

Evaluation of COPD using CT imaging and the synergistic role of impulse oscillometry

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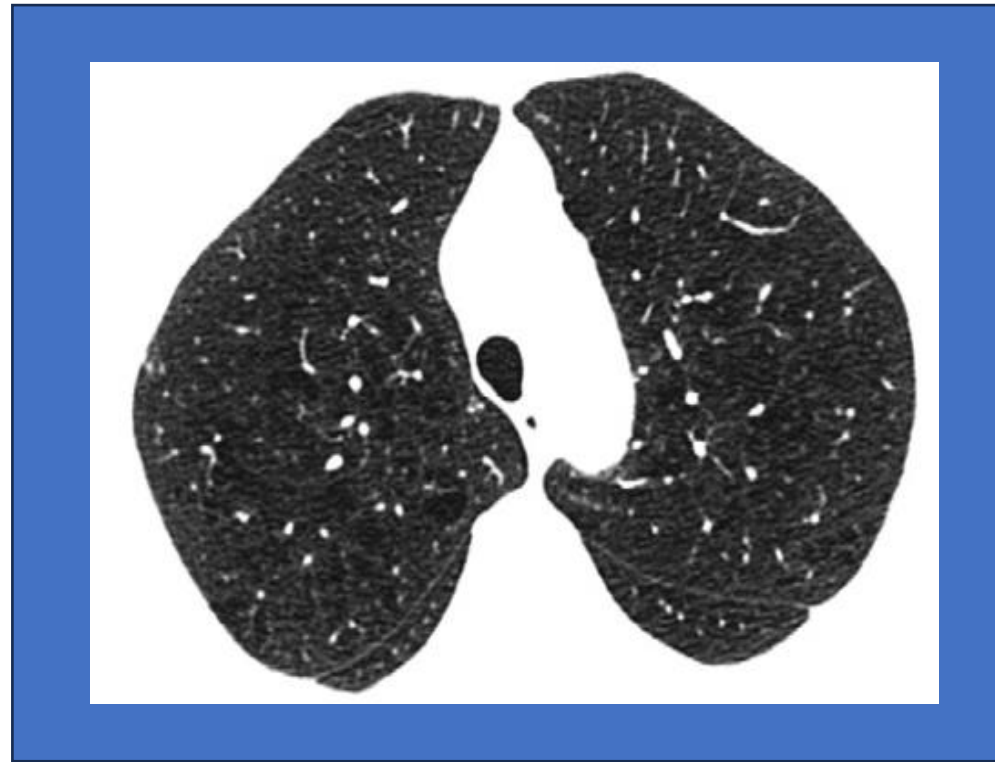
Contents

- Quantification of CT imaging in COPD
 - Emphysema
 - Direct airway measurement
 - Small airway measurement : Quantification of air trapping
- Impulse oscillometry for small airway disease and early detection of disease progression

Quantification of CT imaging in COPD

Assessment to diagnose the patients as COPD?

- COPD is diagnosed as the spirometry, by the presence of a post-bronchodilator FEV₁/FVC ratio less than 0.70.



COPD ?

M/55 with smoker, FEV₁/FVC > 0.7

Quantitative imaging parameters in COPD

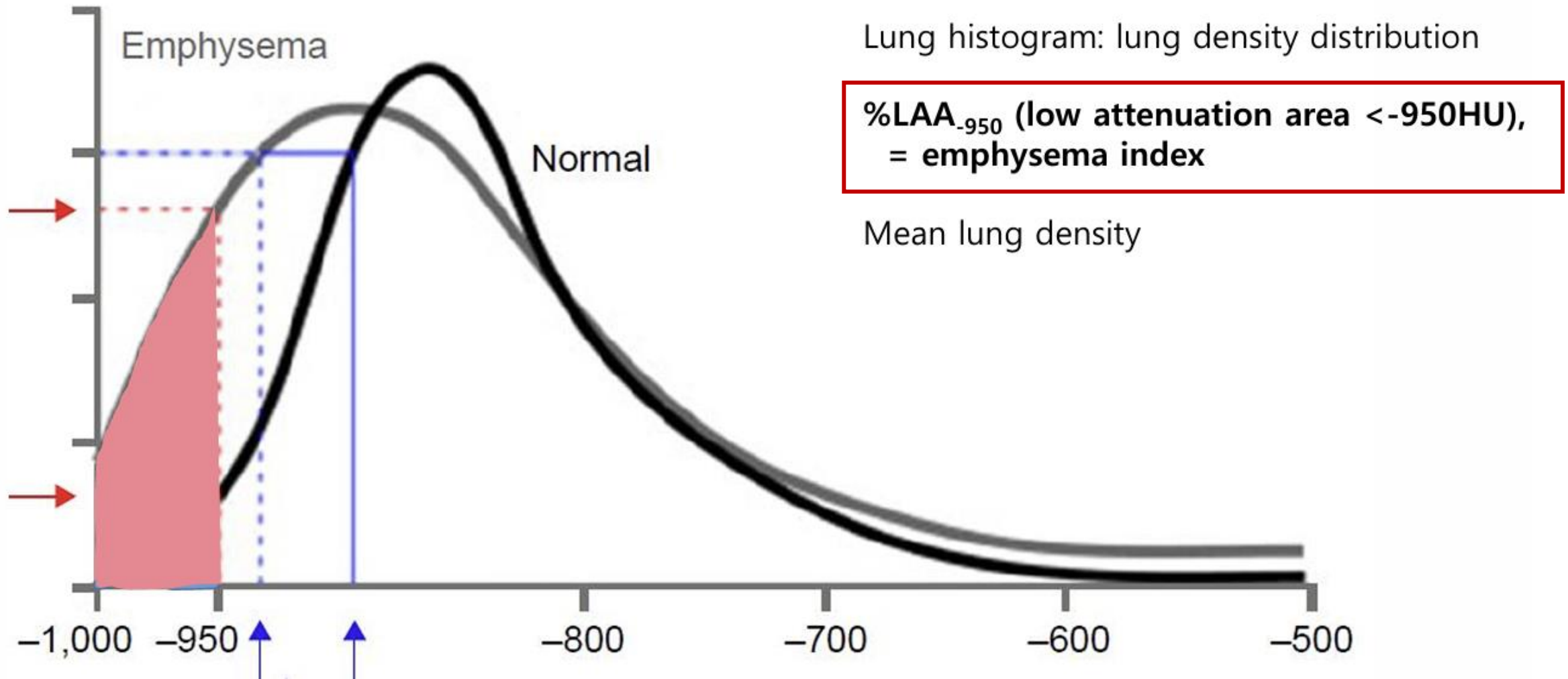
- Major components of COPD
 - Emphysema
 - Small airway disease - Direct airway measurement
 - Quantification of air trapping

- Comorbidities
 - pulmonary vessel alterations
 - atherosclerosis
 - cachexia
 - osteoporosis

Quantitative CT measurement of emphysema

- Emphysema appears as a region of relatively lower CT attenuation, expressed as **lower Hounsfield units (HU)**.
- The most commonly accepted threshold value is -950 HU, **with the percentage area of lung less than -950 HU (the emphysema index, or %LAA-950)** being widely used to estimate the emphysema component in COPD patients.

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- The most commonly accepted threshold value is -950 HU, **with the percentage area of lung less than -950 HU (the emphysema index, or %LAA-950)** being widely used to estimate the emphysema component in COPD patients.
- **The measurement of % low attenuation areas, while it correlates moderately well with histologic severity of emphysema, is not a direct measurement of emphysema.**

Quantitative CT measurement of emphysema

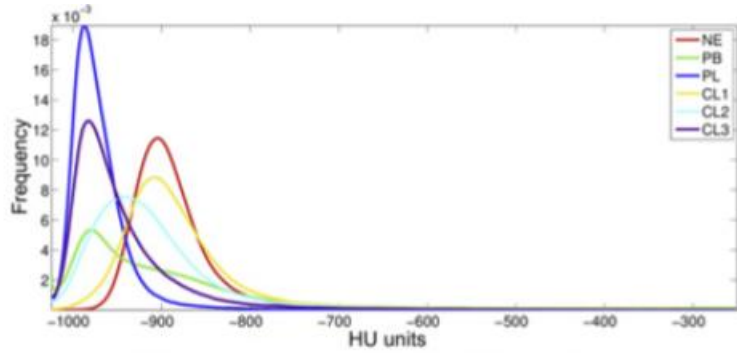


Distinct Quantitative CT Emphysema Patterns Are Associated with Physiology and Function in Smokers

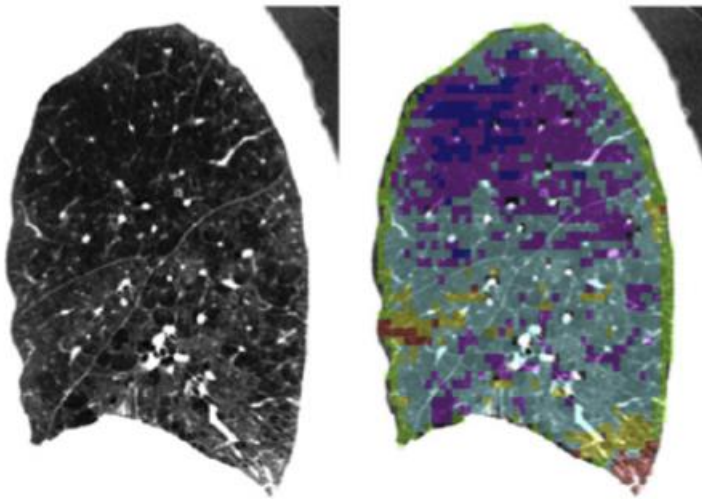
- Between 2007 and 2011, 10,192 non-Hispanic white (n = 6,784) and African-American (n = 3,408) smokers were enrolled into the COPDGene Study as a multicenter study

