



ΕΠΙΣΤΗΜΟΝΙΚΗ ΕΤΑΙΡΕΙΑ  
ΓΙΑ ΤΗ ΜΥΟΣΚΕΛΕΤΙΚΗ ΥΓΕΙΑ

15<sup>ο</sup>

Πανελλήνιο  
Συνέδριο

ΕΠΕΜΥ

28 Σεπτεμβρίου - 1 Οκτωβρίου 2023  
Aquila Atlantis Hotel,  
Ηράκλειο Κρήτης

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Ρευματοειδής Αρθρίτιδα -  
Βασικές αρχές της αξονικής τομογραφίας θώρακος



ΠΑΝΕΠΙΣΤΗΜΙΑΚΟ ΓΕΝΙΚΟ  
ΝΟΣΟΚΟΜΕΙΟ ΗΡΑΚΛΕΙΟΥ

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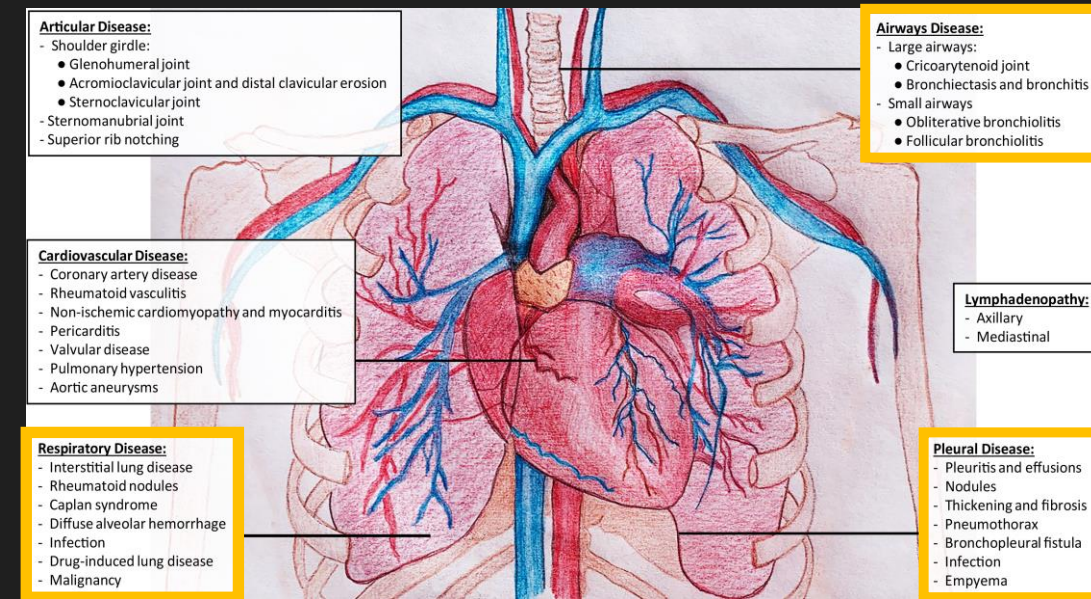
Ιατρός Ακτινολόγος

Επιμελητής Β ΕΣΥ, ΠΑΓΝΗ



# Rheumatoid Arthritis and Lung Disease

- Rheumatoid arthritis (RA) is the most common chronic inflammatory arthritis, affecting 0.5%–1% of adults worldwide and women two to three times more than men. Up to half of all patients with RA exhibit extraarticular manifestations (EAMs)
- Respiratory disease affects approximately 60%–80% of patients with RA and can involve the airways, lung parenchyma, and pleura. Respiratory involvement is the second most common cause of death in RA
- Lung involvement has historically been considered a late manifestation of RA. However, there is increasing evidence that the lung may be a site of RA initiation, as patients may present with parenchymal lung disease in the absence of joint symptoms and demonstrate ACPA-positive sputum and ACPA-negative serum test results



# Rheumatoid Arthritis-Interstitial Lung Disease

- RA-ILD is one of the most common pulmonary manifestations of RA and the second leading cause of mortality, primarily owing to respiratory failure, superimposed infection, and lung cancer. ILD in RA is the only EAM increasing in prevalence
- Clinically significant disease occurs in about 10% of patients, whereas about 30% have subclinical disease
- ILD precedes RA diagnosis in up to 15% of patients, and up to 34% are diagnosed concomitantly
- Risk factors for ILD in RA include cigarette smoking, older age, male sex, and higher disease activity scores

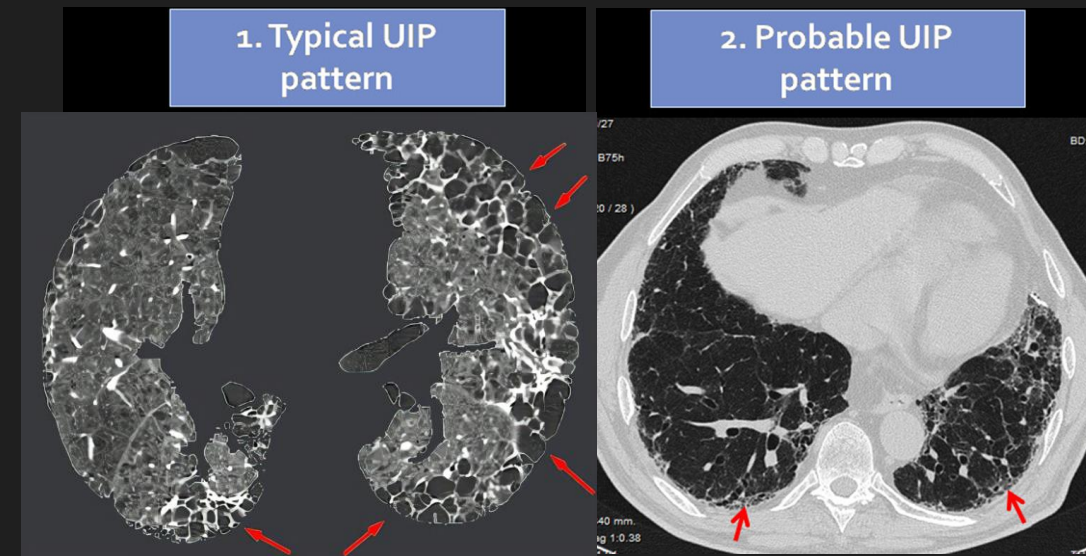
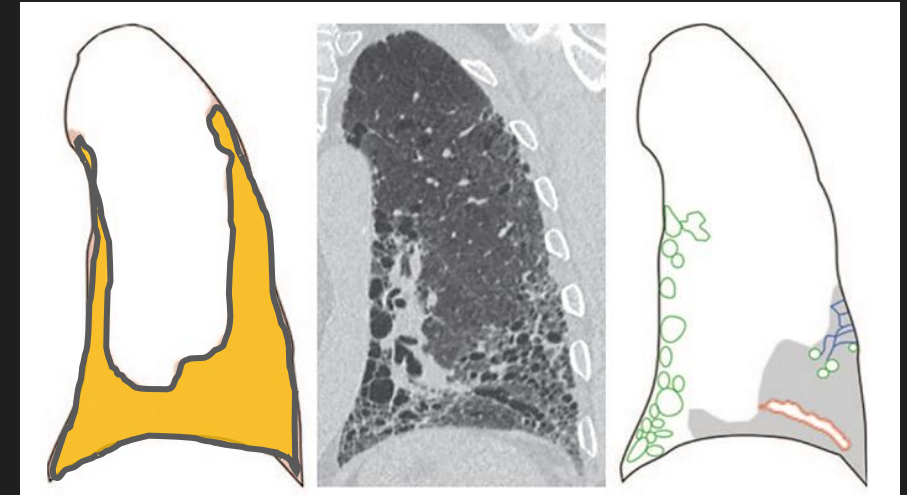
Table 3: Imaging Features of ILD in RA

ILD	Epidemiology	High-Resolution (Thin-Section) CT Features
Usual interstitial pneumonia	Most common, 60% of ILD cases in RA	Heterogeneous fibrosis; basal subpleural predominant; reticular abnormality (coarse and fine); honeycombinglike cystic spaces; peripheral traction bronchiectasis and/or bronchiolectasis
Nonspecific interstitial pneumonia	Second most common, ~30% of ILD cases in RA	Homogeneous fibrosis, basal predominant; immediate subpleural sparing; peribronchovascular involvement common; GGO are greater than reticular abnormalities; traction bronchiectasis (more central)
Organizing pneumonia	Third most common	Variable appearance; peripheral, bronchocentric opacities (consolidative or ground glass); fleeting or migratory consolidation; perilobular opacities; reverse halo sign; crazy-paving pattern
Lymphocytic interstitial pneumonia	Rare	Diffuse or patchy GGO (visualized anywhere lymphoid tissue is present [peribronchovascular, septal, centrilobular, subpleural]); thin-walled cysts (perivascular, lower-lung predominant); thickened interlobular septa and bronchovascular bundles; lymph node enlargement
DAD	Rare	Acute phase: extensive bilateral consolidation and GGO (diffuse GGO and dependent consolidation); reparative (organizing and fibrotic) phase: reticulation and traction bronchiectasis superimposed on areas of GGO and consolidation
Desquamative interstitial pneumonia	Rare	GGOs, mild reticulation; distribution: basal peripheral predominance is more common than diffuse

Note.—DAD = diffuse alveolar damage, GGO = ground-glass opacities.

# RA-ILD: Usual Interstitial Pneumonia (UIP)

- UIP is the most common ILD pattern of fibrosis in RA (60% of cases)
- UIP in RA has the worst prognosis of all ILD patterns in RA, with survival rates mirroring those for idiopathic pulmonary fibrosis and shorter survival times compared with other CTDs with an usual interstitial pneumonia pattern.
- Main HRCT features include **basilar** and **peripheral** predominant fibrosis, with **peripheral traction bronchiectasis and/or bronchiolectasis**.
- **Honeycombing** may or may not be depicted. The distribution of fibrosis is typically heterogeneous and may be a asymmetric.



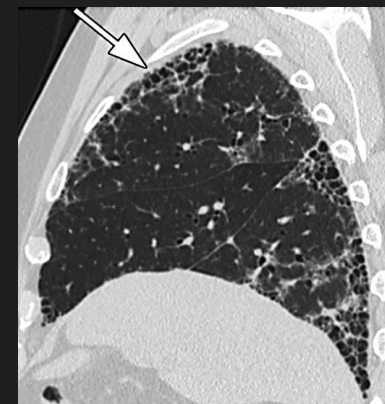
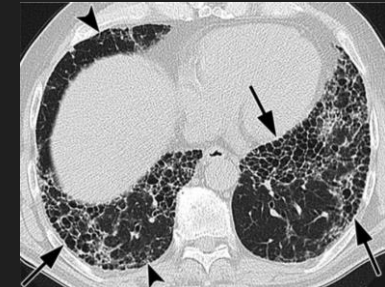
# RA-ILD: Usual Interstitial Pneumonia (UIP)

- The imaging appearances of RA-ILD owing to RA and idiopathic pulmonary fibrosis may be identical, making the distinction challenging
- Chung et al have described three features favoring CTDs with UIP over IPF:

A) exuberant honeycombing

B) straight-edge sign

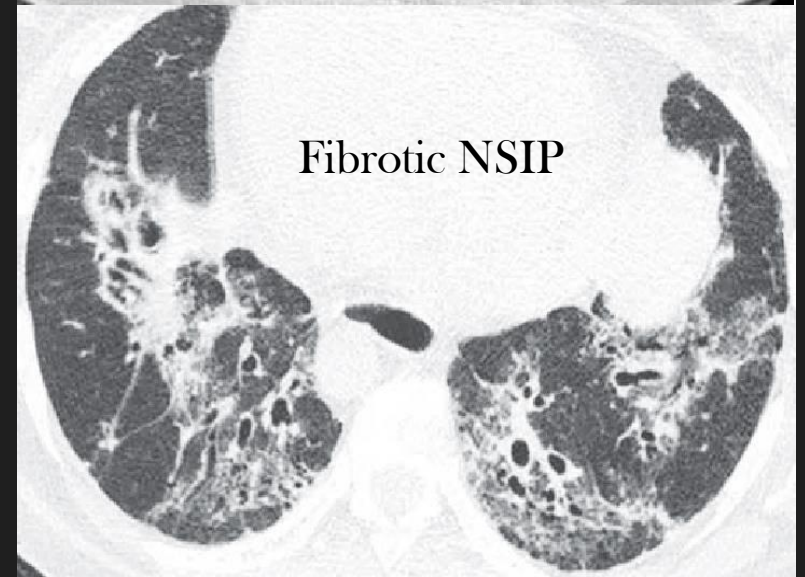
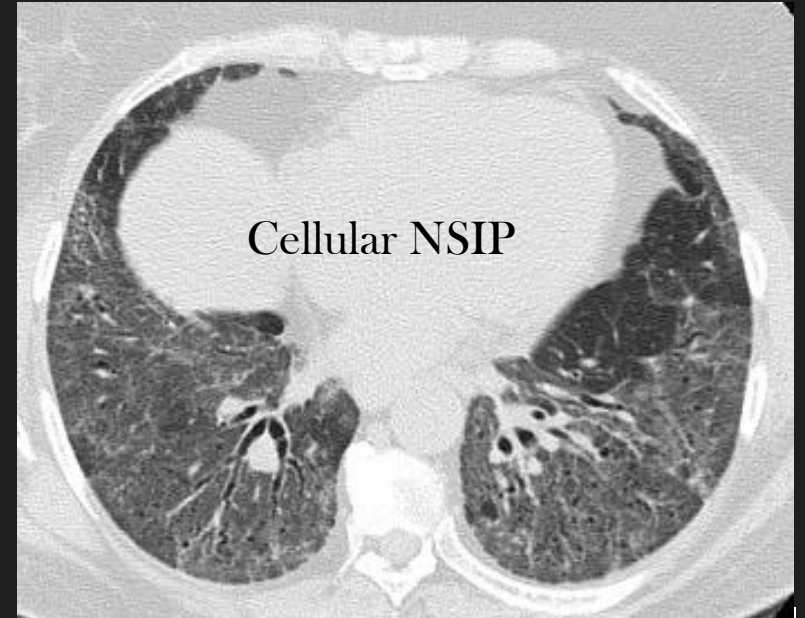
C) anterior upper lobe involvement



- The presence of rheumatoid nodules or pleural disease (~ 15-20 % of cases) also suggests ILD in RA

