
HRCT in the management of diffuse and interstitial lung diseases

For many years now, computer tomography (CT) has been the most effective radiological examination technique to visualise the lungs, as thin-section CT offers a highly detailed overview of the pulmonary parenchyma. This technique is therefore generally regarded as the gold standard for imaging of the normal and pathological lung.

BY: PROF. J.A. VERSCHAKELLEN

Many studies have shown that thin-section computer tomography (CT) has a high diagnostic value, especially in the study of pulmonary disorders predominantly affecting the pulmonary interstitium and pulmonary diseases that spread diffusely across the lung. In addition, CT has been successfully used during follow-up of these pulmonary abnormalities. The technique has also contributed towards a better understanding of the clinical and pathological evolution of certain lung disorders.

The high diagnostic value of CT is the result, on the one hand, of the fact that this technique is able to define the appearance pattern of abnormalities caused by the lung disease (i.e. the way the disease manifests itself) better and more correctly. On the other hand, CT is able to show the distribution pattern of the disease (the way in which the disorder spreads across the lungs) more accurately. Indeed, together with the study of clinical examination findings, the study of the appearance pattern and the distribution pattern constitute the main components that help us to interpret the CT images and

establish the correct diagnosis or differential diagnosis.

The first section of this brief overview of the value of CT in the diagnostic workup of interstitial lung diseases (ILD) discusses the technical aspects and the term high-resolution CT (HRCT). The next section explains when and how CT can be useful for the diagnosis and follow-up of diffuse ILD. Special attention is given to the role of CT in the multidisciplinary diagnosis of usual interstitial pneumonia (UIP) and idiopathic pulmonary fibrosis (IPF). Finally, the article briefly discusses how a CT examination of the lungs is approached to achieve the best possible interpretation of the abnormalities.

Technical aspects

Optimal visualisation of the lung parenchyma is achieved by producing thin-section images (0.5-1mm) and using special computer algorithms that increase detail. Initially these high detailed images were produced by making thin-section images every 10–20 mm, with patients holding their breath after a deep inhalation (the so-called sequential acquisition technique). This type of HRCT examination provided some twenty highly detailed images of the pulmonary parenchyma, sometimes supplemented with images obtained after exhalation or



Johnny Verschakelen is professor of radiology at the Catholic University of Leuven and senior staff member responsible for chest radiology at the Department of Radiology, University Hospitals Leuven. He has a widespread interest in all aspects of chest radiology, with a particular interest in CT of the lungs. He is past president of the Fleischner Society, founding member, member of the board and past president of the European Society of Thoracic Imaging and is member of various scientific societies. His interests comprise all aspects of chest radiology, particularly computer tomography of the lungs. He is reviewer for several journals. He is author and co-author of over 150 scientific publications in international journals and books and invited lecturer worldwide. In 2015 he received the life time achievement award of the ild care foundation. e-mail: johnny.verschakelen@uzleuven.be.

with the patient in prone position. Since not all of the parenchyma was visualised by this technique, it was only suitable for disorders that spread diffusely across the lungs, such as ILD. Nowadays, however, the multidetector spiral CT (MDCT) technique is used.¹ MDCT provides volumetric CT scans allowing to produce contiguous highly detailed images of the entire thorax. Thus, highly detailed images can be obtained of the entire lungs, with no parts being skipped. In addition, the images are no longer limited to cross-sections in a direction perpendicular to the patient's longitudinal axis, but other planes can be visualised as well (e.g. frontal [figures 1 and 2] and sagittal), and there is even the option of obtaining three-dimensional reconstructions or using special post processing techniques such as minimum and maximum intensity projections (figure 3).

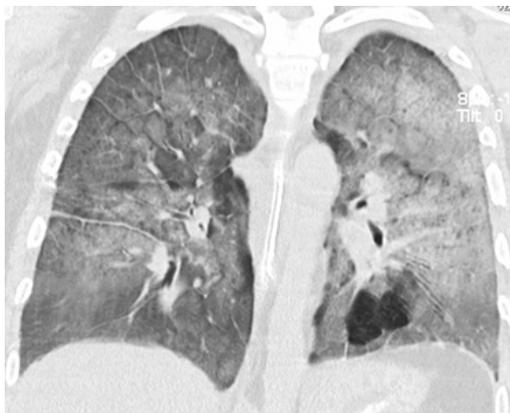


Figure 1. The CT image of this patient with ARDS shows a combination of ground-glass opacifications (right lung) and lung consolidation (left lung) with a linear pattern (best seen in the right lung).