	All Subjects	GOLD U*	GOLD 0 [†]	GOLD 1	GOLD 2–4
N	9,313	1,113	4,069	746	3,385
Age, mean (SD)	60 (9)	57 (8)	57 (8)	62 (9)	63 (9)
Sex, % female	46	54	47	42	44
Race, % African-American	32	42	40	22	22
Pack-years, median (IQR)	39 (27)	38 (26)	34 (23)	40 (26)	47 (32)
FEV ₁ , % of predicted, mean (SD)	77 (25)	71 (8)	98 (12)	91 (9)	51 (18)
Emphysema at –950 HU, median (IQR)	2 (6)	1 (1)	1 (2)	3 (6)	8 (18)
NE, median (IQR)	64 (43)	72 (25)	74 (22)	60 (36)	32 (48)
CL1, median (IQR)	24 (16)	23 (18)	21 (15)	26 (15)	26 (16)
CL2, median (IQR)	5 (16)	2 (4)	2 (4)	7 (13)	22 (33)
CL3, median (IQR)	0 (1)	0 (0)	0 (0)	0 (1)	1 (7)
PL, median (IQR)	0 (0)	0 (0)	0 (0)	0 (0)	0 (3)
PB, median (IQR)	2 (4)	2 (2)	2 (2)	3 (4)	5 (7)

Distinct Quantitative CT Emphysema Patterns Are Associated with Physiology and Function in Smokers

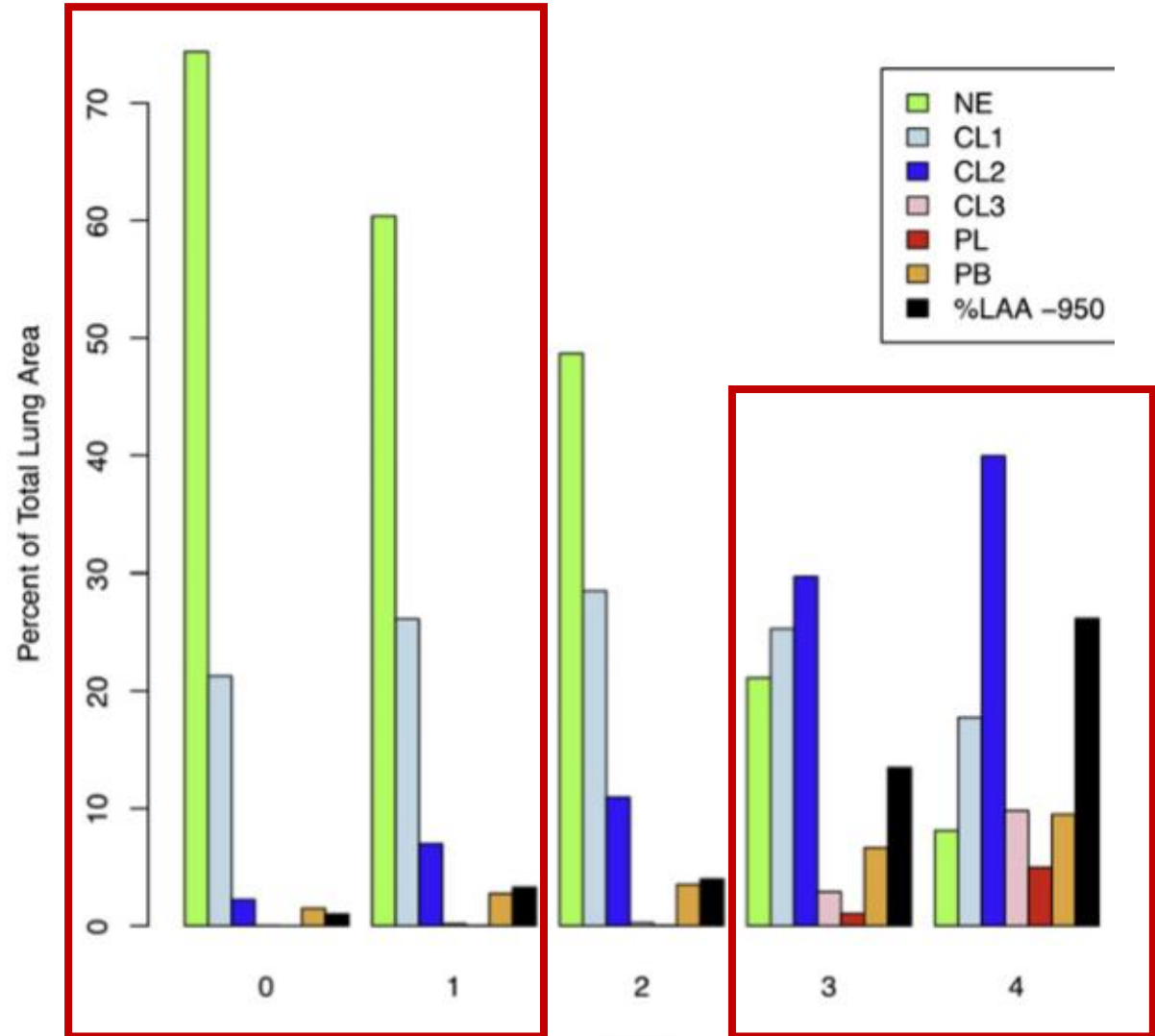


NE: Normal (non emphysema) CL1: Mild Centrilobular
 PB: Pleural-based CL2: Moderate Centrilobular
 PL: Panlobular CL3: Severe Centrilobular



Legend for CT patterns:

- Non-Emphy. (Red)
- Mild Centrilob. (Yellow)
- Moderate Centrilob. (Blue)
- Severe Centrilob. (Purple)
- Panlobular (Dark Blue)
- Pleural-based (Green)



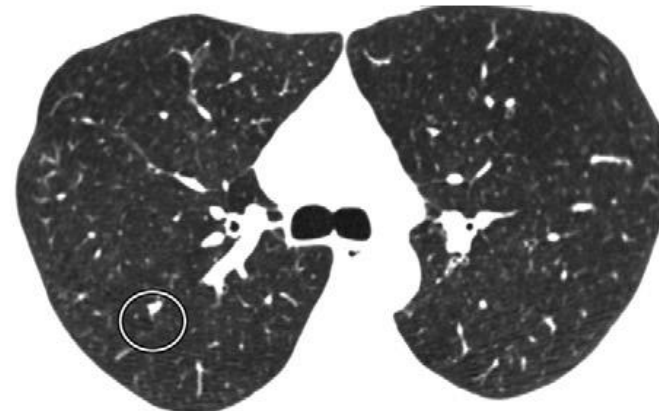
Visual classification of emphysema & association with mortality

- From 2007 to 2011 in COPDGene cohort, 3171 smoker had data available for both visual emphysema CT scores and survival.
- Severity of emphysema was also evaluated quantitatively by using LAA-950.



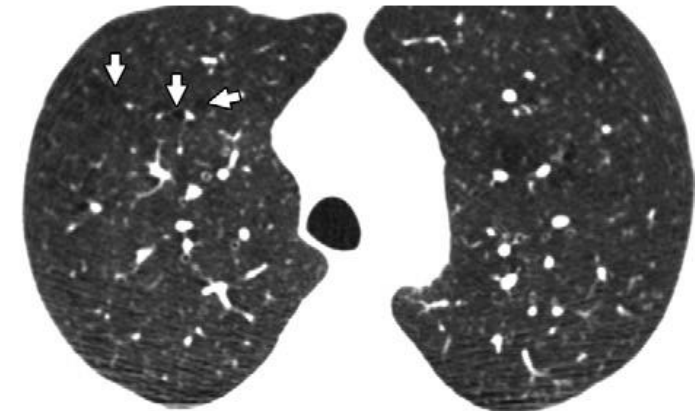
a.

Normal



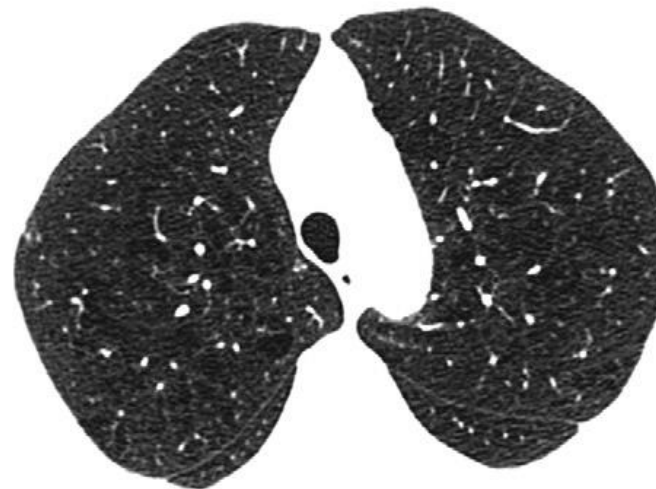
b.

<0.5%, trace



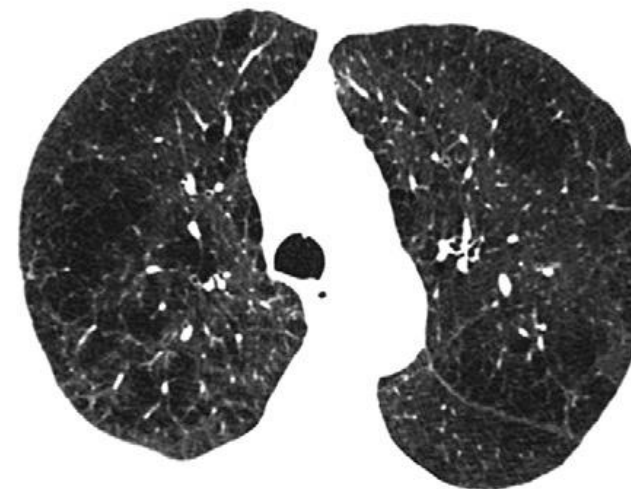
c.

