
제 17차 천식연구회 COPD연구회 공동 심포지엄

TEN SUBTYPES OF COPD BY INTEGRAL METHOD

2021년 3월 6일

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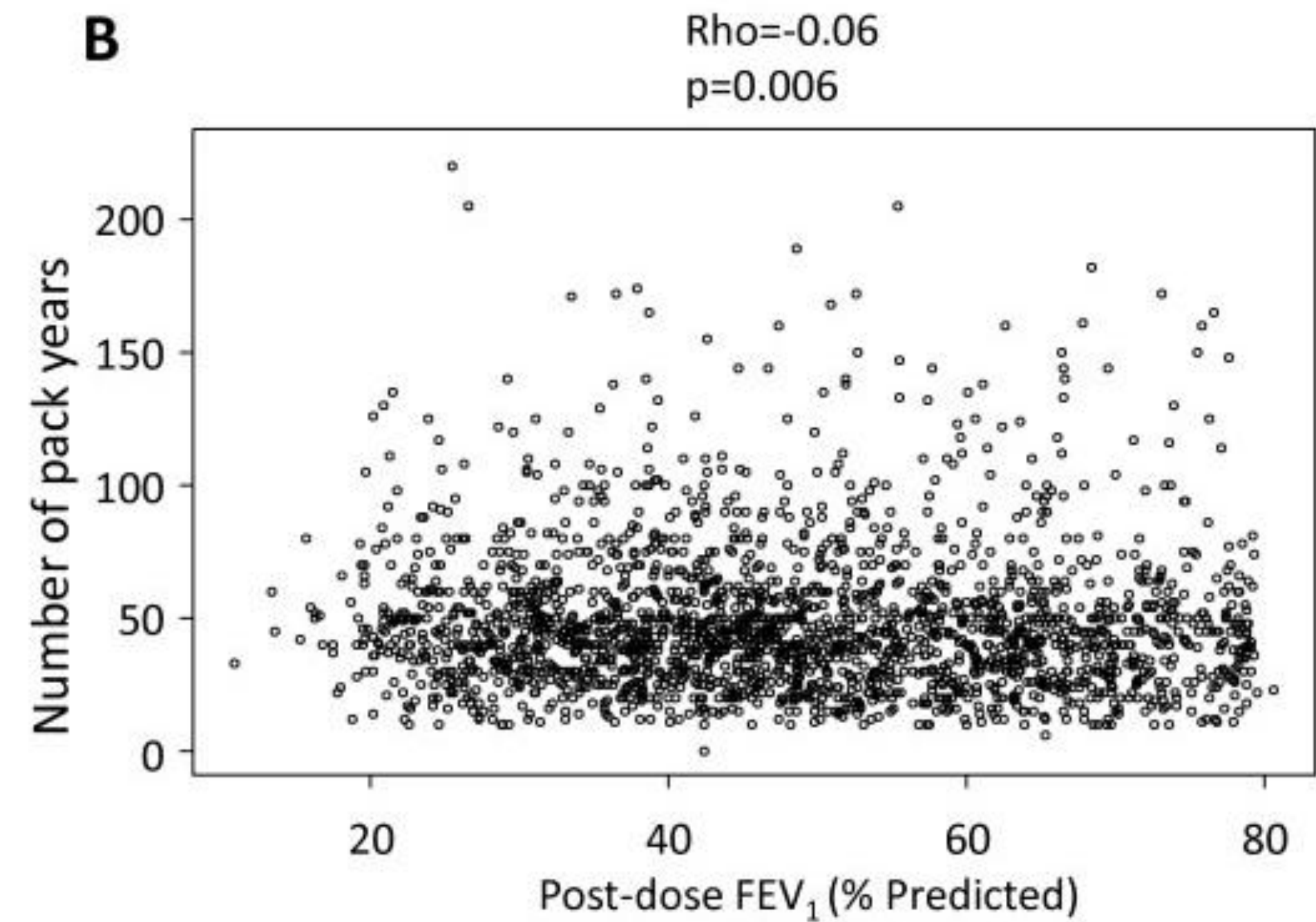
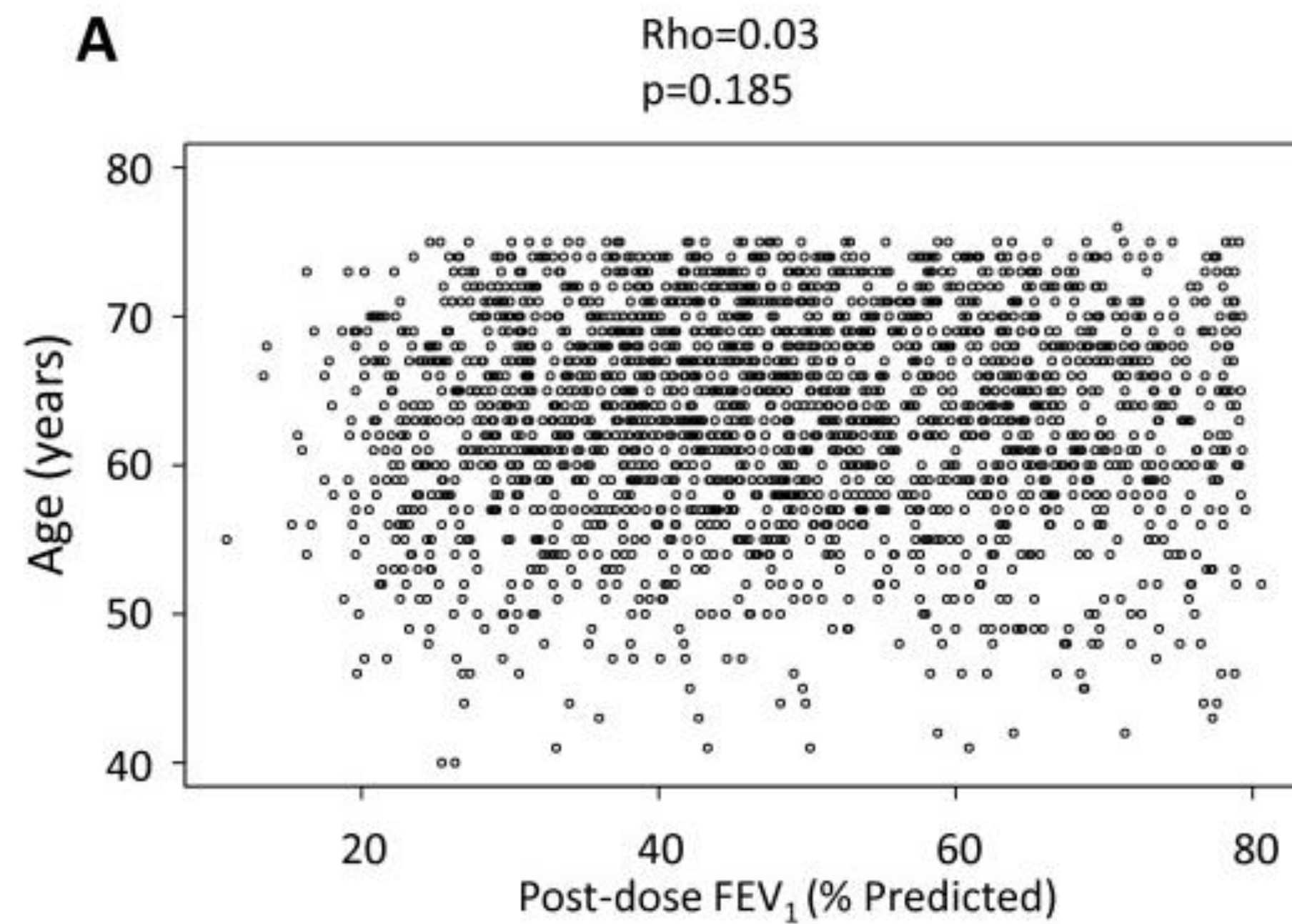
THE DIAGNOSIS OF COPD

- Symptoms compatible with COPD (dyspnea, cough, progressive limitation of activity)
- Spirometry : airflow limitation FEV1/FVC ratio <0.7 after administration of an inhaled bronchodilator (GOLD guideline 2020)

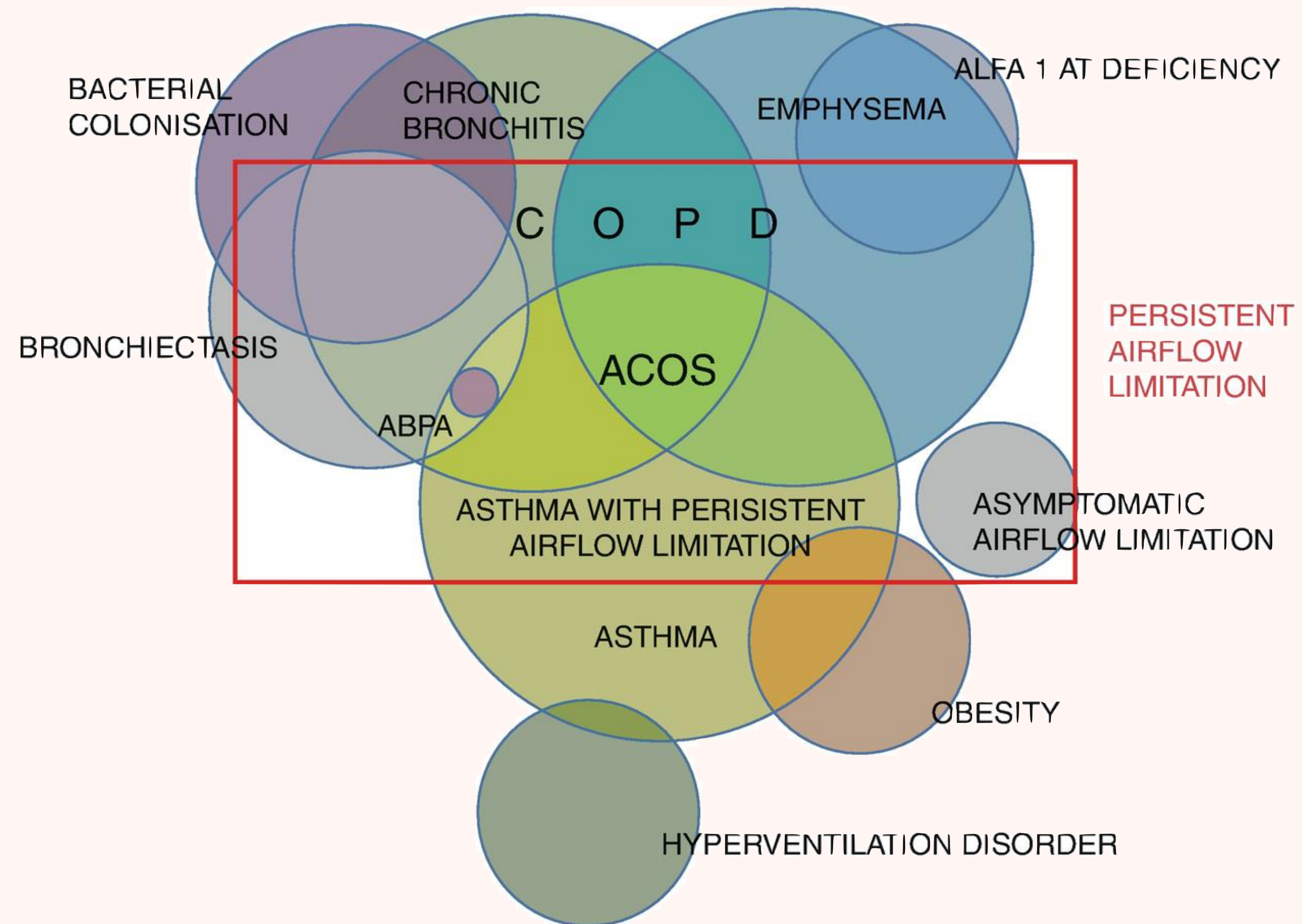
VALUE OF PFT (SPIROMETRY) FOR COPD

- **The cornerstone of the diagnostic evaluation of patients with suspected COPD**
 - **The severity of the airflow limitation**
 - **Assess the response to medications**
 - **Follow disease progression**
 - **useful tool to assess COPD severity.**
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HETEROGENEITY OF COPD BY SEVERITY OF AIRFLOW LIMITATION (GOLD)



HETEROGENEITY OF COPD BY SEVERITY OF AIRFLOW LIMITATION (GOLD)