Thus, high-resolution thin-section imaging is no longer reserved only for the study of diffuse ILD, but is now available for the study of all lung diseases. Although the term HRCT was initially only used to indicate the conventional sequential technique, it is now also used when highly detailed images are obtained with a spiral scanning technique. Since both techniques involve very thin cross-sectional images (usually between 0.5 and 1 mm), the term 'thin-section CT' is also used.

The use of the spiral acquisition technique for thin-section CT results in much larger numbers of images, and hence often in more diagnostic information in patients with lung disease (especially since sections in



Figure 2. Patient with follicular bronchiolitis. The central and lower parts of both lungs show multiple nodular opacifications and branching lines that in some places mimic a 'tree-in-bud'. The centrilobular localisation is characteristic of small airways disease.



Figure 3. Maximum intensity projection (MIP) CT image of a patient with pulmonary tumour thrombotic microangiopathy. Metastatic tumour cells have filled up the distal small centrilobular arterioles (arrows).

other planes can be obtained). In addition, during the same examination and without the need for additional image acquisitions, the spiral technique can provide high-quality images of mediastinal abnormalities (such as enlarged lymph nodes in sarcoidosis patients) or vascular disorders (such as pulmonary embolisms). However, it should be emphasized that the spiral technique may expose the patient to higher radiation dosages, especially when additional expiratory and prone scans are performed.² Fortunately, the x-ray detectors used in CT scanners have improved and X-ray dose necessary to produce high quality images has decreased. In addition many image processing techniques have been and are still being developed to improve image quality despite lower radiation dose.³⁻⁵

Value of thin-section CT in the diagnostic workup of diffuse ILD

Soon after the introduction of HRCT in clinical practice it became clear that this technique was considerably better for the detection of diffuse ILD than conventional chest radiography.⁶ Patients with diffuse lung disorders sometimes show no abnormalities on X-ray, while, due to its greater contrast resolution, CT does detect abnormalities (figure 4). At the same time, since sectional images do not have the problem of superimposed features, there is less danger of false-positive results. Hence, a CT examination may be indicated in case of clinically suspected ILD and inconclusive or normal chest radiographs. The sensitivity and specificity for the detection of diffuse ILD are indeed found to be higher with CT than with conventional chest radiography. In addition, many researchers have shown that CT not only detects pulmonary abnormalities at an earlier stage than chest radiography, but that its diagnostic accuracy is also higher than that of chest radiography, that is, CT is more likely to produce the correct diagnosis.^{7,8} Nevertheless, the research findings also show considerable variation in diagnostic accuracy across the various studies.⁹ Some researchers reported finding the correct diagnosis in 89% of cases among the 3 most likely diagnoses indicated by CT,⁶ while others found it in only 59% of cases.⁹ Major causes of these discrepant reports probably include differences in the CT technique used, the patient selection, the radiologist's level of experience and the difference between prospective and retrospective study designs. But the main cause is whether the clinical information is available and used when interpreting the CT findings. This was already shown by Grenier et al.⁸, who studied 305 patients with ILD and found that the correct diagnosis could be established in 29% of cases purely on the basis of clinical characteristics. This percentage rose significantly to 36% when the chest radiograph was also taken into account, and to 61%