<5%, mild



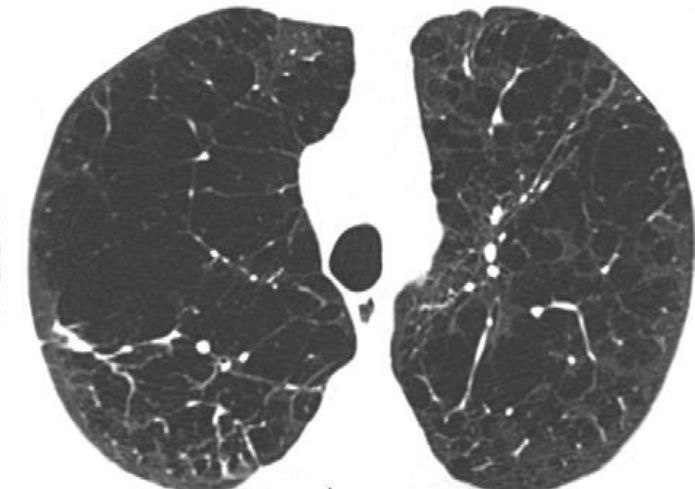
d.

Mean 10.1%, moderate



e.

Mean 23.5%, confluent

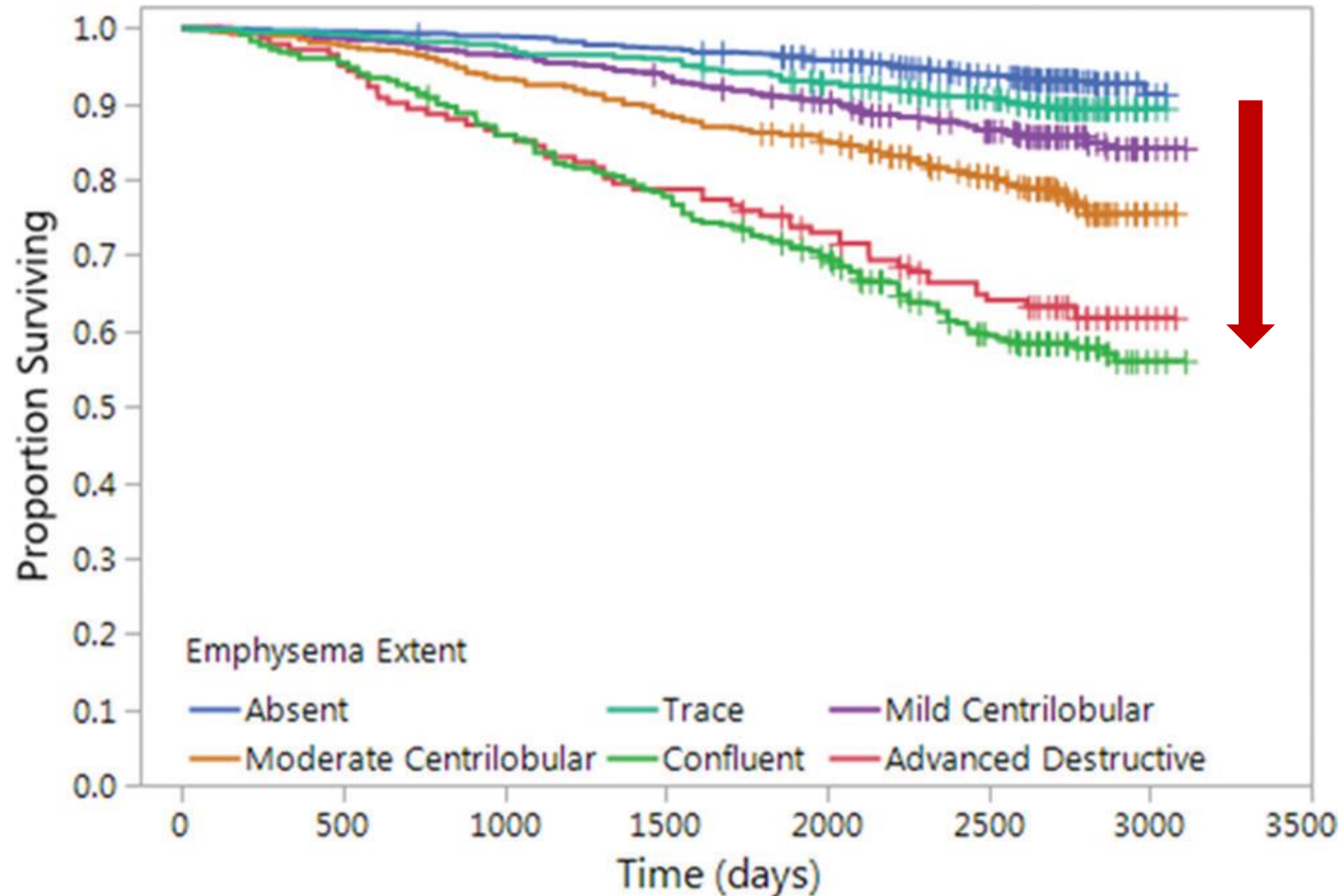


f.

Mean 34.0%, advanced destructive

Visual classification of emphysema & association with mortality

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- Severity of emphysema was also evaluated quantitatively by using LAA-950.



CT imaging in KOCOSS cohort

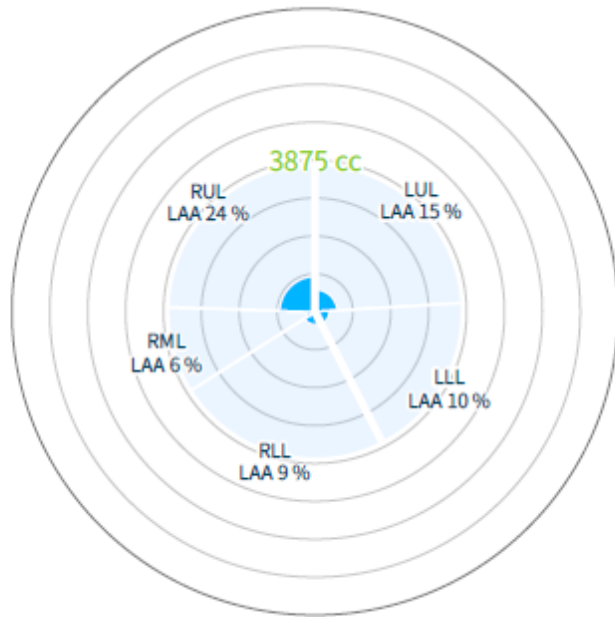
- From the KOCOSS cohort, Chest CT of **484 patients with COPD** have analyzed.

LAA (≤ -950 HU) 14 % D-Slope -3.95

INSP

* According to the Fleischner Society Statement (Lynch DA, et al., Radiology 2015), there is no significant emphysema if LAA is less than 6%.

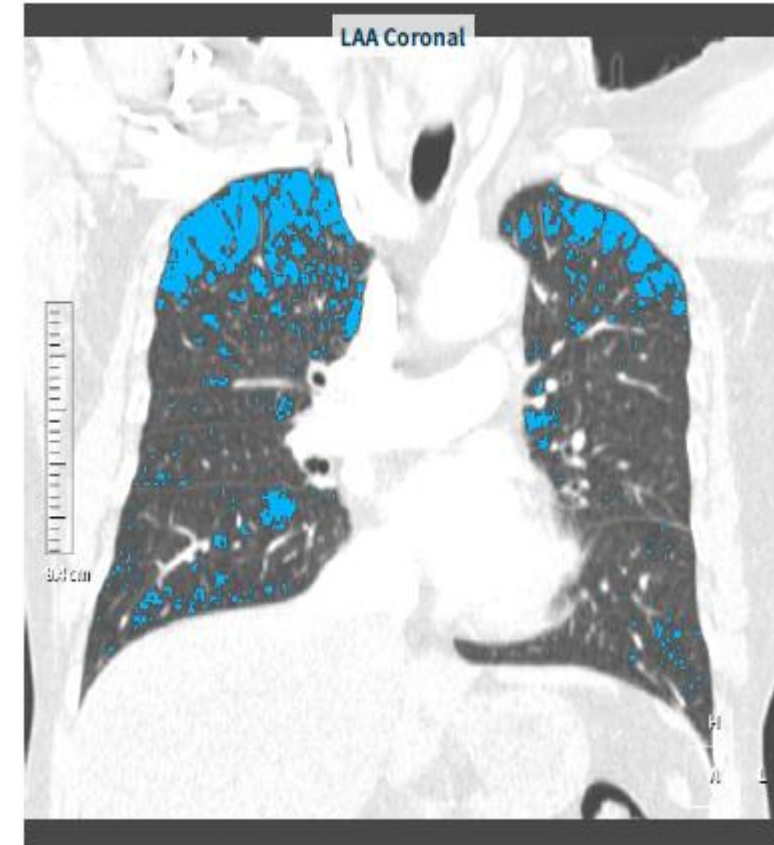
LAA Chart



Rt. Lung: 15 % Lt. Lung: 13 %

LAA Table

Regions	Volume	LAA	MLD	PI-15
Whole Lungs	3875 cc	14 %	-826 HU	-946 HU
Rt. Lung	2231 cc	15 %	-834 HU	-949 HU
Lt. Lung	1644 cc	13 %	-816 HU	-942 HU
RUL	949 cc	24 %	-862 HU	-974 HU
RML	367 cc	6 %	-842 HU	-929 HU
RLL	915 cc	9 %	-801 HU	-927 HU
LUL	932 cc	15 %	-832 HU	-950 HU
LLL	712 cc	10 %	-795 HU	-929 HU

