





# Radiological perspective of COVID-19 pneumonia: The early features and progressive behaviour on high-resolution CT

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## Introduction

In the past two decades, severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) has caused severe respiratory diseases SARS and MERS in endemic areas, respectively.<sup>1,2</sup> In December 2019, an outbreak of pneumonia caused by a novel coronavirus (SARS-CoV-2) named Coronavirus disease 2019 (COVID-19) began in Wuhan, China, and rapidly evolved into a pandemic.<sup>3</sup> SARS-CoV-2 has approximately 80% genome sequence identity with SARS-CoV and similarly uses angiotensin-converting enzyme-2 (ACE-2) as a functional receptor.<sup>4</sup> High ACE-2 expression is known in alveolar type II cells (AT2) of the lung and many patients infected with COVID-19 develop pneumonia.

Many researchers have reported the chest CT manifestations of COVID-19 pneumonia, and chest CT is recognized as a key tool for medical triage of patients suspected of having COVID-19 who present with moderate-severe clinical features and a high pre-test probability of disease.<sup>5,6</sup> High-resolution CT (HRCT) of the lung is well

## Summary

Since the outbreak of Coronavirus disease 2019 (COVID-19) in China, many researchers have reported the chest CT manifestations of COVID-19 pneumonia. High-resolution CT (HRCT) of the lung can provide important clues to understand the progressive behaviour of COVID-19 pneumonia. This pictorial essay discusses the early features and potential progressive behaviour of COVID-19 on HRCT of the lung.

**Key words:** COVID-19; pneumonia; HRCT.

established for diagnosing and managing many pulmonary diseases,<sup>7</sup> and it can provide important clues to understand the characteristics of COVID-19 pneumonia. This pictorial essay discusses the early features and potential progressive behaviour of COVID-19 pneumonia on HRCT.

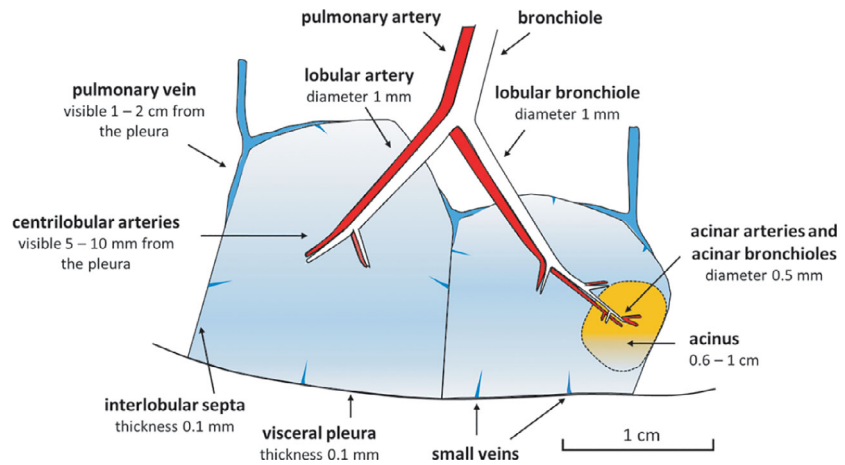
## Lobular anatomy

The secondary pulmonary lobule (SPL) refers to the smallest unit of lung structure separated by the interlobular septa containing pulmonary veins, lymphatics and connective tissue.<sup>8</sup> The anatomy of the SPL with its structures, dimensions and visibility on HRCT is shown in Fig. 1. Small veins peripherally located in the interlobular septa and visceral pleura between the acini (assumed interacinar septa) are also included, which help to understand the characteristics of COVID-19 pneumonia.

## Distribution at SPL level

The distribution patterns of the lesion at the SPL level in pulmonary diseases are shown in Fig. 2. Centrilobular

**Fig. 1.** Secondary pulmonary lobule (SPL) with its structures, dimensions, and visibility on HRCT.



pattern (A) consists of nodular opacities at the acinus level typically observed in pulmonary tuberculosis and mycoplasma pneumonia. Bronchovascular pattern (B) consists of thickening of bronchovascular bundles typically observed in bronchopneumonia. Panlobular patterns (C,D) consist of dense or ground-glass opacities (GGOs) typically observed in bacterial pneumonia and cryptogenic organizing pneumonia. Perilymphatic pattern (E) consists of nodular opacities or thickening or both along lymphatics located in peri-bronchovascular bundles and interlobular septa typically observed in sarcoidosis, lymphangitis carcinomatosa and interstitial lung oedema. Perilymphatic distribution is sometimes accompanied by an intralobular reticular pattern (F) consisting of fine crossing lines of opacity separated by a few millimetres (assumed thickening of interacinar septa). The combination of the ground-glass panlobular pattern (D) and reticular pattern (F) is known as a crazy-paving appearance (G), which is typically observed in pulmonary alveolar proteinosis (PAP) and acute respiratory distress syndrome (ARDS). Collapsed pattern (H) consists of air-space consolidation with volume loss typically observed in later stages of bacterial pneumonia.