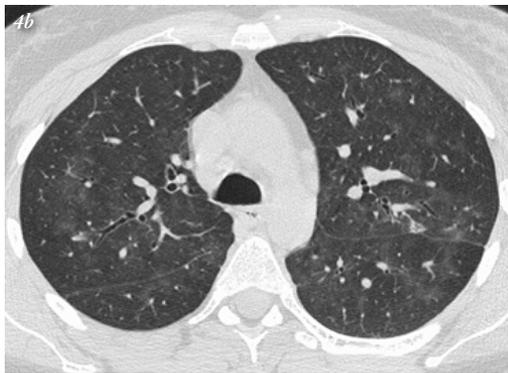
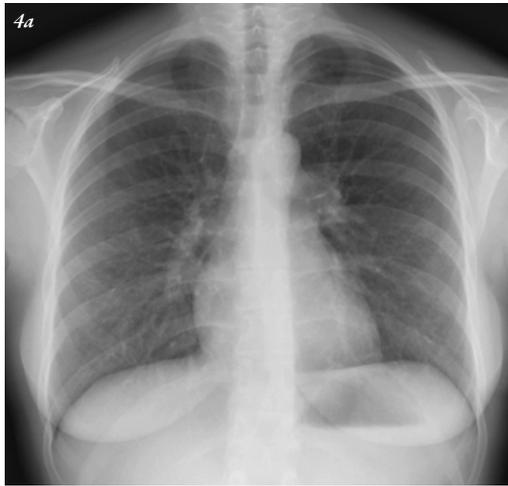


Figure 4. Patient with extrinsic allergic alveolitis. Despite the normal chest radiogram (a), the CT scan clearly shows ground-glass opacifications in both lungs (b).

when the CT findings were additionally included in the diagnostic decision-making process. In their study, CT was particularly valuable for the diagnosis of sarcoidosis (figure 5), Langerhans cell histiocytosis (figure 6), hypersensitivity pneumonitis (figures 4 and 7) and lymphangitic spread of cancer (figure 8). Others later showed that CT is also a valuable technique for the diagnosis of idiopathic pulmonary fibrosis (figure 9), coal

miners' pneumoconiosis and silicosis, alveolar proteinosis, lymphangiomyomatosis and organising pneumonia. In a more recent paper, Aziz et al.¹⁰ compared the clinical data of 168 patients suspected of



Figure 5. Patient with pulmonary sarcoidosis. The lung shows multiple, relatively dense and sharply defined nodules. The nodules are located subpleurally, around the bronchovascular structures and in the interlobular septa: they exhibit a lymphatic distribution pattern.



Figure 6. Patient with Langerhans cell histiocytosis. Multiple small cystic lesions in both lungs.

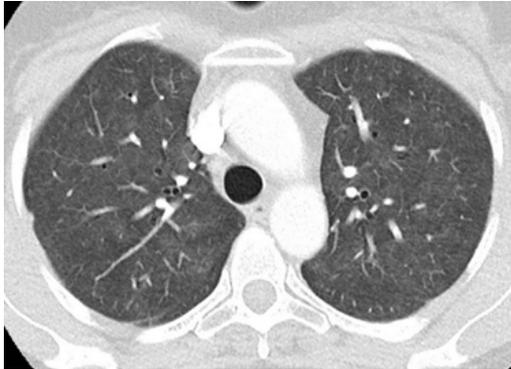


Figure 7. Patient with extrinsic allergic alveolitis. Ground-glass opacifications are diffusely distributed over both lungs. In the appropriate clinical context, this makes the CT image highly suggestive of this disorder.

having diffuse ILD before and after the findings of CT examinations were incorporated in the decision-making process. The comparison showed that the first-choice diagnosis changed in 50% of cases and that the confidence in the most likely diagnosis increased after CT data were included in the decision-making process. In addition, the opinion on the value of and need for bronchoalveolar lavage and thoracoscopic biopsy as diagnostic tools changed in 24–29% of the cases. The number of thoracoscopic biopsies deemed necessary fell from 26.8 % to 11.2% after inclusion of the CT findings.