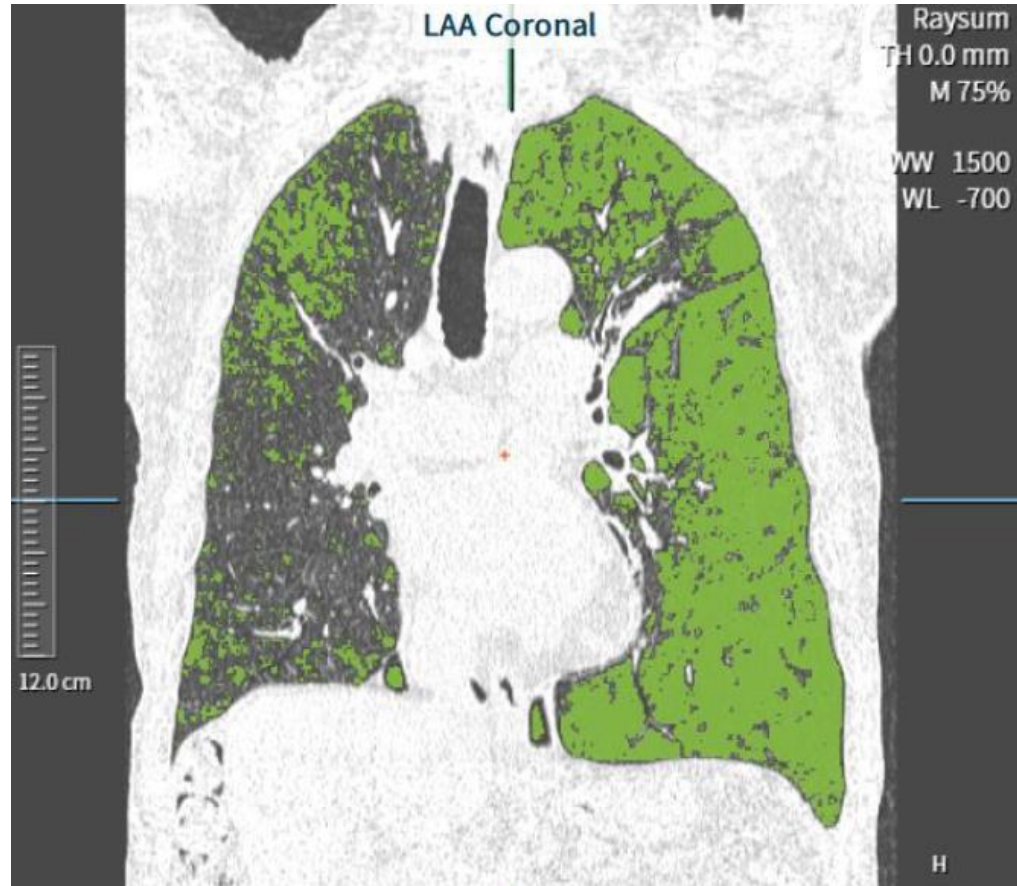


Technical hurdle in emphysema quantification of KOCOSS cohort

- Radiation dose
- CT from different companies - GE, Philips, SIEMENS
- Reconstruction kernel
- Reconstruction thickness - Smart slicer
- Respiration

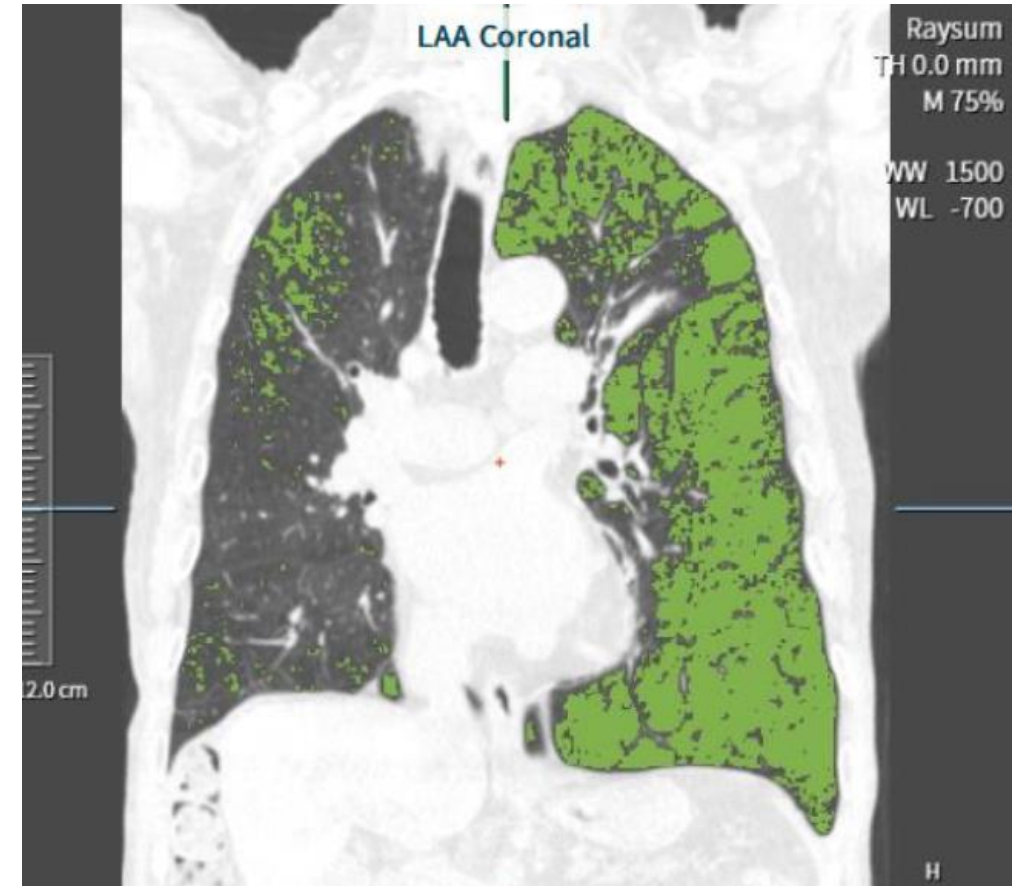
Difference between sharp and smooth kernel

LAA ($\leq -950\text{HU}$) 50%



Sharp kernel

LAA ($\leq -950\text{HU}$) 41%



Smooth kernel

Kernel conversion of emphysema in KOCOSS cohort

	Total N=484
Age (years)	67.78±8.14
Male sex (n, %)	444 (91.74)
Smoking status	
Never-smoker	67 (13.84)
Ex-smoker	314 (64.88)
Current smoker	103 (21.28)
Smoking amount (packs/years)	39.76±23.19
BMI	23.68±3.32
mMRC (mean, SD)	1.16±0.94
CAT score (mean, SD)	12.19±7.78
SGRQ-c score (mean, SD)	25.57±19.58
Pre-bronchodilator FVC (L)	3.48±0.87
Pre-bronchodilator FVC (%)	83.73±16.4
Pre-bronchodilator FEV ₁ (L)	1.89±0.68
Pre-bronchodilator FEV ₁ (%)	63.56±19.85
Post-bronchodilator FEV ₁ /FVC	0.56±0.13
GOLD stage	
Stage 1	102 (21.07)
Stage 2	261 (53.93)
Stage 3	104 (21.49)
Stage 4	17 (3.51)

[Correlation between emphysema index and variables]

	Original	Converted
FEV ₁	-0.35	-0.41
DLco	-0.44	-0.41
RV/TLC	0.31	0.42
mMRC	0.22	0.25
CAT scores	0.05	0.12
SGRQ-c scores	0.13	0.21
6MWD	-0.04	0.15

Uprising interest about CPFE and assessment of ILA/ILD

ILA/ILD (fibrosis)

Pattern N - Pattern of normal area without lesion

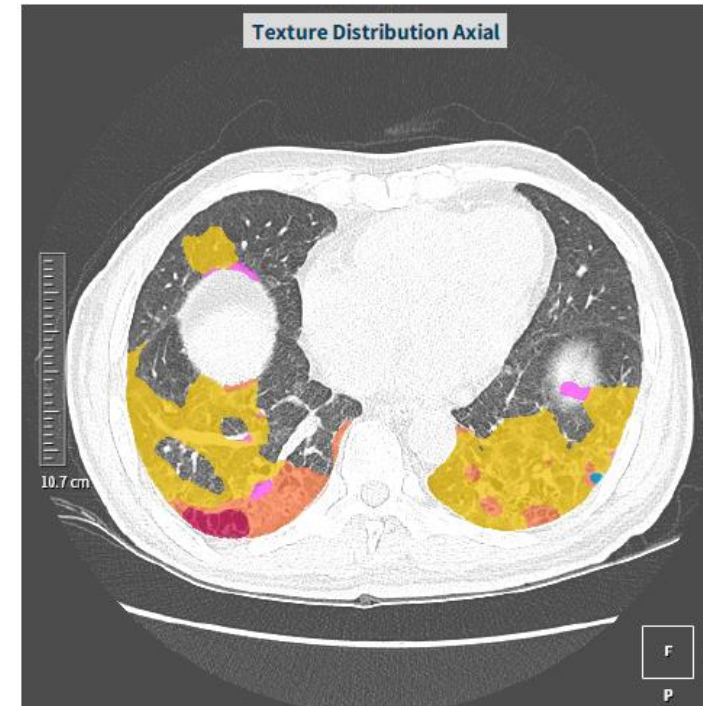
Pattern E - Pattern of dilated alveolar space

Pattern G - A pattern that looks like cloudy glass

Pattern R - Reticulated intricately intertwined pattern

Pattern H - honeycomb pattern

Pattern C - Pattern in the form of hardened soft tissue



	Whole Lungs	Rt. Lung	Lt. Lung
Volume	3699 cc	1898 cc	1801 cc
Pattern H	1 %	2 %	0 %
Pattern R	6 %	8 %	4 %
Pattern G	14 %	16 %	12 %
Pattern C	0 %	0 %	0 %
Pattern E	2 %	2 %	1 %
Pattern N	77 %	71 %	83 %