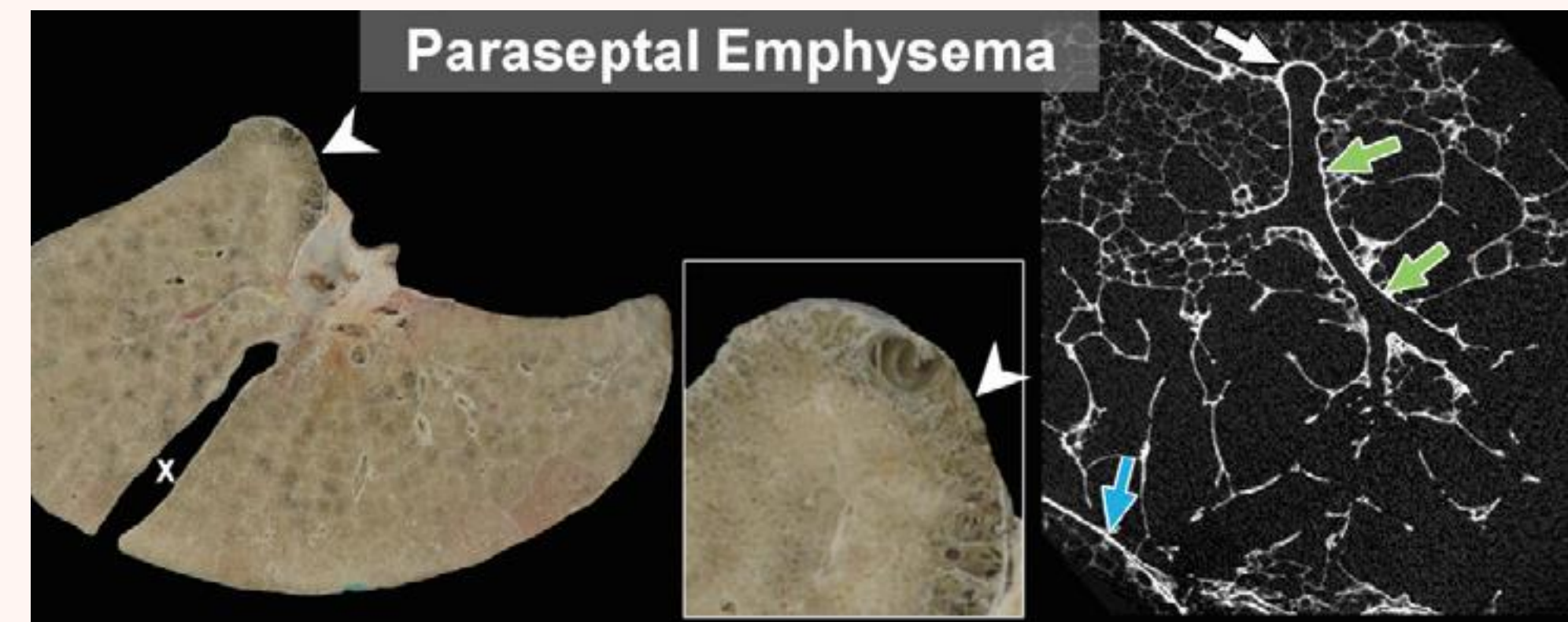
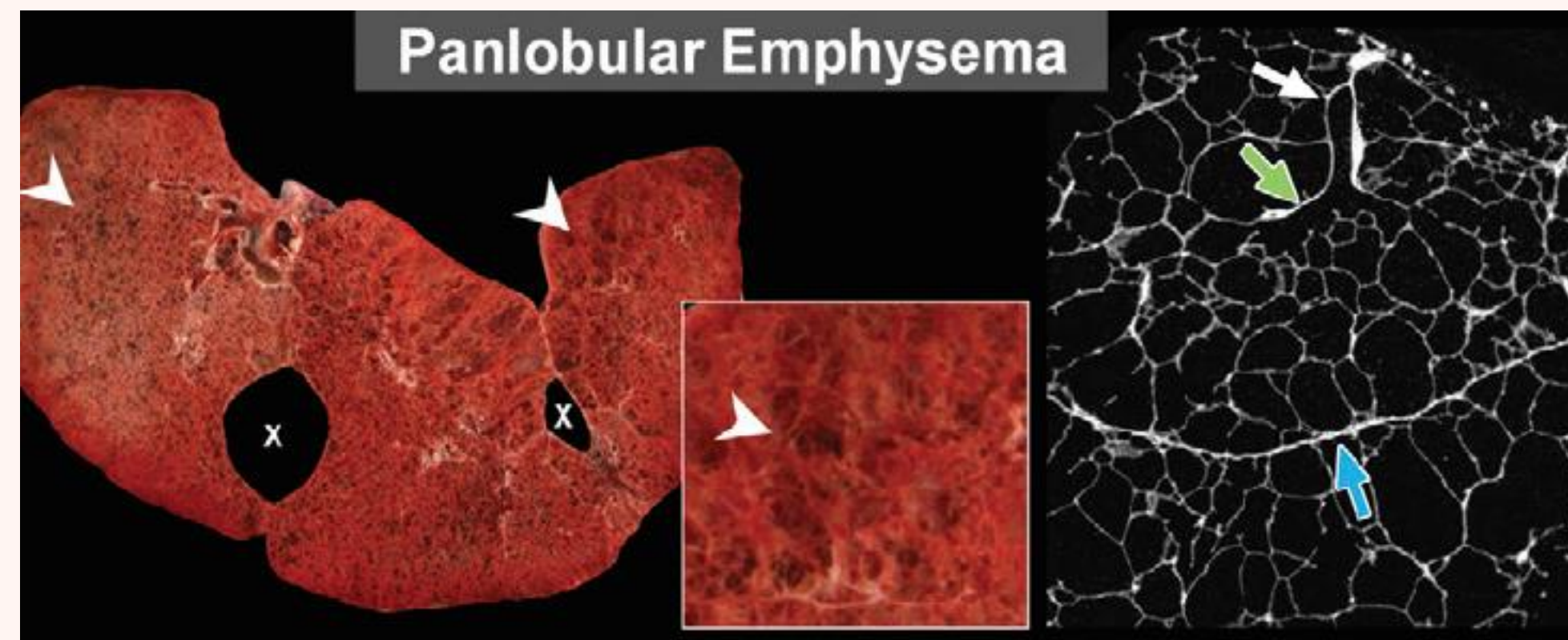
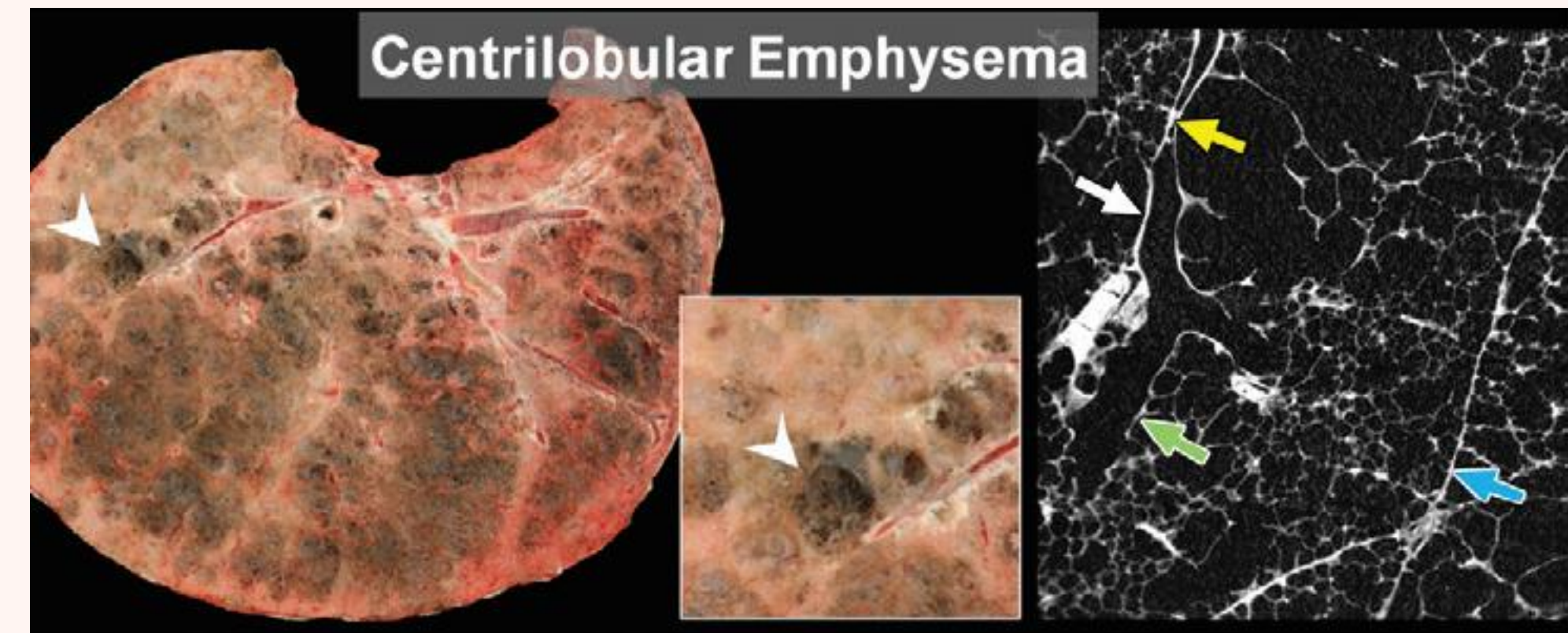
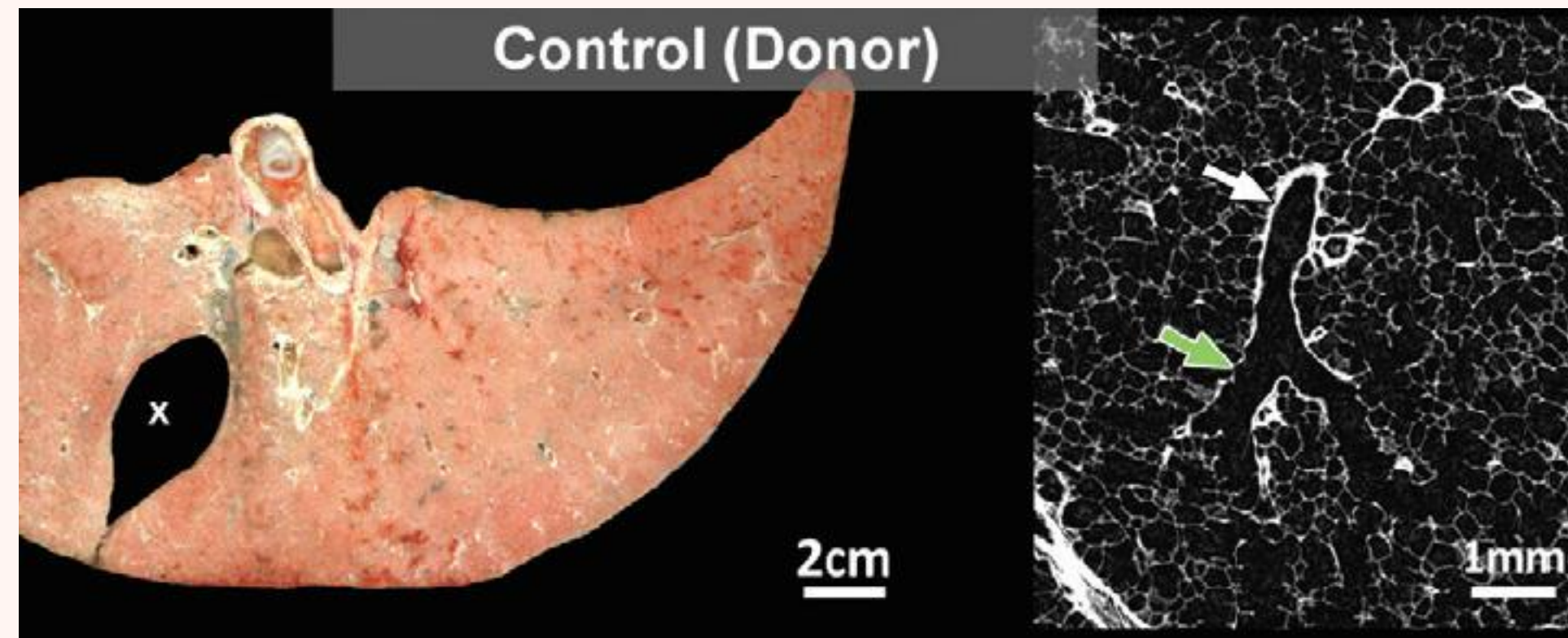
VISUAL CT IMAGING EVALUATION

- A various patterns of abnormalities (emphysema, airway inflammation, small airway disease)
- provide information about emphysema distribution
- correlate well with the patterns recognized on pathology.