What all of the above shows is that the diagnostic workup of diffuse ILD is a team effort. To begin with, the clinician and radiologist must collaborate closely, as combining the clinical and radiological information can in a number of cases lead to a definitive or highly likely diagnosis, so that invasive lung biopsies can be avoided.¹¹ Nevertheless, there will also be cases where the clinical picture and the radiological images do not fully agree, or where the typical clinical picture does not correspond with what is suggested by the CT image, or vice versa. This is why the role of the third player in the team, the

pathologist, is very important. In a number of cases it will still be necessary to have a biopsy and tissue examination. In such cases, CT can be used to guide the biopsy procedure (to avoid fibrotic areas in the lung, to indicate areas where the lung disorder is probably active, or to choose between a transbronchial and a thoracoscopic approach). Correlating the microscopic picture of the lung disorder obtained from examining small tissue samples from a few sites in one lung with the ‘submacroscopic’ image of the entire lungs obtained with thin-section CT is an essential approach to arrive at a reliable diagnosis.¹² Although CT has thus reduced the need for biopsies for many of the patients with diffuse ILD, biopsy and tissue examination still has an important role to play for a number of patients. For these patients, the CT findings can help in deciding on the best site and

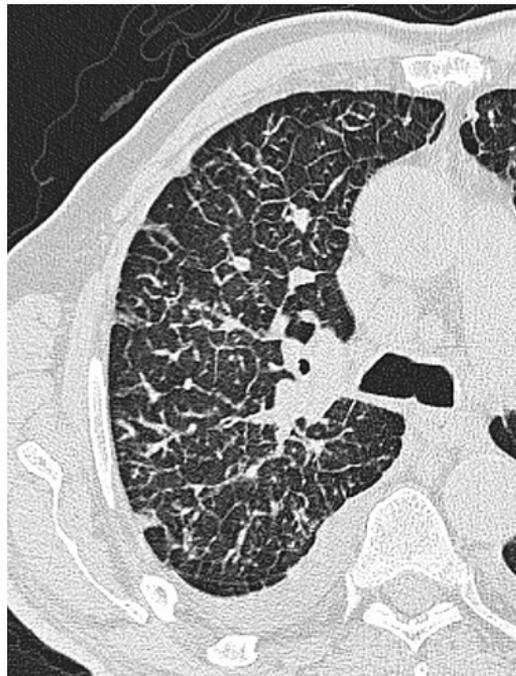


Figure 8. Patient with lymphangitic spread of cancer. Thickening of the interlobular septa has led to a linear pattern.

type of the biopsy and in interpreting the microscopic findings.¹³

Thin-section CT in the workup of IPF

IPF is a specific form of chronic fibrosing interstitial pneumonia with unknown etiology which is limited to the lung and associated with histological appearance of usual interstitial pneumonia (UIP). In 2011 the ATS/ERS/JRS/ALAT international evidence based guidelines on the diagnosis and management of IPF were published.¹⁴ These widely used guidelines, provide diagnostic criteria based on clinical, radiological and histopathological features and emphasize the need for a close communication between clinician, radiologist and, when appropriate, pathologist. Based on appearance and distribution of CT abnormalities, imaging features are described that suggest UIP (UIP pattern), possible UIP (possible UIP pattern), or should be seen as inconsistent with UIP (inconsistent with UIP pattern). UIP is suggested when subpleural, basal reticular abnormalities and honeycombing often associated with traction bronchiectasis are present and when some features (upper, mid-lung, peribronchovascular predominance, extensive ground-glass, profuse micronodules, multiple cysts, diffuse mosaic attenuation, segmental consolidation) listed as inconsistent with UIP are absent (figure 9e and 9f). The presence of honeycombing is considered critical for making a definite diagnosis and when absent despite other imaging features that meet criteria for UIP being present the imaging features are regarded as representing possible UIP (figure 9a, 9b, 9c and 9d). The difference between the “typical” UIP pattern and the two other patterns (possible and inconsistent) is important because according to these guidelines only the UIP pattern directly obviates surgical lung biopsy in a patient with clinical suspicion of IPF. Unfortunately honeycombing on CT indicates advanced and end-stage fibrosis and starting therapy in this stage

may be not as effective as beginning therapy in an earlier stage. In addition, it has been shown that there is significant interobserver variability in the CT assessment of honeycombing¹⁵ (figure 9c and 9d) while performing a surgical lung biopsy turns out to be impossible in an important number of patients with possible UIP.