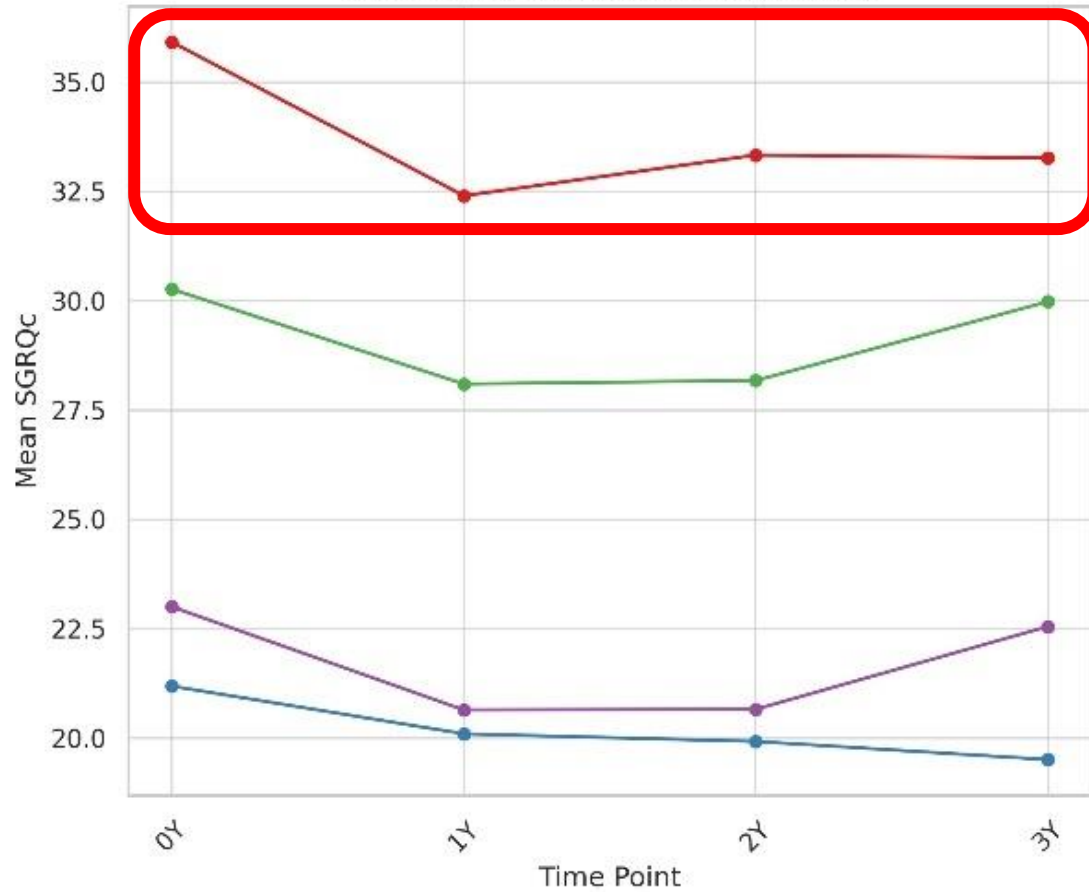
Adding the effect of fibrosis in COPD population

Total (n=587)	Fibrotic ILA of whole lung	
Emphysema of whole lung	≥ 1%	< 1%
≥ 5%	CPFE (n=54)	Emphysema (n=217)
< 5%	COPD with ILA (n=55)	Minimal change type (n=261)

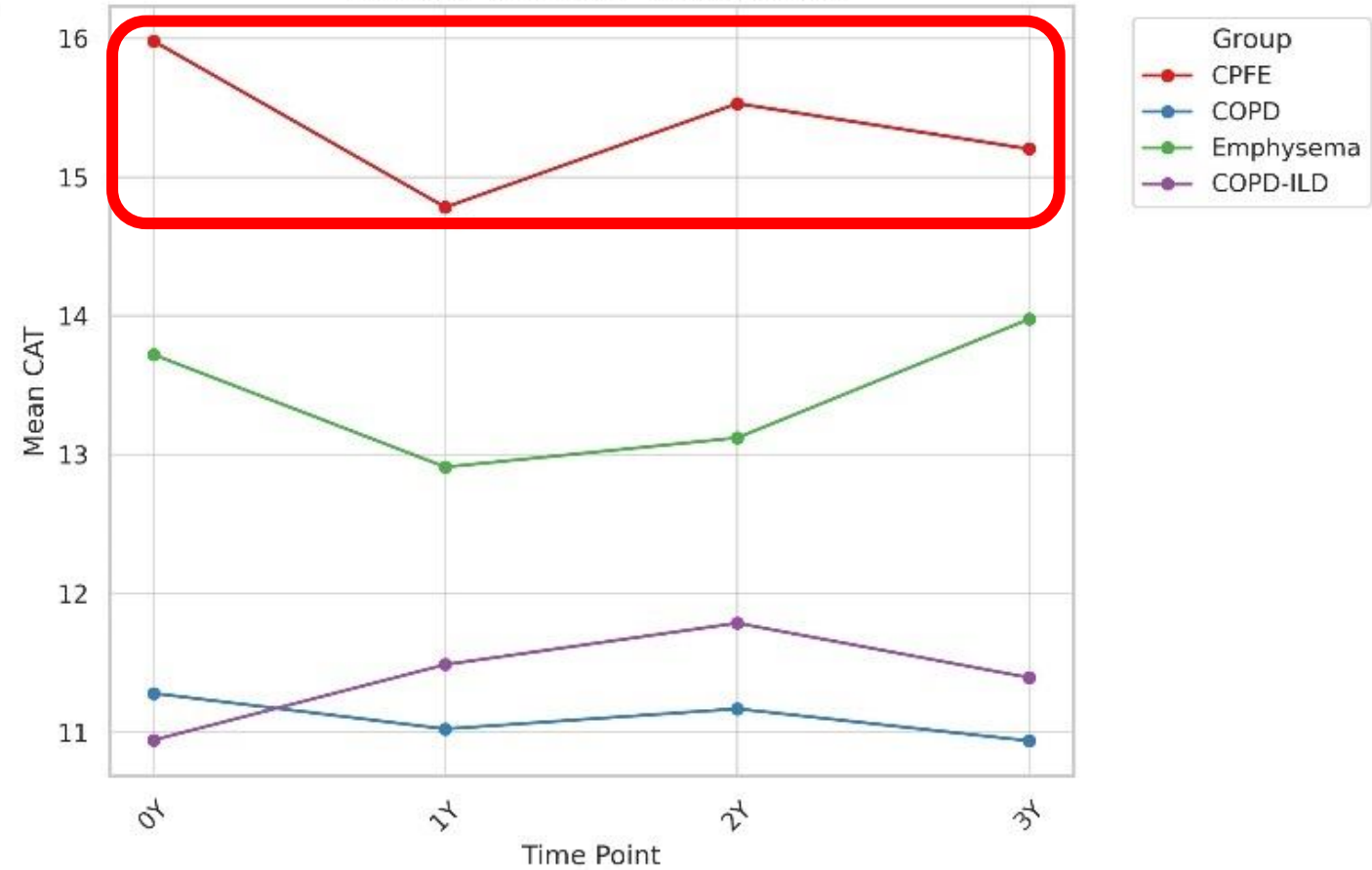
Lung function (mean ± SD)	CPFE (N=54)	Emphysema (N=217)	COPD with ILA (N=55)	Minimal change type (N=261)	p-value
TLC (L)	5.93±0.76	6.23±1.12	5.36±1.02	5.70±1.05	< 0.01
TLC (%)	97.2±12.2	104.3±14.2	88.2±13.2	94.4±12.7	< 0.01
BDR FVC (L)	3.39±0.74	3.43±0.92	3.16±0.69	3.53±0.85	0.04
BDR FVC (%)	80.6±15.0	84.5±17.2	77.7±15.7	84.6±15.2	0.02
BDR FEV1 (L)	1.65±0.51	1.60±0.64	1.92±0.55	2.14±0.67	< 0.01
BDR FEV1 (%)	56.3±18.0	55.1±18.5	68.4±18.6	71.1±17.2	< 0.01
DLCO (%)	48.5±20.8	60.9±19.5	62.4±16.9	77.0±18.3	< 0.01