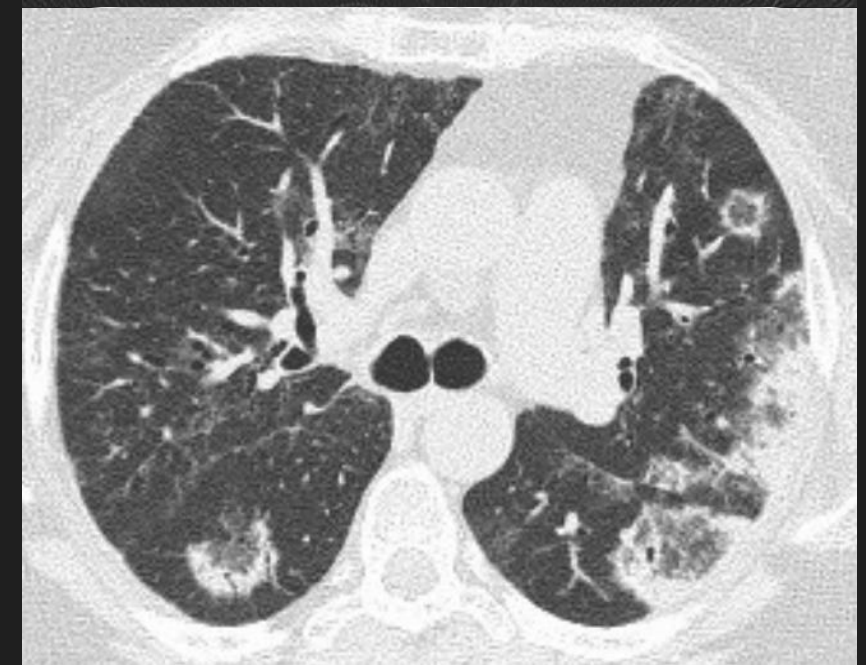
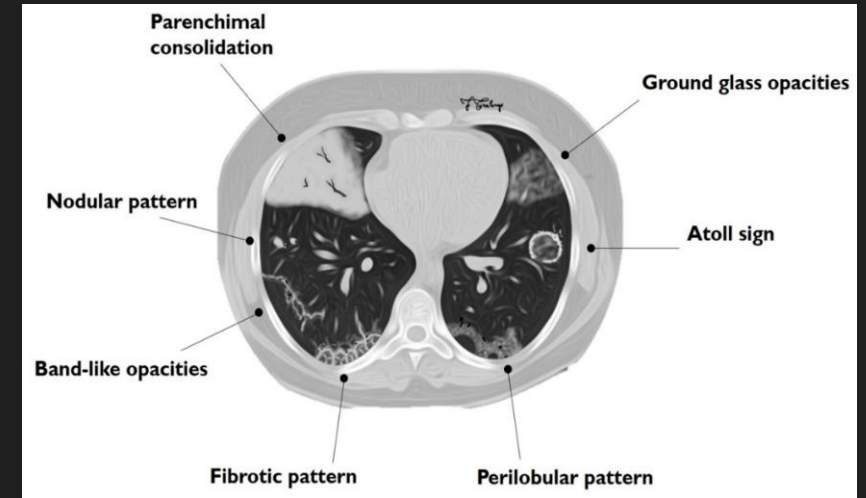
# RA-ILD: Non Specific Interstitial Pneumonia (NSIP)

- **NSIP** is the second most common ILD pattern in RA (approximately one-third of cases)
- Is associated with longer joint disease duration, lower risk of disease progression, better treatment response, and better outcomes overall compared with UIP
- CT findings include **ground glass opacities** as a dominant feature: can be symmetrically or diffusely distributed in all zones (86%) or display a basal peripheral predominance (68%) and **fine reticulation**, with or without immediate subpleural sparing, **thickening of bronchovascular bundles** and **traction bronchiectasis**
- Fibrosis is typically homogeneous and symmetric, and traction bronchiectasis is often relatively central compared with that of usual interstitial pneumonia

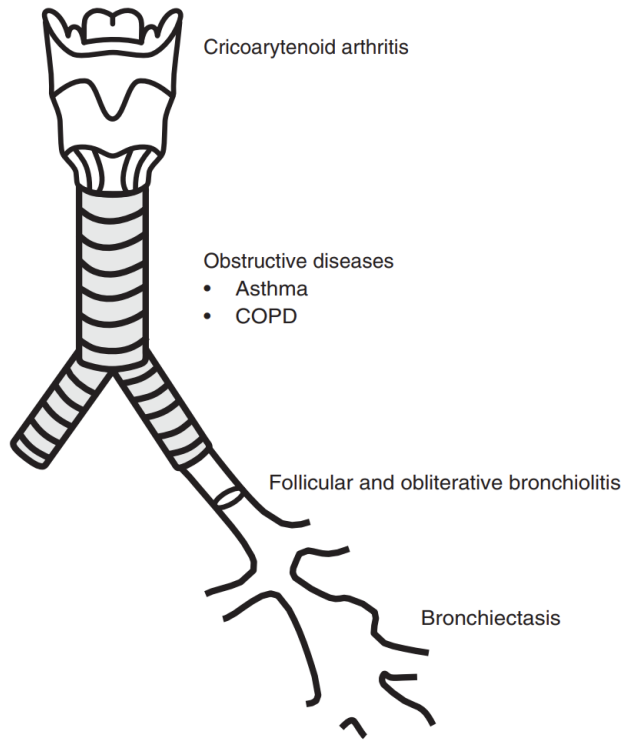


# RA-ILD: Organizing Pneumonia (OP)

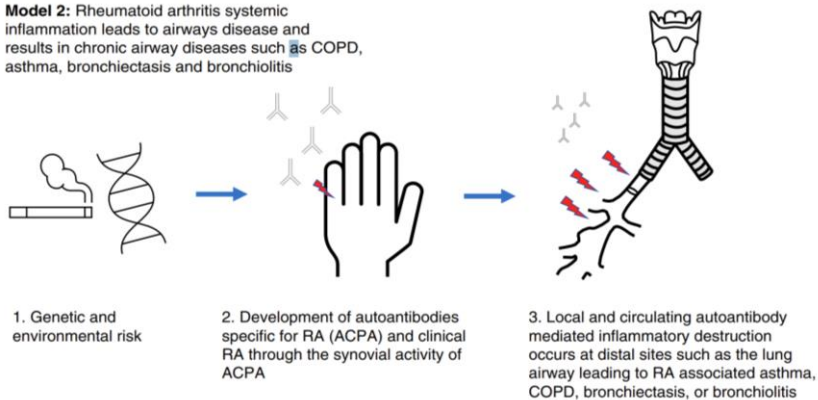
- The third most common ILD in RA (11% of cases), OP is a nonspecific response to alveolar epithelial injury, characterized by polypoid plugs of granulation tissue within alveolar ducts, alveoli, and terminal bronchioles, with alveolar septal inflammation
- OP can occur alone or with other ILD patterns and has an overall good prognosis.
- CT features of organizing pneumonia vary and commonly include **peripheral and/or peribronchovascular consolidations**, **ground-glass opacities**, peribronchovascular opacities and **nodules**
- A **reverse halo sign (Atoll sign)**, characterized by central ground-glass opacity surrounded by a complete or incomplete ring of peripheral consolidation. The abnormalities are often fleeting or migratory



# Rheumatoid Arthritis and Airways disease

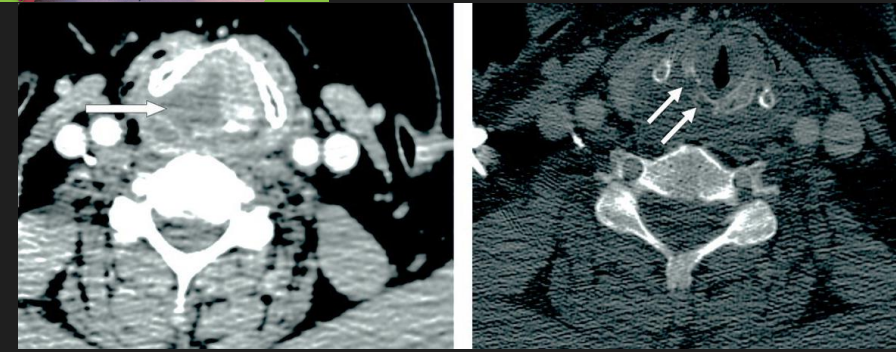


**Model 2:** Rheumatoid arthritis systemic inflammation leads to airways disease and results in chronic airway diseases such as COPD, asthma, bronchiectasis and bronchiolitis



- Airways disease in RA can involve the large and small airways **from the cricoarytenoid joint** in the larynx to the **smallest bronchioles**.
- It has been observed that 39 to 60% of RA patients develop airway-related morbidities in their lifetime. The incidence increases with disease duration
- Airway diseases such as asthma, chronic obstructive pulmonary disease (COPD), bronchiectasis, and bronchiolitis result as a **direct manifestation of RA autoantibody-mediated inflammation** and represent a unique autoimmune endotype of airway disease
- HRCT and PFTs can be very helpful in diagnosing large airway involvement, although HRCT has a tremendous diagnostic sensitivity for small airway involvement in RA patients

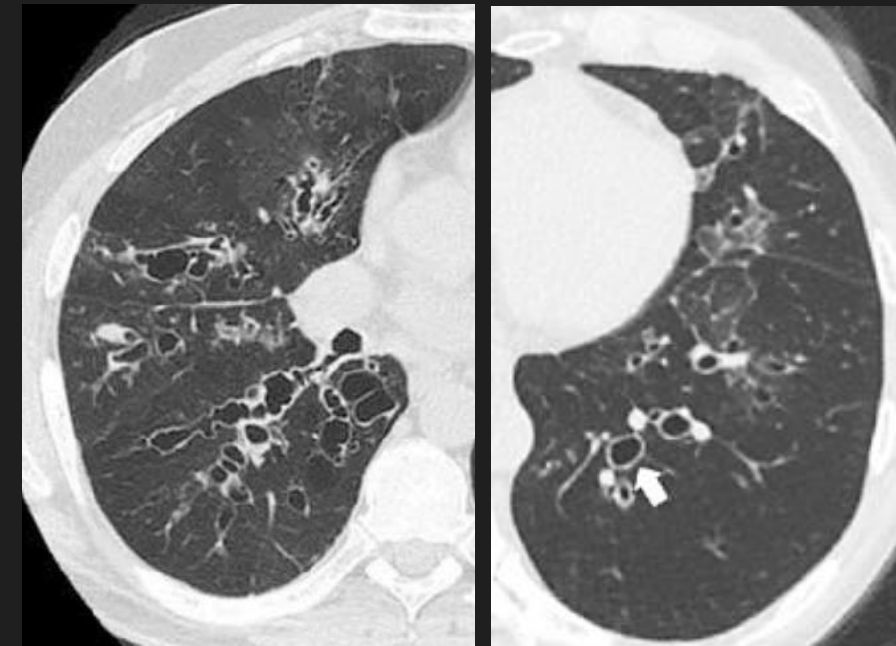




Cricoarytenoid arthritis

# RA-related large airway disease

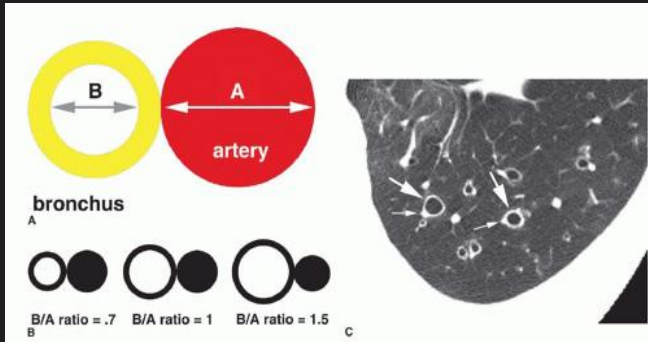
- Large airway abnormalities include **cricoarytenoid arthritis** and **bronchiectasis**. The incidence of bronchiectasis in RA is approximately 30%–40%, sometimes preceding RA onset or presenting early in the disease course



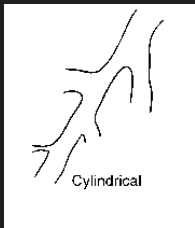
Bronchiectasis

- Pathogenesis of bronchiectasis is incompletely understood but is likely in part owing to an inflammatory milieu related to RA, which leads to RA-autoantibody production and recurrent infection

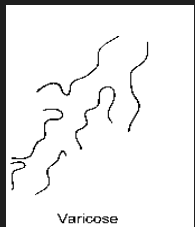
# Bronchiectasis in RA



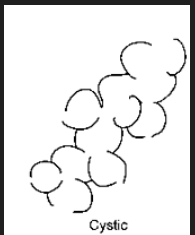
Cylindrical



Varicose



Cystic



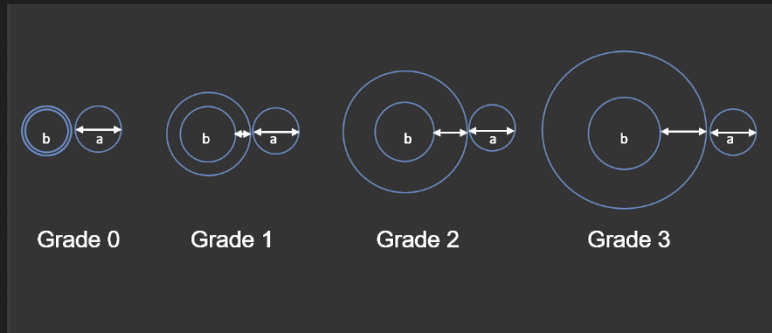
Typically found in at least two lobes and often affects the lungs diffusely

Allain J et al. Prevalence of symptomatic bronchiectasis in patients with rheumatoid arthritis. Rev Rhum Engl Ed 1997;64:531-537

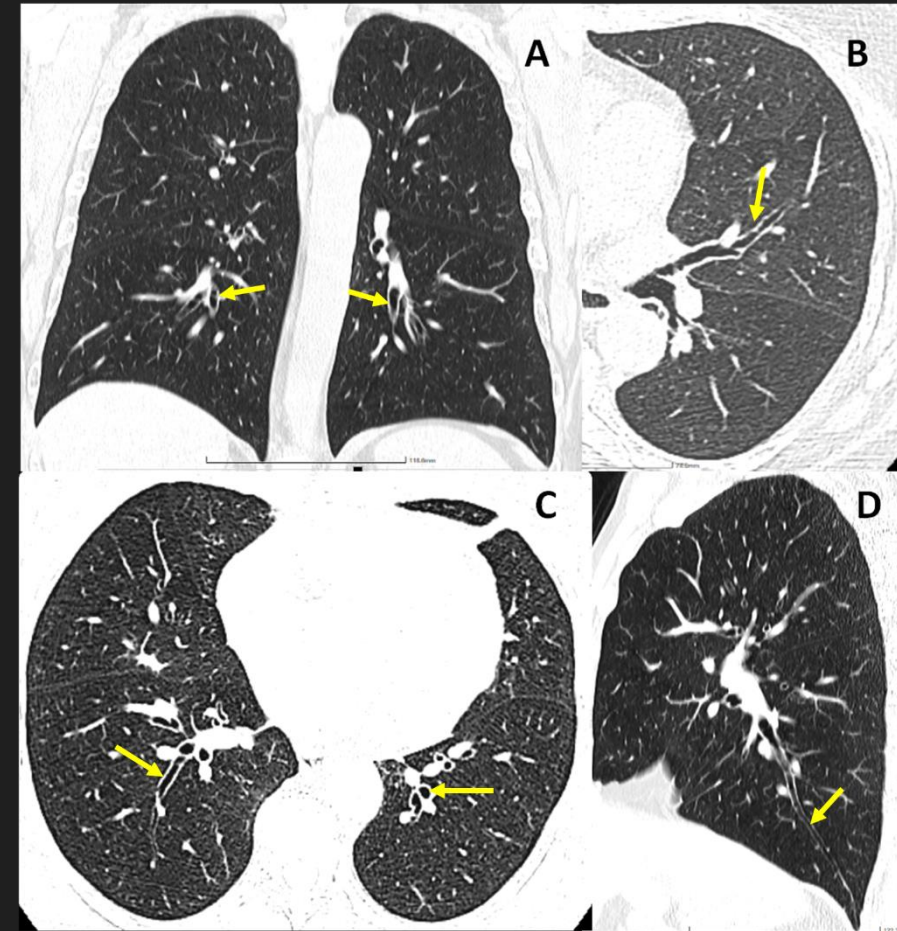
Groner KG et al. Thoracic Manifestations of Rheumatoid Arthritis. RadioGraphics 2021; 41:32-55

# Bronchial wall Thickening (BWT)

- Probably the most common HRCT findings in RA patients with respiratory symptoms is bronchial wall thickening. Grade and extent of BWT is usually correlated with FEF25-75, FEF75, and FEF50



- Grade 0: absence of BWT, Grade 1: < 50%, Grade 2: 50-100% and Grade 3: > 100% of the adjacent artery diameter



Detorakis EE, et al. Evolution of imaging findings, laboratory and functional parameters in rheumatoid arthritis patients after one year of treatment with anti-TNF- $\alpha$  agents. Clin Exp Rheumatol. 2017 Jan-Feb;35(1):43-52.