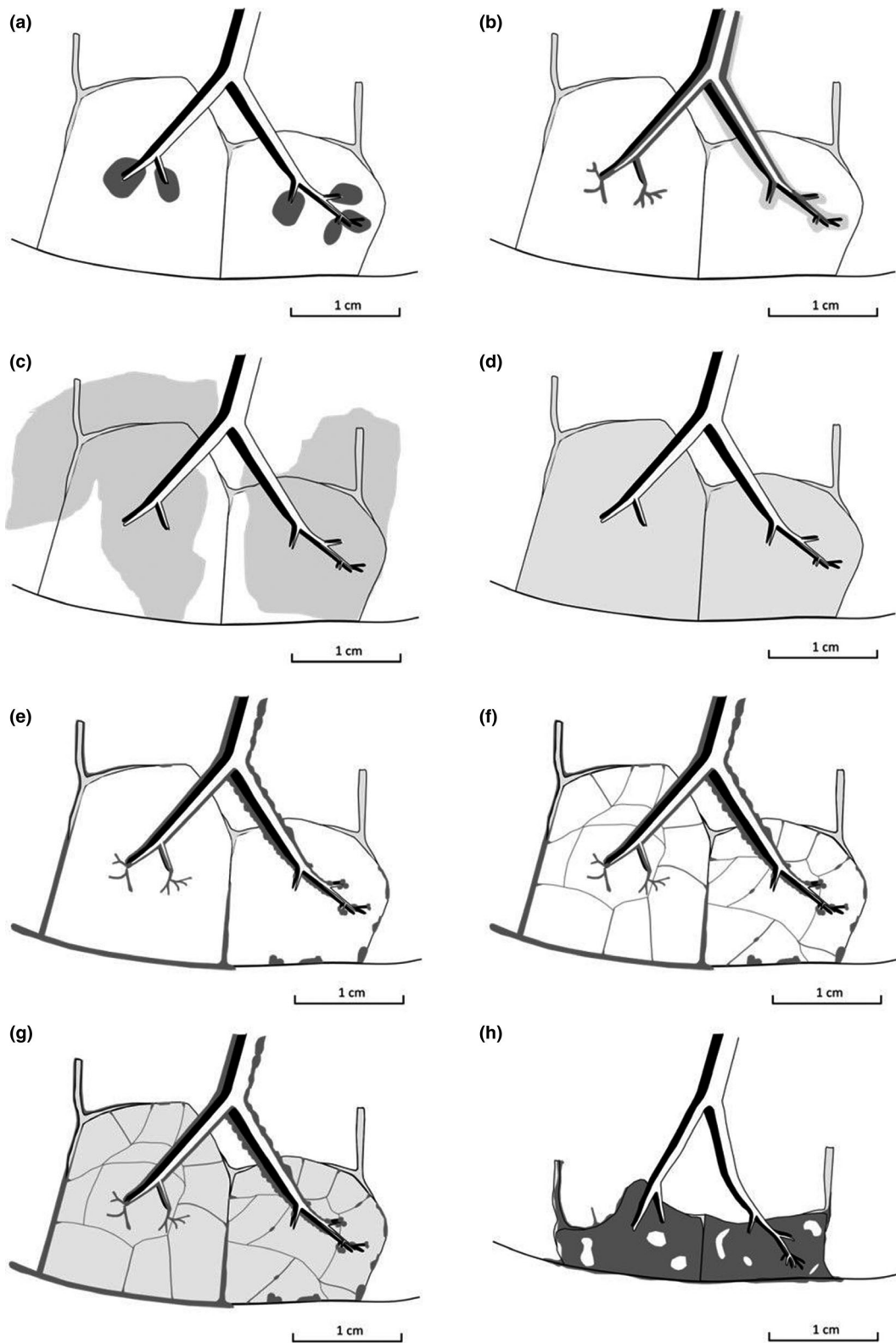
### HRCT findings of COVID-19 pneumonia

COVID-19 pneumonia demonstrates almost all distribution patterns on HRCT. The most representative early finding on HRCT is the patchy GGOs around the size of an acinus in a centrilobular distribution (Fig. 3a). The centrilobular distribution of GGOs indicates bronchiolar infection of SARS-CoV-2. GGOs easily become fused together across interlobular septa (Fig. 3b). Due to the high affinity of SARS-CoV-2 for ACE-2 expressed in AT2 of the lung, the lesions mainly exist and progress in lung alveoli resulting in the peripherally located GGOs. In contrast, the centrilobular small nodules reflecting bronchiolitis were not observed.