Results – 3yr f/u of PROs

Mean SGRQc values over time by Group

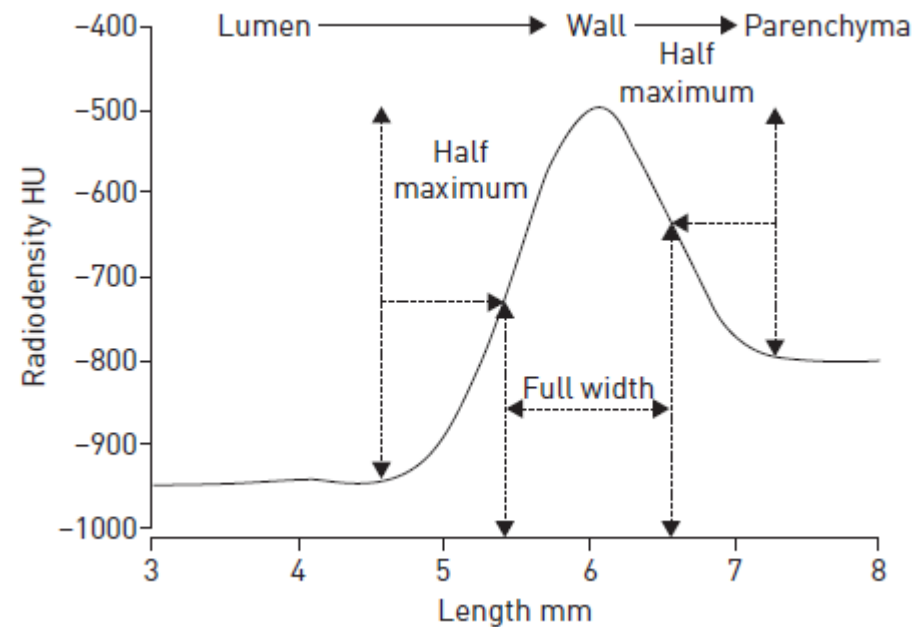


Mean CAT values over time by Group

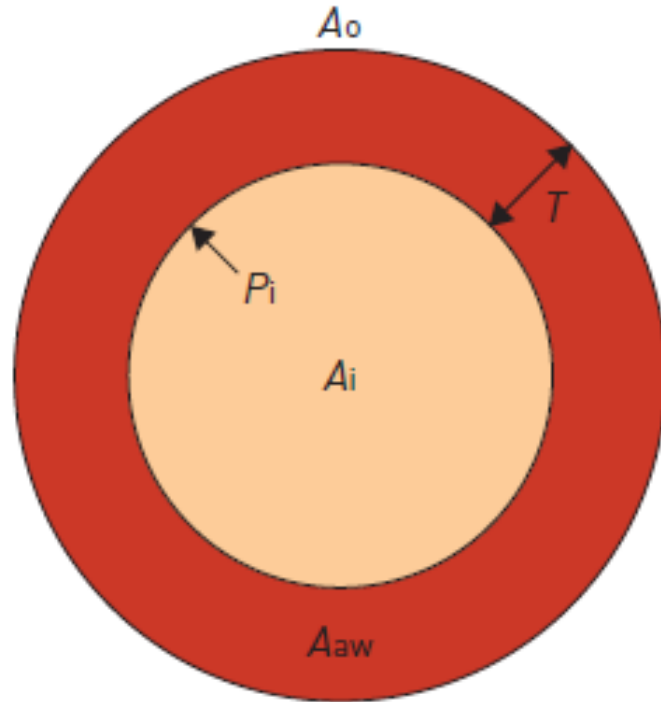


Airway measurement in COPD

- Small airway disease - Direct airway measurement
 - Quantification of air trapping
- Airway wall remodelling is an important feature in COPD, but the limited resolution of CT means only large and intermediate-sized airways can be visualized directly.
- One of the automated methods is the “full width at half maximum” principle.



Airway measurement in COPD

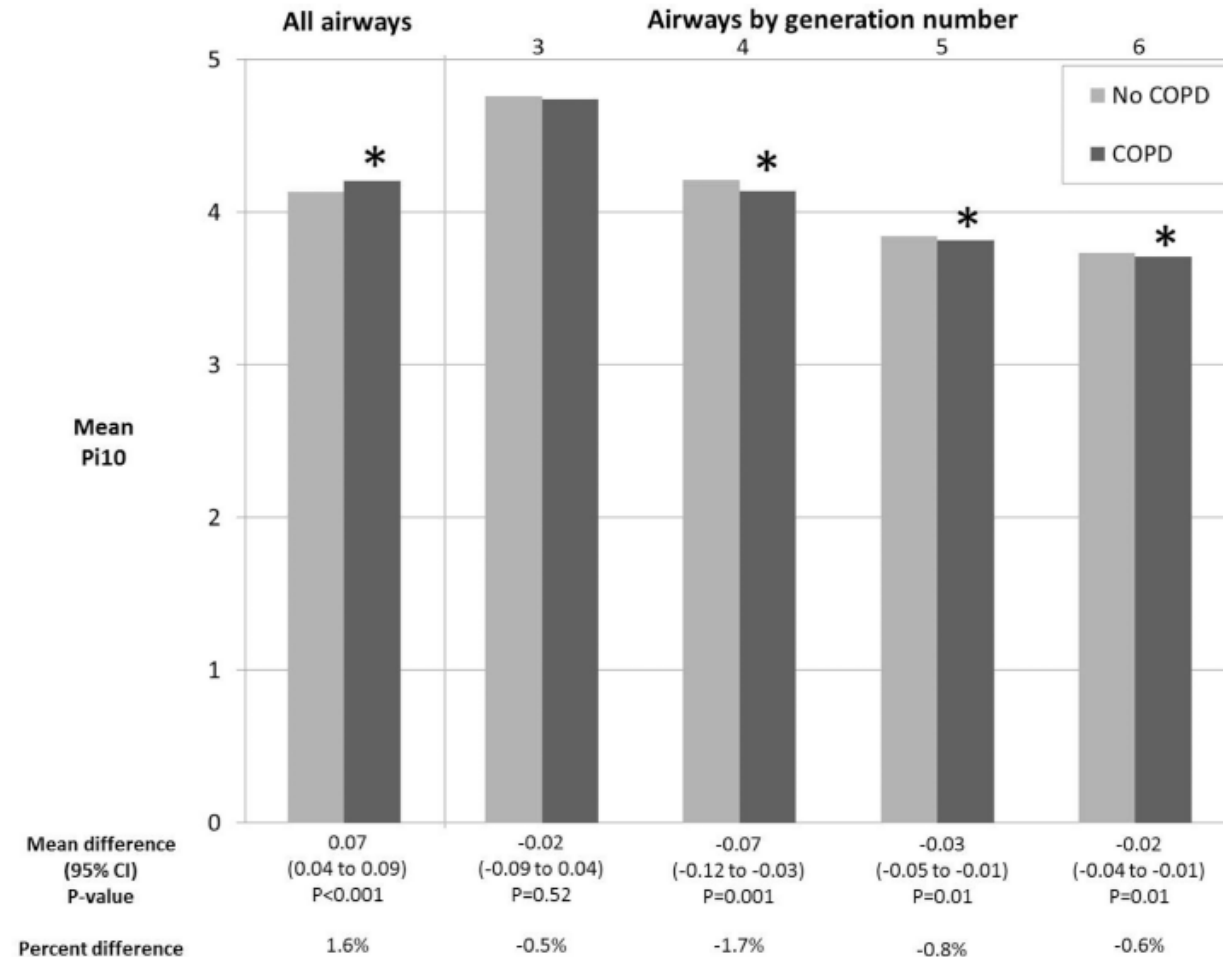


$$\%WA = \frac{A_{aw}}{A_o} \times 100$$

- A_{aw} : airway wall area
- T : wall thickness
- A_o : total airway area
- A_i : inner area
- P_i : internal perimeter
- $\%WA$: percentage wall area

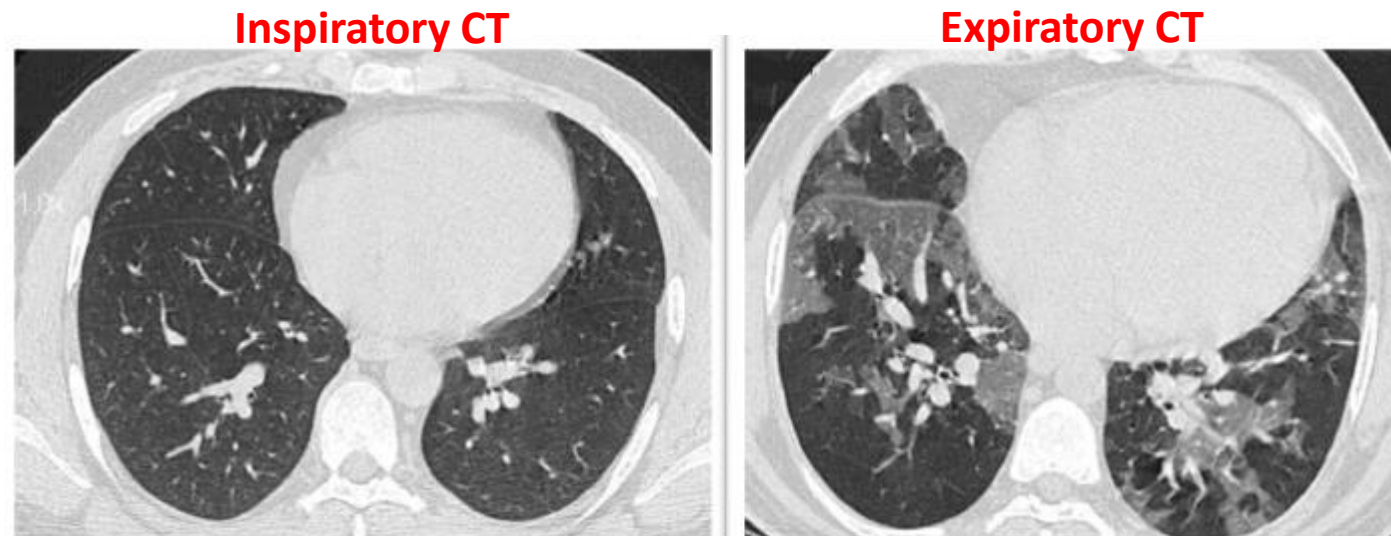
Thinner airway walls in COPD from MESA COPD study

- The MESA COPD Study and SPIROMICS recruited smokers with COPD and controls aged 50–79 years and 40–80 years.