Guidelines in clinical practice

In addition the practical use of these criteria has been questioned by many observations. Walsh et al showed that the interobserver agreement for the ATS/ERS/JRS/ALAT CT criteria for UIP is only moderate among thoracic radiologists, irrespective of their experience.¹⁶ In addition, Raghu et al.¹⁷ showed that in a group of patients suspected of having IPF who had both CT and surgical lung biopsy samples, 108/111 (97%) patients with CT criteria of UIP had histologically confirmed UIP, but also 79/84 (94%) patients who met CT criteria for possible UIP did so. In addition, Yagihashi et al. found, in a study focussing on discordance between imaging and histologic diagnoses of UIP, that in a group of 75 patients with CT features inconsistent with UIP 71 (94.7%) had histologically definite or probable UIP. These patients were younger and less likely to be smokers.¹⁸ Another study looked at previous and subsequent CT examinations before patients developed typical CT and also clinical criteria of IPF and concluded that radiologists can effectively diagnose UIP and in the proper clinical settings IPF in the absence of honeycombing.¹⁹ Criteria that suggest UIP in this study included: peripheral reticulation with lobular distortion, lower lobe predominance but some upper lobe involvement, non-segmental distribution, heterogeneous appearance, traction bronchiectasis with or without honeycombing given that other CT patterns like nodular, cystic, mosaic attenuation or ground-glass and consolidation patterns are not dominantly present or that the lungs are not showing extensive paraseptal or

centrilobular emphysema (figure 9a, 9b, 9c and 9d). So it becomes obvious that IPF can and should be diagnosed earlier before CT honeycombing develops and that with a possible UIP pattern on CT in the appropriate clinical settings, the diagnosis of IPF can be made by a multidisciplinary group of experts without surgical lung biopsy.¹⁷ This surgical lung biopsy can then be reserved for those patients with an important discordance between clinical and CT findings.

Interpreting a thin-section CT scan to diagnose diffuse ILD

As was explained above, the interpretation of a CT examination of the lungs is based on recognising the appearance and distribution pattern of abnormalities.²⁰⁻²³ The first phase involves classifying the abnormalities in one of the following appearance patterns:

1. Nodular pattern: the most obvious abnormality is the presence of large numbers of nodules²⁴ (figure 5).
2. Linear pattern: the most striking feature is the lines running across the pulmonary parenchyma; these may look like a web, which is why this is also known as the reticular pattern²⁵ (figure 8).
3. Increased pulmonary attenuation: parts of the lung appear less translucent, that is, density has arisen. Two types are distinguished: ground-glass opacities and pulmonary consolidations²⁶ (figure 10),
4. Reduced pulmonary attenuation: parts of the lung appear more translucent, that is, density has decreased. This may be caused by reduced pulmonary perfusion, cysts and cyst-like lesions, and pulmonary emphysema²² (figure 6).

It is important to emphasize that it is not always easy to identify a particular pattern. Certain diseases may present a combination of two or more patterns (figures 1, 9) or one pattern may be replaced by another in the course of the disease. One should always try to identify

the most dominant pattern. The second phase comprises attempts to localise the abnormalities as accurately as possible. Some disorders, like sarcoidosis, Langerhans cell histiocytosis and centrilobular emphysema, preferentially affect the upper parts of the lung. Others, like idiopathic pulmonary fibrosis (IPF), panlobular