Terasaki H, et al. Respiratory symptoms in rheumatoid arthritis: relation between high resolution CT findings and functional impairment. Radiat Med. 2004 May-Jun;22(3):179-85

# Small Airway disease in RA

The reported prevalence of small airways disease in RA patients, varies among studies, ranging from 8% to 65% and bronchiolar abnormalities on HRCT scans are associated with RA duration

## INSPIRATORY SCAN

- **Follicular bronchiolitis**

HRCT is the mainstay of diagnosis and can demonstrate findings before clinical symptoms

- **Obliterative (constrictive) bronchiolitis**

Usually has a more severe and acute clinical presentation.

## EXPIRATORY SCAN

- **Air trapping**

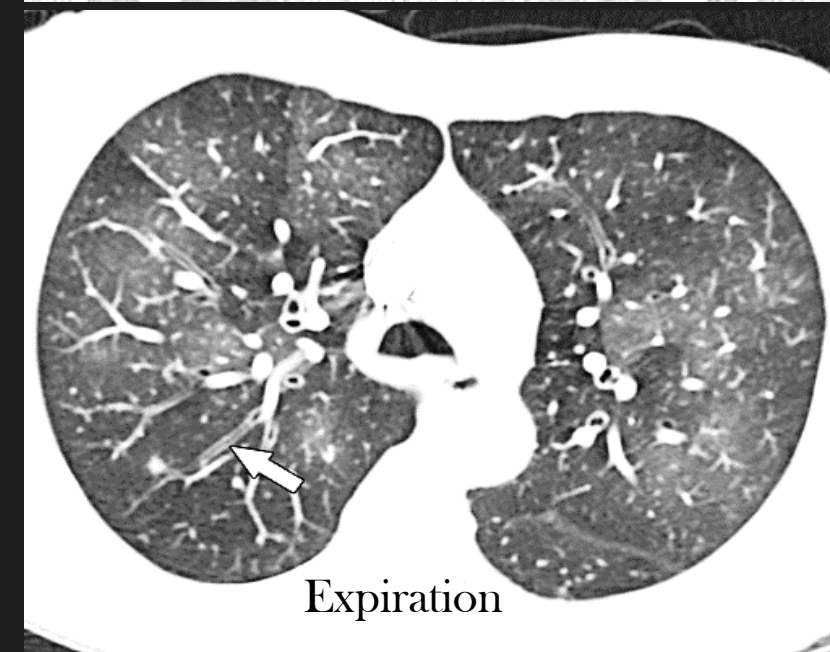
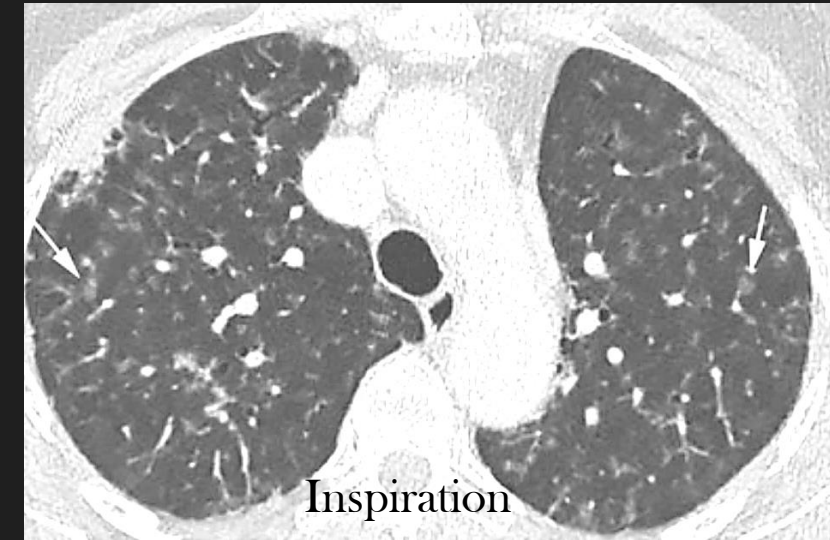
Shaw M, Collins BF, Ho LA, Raghu G: Rheumatoid arthritis-associated lung disease . Eur Respir Rev. 2015, 24:1-16

Hayakawa H, et al. Bronchiolar disease in rheumatoid arthritis. Am J Respir Crit Care Med. 1996, 154:1531-1536.

Lin E, et al. Obliterative bronchiolitis associated with rheumatoid arthritis: analysis of a single-center case series. BMC Pulm Med. 2018, 18:105

# Follicular Bronchiolitis (FB)

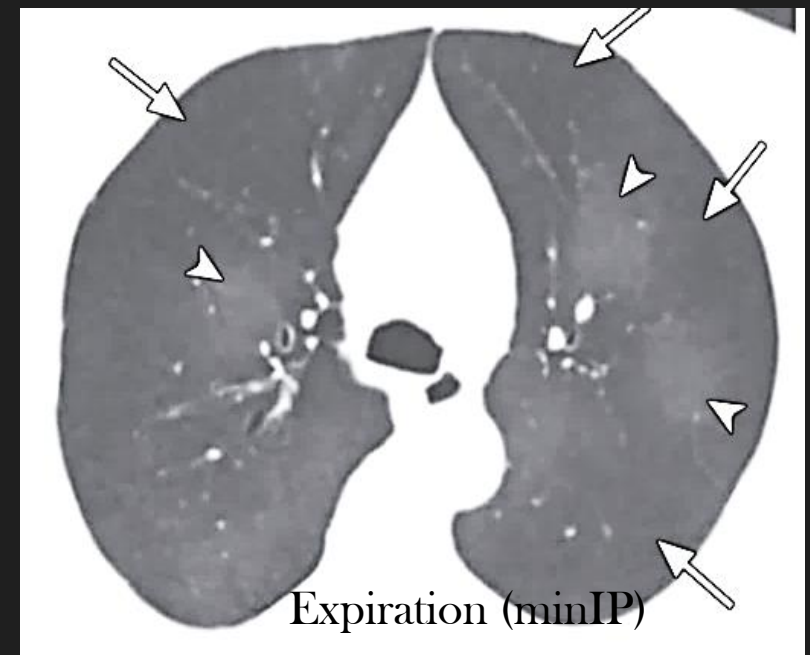
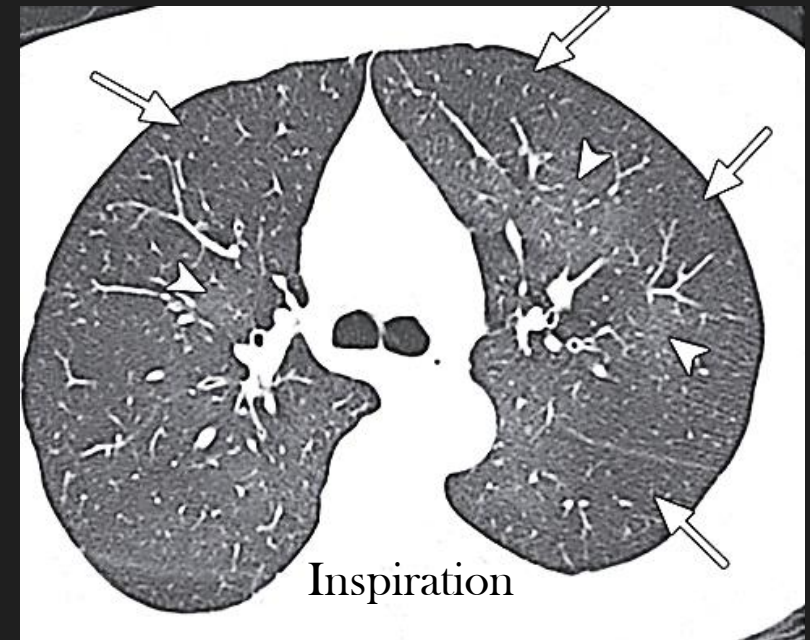
- HRCT findings associated with FB: **centrilobular nodules** (less than 3mm), **hyperinflation**, mosaicism, and **air trapping**, although these findings are nonspecific. HRCT findings of bronchiolitis have several overlapping features with asthma, which can make the two diseases difficult to distinguish radiographically
- Diagnosis of this condition is typically made on lung tissue examination after a surgical lung biopsy
- Histopathology reveals hyperplasia of bronchiole associated lymphoid tissue, accompanied by narrowing of the bronchiole lumen



# Obliterative Bronchiolitis (OB)

(constrictive bronchiolitis/Bronchiolitis obliterans)

- RA is the most implicated connective tissue disease for OB.
- Imaging findings of OB are **bronchial wall thickening**, **diffuse pulmonary infiltrates**, and lobular areas of decreased attenuation with **mosaicism** indicating **air trapping**
- Histopathologic examination of OB reveals concentric fibrosis of the bronchial wall with severe narrowing of the bronchiole lumen



