mueller-Mang 2007¹

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