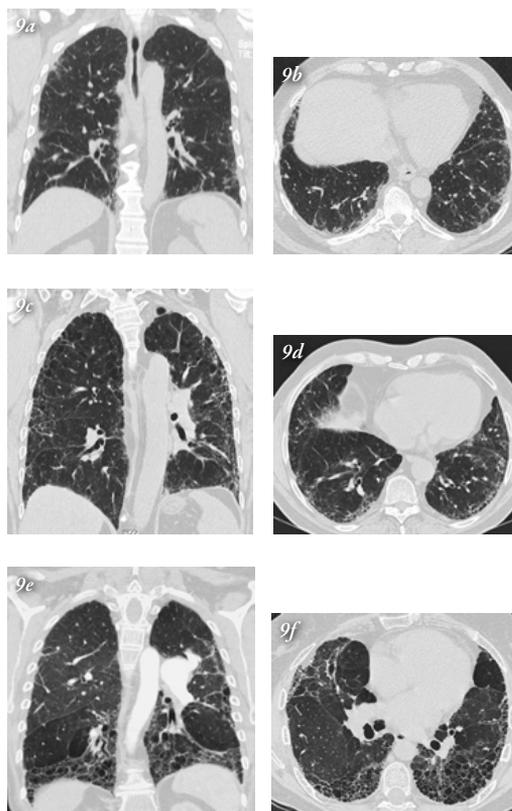


Figure 9. Three patients with idiopathic pulmonary fibrosis. Early disease (a and b) irregular lines at the periphery of the lung with lobular distortion, lower lobe predominance but some upper lobe involvement, non-segmental distribution and heterogeneous appearance; only few traction bronchiectasis. More advanced disease (c and d) : abnormalities are more pronounced with obvious small cystic abnormalities and traction bronchiectasis. Advanced disease (e and f) : irregular lines with larger cystic lesions (honeycombing) and extensive lung deformation and traction bronchiectasis.

emphysema and organising pneumonia, particularly affect the lower pulmonary fields, while disorders such as extrinsic allergic alveolitis (EAA) or lymphangio-matosis (LAM) usually have no preference for a particular part of the lung. In sarcoidosis, the involvement of the lung develops particularly in a central peribronchovascular pattern, whereas the abnormalities in IPF and organising pneumonia are usually situated peripherally and subpleurally.

The high level of detail provided by CT scans makes it possible in a number of cases to determine the localisation and distribution pattern in even more detail (submacroscopic distribution). It is often possible to determine whether the pathology has spread in or along the airways (figure 2, 11), the blood vessels (arteries [figure 3] or veins) or the lymphatic vessels (figure 5, 8), and whether the pathology appears to affect mainly the interstitium (figure 9) or the air spaces (figure 10). The submacroscopic distribution is mostly determined by relating the distribution of the abnormalities to the various components of the secondary pulmonary lobule.²⁷



Figure 10. Patient with eosinophilic pneumonia. Both lungs show ground-glass opacities, while the left lower lobe shows a poorly defined area of lung consolidation. This consolidation shows an air-filled airway, an 'air bronchogram' (arrows).

The secondary pulmonary lobule is defined as the smallest unit of lung tissue that is surrounded by connective tissue. This pulmonary unit has been known for a long time, but has regained popularity since the introduction of thin-section CT, and is now used as the reference structure when studying the fine distribution of abnormalities in the lung.

Such a pulmonary unit has a size of approximately 0.5 - 3 cm and has a polygonal shape. At the centre of the lobule there is a small airway (bronchiole) accompanied by a small artery (arteriole). This bronchiole and arteriole then divide into smaller branches, eventually forming the alveoli and capillaries, respectively. The capillaries then collect in venules, which eventually discharge into larger veins situated in the septa between the various lobules. These septa are called interlobular septa; they are connective tissue septa that belong to the peripheral pulmonary interstitium and also contain lymphatic vessels. Lymphatic vessels are also present at the centre of the lobule, but not around the alveoli. The centre of the lobule also contains connective tissue around the



Figure 11. Patient with mycoplasma pneumonia. Multiple poorly defined nodules in both upper fields. The centrilobular localisation indicates a bronchial distribution pattern.

arteriole and bronchiole (the axial interstitium). This is distally connected to the parenchymatous interstitium, which extends between the alveoli and continues proximally around the larger bronchovascular structures. From the interlobular septa, intralobular septa extend towards the centre of the lobule.

Together with the interlobular septa, these intralobular septa belong to the peripheral interstitium. For a correct understanding of the lymphatic distribution pattern, it is necessary to know that the lymphatic vessels extend proximally from the centre of the lobule to envelop the large bronchovascular structures and are also situated in the subpleural spaces.