physiologic impairment

- considerable observer variation for quantitative assessment of severity.
-

COMPARISON OF FROZEN LUNG SLICES AND MICRO-CT IMAGES



A STATEMENT OF THE FLEISCHNER SOCIETY

➤ CT defined subtypes of COPD

Emphysema

mild CLE
moderate CLE
confluent emphysema

upper lobe
predominant

Advanced Destructive emphysema

lower lobe
predominant

Paraseptal Emphysema

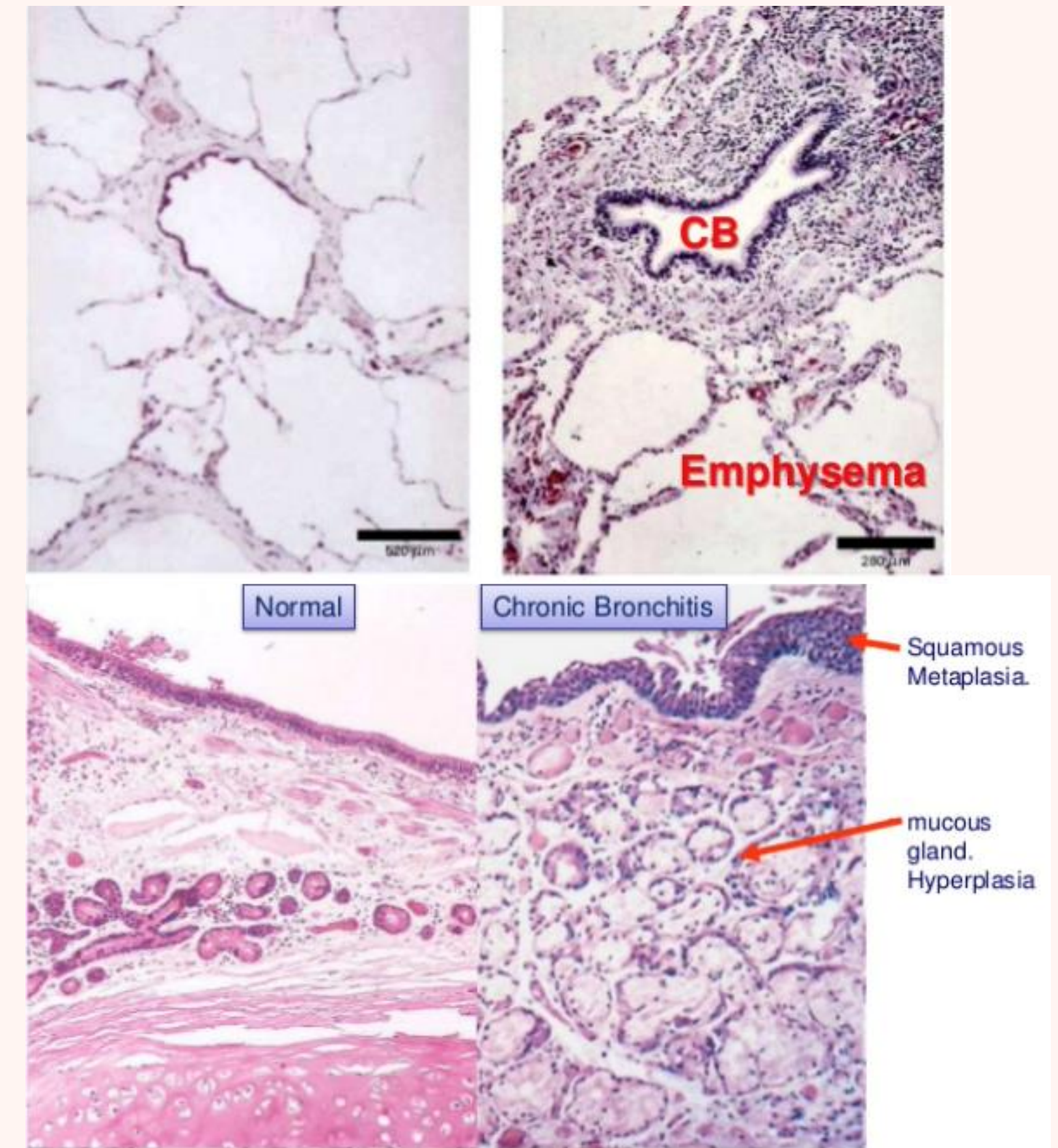
Panlobular emphysema (PLE)

A1AT deficiency

Airway Predominant Diseases

Bronchial Disease

Small Airway Disease



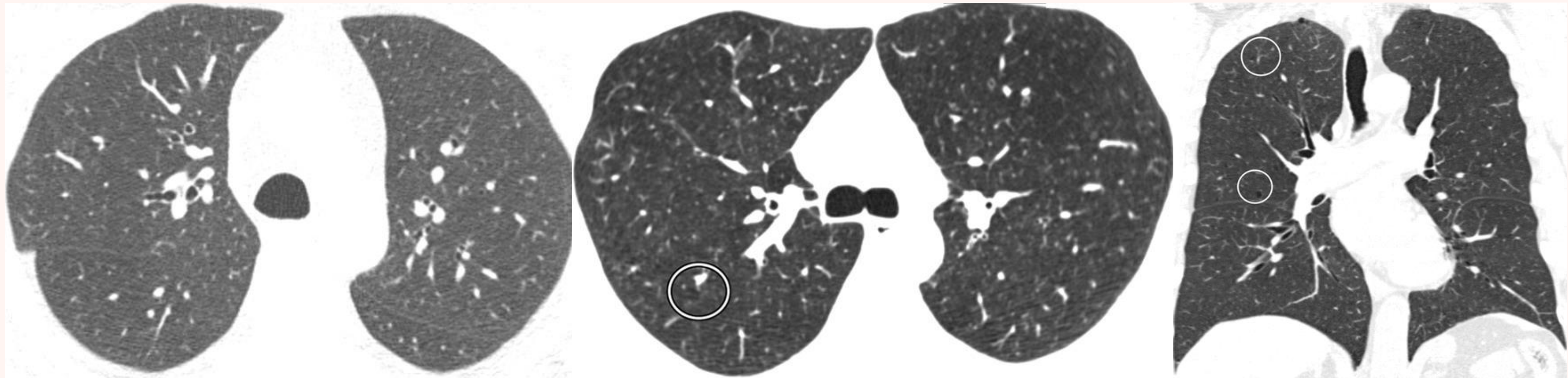
VISUALLY DEFINED PATTERNS OF CLE

➤ Centrilobular Emphysema (CLE)

- Trace CLE : minimal centrilobular lucencies, occupying <0.5% of a lung zone
 - Mild CLE : scattered centrilobular lucencies, usually separated by large regions of normal lung, involving an estimated 0.5-5% of a lung zone.
 - Moderate CLE: many well-defined centrilobular lucencies, occupying more than 5% of any lung zone
 - Confluent CLE : coalescent centrilobular or lobular lucencies including multiple regions of lucency's that span several secondary pulmonary lobules, but not involving extensive hyper expansion of secondary pulmonary lobules or distortion of pulmonary architecture.
 - Advanced Destructive emphysema (ADE) : pan lobular lucencies, with hyperexpansion of secondary pulmonary lounges and distortion of pulmonary architecture.
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VISUALLY DEFINED PATTERNS OF CLE ;STATEMENT OF THE FLEISCHNER SOCIETY

➤ Centrilobular Emphysema (CLE), trace CLE



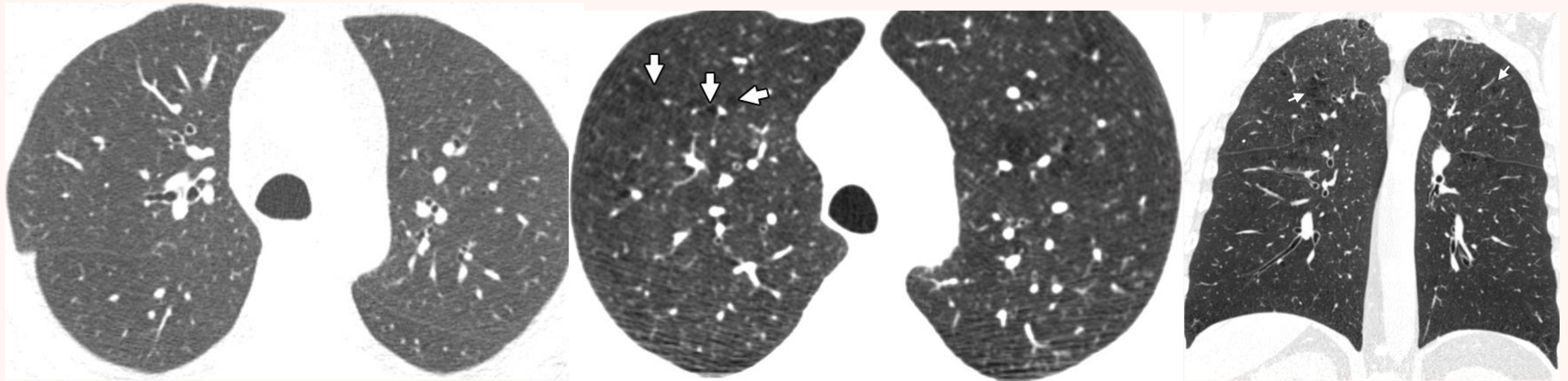
Normal

Trace CLE

involved less than 0.5% of the lung zone

VISUALLY DEFINED PATTERNS OF CLE ;STATEMENT OF THE FLEISCHNER SOCIETY

➤ Centrilobular Emphysema (CLE), mild CLE



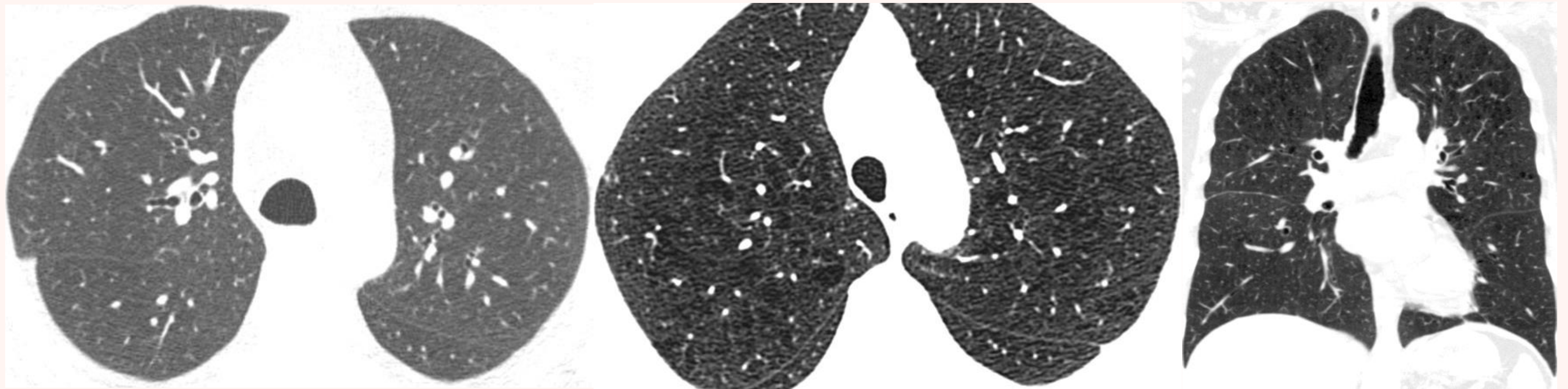
Normal

mild CLE

involved 0.5%–5.0% of the lung zone.