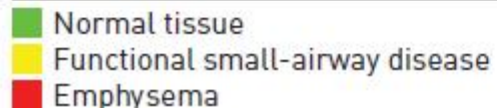
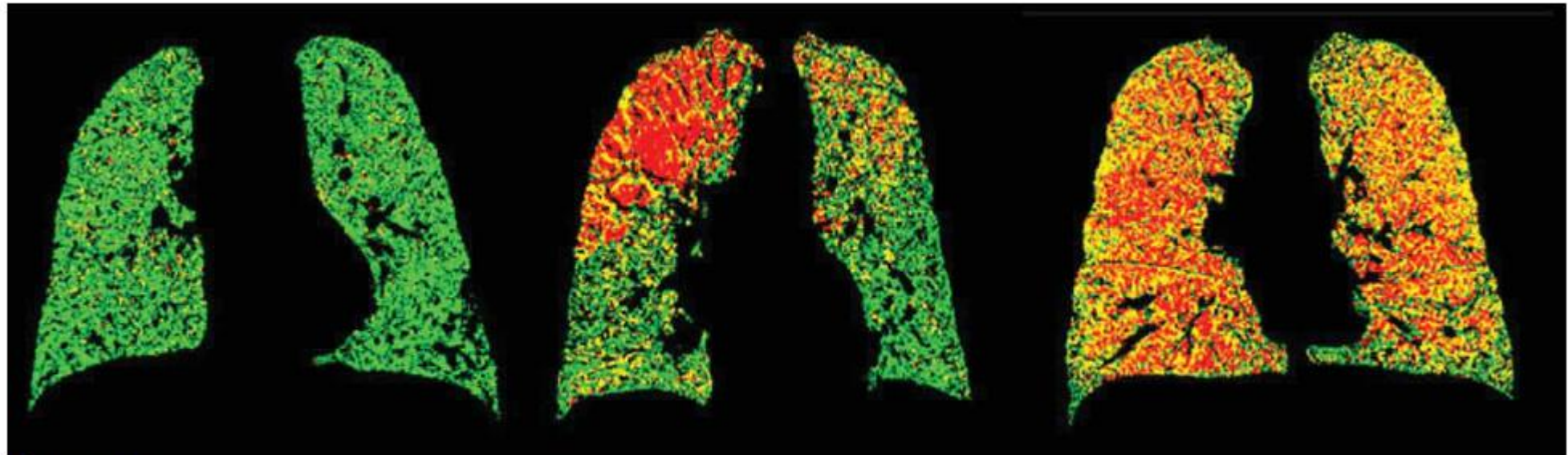
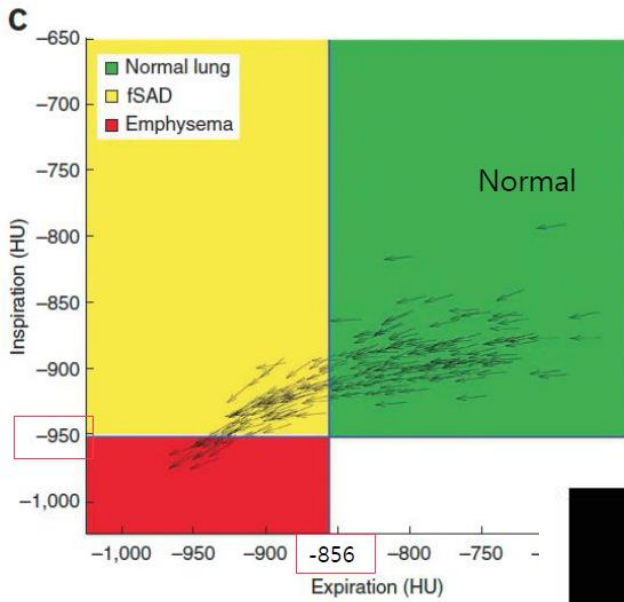


Assess to airway impairment in COPD

- Chest CT should be a useful tool at assessing the morphology of the large and intermediate-sized airways.
- However, there are still many uncertainties regarding this technology and measurements, and no definite evidence has shown that this is a particularly useful tool in COPD.
- **The small airways** are the main contributor to the airflow obstruction seen in COPD.
- There is currently no gold standard for measuring this small-airway disease and so better methods are required, and considerable research is ongoing in this area.
- The indirect sign of gas trapping can be used as a surrogate marker, and **the parametric response mapping (PRM)** using inspiratory and expiratory scan can be performed.



Parametric Response Mapping in COPD

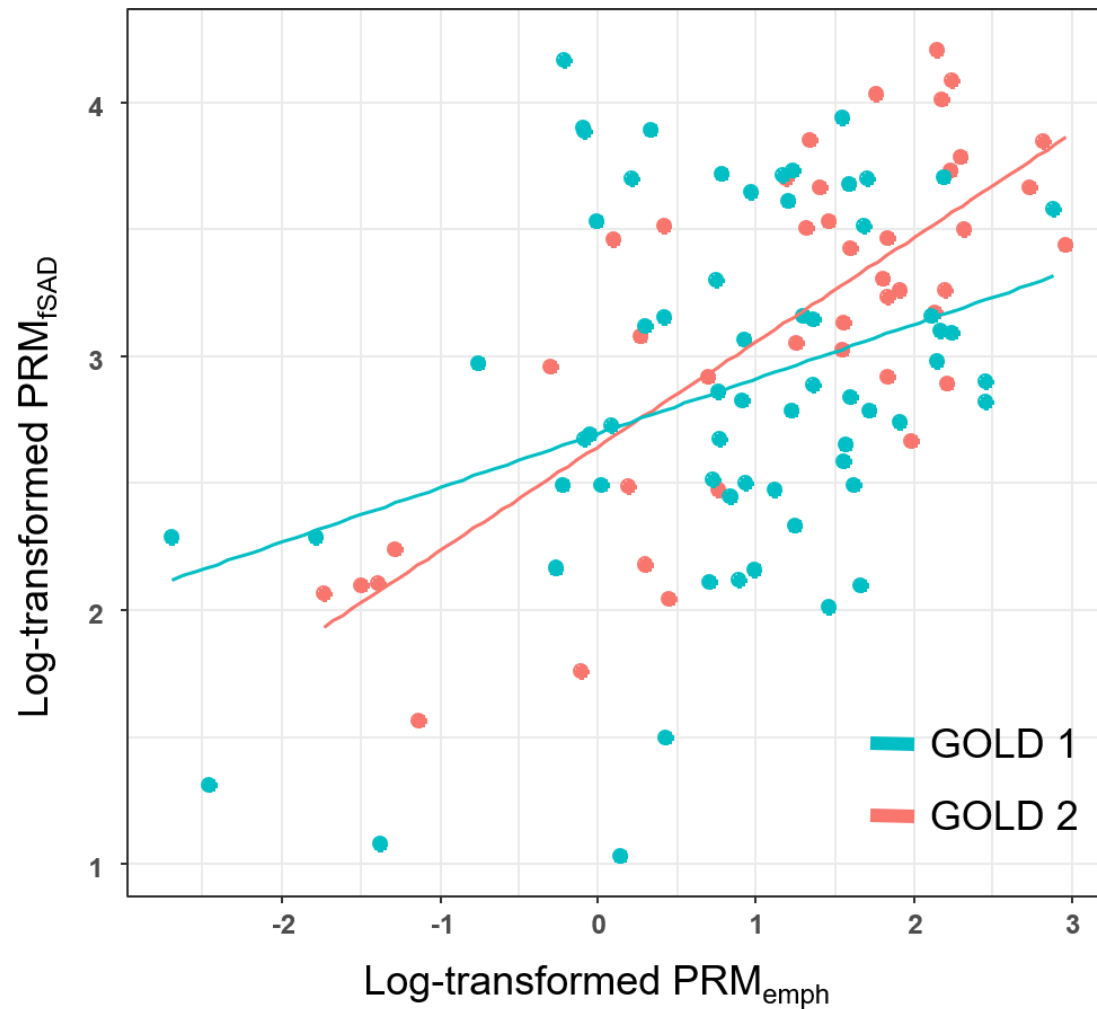


Longitudinal PRM on CT for fSAD and emphysema in COPD

- Longitudinal CT data of the COPD in Dusty Areas (CODA) cohort from 2012 to 2014

	Overall	GOLD 1 (n = 63)	GOLD 2 (n = 43)	P-value
Age (years)	70.9 (6.6)	72.2 (5.4)	69.0 (7.6)	0.013
Sex (male)	88 (83.0)	50 (79.4)	38 (88.4)	0.342
BMI (kg/m²)	23.6 (3.2)	24.0 (2.9)	23.1 (3.6)	0.15
Smoking status				0.2
Never	28 (26.4)	20 (31.7)	8 (18.6)	
Ever	78 (73.6)	43 (68.3)	35 (81.4)	
mMRC grade				
≥2	39 (36.8)	23 (36.5)	16 (37.2)	1.0
CAT				
≥10	76 (71.7)	45 (71.4)	31 (72.1)	1.0
Exacerbation in previous year				
≥2 moderate or ≥1 severe	3 (2.8)	1 (1.6)	2 (4.7)	0.736
Charlson comorbidity index				
≥2	12 (11.3)	8 (12.7)	4 (9.3)	0.818
Inhaler therapy	16 (15.1)	5 (7.9)	11 (25.6)	0.027
Lung function testing				
FVC (L)	3.1 (0.7)	3.2 (0.7)	2.9 (0.7)	0.017
FVC, % pred	94.8 (14.7)	101.8 (12.2)	84.5 (11.6)	<0.001
FEV ₁ (L)	2.0 (0.5)	2.2 (0.5)	1.8 (0.4)	<0.001
FEV ₁ , % pred	84.1 (15.8)	93.8 (12.1)	69.7 (7.3)	<0.001
FEV ₁ /FVC (%)	64.8 (6.9)	67.2 (5.6)	61.2 (7.2)	<0.001
PRM value				
PRM _{emph} (%)	4.3 (3.9)	3.6 (3.3)	5.4 (4.6)	0.022
PRM _{fSAD} (%)	24.3 (15.0)	22.1 (14.2)	27.5 (15.7)	0.065