Nodular pattern

This pattern is characterised by the presence of multiple nodular opacities with a maximum diameter of 3 cm each. The CT interpretation of the nodular pattern is based on studying the size of the nodules, their boundaries (which can be sharp, as in figure 5 or vague as in figure 11), their density and their distribution (in and around the lymphatic vessels (figures 5, 8), at the centre of the lobule (figure 11) or randomly distributed).²⁴

Linear pattern

This pattern is characterised by the presence of a number of lines. Since these lines often intersect, the pattern is also known as the 'reticular pattern'. The CT interpretation of this pattern is mainly based on studying the appearance (smooth versus irregular boundaries) and the localisation of the lines. Linear opacities are seen when the interstitium is thickened (figure 9), when the lymphatic vessels are affected (figures 5,8), when the blood vessels have a larger than normal diameter and when the wall of the airway is thickened or the lumen of smaller or larger airways is obstructed (figure 2).²⁵

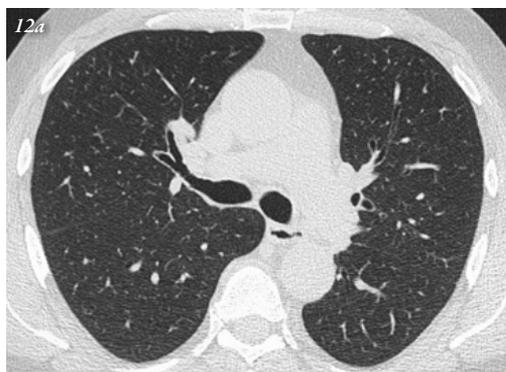


Figure 12. Patient with post-infection constrictive bronchiolitis (a) inspiration; (b) expiration). While the lungs seem normal on the inspiratory CT (a), the expiratory CT shows inhomogeneous lung attenuation: attenuation is decreased in some parts and increased in others (mosaic attenuation).

The reduced attenuation is due to reduced perfusion secondary to hypoventilation due to small airways obstruction, while the increased attenuation is caused by redistribution of the capillary blood to the normal parts of the lung. The fact that the mosaic attenuation is only seen on the image obtained after deep exhalation indicates small airways narrowing with air-trapping.

Increased attenuation

This pattern arises when the density of the lung increases. This can happen as a result of an increase in the amount of tissue or of the tissue becoming denser, or it can be due to an increase in the volume of blood in the small blood vessels. Finally, the density also increases if the amount of air in the lung decreases relative to the amount of tissue, which is seen, for instance, when pulmonary volume is lost or when alveoli are partially or completely filled up.

The term 'ground-glass opacification' (figures 1, 4, 10, 7) is used when the increase in density is limited and the blood vessels and airways can still be seen on the CT scan through the whiter lung tissue. The term 'pulmonary consolidation' is used when the density has increased so much that the blood vessels and bronchi are no longer visible (figure 1). Sometimes the air in the airways is still visible, and the image is then described as an 'air bronchogram' (figure 10).

Whereas pulmonary consolidation is always pathological, ground-glass opacification can also occur under certain normal physiological conditions. It is seen, for instance, after a deep exhalation or in the dorsal parts of the lung when the patient is lying supine, as this means that these parts are then more strongly perfused due to gravity.²⁶

Decreased attenuation

The causes of decreased attenuation are the opposite of those causing increased attenuation. Decreased attenuation is seen when there is an abnormal increase in the volume of air in a particular part of the lung, for instance due to 'air-trapping' behind a narrowed small airway (figure 12), when less than the normal volume of blood circulates through the capillaries (reduced perfusion), but also due to pulmonary tissue destruction as in pulmonary emphysema or the development of pulmonary cysts (figure 6). Decreased pulmonary attenuation is always pathological.²²

Practice recommendations

Thin-section or high-resolution CT plays an important role in the diagnostic workup of diffuse and interstitial lung diseases. Optimal use of the CT findings requires close collaboration between clinician, radiologist and pathologist, as the contributions of clinical, CT and microscopic information to the diagnostic workup for ILD are greatly increased by examining and interpreting this information in an integrated manner.