VISUALLY DEFINED PATTERNS OF CLE ;STATEMENT OF THE FLEISCHNER SOCIETY

➤ Centrilobular Emphysema (CLE), moderate CLE

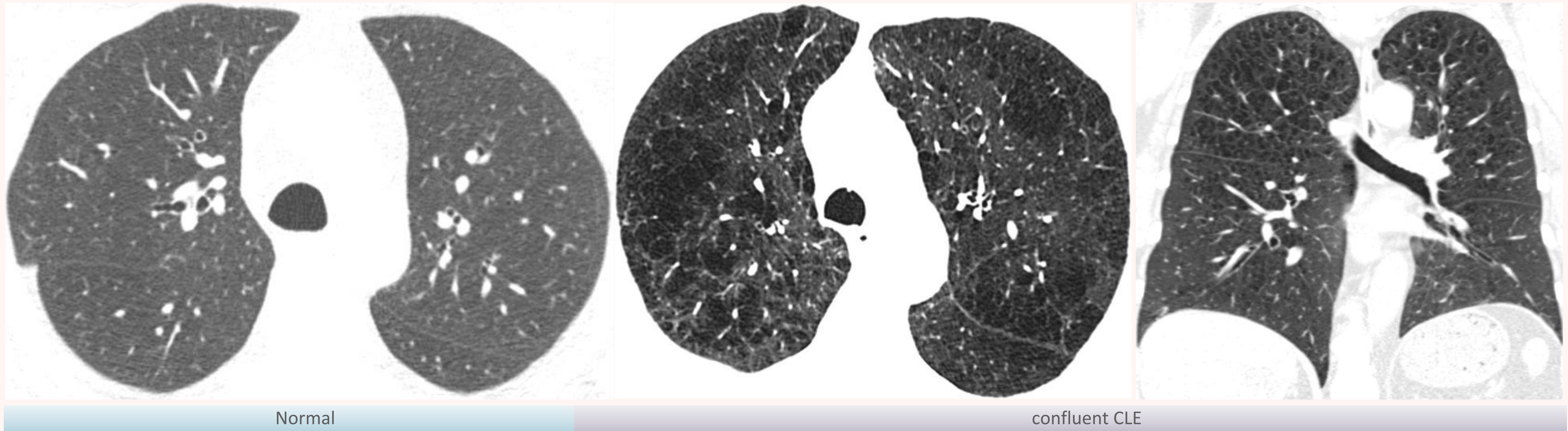


Normal

moderate CLE
involved more than 5% of the lung zone

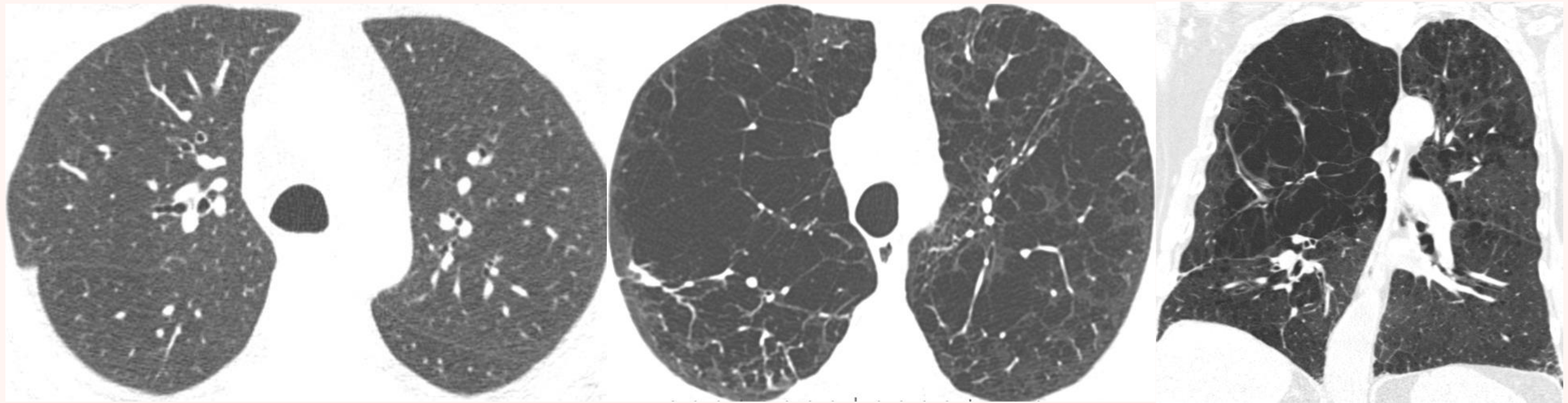
VISUALLY DEFINED PATTERNS OF CLE ;STATEMENT OF THE FLEISCHNER SOCIETY

➤ Centrilobular Emphysema (CLE), confluent CLE



VISUALLY DEFINED PATTERNS OF CLE ;STATEMENT OF THE FLEISCHNER SOCIETY

➤ Centrilobular Emphysema (CLE), Advanced destructive emphysema CLE



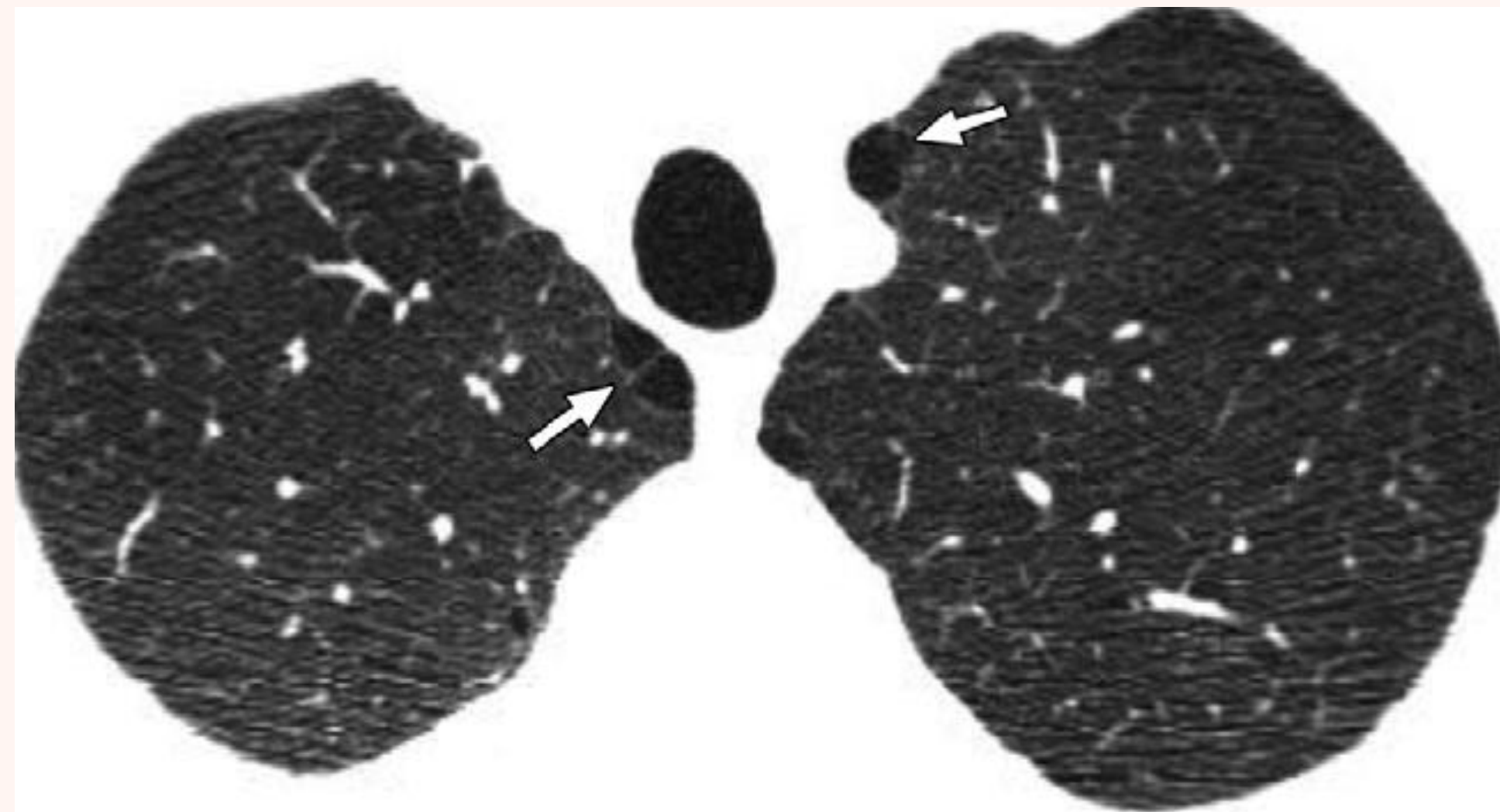
Normal

Advanced destructive emphysema
with vascular distortion.

VISUALLY DEFINED PATTERNS OF PSE

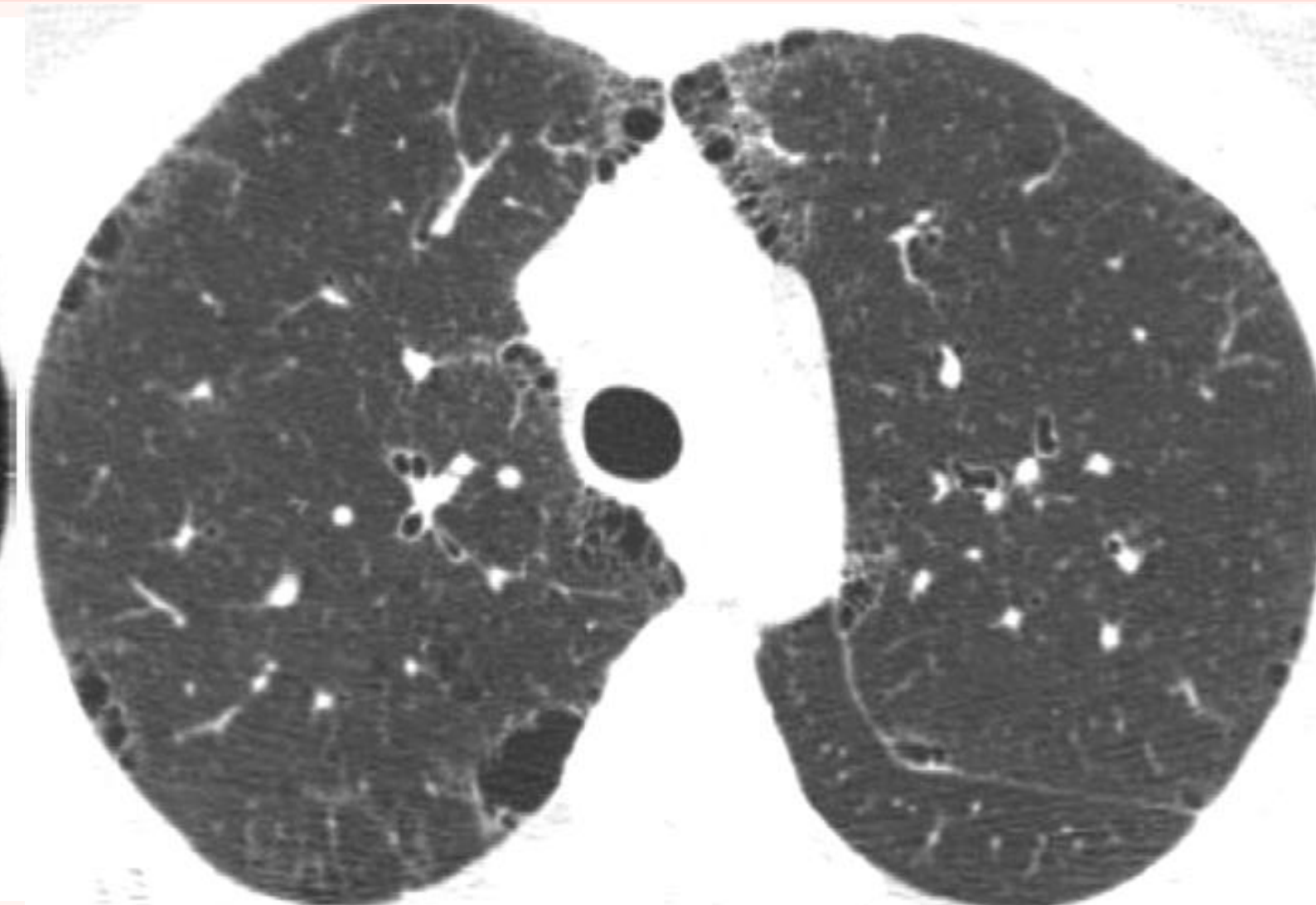
➤ Paraseptal Emphysema, PSE

Mild PSE



small (<1cm diameter), well demarcated rounded juxtaleural lucencies, aligned in a row along a pleural margin, sometimes including along an interloper fissure, and sometimes including a few small rounded lucencies immediately central to the juxtaleural lucencies.

Substantial PSE

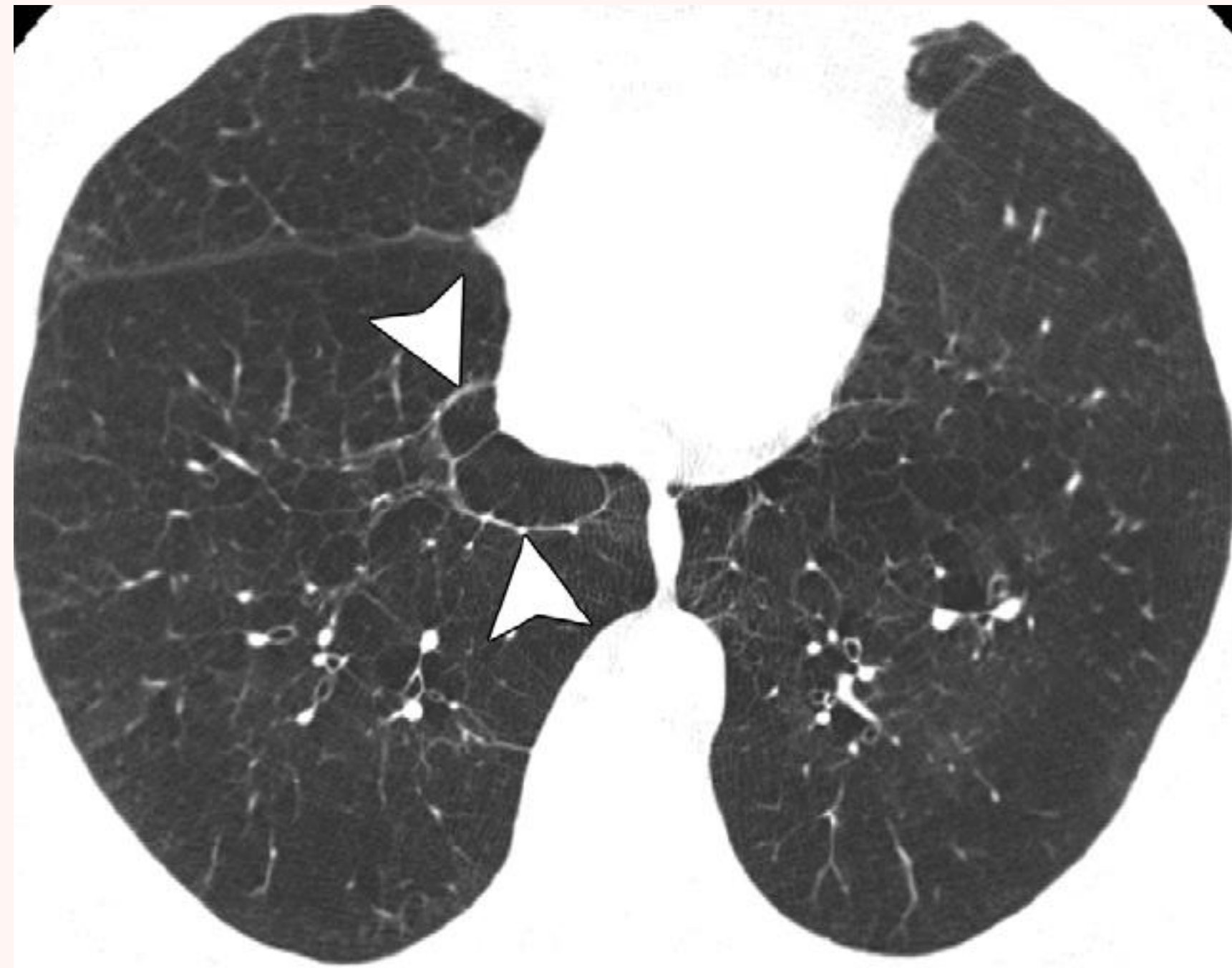


mainly large (>1cm diameter) juxtaleural cyst-like lucencies or bull, involving more than the lung apices, aligned in a row along a pleural margin, and sometimes including adjacent to an interlobar fissure.