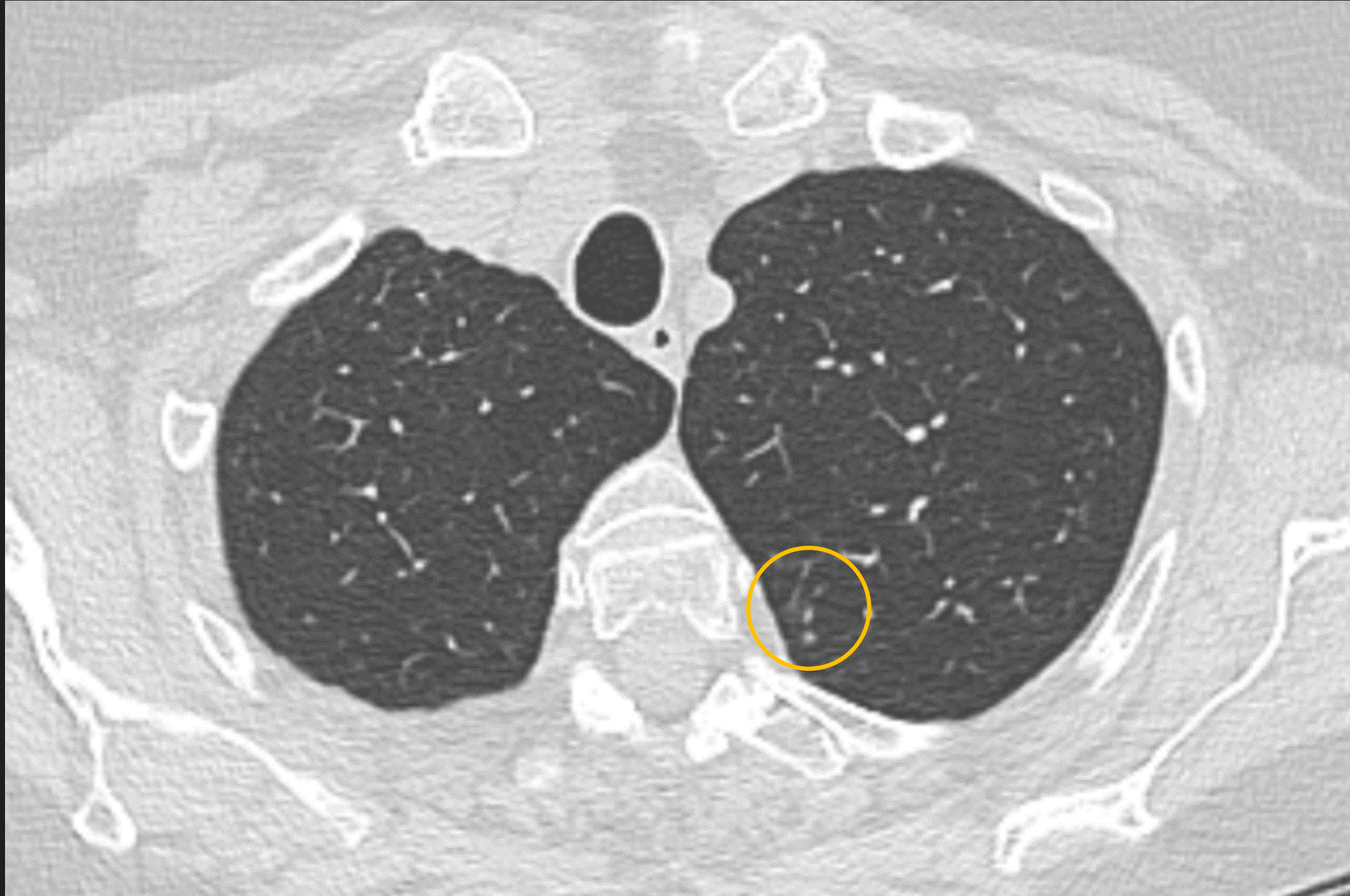
Παρουσίαση περιστατικού

Inspiratory phase

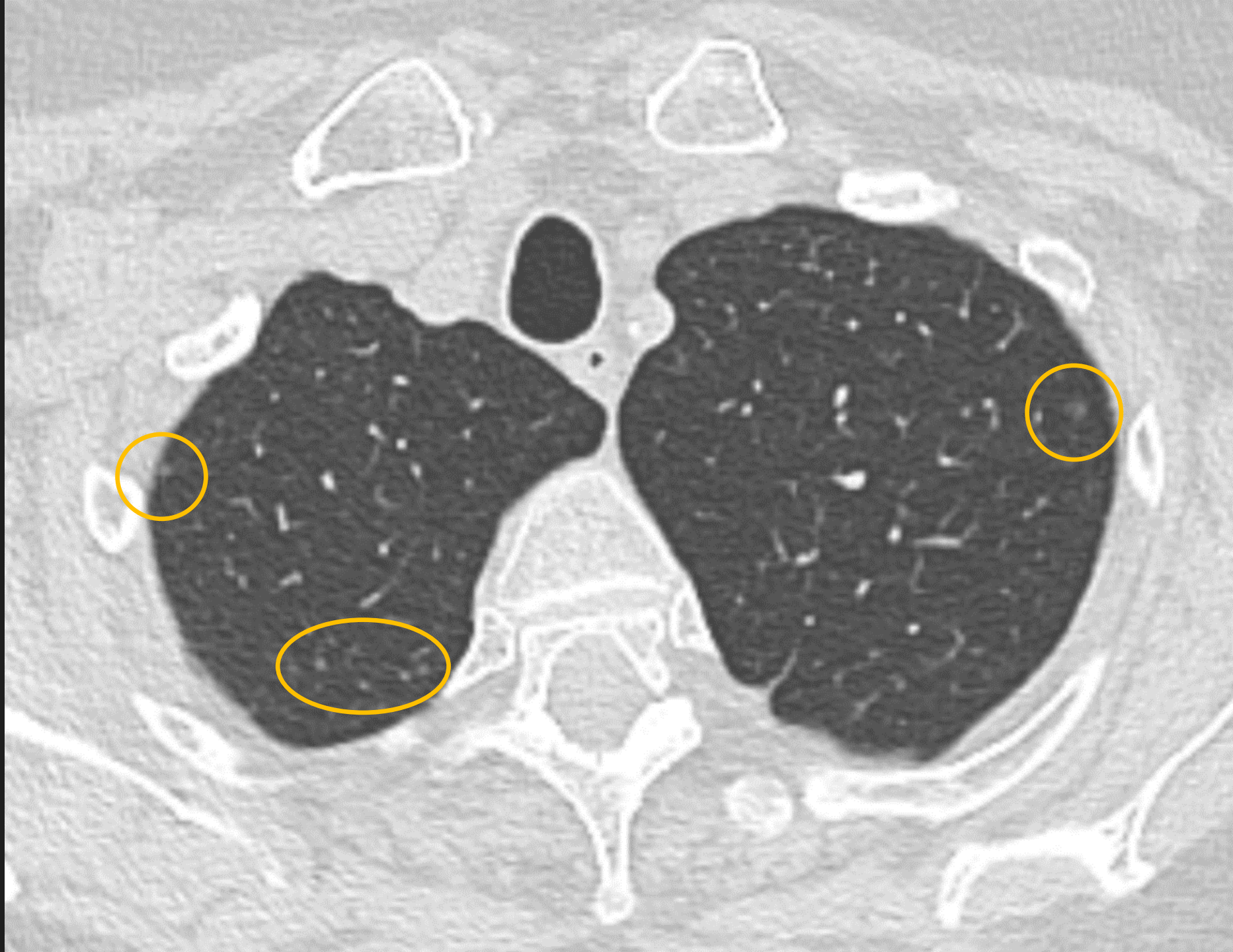




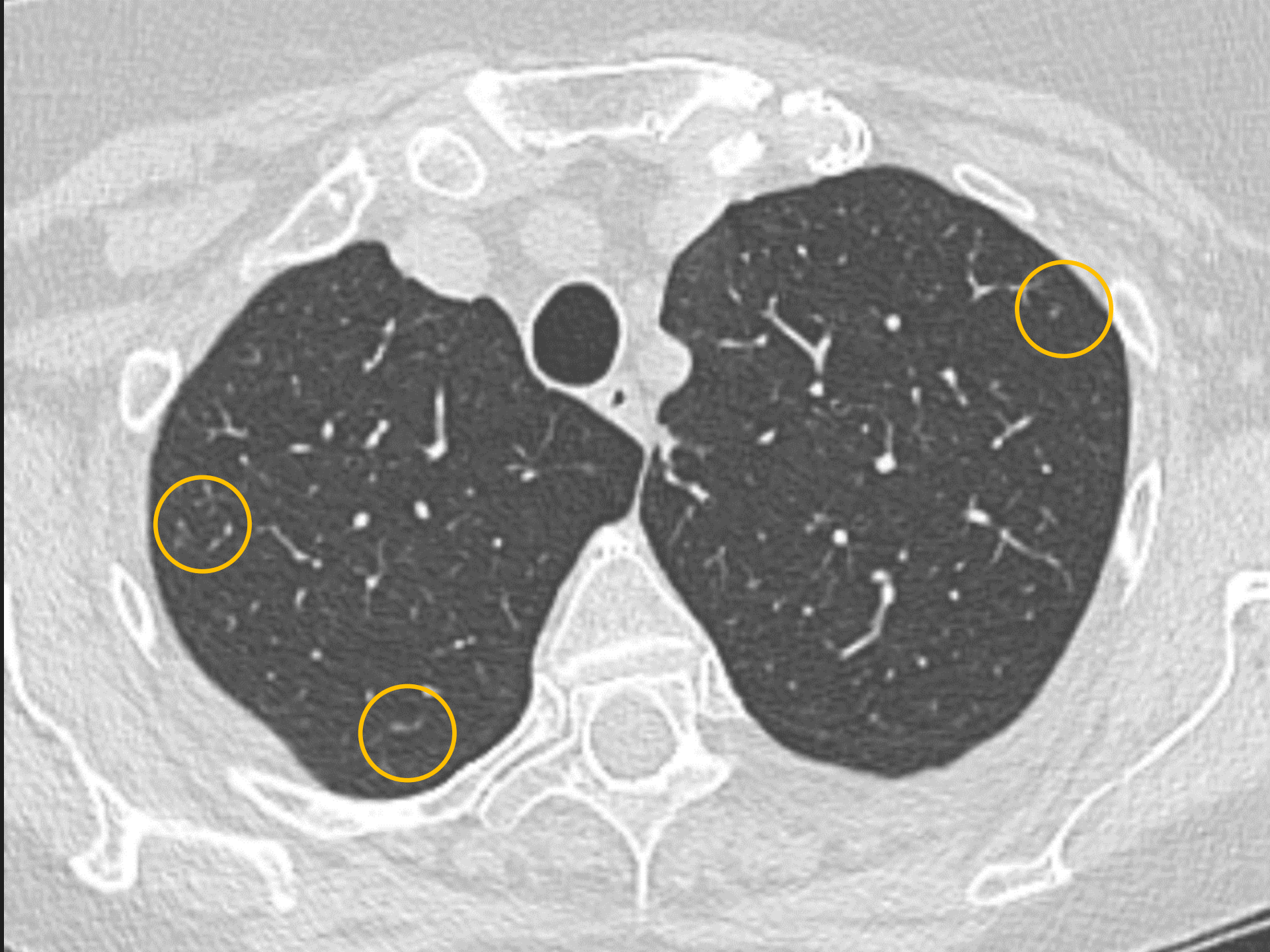
Inspiratory phase



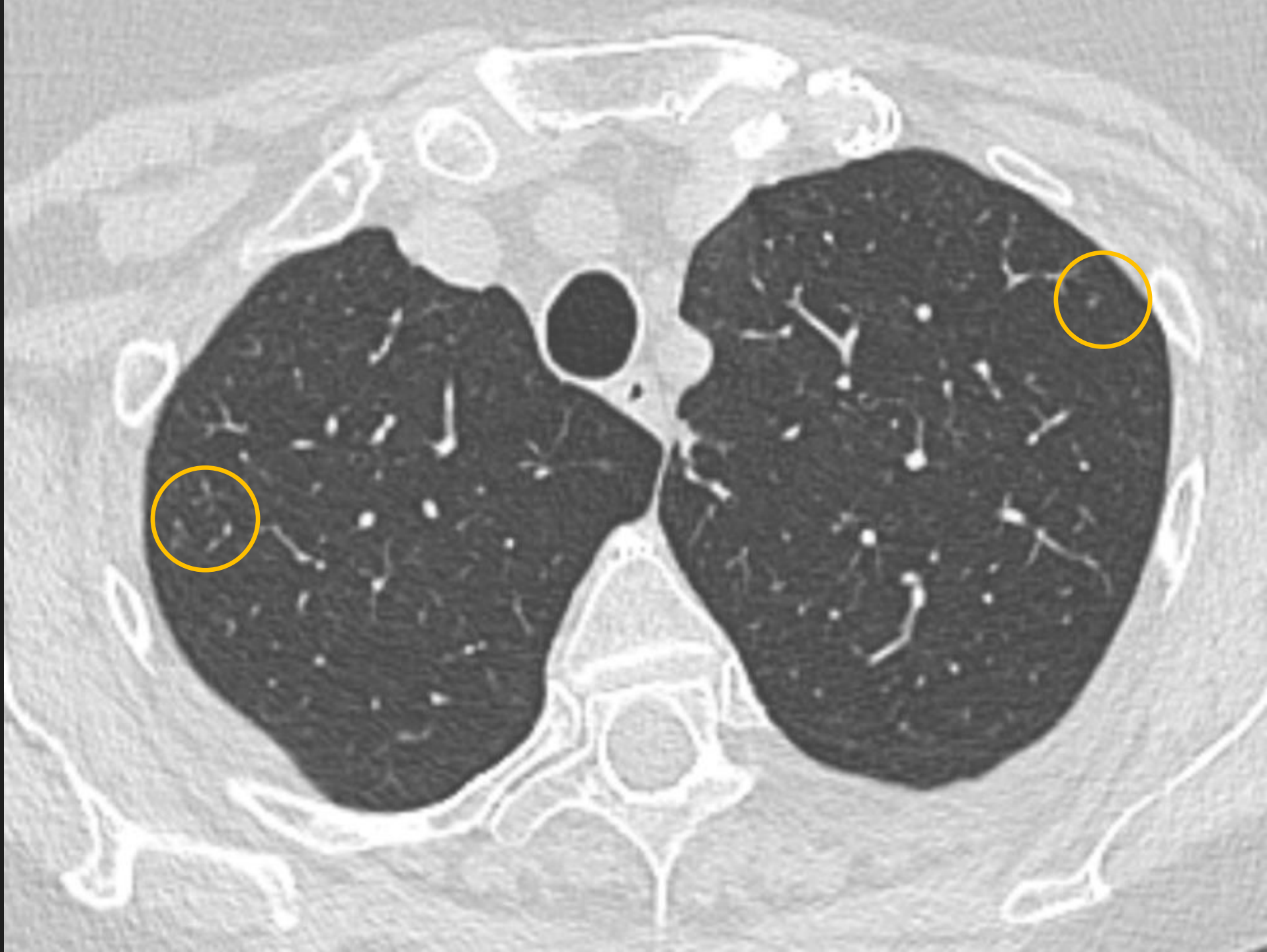
Inspiratory phase



Inspiratory phase



Inspiratory phase



Inspiratory phase



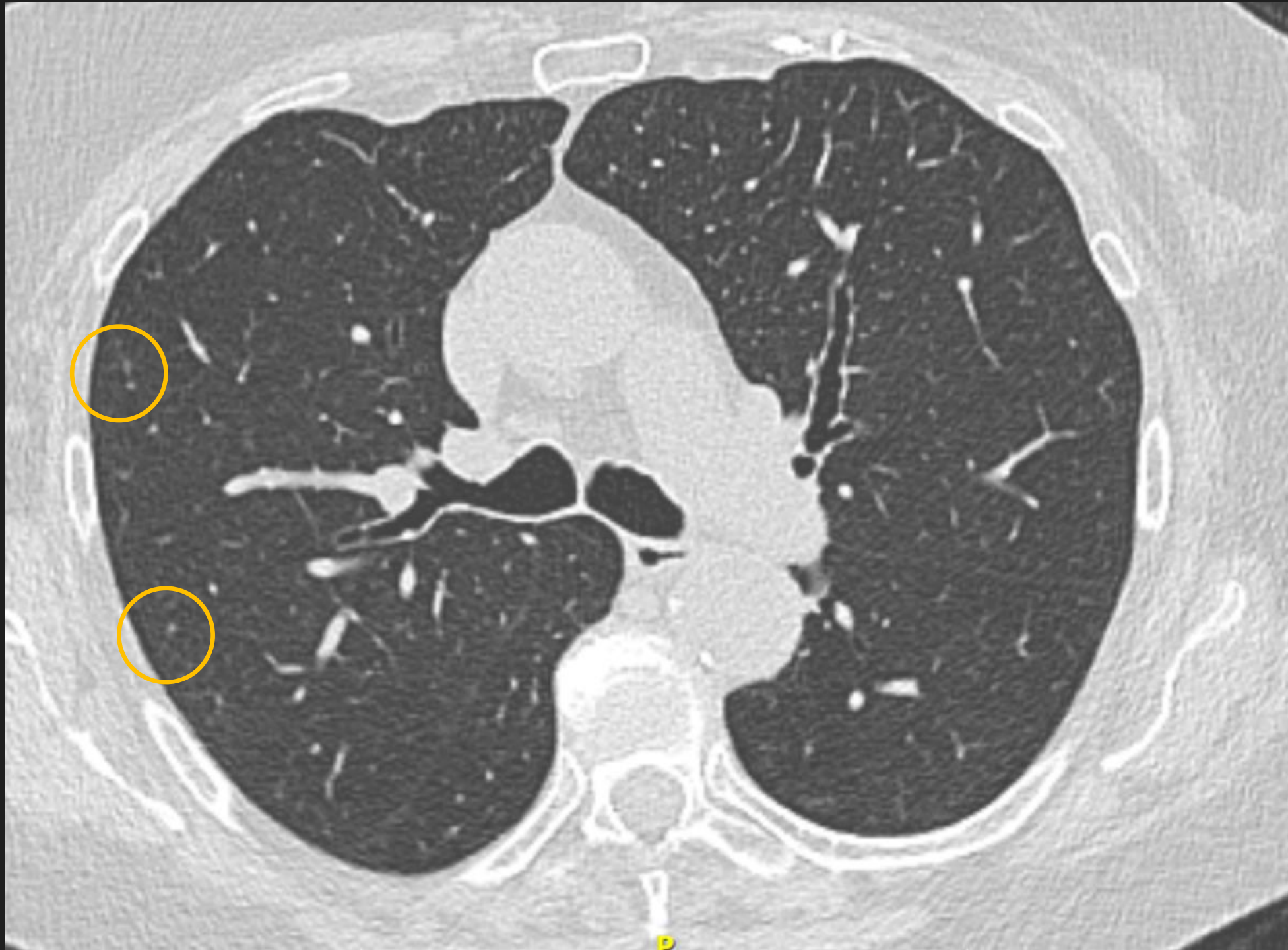
Inspiratory phase



Inspiratory phase



Inspiratory phase





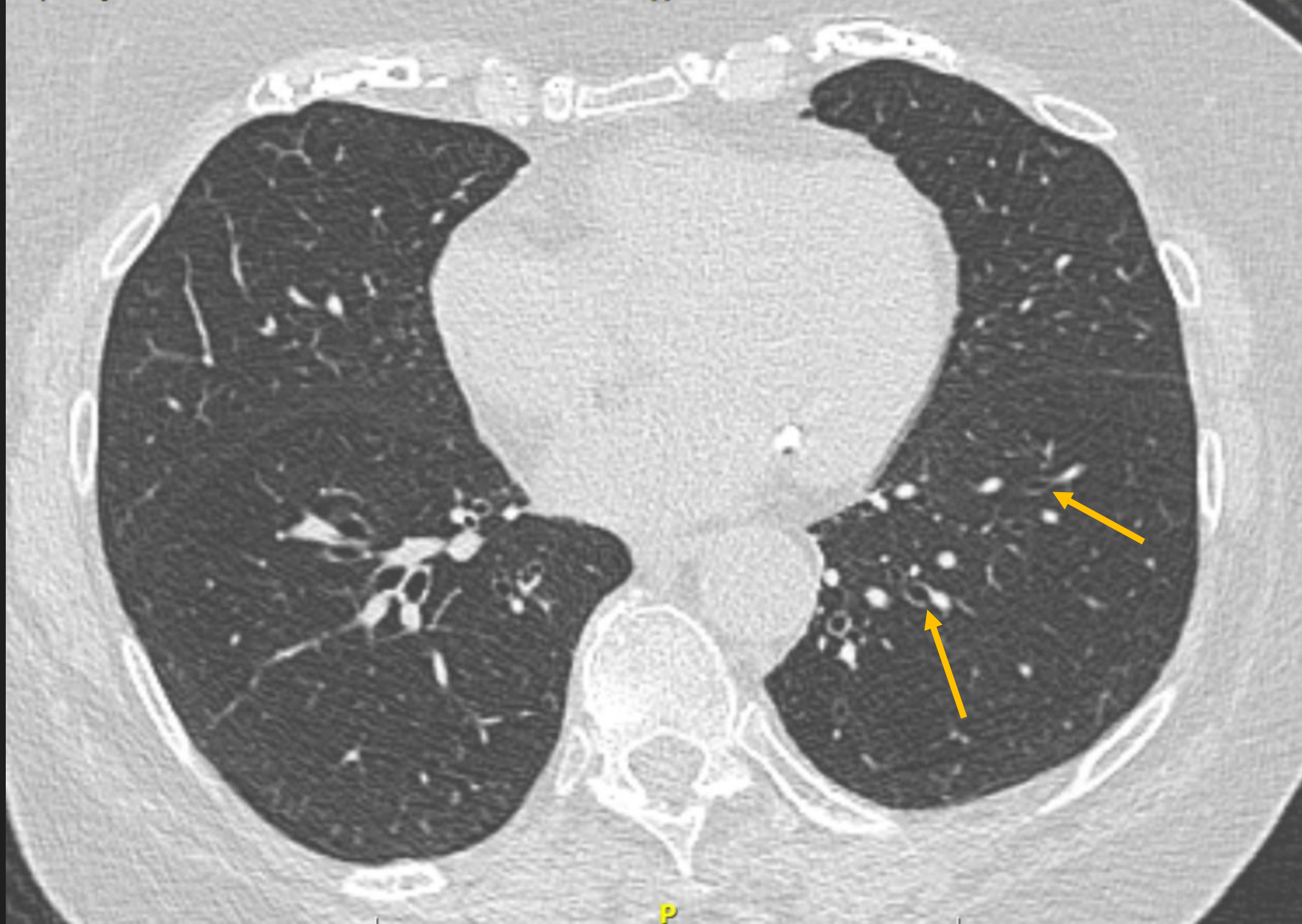
Inspiratory phase