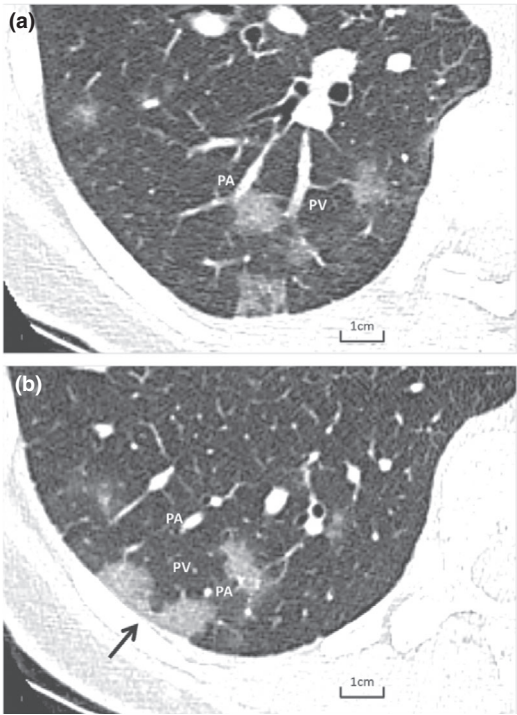
In some patients whose respiratory symptoms progressed, GGOs (Fig. 4a) significantly progressed with partial volume loss and interstitial lines in the lung periphery (Fig. 4b). The volume loss (collapsed pattern: Fig. 2h) can be evaluated by the changes in the position of peripheral vessels and interlobar pleura. The peripheral interstitial lines are interlobular septal thickening, termed Kerley B lines, commonly due to mild pulmonary oedema (Fig. 4b).

One of the other representative HRCT findings is the crazy-paving appearance referring to the appearance of GGOs with superimposed inter- and intralobular septal thickening (Fig. 5). In COVID-19 pneumonia, the crazy-paving appearance can be observed in both severe and non-severe patients with disease progression or at the peak stage. It is typically found in patients with PAP and ARDS (Fig. 2g). PAP is a rare lung disorder characterized by an abnormal accumulation of surfactant proteins. The pathological findings of early-stage COVID-19 pneumonia were described as prominent proteinaceous exudates with granules in alveolar spaces, pneumocyte hyperplasia and interstitial thickening.<sup>9</sup> These pathological findings are similar to those of PAP. ARDS is recognized as the severe form of acute lung injury consisting of alveolar oedema and interstitial inflammation, which is one of the major phenotypes of COVID-19.<sup>10</sup> The entry of SARS-CoV-2 into AT2 and subsequent proinflammatory cytokine release (cytokine storm) may cause ARDS and the crazy-paving appearance on HRCT.

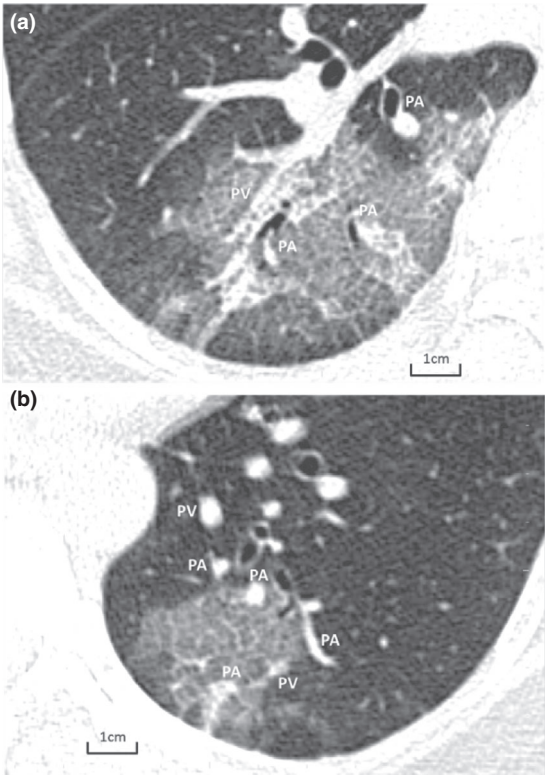
CT halo and reversed halo signs<sup>11,12</sup> can be observed in COVID-19 pneumonia (Fig. 6a,b, respectively). Although the CT halo sign was classically described in haemorrhagic nodules, typically observed in angio invasive fungal infections and vasculitis, viral infections and organizing pneumonia are known as differential causes for the halo sign. The reversed halo sign, defined as an area with GGO surrounded by partial or complete rings of consolidation, typically develops longer after symptom