VISUALLY DEFINED PATTERNS OF EMPHYSEMA

- **Panlobular Emphysema**

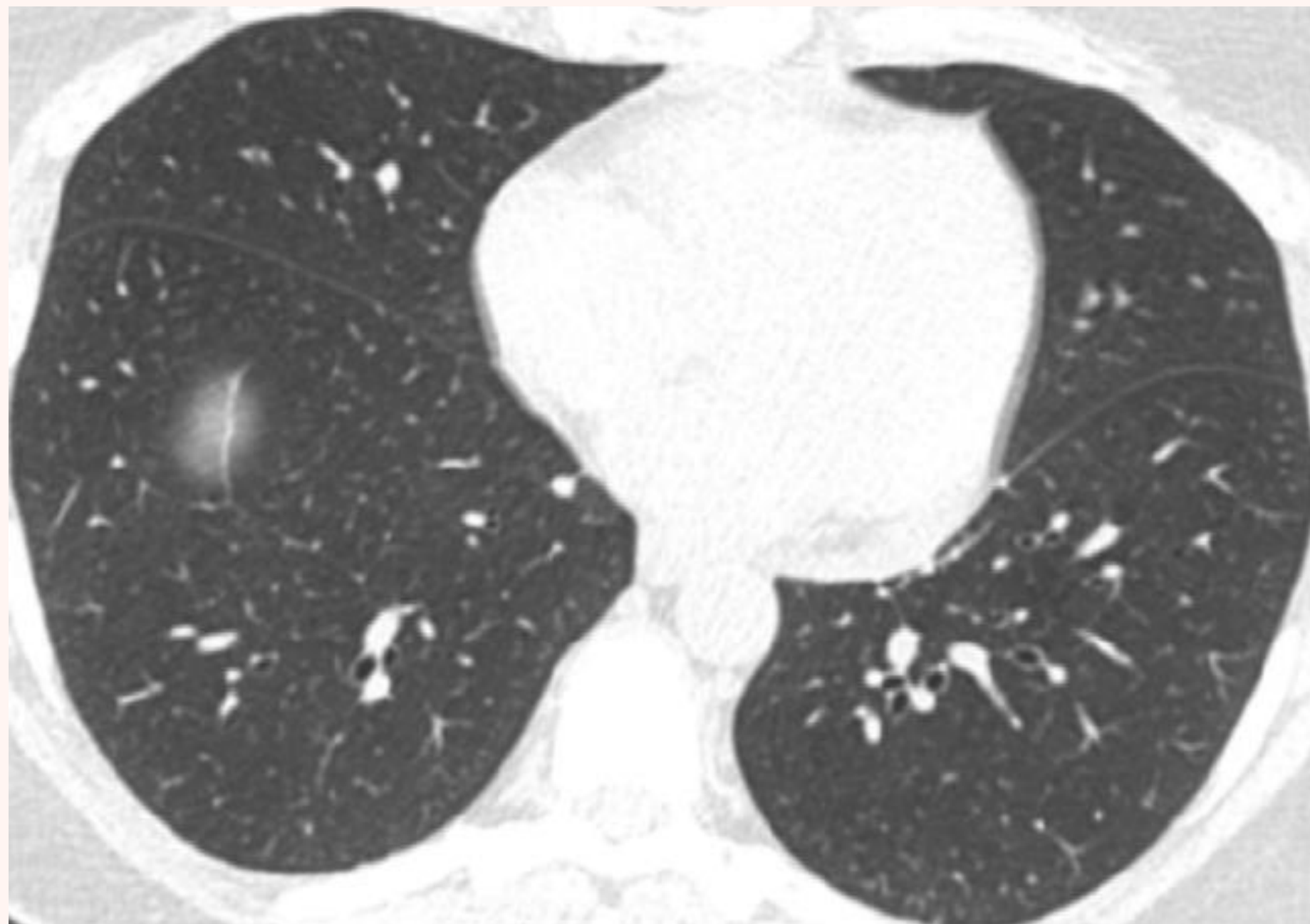
- **Associated with A1AT deficiency: most commonly, a lower lobe predominant pattern involving generalized destruction of all acini more or less equally.**



VISUALLY DEFINED PATTERNS OF AIRWAY

- **Airway disease : in the absence of emphysema as a predominant expression of COPD**

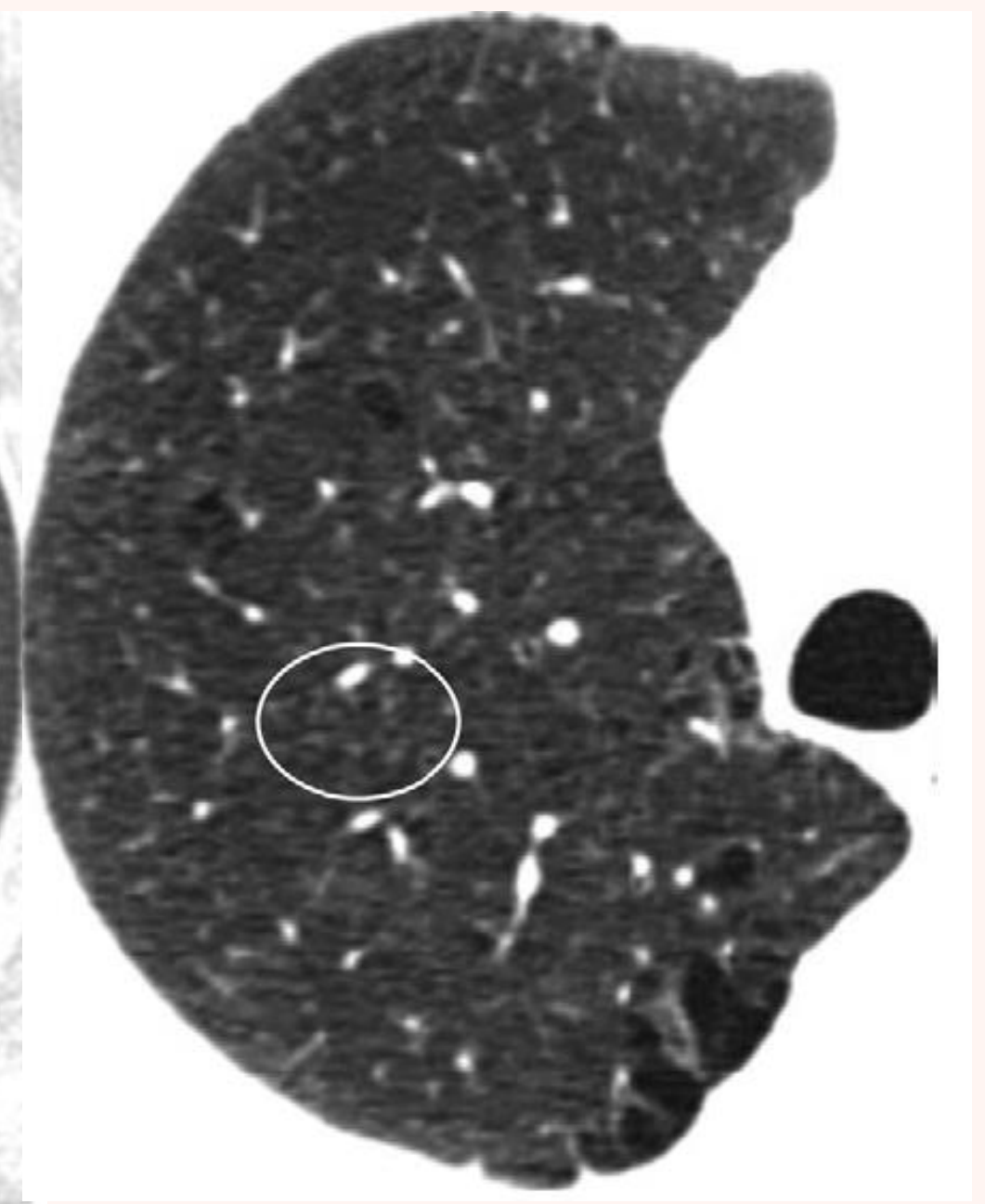
Normal



Bronchial Disease



Small Airway Disease



VISUAL CT IMAGING EVALUATION

- A various patterns of abnormalities (emphysema, airway inflammation, small airway disease)
- provide information about emphysema distribution
- correlate well with the patterns recognized on pathology.

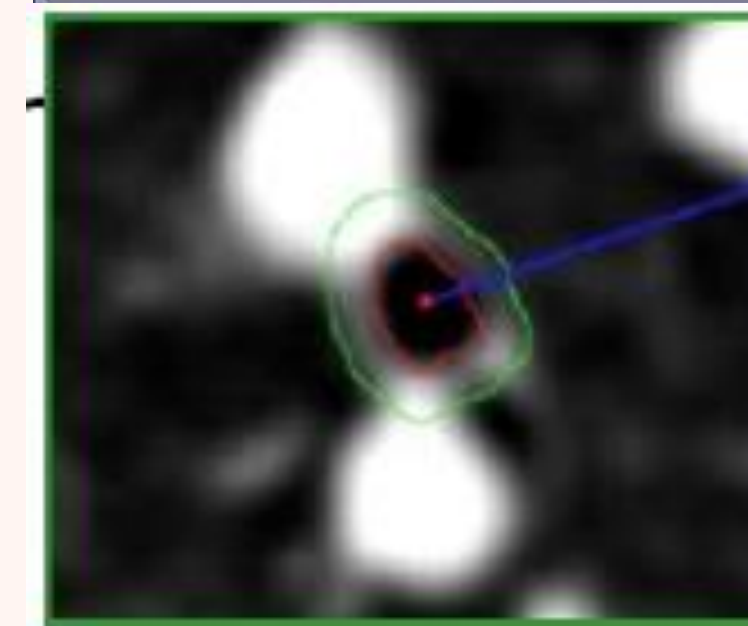
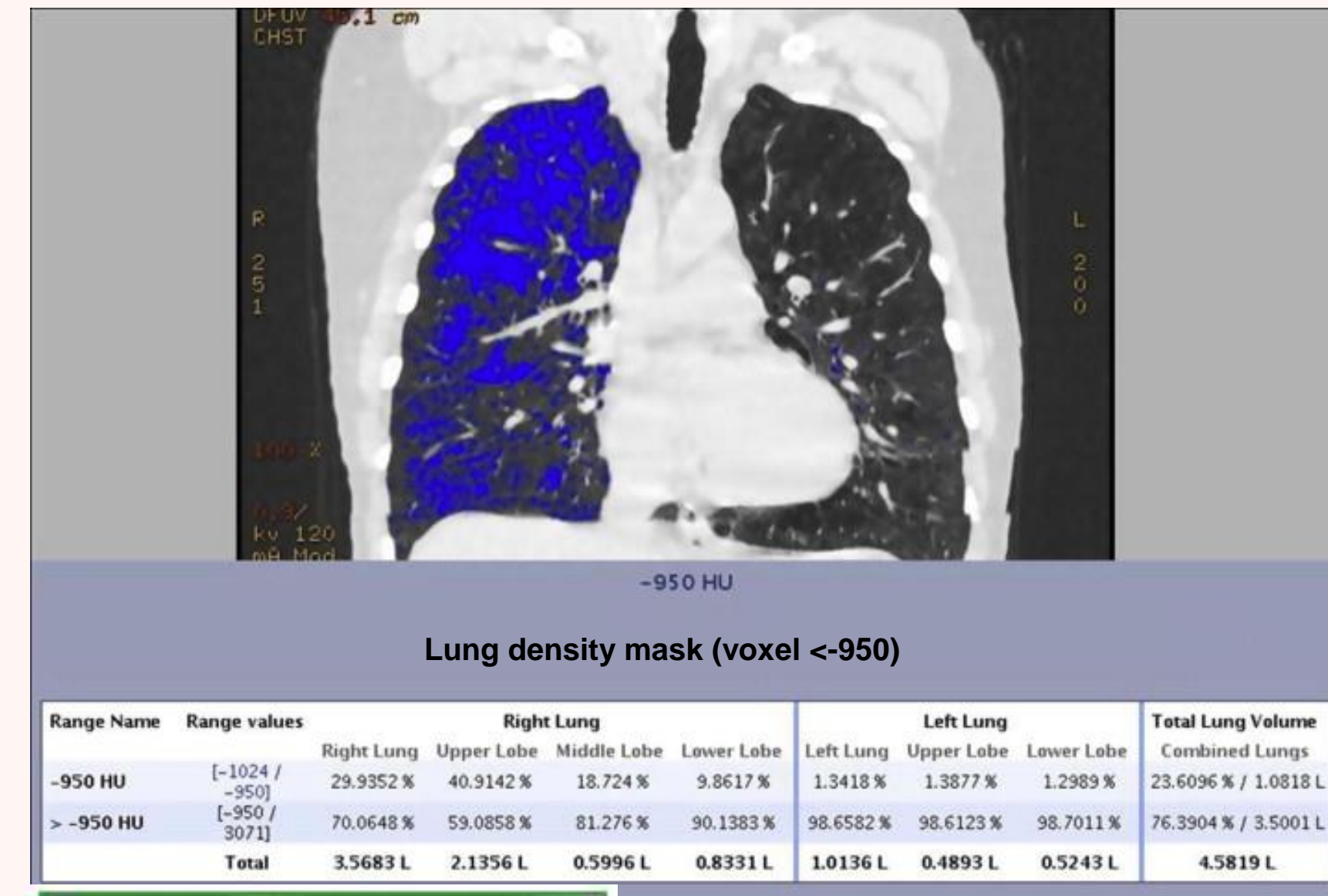
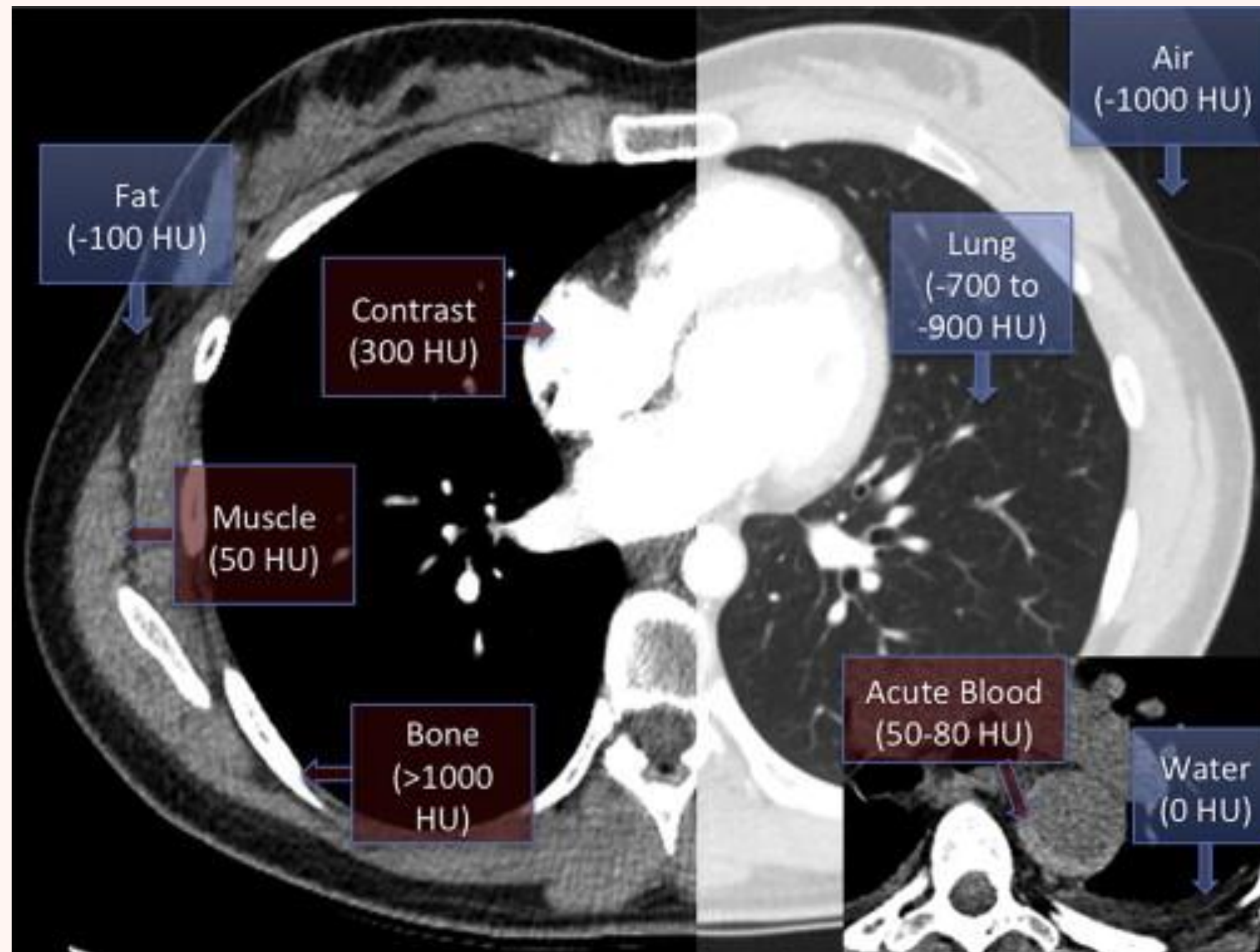
physiologic impairment