Inspiratory phase



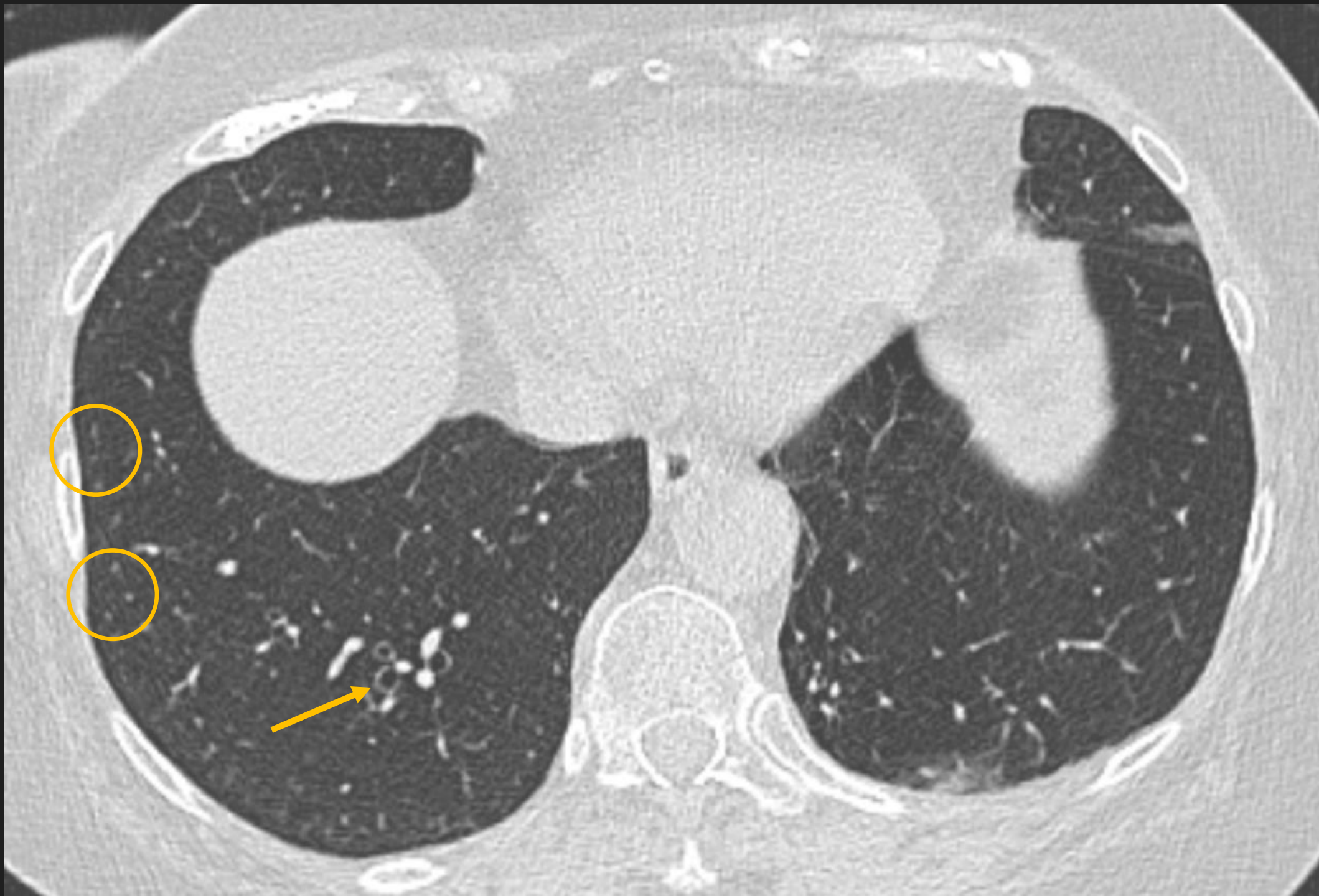
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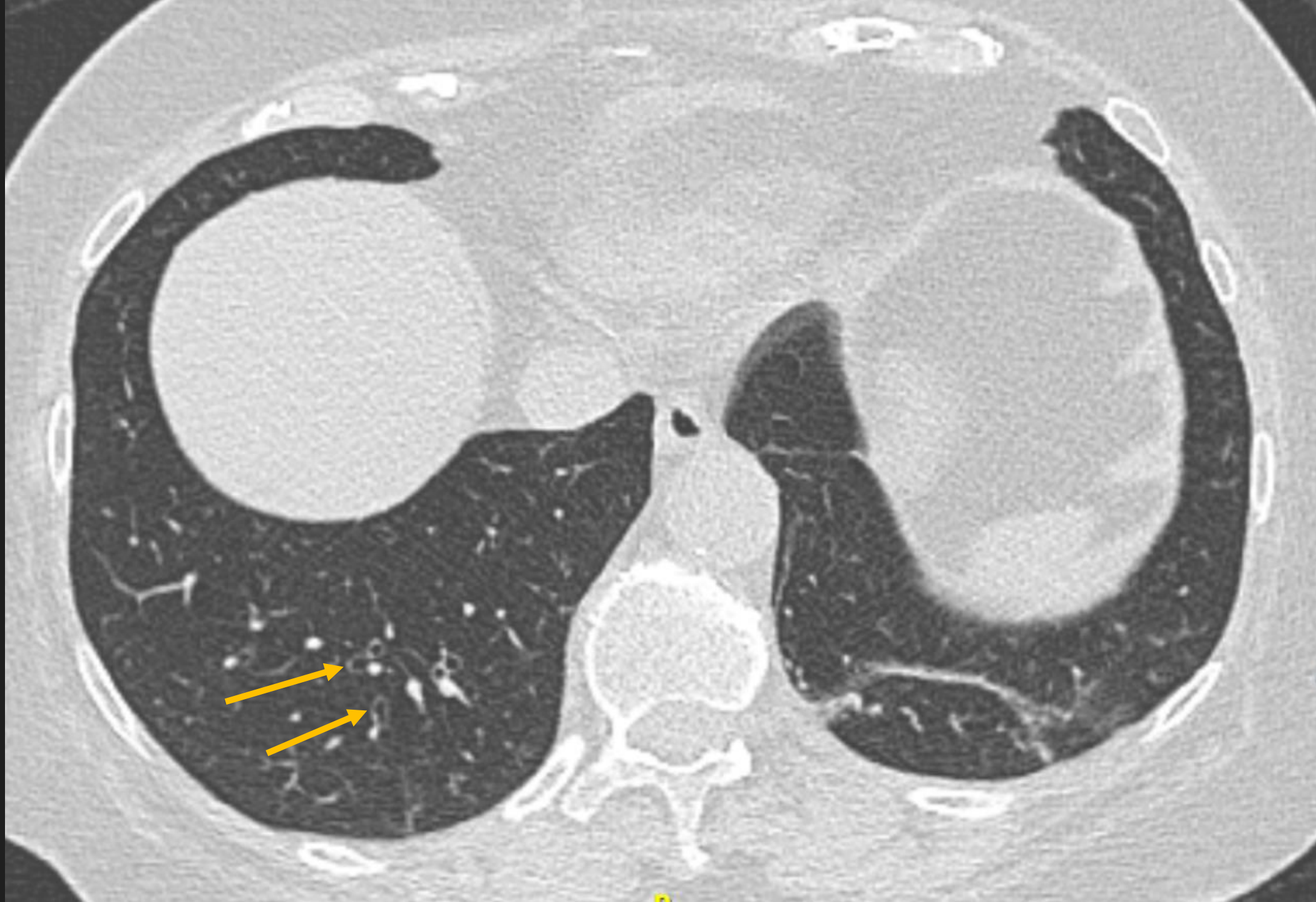
Inspiratory phase



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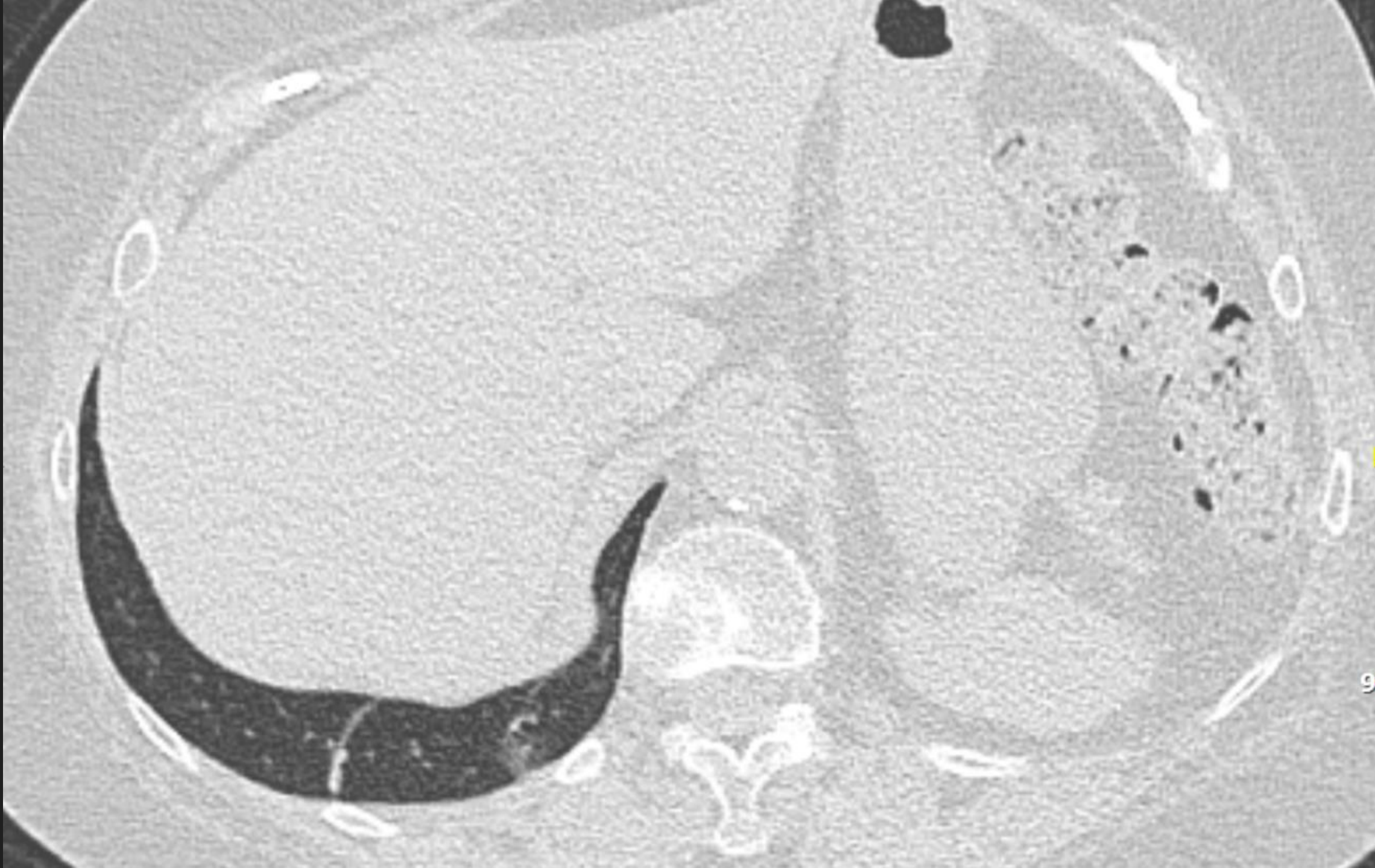


Inspiratory phase





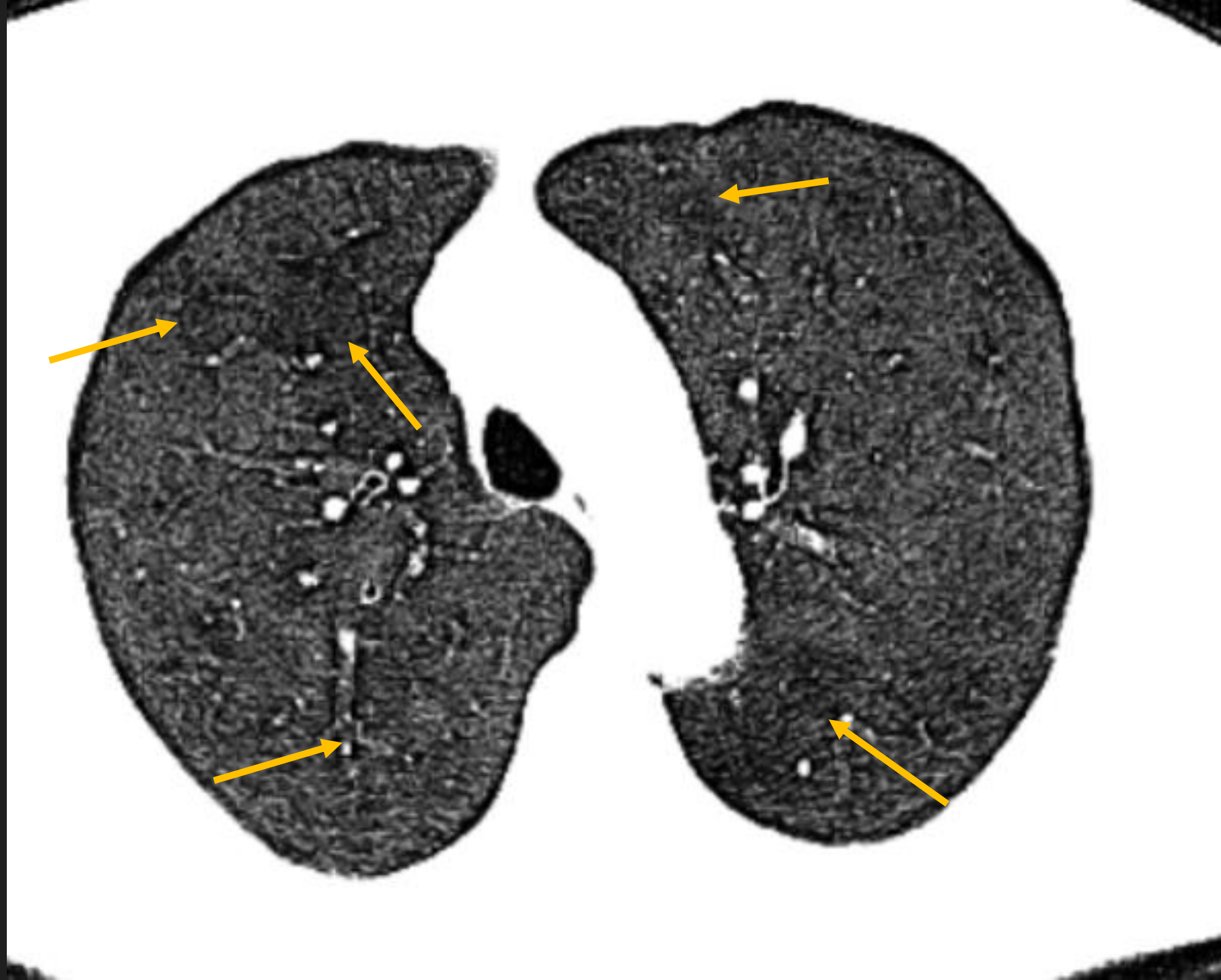
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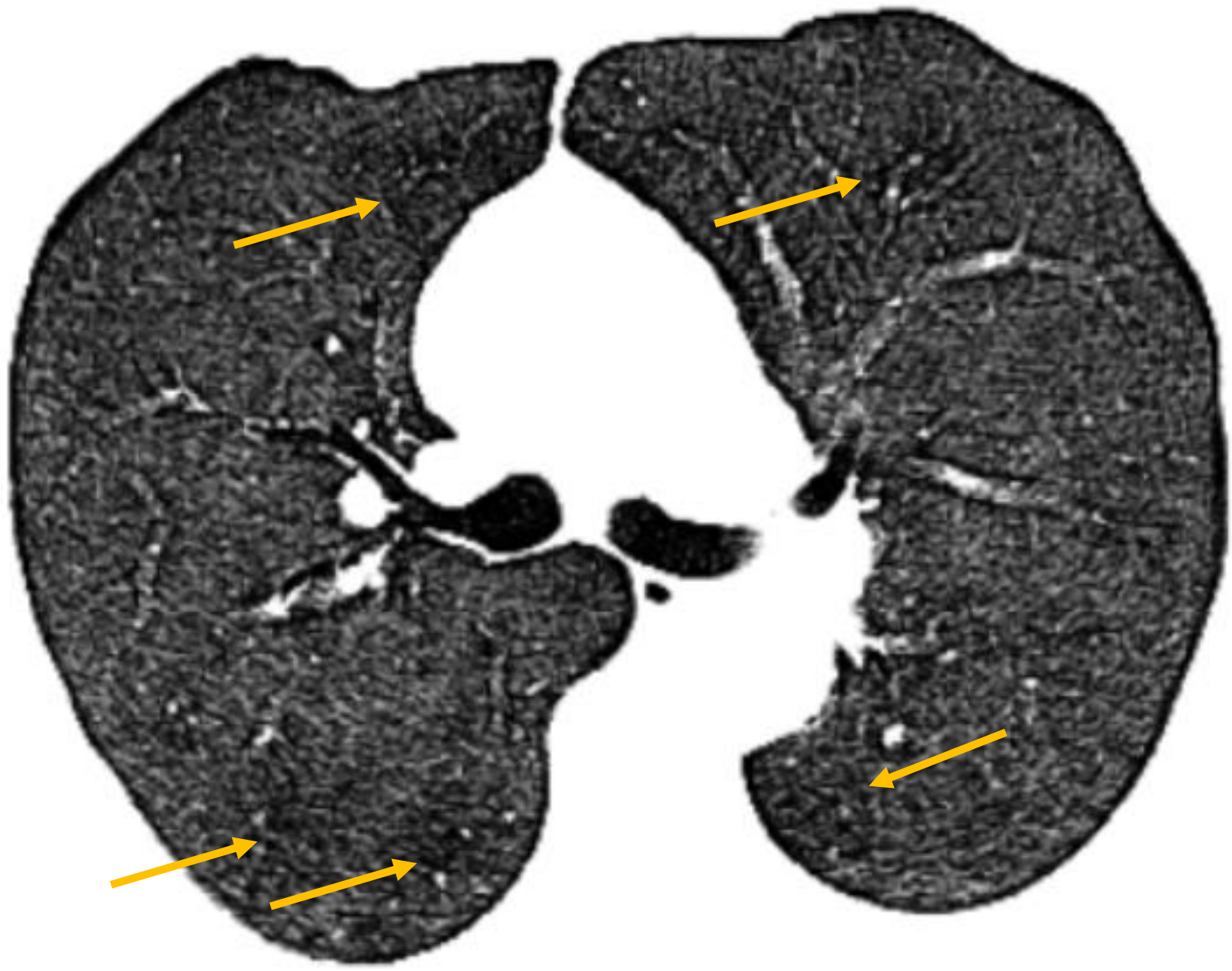
Inspiratory phase  
minIP projection