References

1. Prokop M. Multisection CT: technical principles and future trends. *Eur Radiol* 2003; 13 Suppl 5: M3-13.
2. Imhof H, et al. Spiral CT and radiation dose. *Eur J Radiol* 2003; 47(1): 29-37.
3. den Harder AM, et al. Achievable dose reduction using iterative reconstruction for chest CT: A systematic review. *Eur J Radiol* 2015; 84: 2307-13.
4. Rawat U, et al. ACR White Paper-Based Comprehensive Dose Reduction Initiative in radiation dose for chest CT. *J Am Coll Radiol* 2015;12: 1251-6.
5. Pontana F, et al. Effect of iterative reconstruction on the detection of systemic sclerosis-related ILD. *Radiology* 2016; 279(1): 297-305.
6. Mathieson JR, et al. Chronic diffuse infiltrative lung disease: comparison of diagnostic accuracy of CT and chest radiography. *Radiology* 1989; 171: 111-16.
7. Padley SP, et al. Comparative accuracy of HRCT and chest radiography in the diagnosis of chronic diffuse infiltrative lung disease. *Clin Radiol* 1991; 44(4): 222-26.
8. Grenier P, et al. Chronic ILD: diagnostic value of chest radiography and HRCT. *Radiology* 1991; 179: 123-132.
9. Nishimura K, et al. The diagnostic accuracy of

-
- HRCT in diffuse infiltrative lung diseases. *Chest* 1993; 104: 1149-55.
10. Aziz ZA, et al. ILD: effects of thin-section CT on clinical decision making. *Radiology* 2006; 238: 725-33.
 11. Wells AU. HRCT in the diagnosis of diffuse lung disease. *Semin Respir Crit Care Med* 2003; 24: 347-56.
 12. Colby TV, et al. Anatomic distribution and histopathologic patterns in ILD correlation with HRCT. *J Thorac Imaging* 1996; 11: 1-26.
 13. Quigley M, et al. ILD: synergy between radiology and pathology. *Histopathology* 2006; 49: 334-42.
 14. Raghu G, et al. An official ATS/ERS/JRS/ALAT statement: IPF: evidence-based guidelines. *AJRCCM* 2011; 183: 788-824.
 15. Watadani T, et al. Interobserver variability in the CT assessment of honeycombing in the lungs. *Radiology* 2013; 266: 936-44.
 16. Walsh SL, et al. Interobserver agreement for the ATS/ERS/JRS/ALAT criteria for a UIP pattern on CT thorax. *Thorax* 2016; 71: 45-51.
 17. Raghu G, et al. Diagnosis of LPF with HRCT in patients. *Lancet Respir Med* 2014; 2: 277-84.
 18. Yagihashi K, et al. Radiologic-pathologic discordance in biopsy-proven usual interstitial pneumonia. *Eur Respir J* 2016; 47(4): 1189-97.
 19. Gruden JF, et al. Diagnosis of UIP in the absence of honeycombing: evaluation of specific CT criteria with clinical follow-up. *Am J Roentgenol* 2016; 206: 472-80.
 20. Ellis SM, Hansell DM. IIPs: imaging-pathology correlation. *Eur Radiol* 2002; 12: 610-26.
 21. Collins J. CT signs and patterns of lung disease. *Radiol Clin North Am* 2001; 39(6): 1115-1135.
 22. Verschakelen J, De Wever W. *Computed Tomography of the Lung - A Pattern Approach*. Springer Verlag, Berlin Heidelberg, 2007.
 23. Schaefer-Prokop C, et al. HRCT of diffuse ILD: key findings. *Eur Radiol* 2001; 11: 373-92.20.
 24. Lee KS, et al. Diffuse micronodular lung disease: HRCT and pathologic findings. *J Comput Assist Tomogr* 1999; 23: 99-106.
 25. Kang EY, et al. Interlobular septal thickening; patterns at HRCT. *J Thorac Imaging* 1996; 11: 260-64.
 26. Collins J, Stern EJ. Ground-glass opacity at CT: the ABCs. *Am J Roentgenol* 1997; 169: 355-67.
 27. Webb WR. Thin-section CT of the secondary pulmonary lobule: the 2004 Fleischner lecture. *Radiology* 2006; 239: 322-38.