- **considerable observer variation for quantitative assessment of severity.**
-

QUANTITATIVE CT IMAGING

- **Help assess the severity and lobar distribution of emphysema**
 - **correlate better than visual CT scoring with macroscopic measurements of emphysema**
 - **the highest correlation between QCT metrics and histology**
 - **variation in lung volume, technical CT parameters(reconstruction algorithm), and cigarette smoking status**
-

QUANTITATIVE CT IMAGING



Pi 10 :
Extrapolated square root of wall area of ideal airway of 10mm internal perimeter

QUANTITATIVE CT IMAGING : EMPHYSEMA

- **the density mask technique : -950 HU (percentage of low attenuation areas %LAA-950) \geq 5%**
- **percentile along the frequency histogram of lung attenuation (1st or 15th percentile; Perc15)**
 - : more powerful for longitudinal evaluation of emphysema**
 - : less sensitive lung volume change**



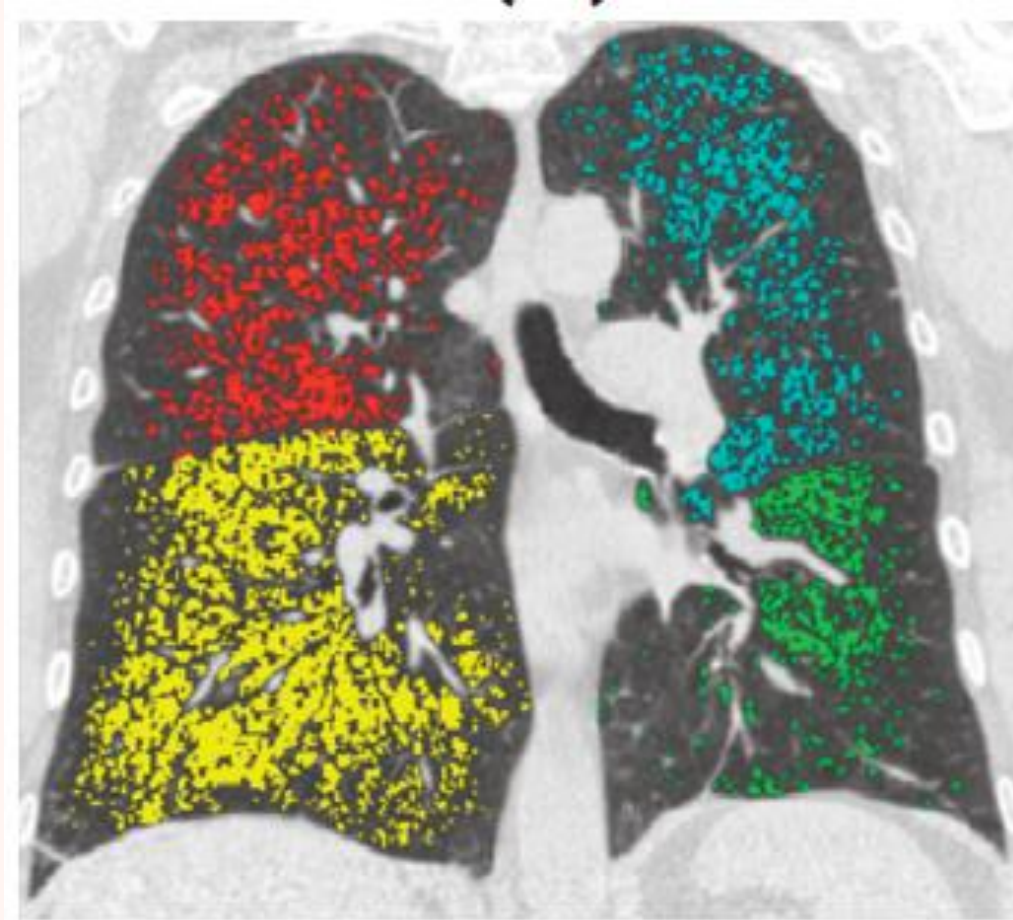
QUANTITATIVE CT IMAGING : AIRTRAPPING

- **End-expiratory** CT, whether obtained at functional residual capacity or at residual volume
- gas trapping by evaluating the % LAA at a threshold of -856 or -850 HU (LAAexp856 or LAAexp850) \geq 20%
- LAAexp850 provided remarkably high correlations ($r=0.85-0.90$) with (FEV1 /FVC) ratio and with FEV1 %