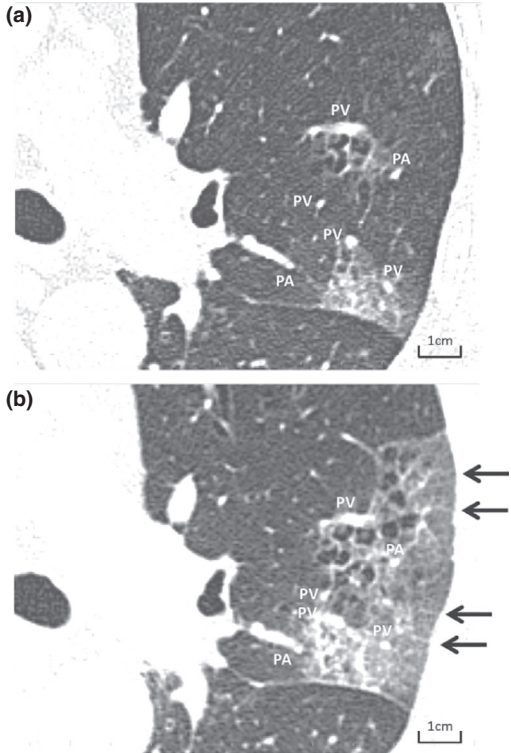
**Fig. 2.** Distribution patterns of the lesion at the SPL level. a: centrlobular, b: bronchovascular, c and d: panlobular, e: perilymphatic, f: reticular, g: crazy-paving, h: collapsed.



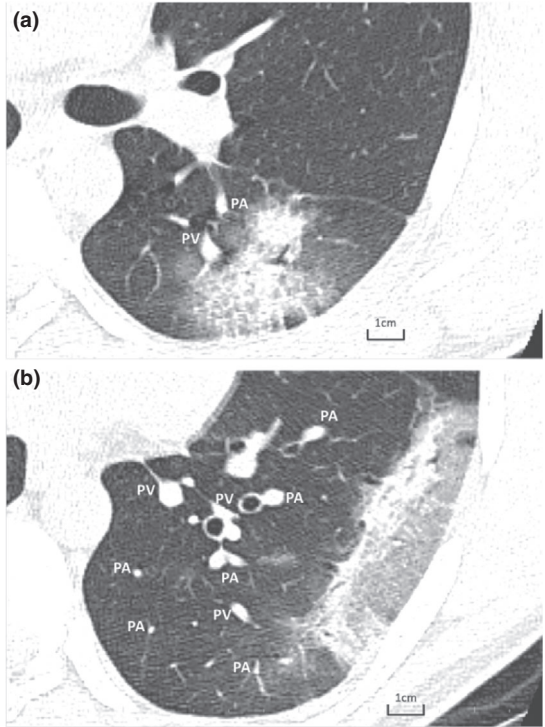
**Fig. 3.** Patchy GGOs in a centrilobular distribution (a) and their fusion (b) in a 53-year-old woman. PA, pulmonary artery; PV, pulmonary vein.



**Fig. 5.** Crazy-paving appearances in a 56-year-old woman.



**Fig. 4.** The GGOs (a) and disease progression (b) with partial alveolar collapse and interstitial oedema observed in a 70-year-old man.



**Fig. 6.** The CT halo (a) and reversed halo signs (b) in a 37-year-old man.

onset, suggesting that this CT finding correlates with the underlying pathophysiology of the disease process as it organizes.<sup>13</sup> These findings suggest that organizing pneumonia is one of the mechanisms of late lung injury in COVID-19 pneumonia.

In conclusion, the initial HRCT finding of COVID-19 pneumonia is patchy GGOs around the size of an acinus in a centrilobular distribution, indicating bronchiolar infection of SARS-CoV-2. Typical findings of bronchiolitis are rare, probably due to the high affinity of SARS-CoV-2 for ACE-2 expressed in alveoli. The GGOs easily become fused together across interlobular septa, and progress with partial alveolar collapse and interlobular septal thickening. The crazy-paving appearance is sometimes observed in non-severe patients with COVID-19 pneumonia, considered to result from the alveolar oedema and interstitial inflammation caused by impaired production of surfactant proteins or proinflammatory cytokine release or both in patients with disease progression or at the peak stage. CT halo and reversed halo signs reflect organizing pneumonia in the stage of late lung injury in COVID-19 pneumonia.

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