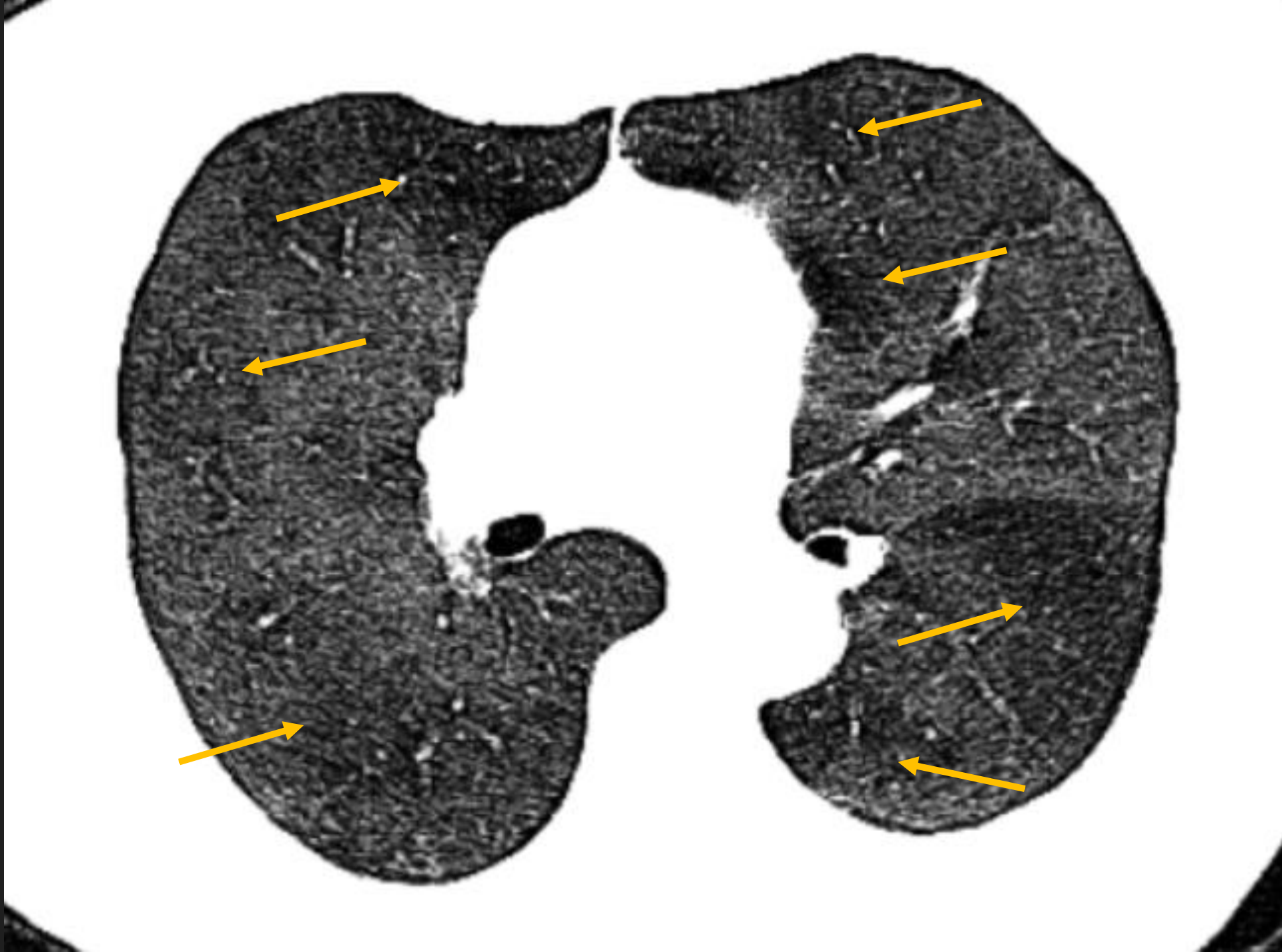
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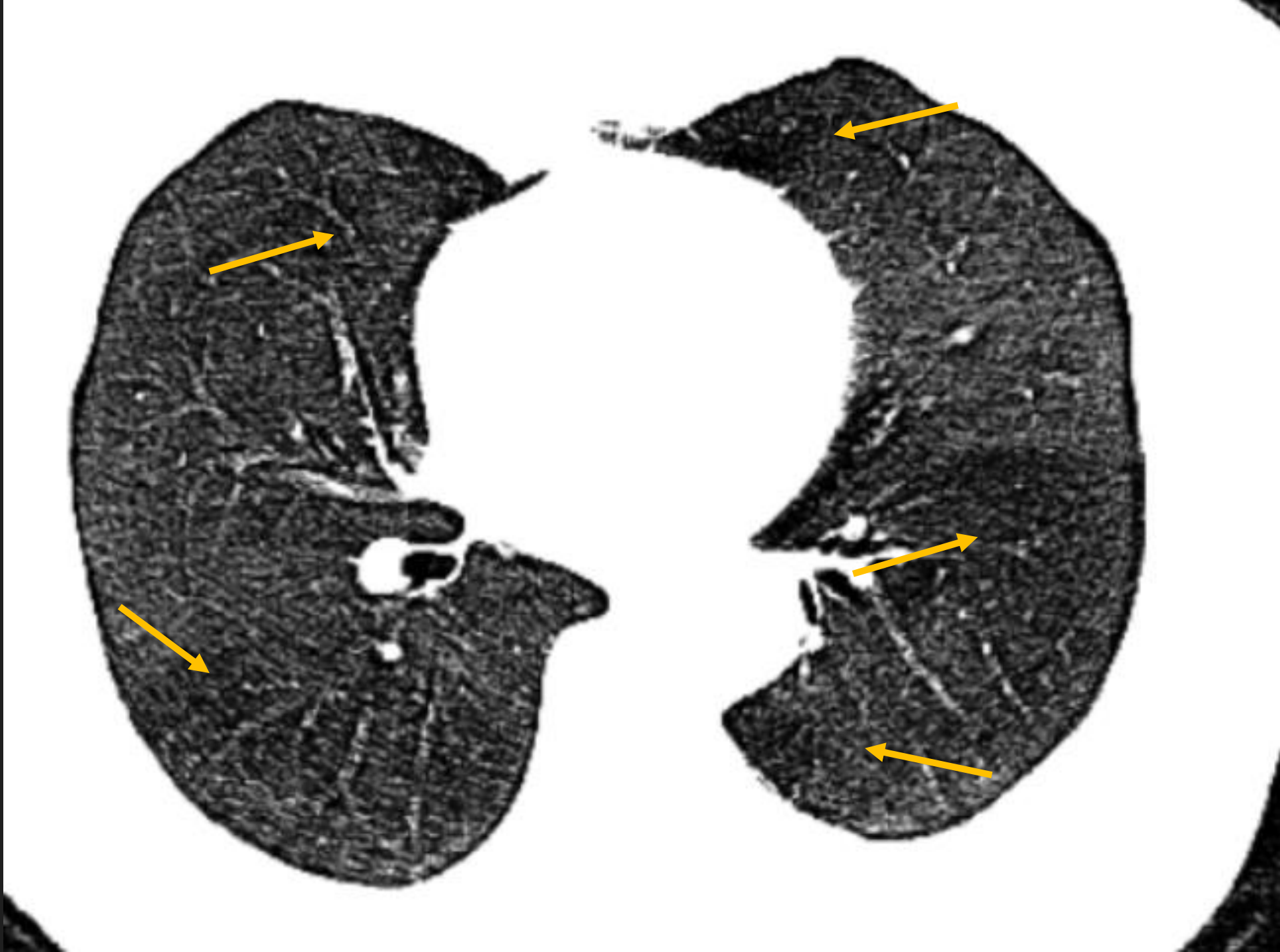
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minIP projection