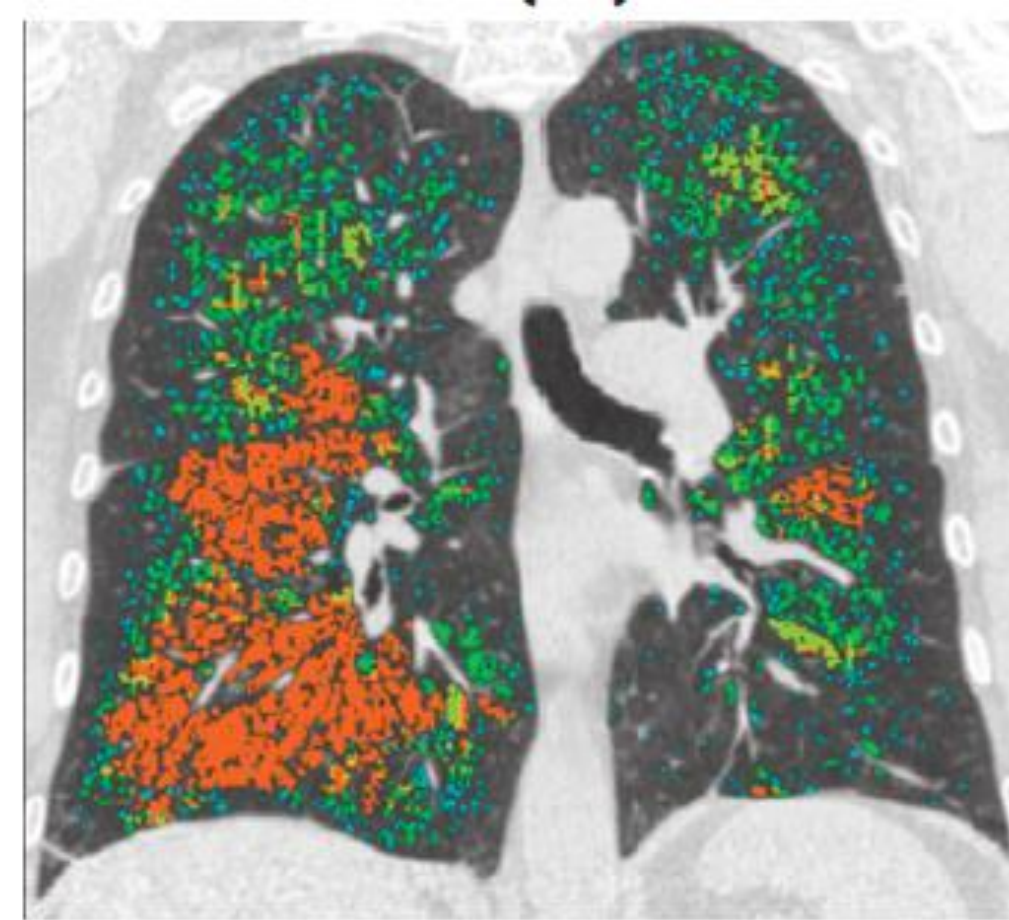


QUANTITATIVE CT IMAGING : AIRTRAPPING

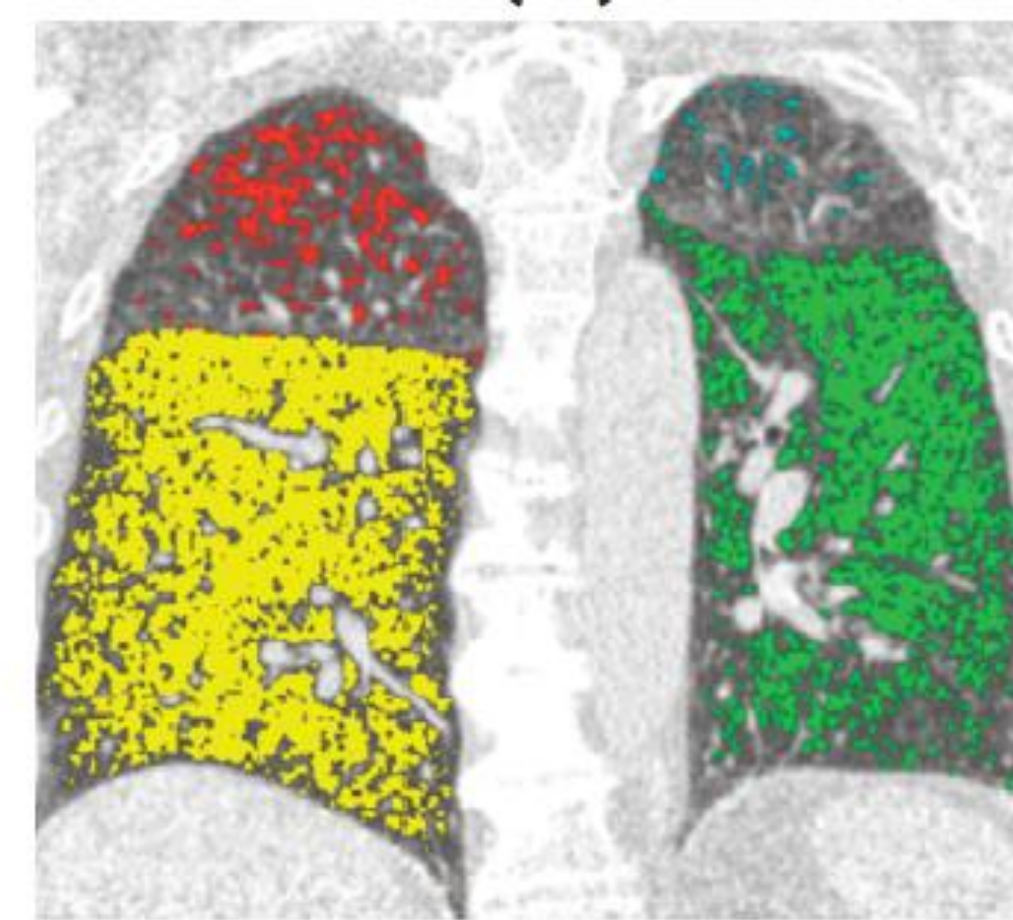
Inspiratory CT



Inspiratory CT



Expiratory CT

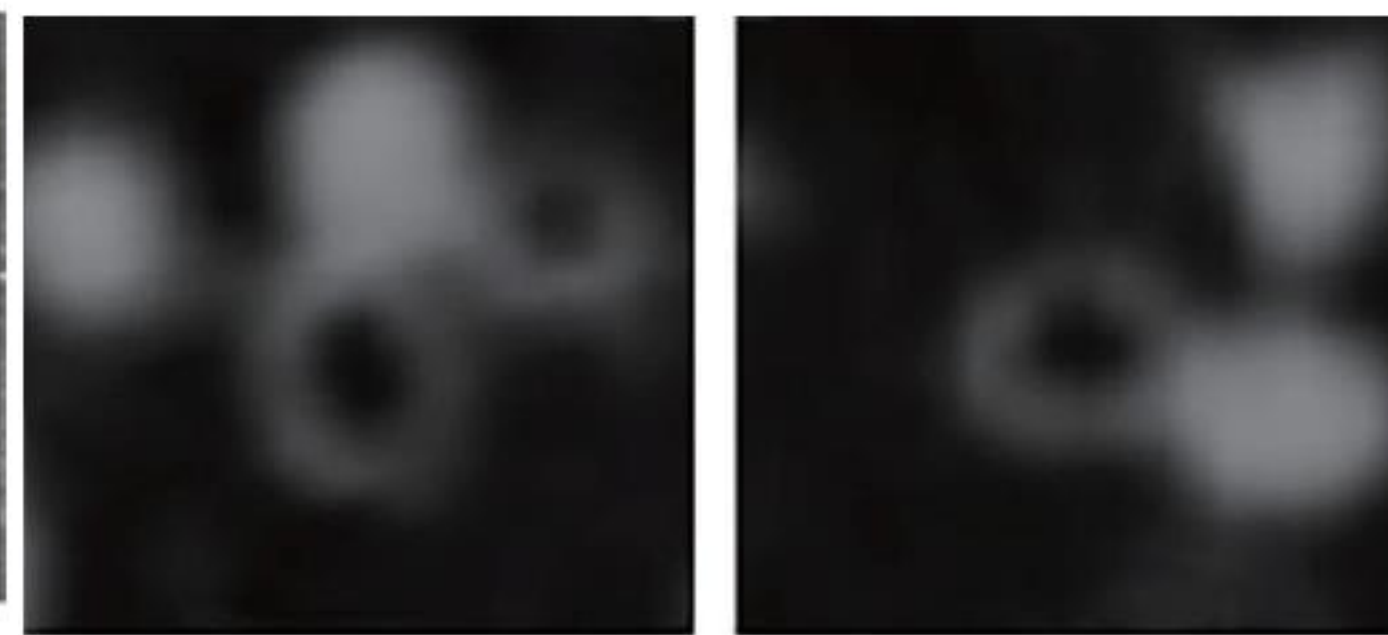
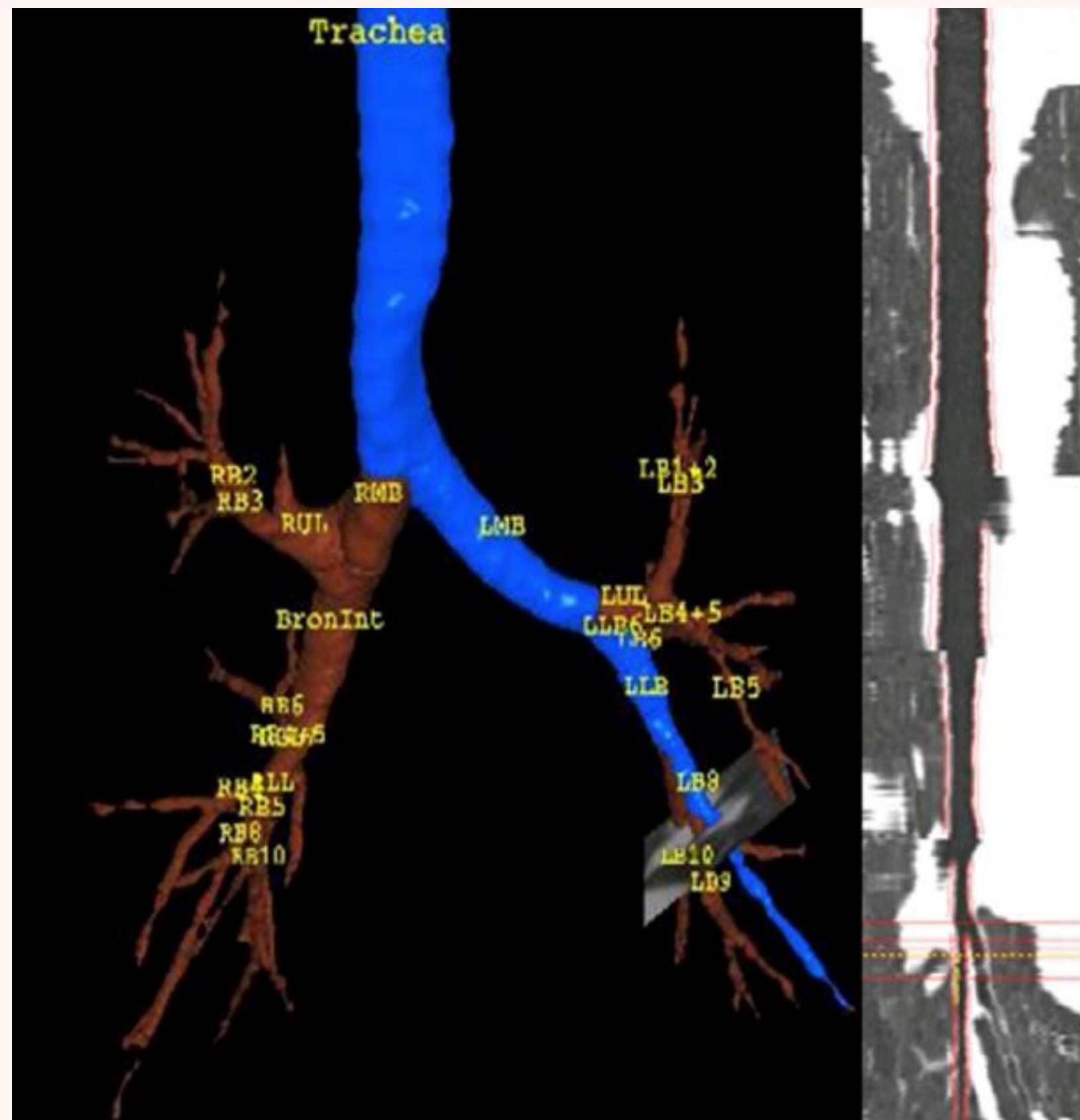


	Red	Yellow	Green
Inspiration	Voxels < -950 HU	voxels > -950 HU	Voxels > -950 HU
Expiration	Voxels < -856 HU	Voxels < -856 HU	Voxels > -856 HU
	emphysema	air trapping	Normal

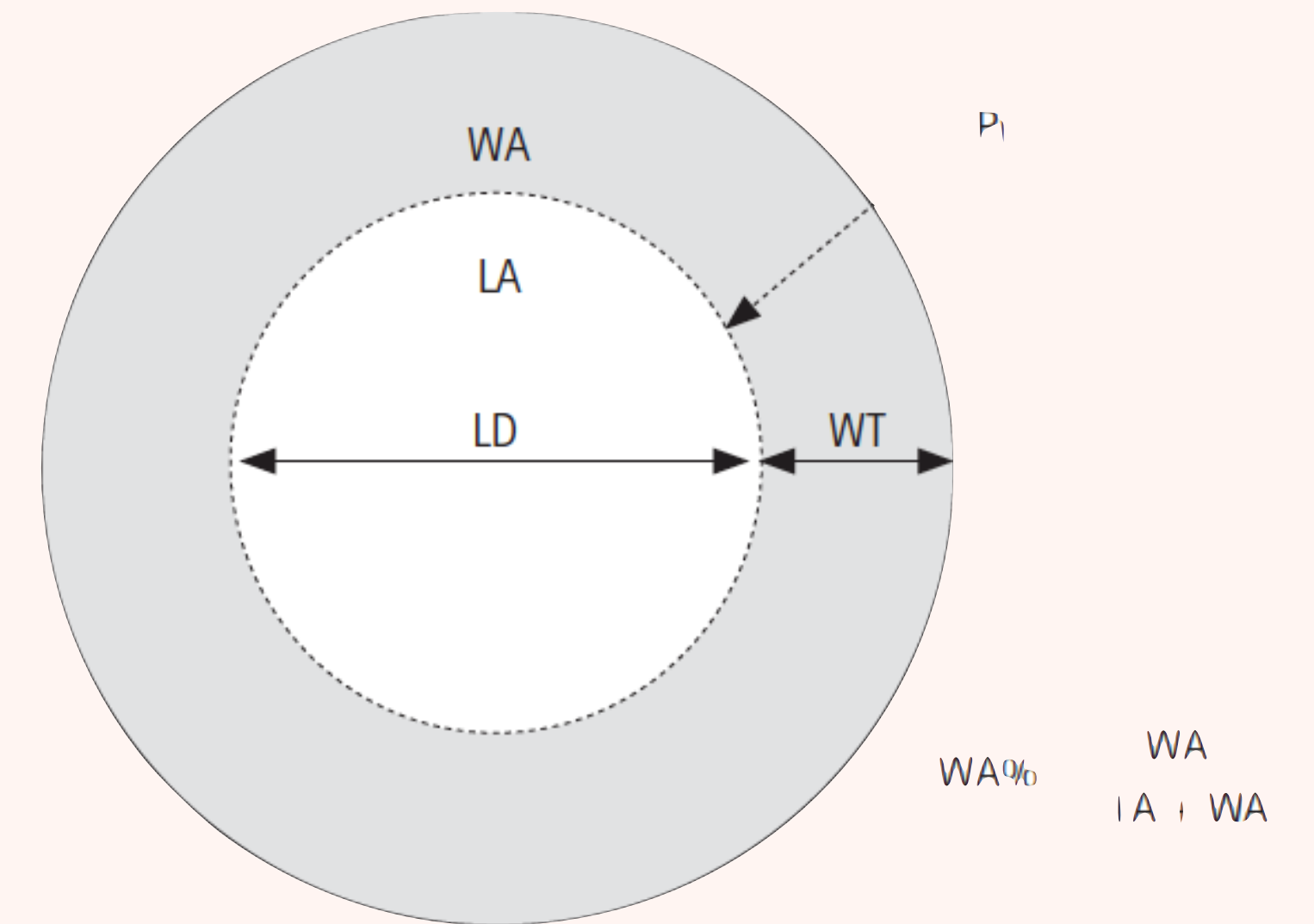
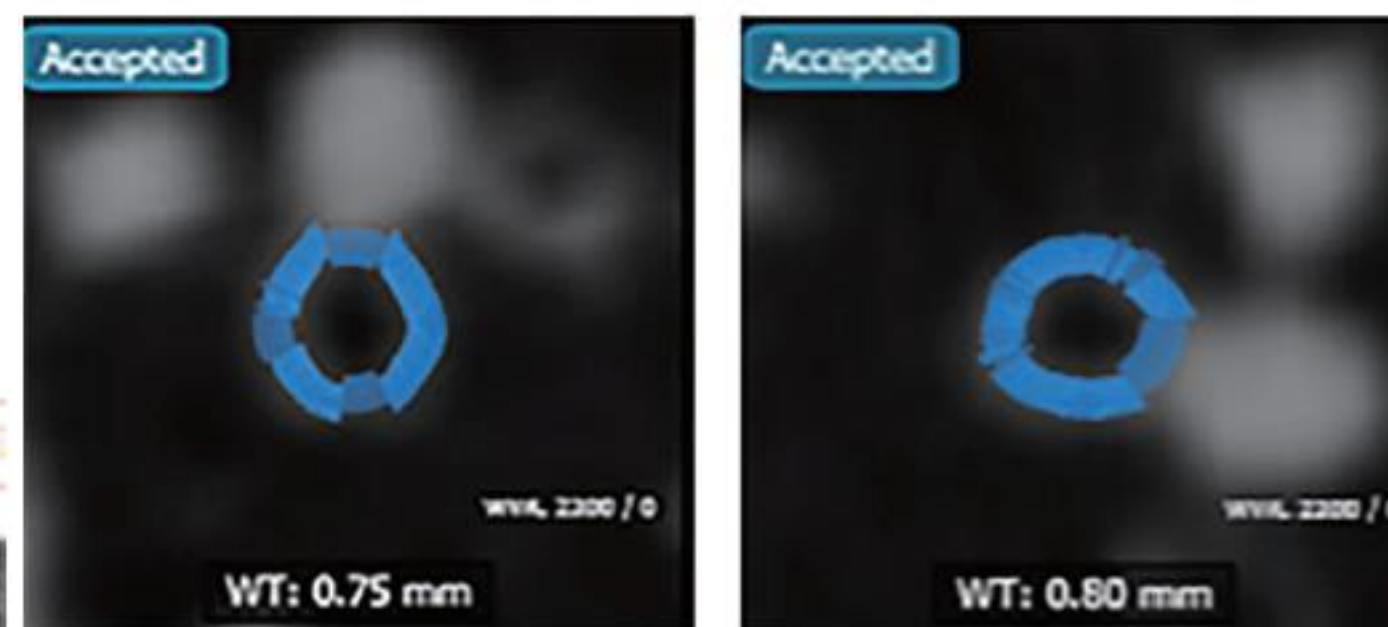
AIRWAY DISEASE