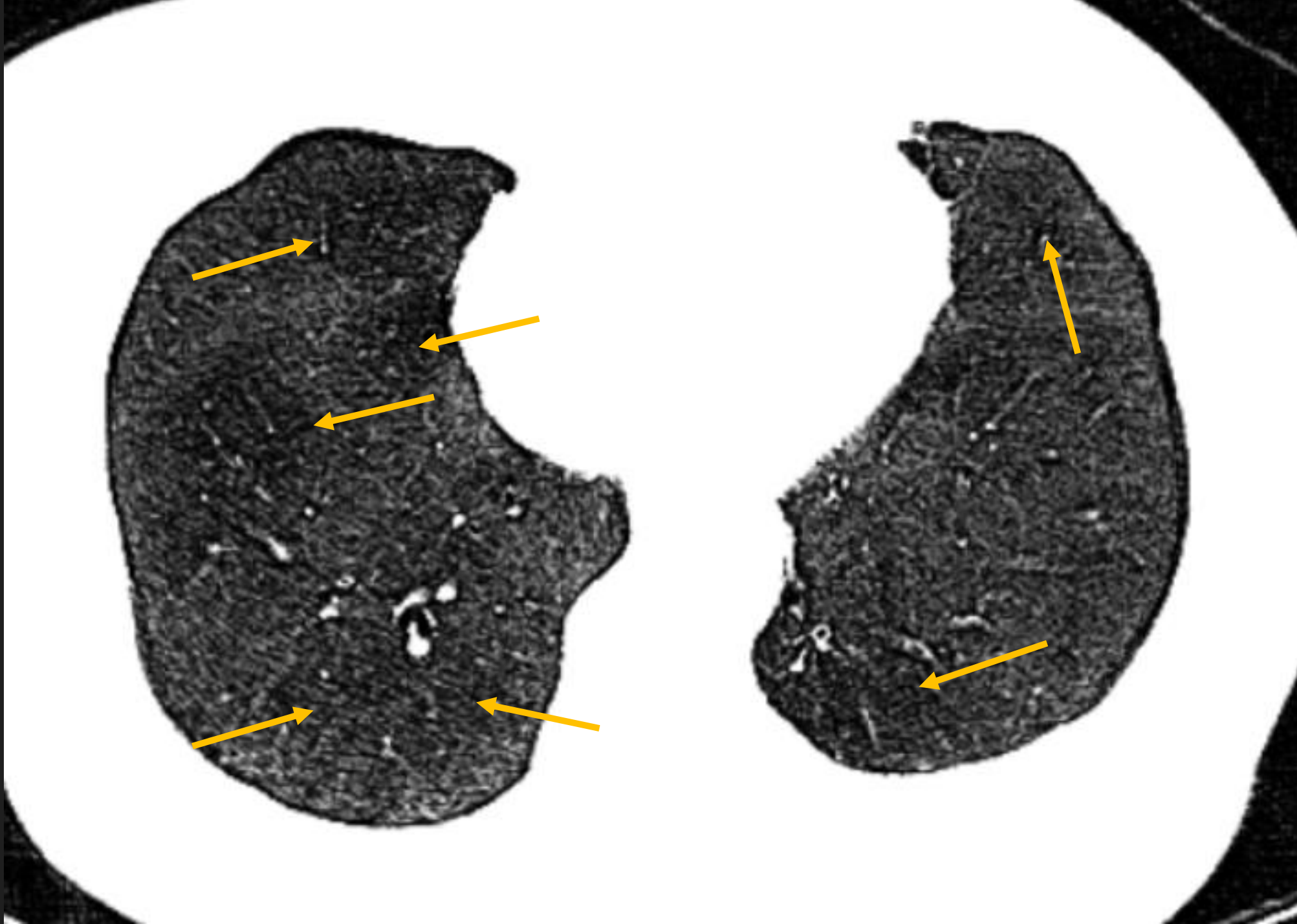
Inspiratory phase  
minIP projection



Inspiratory phase  
minIP projection

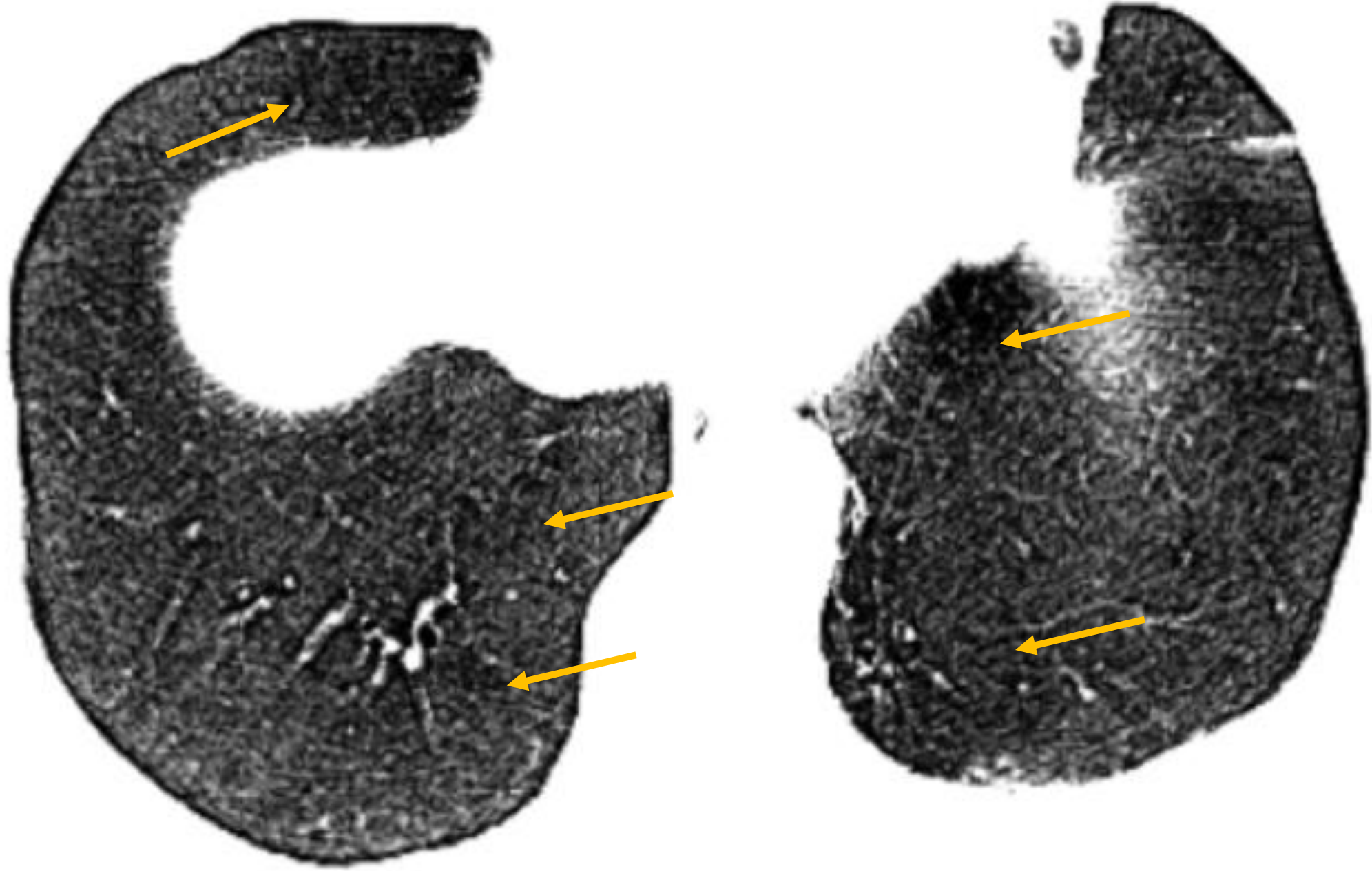


Inspiratory phase  
minIP projection



Inspiratory phase

minIP projection

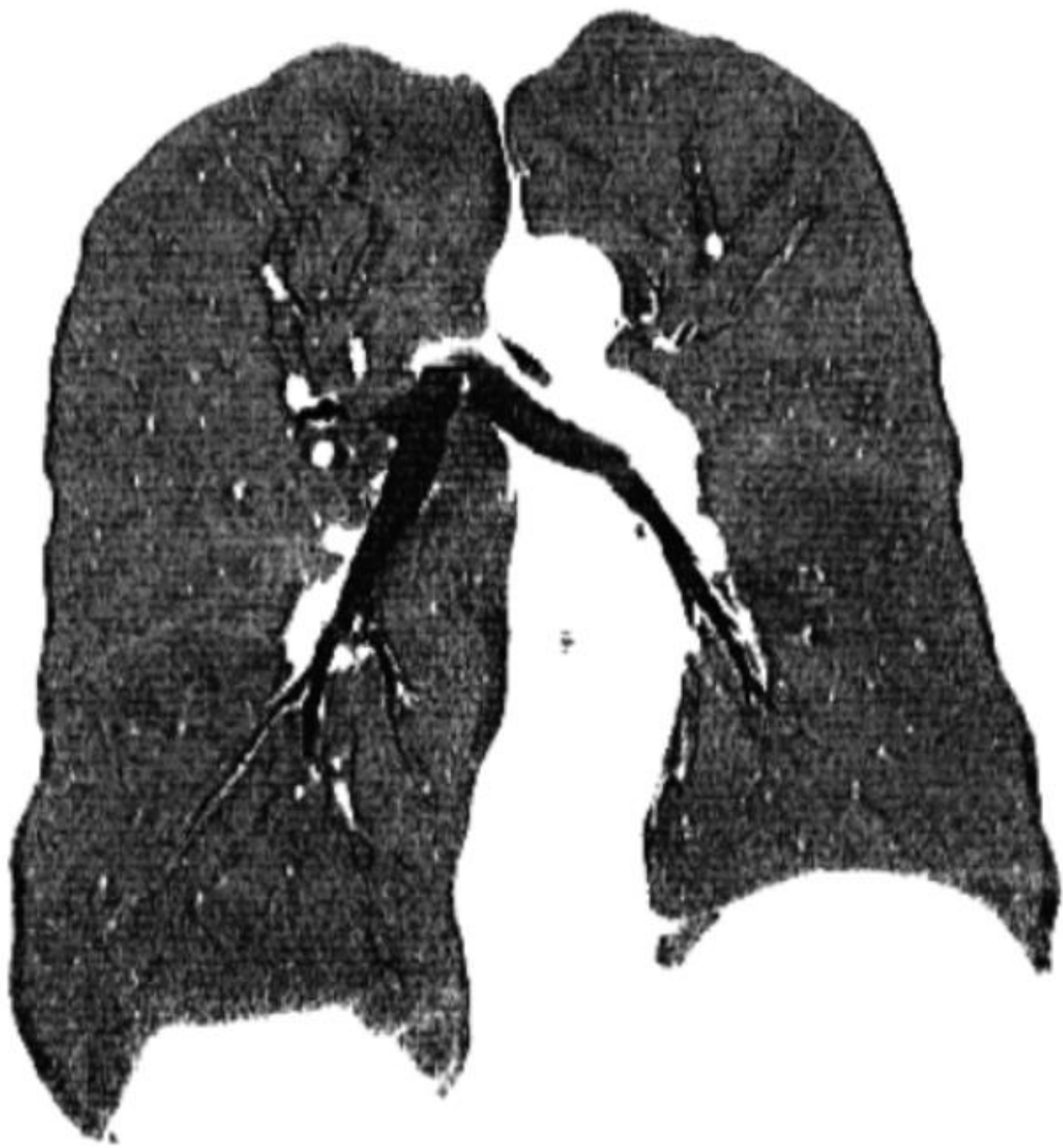




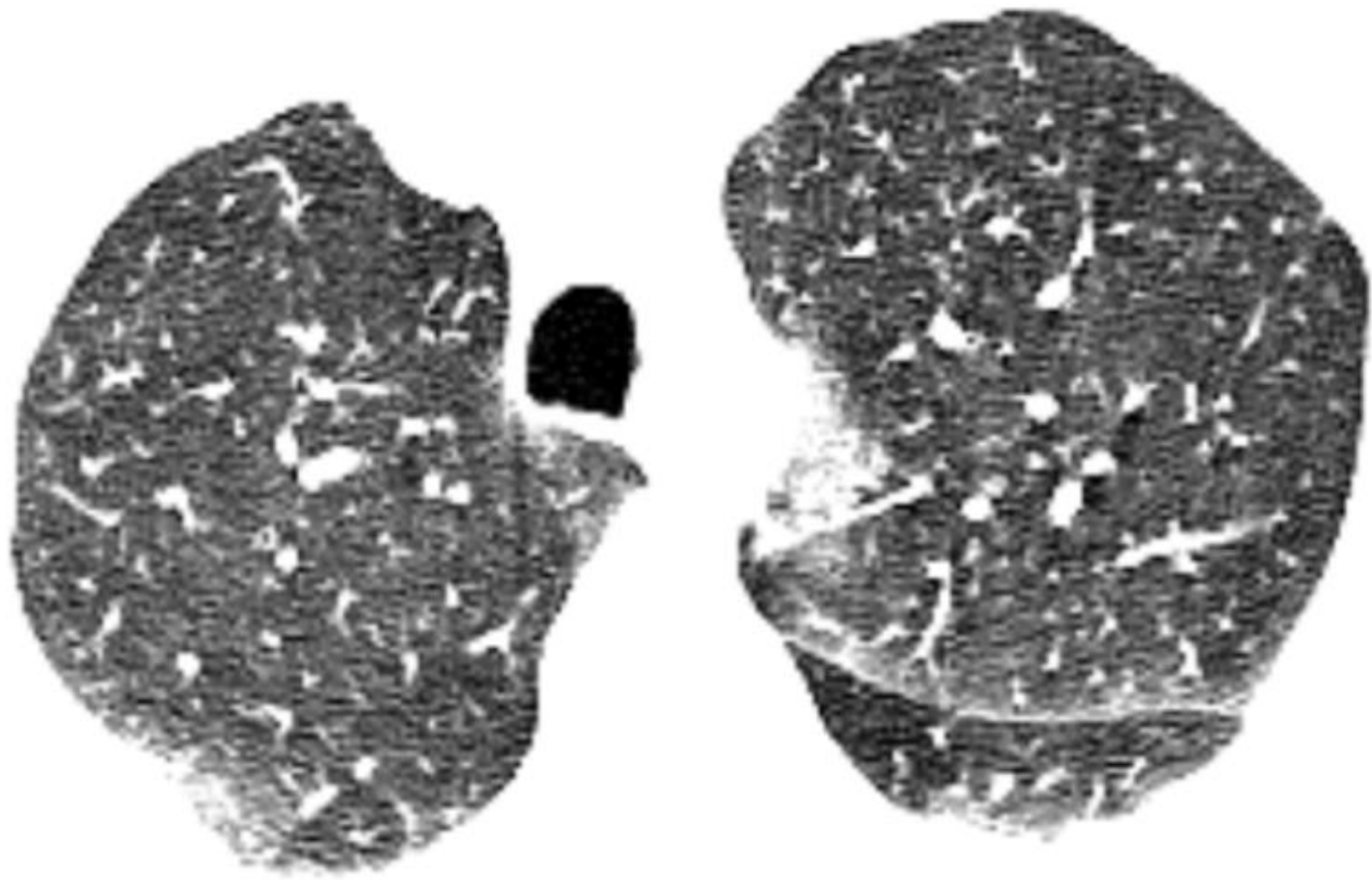
Inspiratory phase  
minIP projection



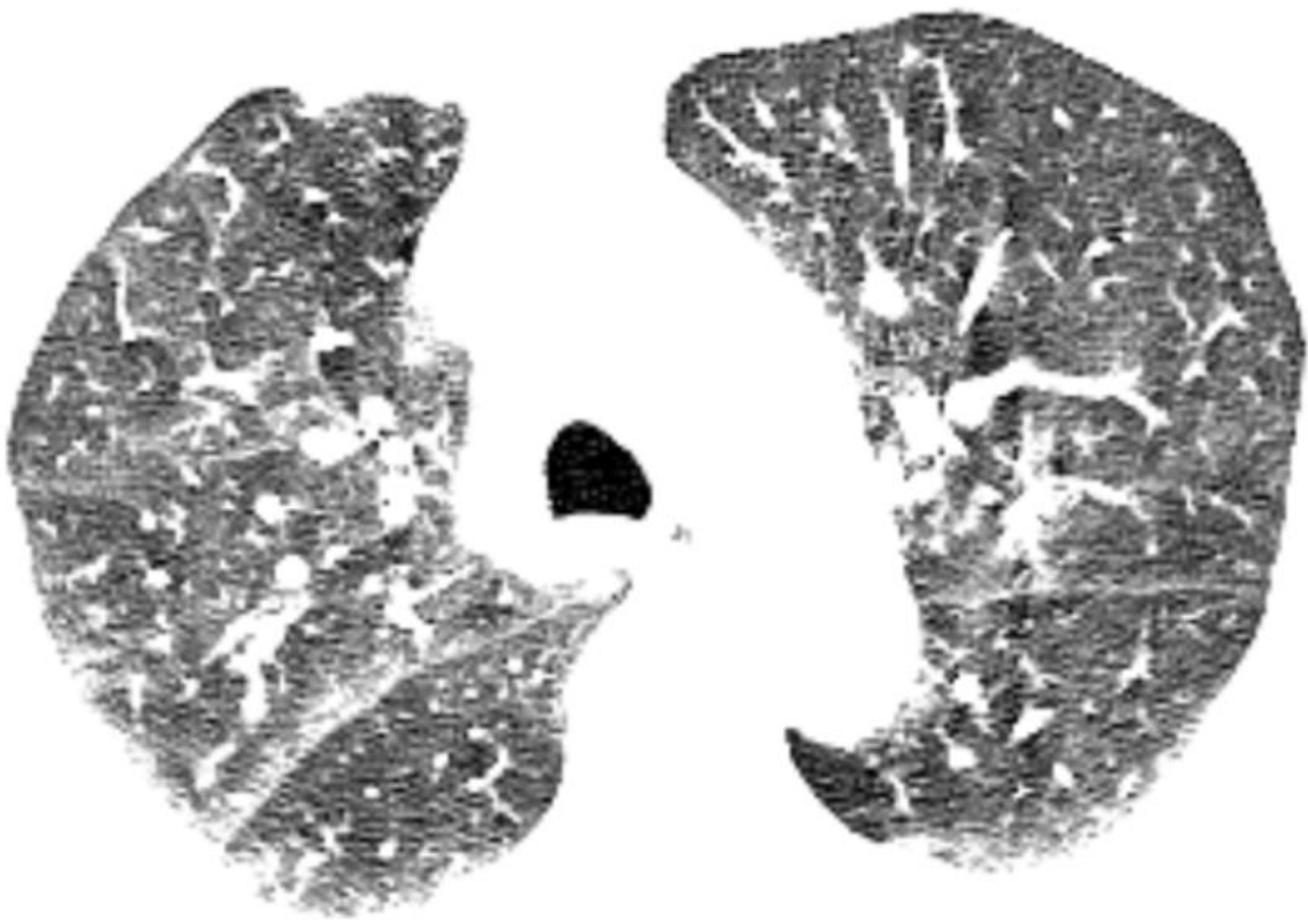
Inspiratory phase  
minIP projection



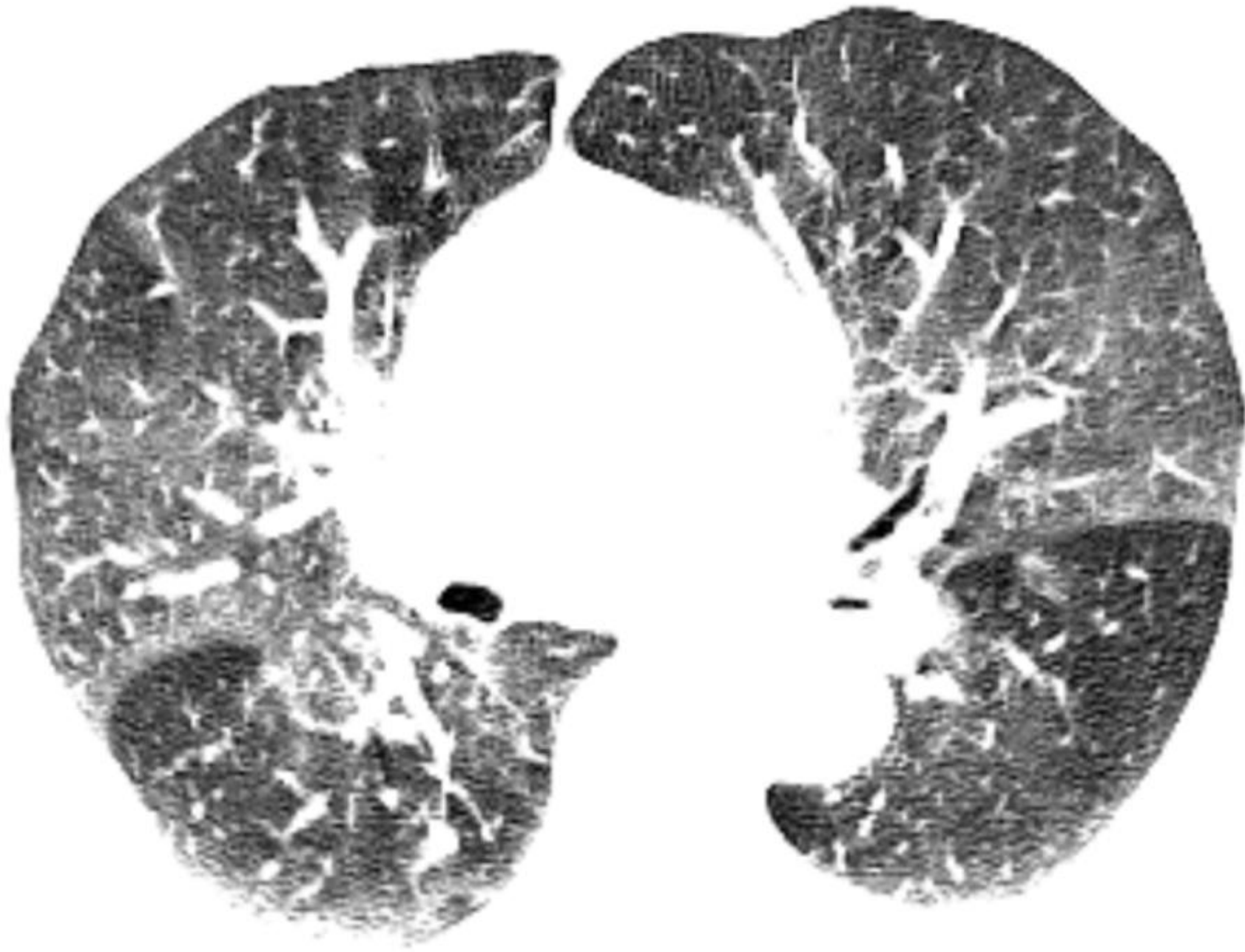
# Expiratory phase



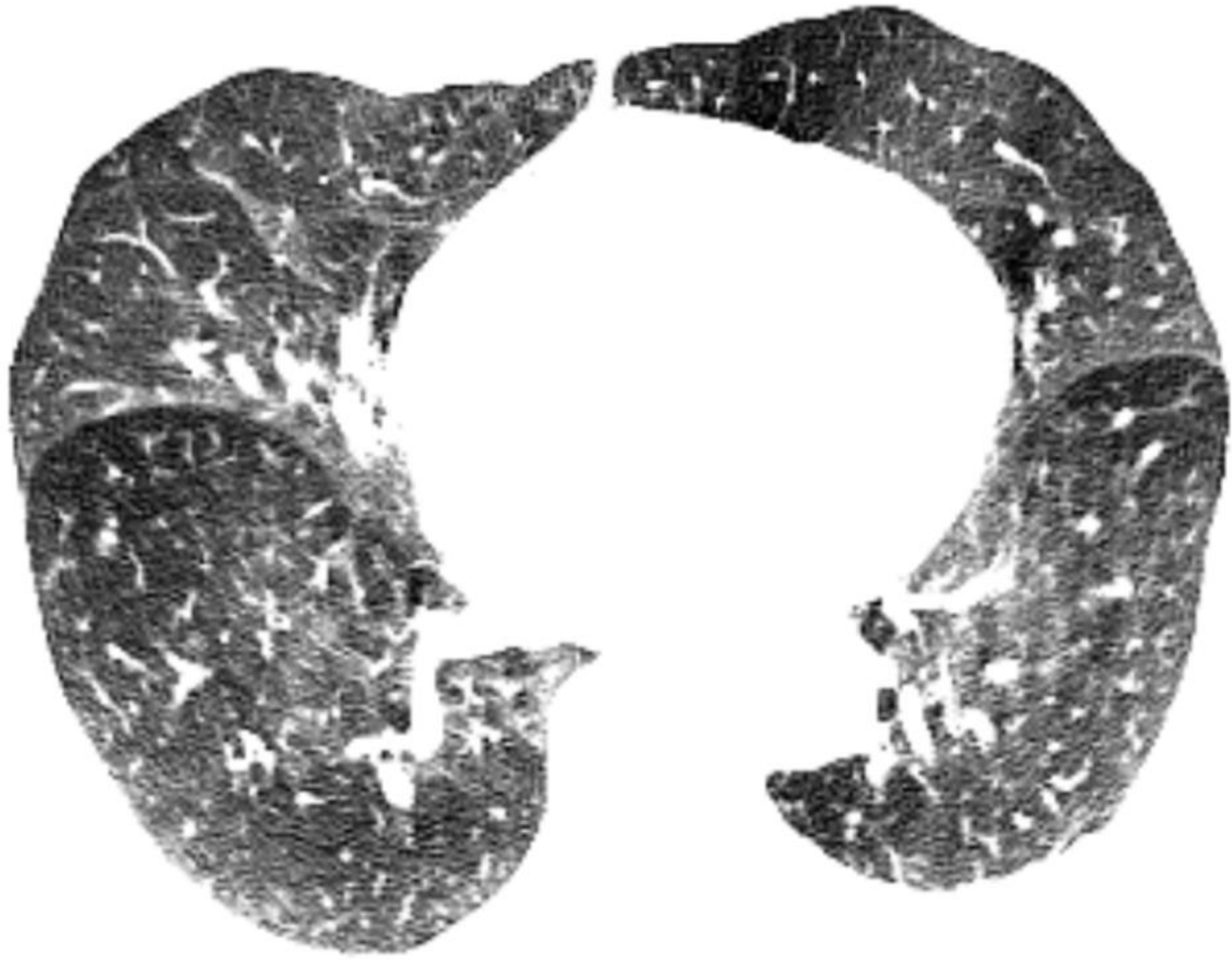
# Expiratory phase



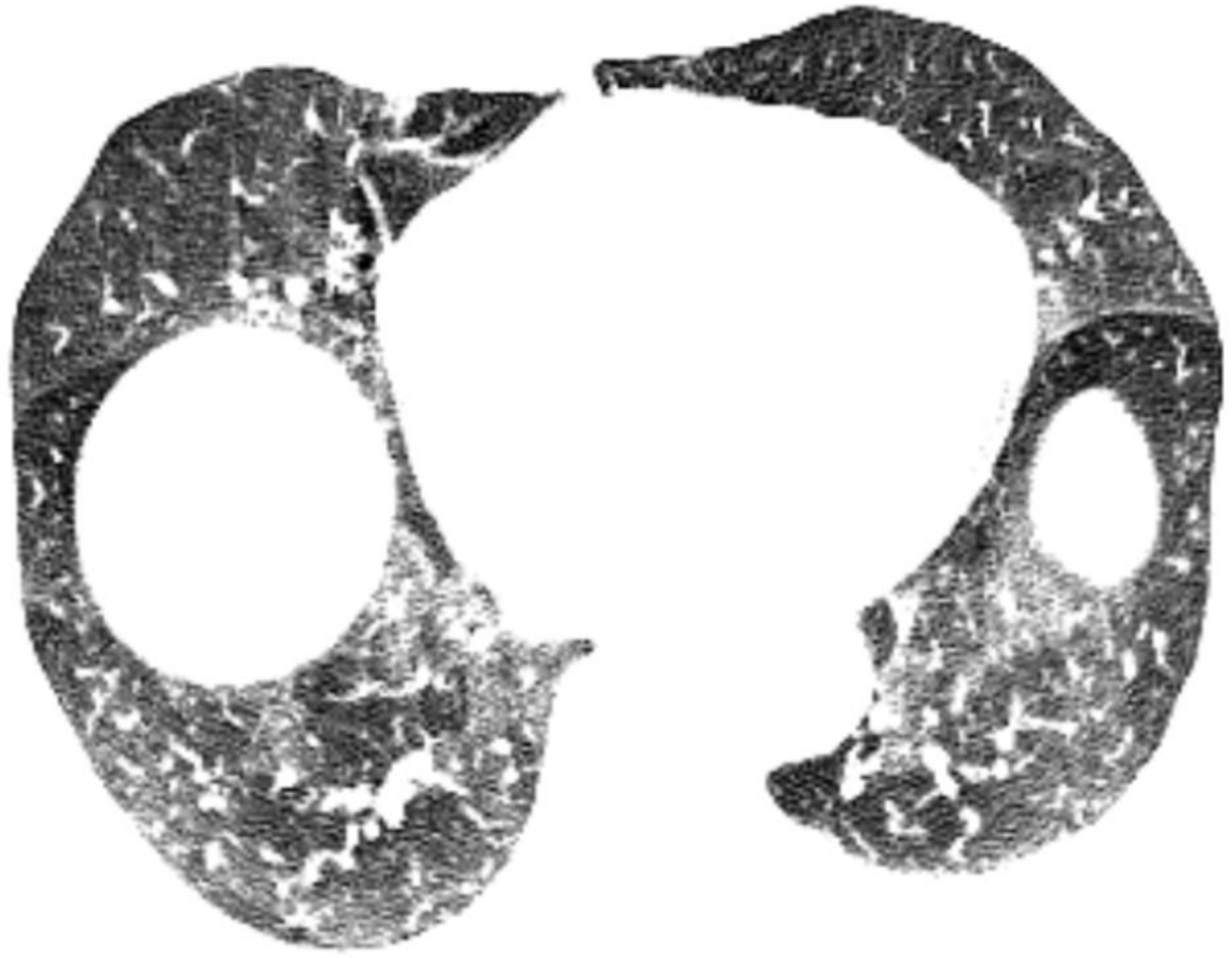
Expiratory phase



Expiratory phase



Expiratory phase



# Συμπερασματικά...

- Η πνευμονική συμμετοχή στη PA είναι συχνότερη και πρωιμότερη απ'όσο πιστεύαμε, καθιστώντας την έγκαιρη διάγνωση απαραίτητη για τον ασθενή

## Η HRCT θώρακος:

- Αποτελεί σημαντική διαγνωστική μέθοδο για την πρώιμη διάγνωση τόσο πιθανής ILD, όσο και προσβολής των αεραγωγών
- Συνεισφέρει στην καλύτερη διαχείριση και παρακολούθηση των ασθενών με πνευμονική συμμετοχή
- Σε περίπτωση υποψίας παθολογίας αεραγωγών, συνιστάται σάρωση σε εισπνοή και εκπνοή
- Συνιστάται ακόμα και σε πρώιμη φάση της PA για τον αποκλεισμό πνευμονικής συμμετοχής

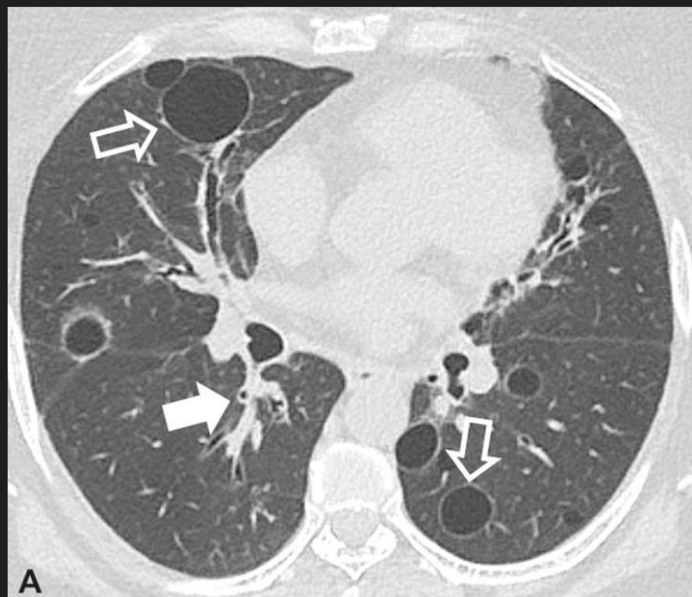


A scenic view of a rocky coastline with clear turquoise water and a sandy beach. The text "Σας Ευχαριστώ" is overlaid on the image.

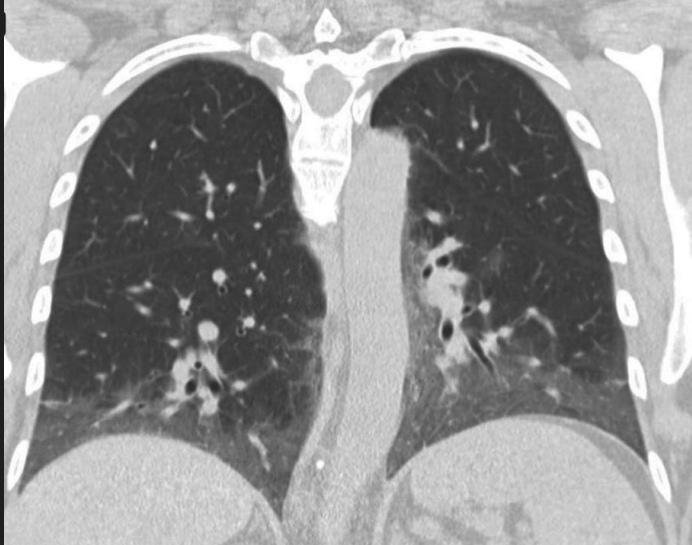
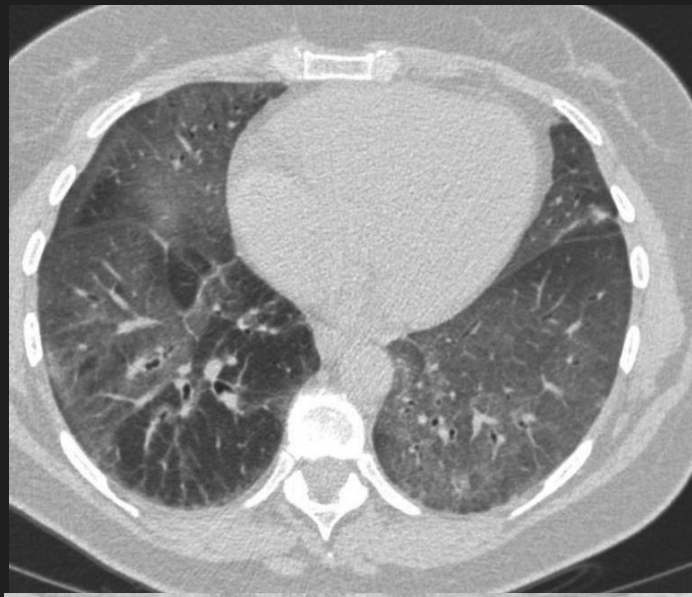
Σας Ευχαριστώ



## Lymphocytic Interstitial Pneumonia (LIP)



## Desquamative Interstitial Pneumonia (DIP)



## Diffuse Alveolar Damage (DAD)



# Drug-Induced ILD

- Hypersensitivity reaction resembling hypersensitivity pneumonitis, eosinophilic pneumonia, pulmonary edema, and diffuse alveolar damage (DAD)
- The not typical manifestations of RA-associated lung disease and should raise suspicion for drug reaction
- Patients presenting with acute onset or rapid progression of symptoms and new imaging abnormalities warrant empirical drug cessation
- Methotrexate : most common CT patterns resemble those of hypersensitivity pneumonitis, less often patterns of DAD, OP, rheumatoid nodules and pleuropericarditis
- Symptoms typically improve within days of drug cessation, although radiographic improvement may take several weeks.

**Table 4: Imaging Features of DILD in RA**

Medications	Drug-induced Reactions	Imaging Features
MTX, rituximab	Hypersensitivity pneumonitis-like reaction	Diffuse centrilobular GGO, air trapping
MTX (reactions occur within 6 months to 2 years), anti-TNF agents, leflunomide (reactions occur within 20 weeks), rituximab, abatacept (reactions are rare)	Noncardiogenic edema, DAD, pneumonitis	Acute, rapid extensive bilateral consolidation and GGO: diffuse GGO and dependent consolidation (acute phase); fibrosis (reparative phase)