- Segmental, subsegmental, and subsubsegmental bronchi of RB1, RB4, RB10 and LB1, LB4, LB10
 - airway wall thickness (WT)
 - luminal diameter (LD)
 - airway wall area percent (% wall area/total bronchial area, WA%)
 - Square root of the wall area at an internal airway perimeter of 10 mm (Pi10)
-

AIRWAY DISEASE



Automatic measurement



LA = lumen area, LD = lumen diameter, Pi = internal perimeter,
 WA = wall area, WA% = wall area percentage, WT = wall thickness

QCT MEASUREMENTS FOR AIRWAY DISEASE CORRELATED WITH PHYSIOLOGICAL INDICES.

Correlation coefficients (p value) between QCT measurements and physiological measurements

QCT parameter	FEVI % predicted	FEVI/FVC ratio	FEF25-75%	Raw	sGaw
%LAA_950ins	-0.575 (<0.001)	-0.685 (<0.001)	-0.425, (<0.001)	0.083 (0.259)	-0.397, (<0.001)
%LAA_856exp	-0.730, (<0.001)	-0.802 (<0.001)	-0.590 (<0.001)	0.254 (<0.001)	-0.592 (<0.001)
RVC—856 to —950	-0.765 (<0.001)	-0.733 (<0.001)	-0.606 (<0.001)	0.266 (<0.001)	-0.515 (<0.001)
E/I-ratio MLD	-0.796 (<0.001)	-0.773 (<0.001)	-0.648 (<0.001)	0.332 (<0.001)	-0.624 (<0.001)
Pi10	-0.289 (<0.001)	-0.212 (0.003)	-0.298 (<0.001)	0.304 (<0.001)	-0.328 (<0.001)
Mean airway wall area% (segmental)	-0.355 (<0.001)	-0.267 (<0.001)	-0.433 (<0.001)	0.434 (<0.001)	-0.489 (<0.001)
Mean airway wall area% (subsegmental)	-0.438 (<0.001)	-0.338 (<0.001)	-0.541 (<0.001)	0.531 (<0.001)	-0.496 (<0.001)
Mean airway wall area% (subsubsegmental)	-0.438 (<0.001)	-0.295 (<0.001)	-0.490 (<0.001)	0.496 (<0.001)	-0.369 (<0.001)
Mean airway wall thickness (segmental)	0.043 (0.555)	-0.029 (0.694)	0.175 (0.016)	-0.253 (<0.001)	0.052 (0.477)
Mean airway wall thickness (subsegmental)	0.102 (0.102)	0.099 (0.177)	0.174 (0.017)	-0.240 (0.001)	0.063 (0.390)
Mean airway wall thickness (subsubsegmental)	0.0038 (0.603)	0.057 (0.434)	0.133 (0.069)	-0.205 (0.005)	0.056 (0.446)
Mean luminal diameter (segmental)	0.306 (<0.001)	0.203 (0.005)	0.445 (<0.001)	-0.496 (<0.001)	0.395 (<0.001)
Mean luminal diameter (subsegmental)	0.352 (<0.001)	0.267 (<0.001)	0.506 (<0.001)	-0.515 (<0.001)	0.416 (<0.001)
Mean luminal diameter (subsubsegmental)	0.324 (<0.001)	0.247 (0.001)	0.471 (<0.001)	-0.485 (<0.001)	0.357 (<0.001)
Visual assessment of severity of airway disease	-0.264 (<0.001)	-0.247 (0.001)	-0.334 (<0.001)	0.211 (0.004)	-0.313 (<0.001)

Subtyping COPD by Using Visual and Quantitative CT Imaging Features



*Jinkyong Park, MD, PhD; Brian D. Hobbs, MD; James D. Crapo, MD; Barry J. Make, MD; Elizabeth A. Regan, MD, PhD; Stephen Humphries, PhD; Vincent J. Carey, PhD; David A. Lynch, MB, BCh; Edwin K. Silverman, MD, PhD; for the COPDGene Investigators**

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INTEGRATE VISUAL AND QUANTITATIVE CT IMAGING PHENOTYPES WITH SPIROMETRY

1 No emphysema or airway abnormality

- All of the following criteria are met:
 - + No quantitative emphysema (LAA-950 <5%)
 - + Absent or trace CLE, and absent or mild paraseptal emphysema on visual analysis
 - + Bronchial wall thickening absent or mild on visual analysis
 - + Absence of significant gas trapping (LAA-856 < 20%)
 - + FEV1/FVC ratio ≥ 0.7 , and/or FEV1 $\geq 80\%$ predicted

2 Paraseptal Emphysema (PSE)

- Substantial PSE by visual score (regardless of other emphysema assessments)

3 Bronchial Airway Disease (BD)

- All of the following criteria are met:
 - + No quantitative emphysema (LAA-950 <5%)
 - + Absent or trace emphysema, and absent or mild paraseptal emphysema on visual analysis
 - + Bronchial wall thickening present on visual analysis

4 Small Airways Disease (SAD)

- All of the following criteria are met:
 - + No quantitative emphysema (LAA-950 <5%)
 - + Absent or trace emphysema, and absent or mild paraseptal emphysema on visual analysis
 - + Bronchial wall thickening absent or mild on visual analysis
 - + One or more positive indices for airway obstruction: Significant gas trapping (LAA-856 >20%) and/or FEV1/FVC ratio <0.7, and FEV1 < 80% predicted

5 Mild Centrilobular Emphysema (CLE)

- One of the following criteria is met:
 - + Absent or mild paraseptal emphysema
 - + Mild CLE by Fleischner visual score or
 - + Absent or trace CLE by Fleischner visual score and LAA-950 $\geq 5\%$ and <10%

6 Mod-to-Severe CLE; Upper dominant

- Absent or mild paraseptal emphysema
- (Upper third)/(lower third) ratio of LAA-950 > 2 and either:
 - Moderate CLE by Fleischner visual score and LAA-950 $\geq 5\%$
- or
- Confluent or advanced destructive emphysema by Fleischner visual score, and LAA-950 $\geq 10\%$

7 Mod-to-Severe CLE; Lower dominant

- Absent or mild paraseptal emphysema
- (Upper third)/(lower third) ratio of LAA-950 < 0.5 and either:
 - Moderate CLE by Fleischner visual score and LAA-950 $\geq 5\%$
- or
- Confluent or advanced destructive emphysema by Fleischner visual score, and LAA-950 $\geq 10\%$

8 Mod-to-Severe CLE; Diffuse

- Absent or mild paraseptal emphysema
- (Upper third)/(lower third) ratio of LAA-950 ≤ 2 and ≥ 0.5 and either:
 - Moderate CLE by Fleischner visual score and LAA-950 $\geq 5\%$
- or
- Confluent or advanced destructive emphysema by Fleischner visual score, and LAA-950 $\geq 10\%$

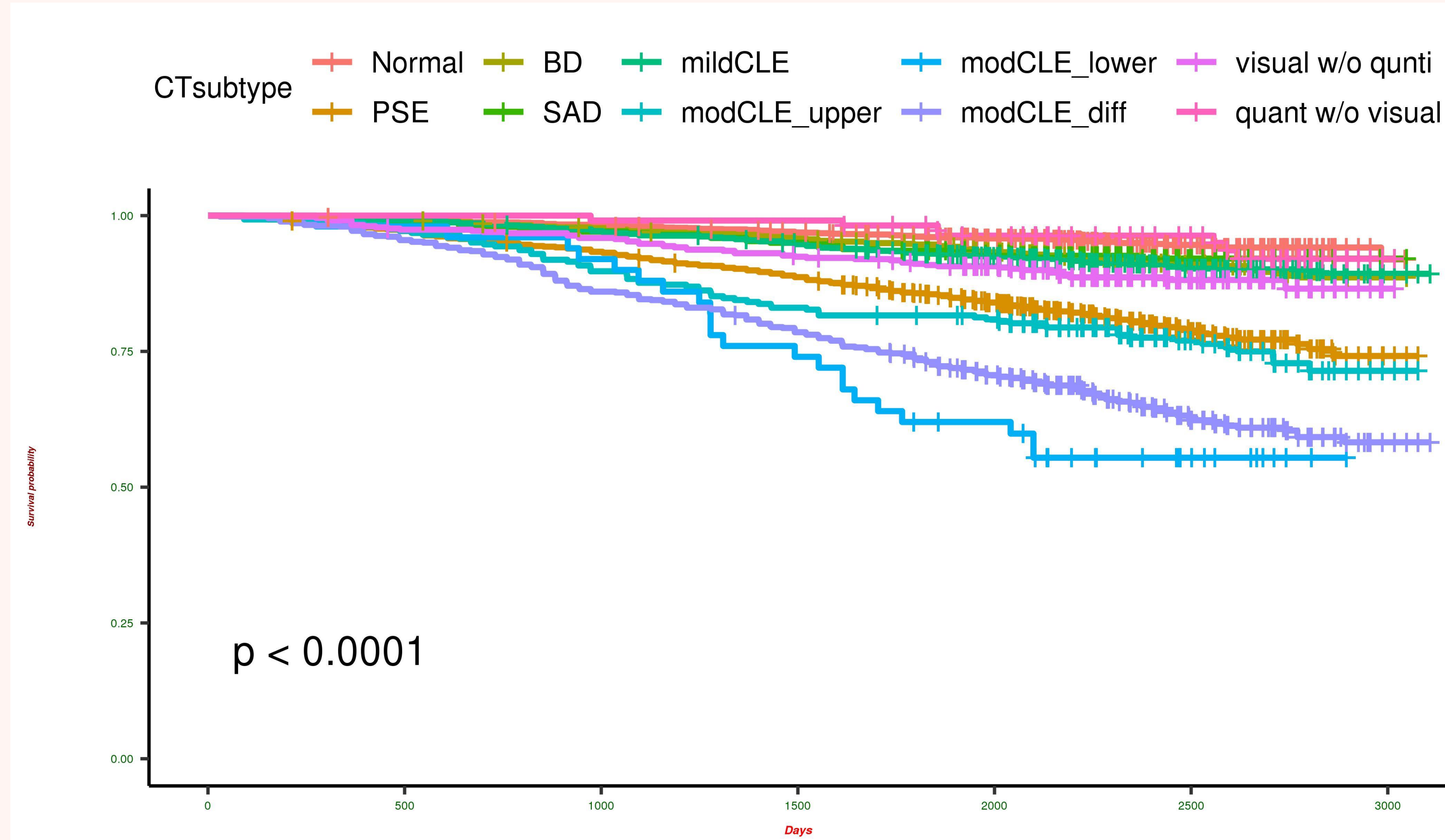
9 Discordant – Visual Emphysema W/O Quantitative Emphysema

- Absent or mild paraseptal emphysema
- Moderate CLE by Fleischner visual score and LAA-950 <5%
- or
- Confluent or advanced destructive emphysema by Fleischner visual score, and LAA-950 <10%

10 Discordant – Quantitative Emphysema W/O Visual Emphysema

- Absent or mild paraseptal emphysema
- Absent or trace emphysema on visual analysis, and LAA-950 $\geq 10\%$

RISK FOR ALL-CAUSE DEATH IN SMOKERS ACCORDING TO INTEGRAL METHOD



SUMMARY

- smokers were categorized into 10 nonoverlapping subtypes based on chest CT imaging and spirometric characteristics
 - These 10 subtypes had substantial differences in their rates of radiological, physiological, and symptom progression, as well as in mortality.
 - the combination of visual and quantitative CT imaging features, which may reflect different underlying pathobiological processes in COPD, may provide a superior approach to classify COPD compared with the use of visual or quantitative CT imaging features alone.
-