Correlation between PRM_{fSAD} and PRM_{emph}



$p < 0.001$ / $p = 0.049$

$p < 0.001$ / $p < 0.001$

Changes in lung function for 6 years

Crude				
PRM _{emph}	FVC change	<i>P</i>	FEV ₁ change	<i>P</i>
All (n = 106)	30.2 (-9.1, 69.4)	0.13	-6.2 (-29.9, 17.6)	0.608
GOLD 1 (n = 63)	2.5 (-61.6, 66.6)	0.937	3.0 (-38.3, 44.3)	0.884
GOLD 2 (n = 43)	38.3 (-10.4, 86.9)	0.119	-11.2 (-38.6, 16.2)	0.413
PRM _{fSAD}	FVC change	<i>P</i>	FEV ₁ change	<i>P</i>
All (n = 106)	-9.0 (-15.5, -2.4)	0.008	-6.0 (-9.9, -2.2)	0.003
GOLD 1 (n = 63)	-4.0 (-10.9, 2.9)	0.249	-3.9 (-8.3, 0.1)	0.083
GOLD 2 (n = 43)	-16.7 (-28.6, -4.9)	0.006	-8.9 (-15.5, -2.5)	0.008

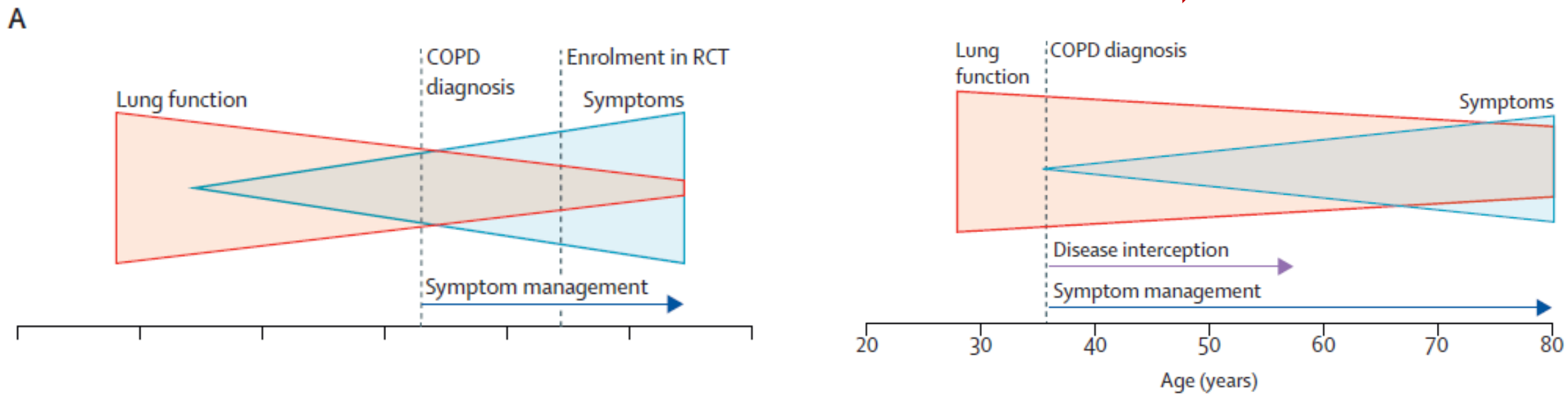
Adjusted				
PRM _{emph}	FVC change	<i>P</i>	FEV ₁ change	<i>P</i>
All (n = 106)	22.9 (-16.1, 61.9)	0.247	-6.7 (-29.1, 15.7)	0.553
GOLD 1 (n = 63)	-3.6 (-68.9, 61.8)	0.913	-1.5 (-15.1, 42.1)	0.944
GOLD 2 (n = 43)	39.5 (-18.1, 97.0)	0.172	-1.9 (-30.7, 26.9)	0.895
PRM _{fSAD}	FVC change	<i>P</i>	FEV ₁ change	<i>P</i>
All (n = 106)	-8.0 (-14.5, -1.6)	0.016	-6.0 (-9.6, -2.4)	0.001
GOLD 1 (n = 63)	-5.6 (-12.7, 1.5)	0.119	-4.2 (-8.9, 0.4)	0.074
GOLD 2 (n = 43)	-26.6 (-40.8, -12.4)	<0.001	-11.8 (-18.9, -4.7)	0.002

Impulse oscillometry for small airway disease and
early detection of disease progression

Towards the elimination of chronic obstructive pulmonary disease: a *Lancet* Commission

Daiana Stolz, Takudzwa Mkorombindo, Desiree M Schumann, Alvar Agusti, Samuel Y Ash, Mona Bafadhel, Chunxue Bai, James D Chalmers, Gerard J Criner, Shyamali C Dharmage, Frits M E Franssen, Urs Frey, MeiLan Han, Nadia N Hansel, Nathaniel M Hawkins, Ravi Kalhan, Melanie Konigshoff, Fanny W Ko, Trisha M Parekh, Pippa Powell, Maureen Rutten-van Mólken, Jodie Simpson, Don D Sin, Yuanlin Song, Bela Suki, Thierry Troosters, George R Washko, Tobias Welte, Mark T Dransfield

Early Detection and Intervention



Emphysema at chest CT in GOLD stage 0 with smoking exposure

Parameter	No Visually Evident Emphysema	Visually Evident Emphysema*	P Value [†]
No. of participants	2116 (51.7)	1979 (48.3)	
No. of deaths	127 (6.0)	166 (8.4)	.003
Demographics			
Age (y)	56 ± 8	57 ± 8	<.001
Height (cm)	170 ± 10	170 ± 9	.70
Weight (kg)	87 ± 19	81 ± 17	<.001
BMI (kg/m ²)	30 ± 6	28 ± 5	<.001
No. of men	1068 (50.5)	1096 (55.4)	.002
Ethnicity			
No. of non-Hispanic white participants	1347 (63.7)	1070 (54.1)	<.001
No. of African American participants	769 (36.3)	909 (45.9)	<.001
Smoking status			
No. of current smokers	1111 (52.5)	1313 (66.3)	<.001
No. of pack-years smoked [‡]	30 (21)	38 (23)	<.001
Comorbidities			
No. of exacerbations in past year	187 (8.8)	168 (8.5)	.69
No. with chronic bronchitis	155 (7.7)	189 (10)	<.01
Functional parameters			
Percentage predicted FEV ₁	98 ± 12	97 ± 11	<.001
FEV ₁ -to-FVC ratio	0.8 ± 0.1	0.8 ± 0.0	<.001
6-minute walk distance (m) [‡]	461.1 (132.6)	445.5 (128.7)	<.001
No. of participants with mMRC dyspnea score answer of yes	736 (34.8)	776 (39.2)	.004
SGRQ [‡]	9 (21)	11 (26)	<.001
%LAA ₋₉₅₀ [‡]	0.90 (2.3)	0.98 (2.3)	<.03
Adjusted lung density (g/L)	94 ± 20	96 ± 21	<.001
FRC _{CT} -to-TLC _{CT} ratio	0.5 ± 0.1	0.5 ± 0.1	<.001

5-yr change in CT parameters, lung function, and PROs

Table 4: Estimated 5-year Mean Change in CT Parameters, Lung Function, and Clinical Status for Participants Stratified by Emphysema Grade according to the Fleischner Society Classification System

Parameter	Trace	Mild	Moderate	Confluent and Advanced De-structive	<i>P</i> Value
ALD (g/L)	-2.01 (-3.11, -0.91)	-4.13 (-5.28, -2.98)	-3.79 (-5.52, -2.05)	-5.63 (-10.09, -1.17)	.006
Perc15 (HU)	-2.68 (-4.37, -1.00)	-4.05 (-5.82, -2.28)	-2.71 (-5.45, 0.03)	-5.77 (-12.97, 1.42)	.50
Natural log %LAA ₉₅₀	0.01 (-0.09, 0.10)	0.26 (0.17, 0.36)	0.35 (0.20, 0.50)	0.37 (-0.02, 0.77)	<.001
FRC _{CT} -to-TLC _{CT} ratio	-0.50 (-1.37, 0.38)	0.13 (-0.80, 1.06)	-1.14 (-2.63, 0.34)	-4.12 (-8.04, -0.21)	.10
(FEV ₁ -to-FVC ratio) · 100	-1.5 (-2.0, -1.0)	-1.9 (-2.4, -1.4)	-3.2 (-4.0, -2.3)	-1.1 (-3.4, 1.1)	.005
FEV ₁ (mL)	-85 (-112, -58)	-97 (-126, -68)	-81 (-128, -34)	-98 (-221, 24)	.90
6MWD (m)	-10.8 (-20.4, -1.5)	-15.0 (-25.5, -4.8)	-15.0 (-31.8, 1.8)	-9.0 (-54.6, 36.6)	.92
SGRQ total	0.67 (-0.83, 2.16)	1.39 (-0.23, 3.00)	-0.04 (-2.63, 2.55)	-0.78 (-7.75, 6.20)	.74
SF36 general	-1.51 (-2.56, -0.47)	-0.73 (-1.85, 0.39)	-1.71 (-3.51, 0.09)	0.66 (-4.28, 5.61)	.56

Changes in lung function for 6 years

Crude				
PRM _{emph}	FVC change	<i>P</i>	FEV ₁ change	<i>P</i>
All (n = 106)	30.2 (-9.1, 69.4)	0.13	-6.2 (-29.9, 17.6)	0.608
GOLD 1 (n = 63)	2.5 (-61.6, 66.6)	0.937	3.0 (-38.3, 44.3)	0.884
GOLD 2 (n = 43)	38.3 (-10.4, 86.9)	0.119	-11.2 (-38.6, 16.2)	0.413
PRM _{fSAD}	FVC change	<i>P</i>	FEV ₁ change	<i>P</i>
All (n = 106)	-9.0 (-15.5, -2.4)	0.008	-6.0 (-9.9, -2.2)	0.003
GOLD 1 (n = 63)	-4.0 (-10.9, 2.9)	0.249	-3.9 (-8.3, 0.1)	0.083
GOLD 2 (n = 43)	-16.7 (-28.6, -4.9)	0.006	-8.9 (-15.5, -2.5)	0.008

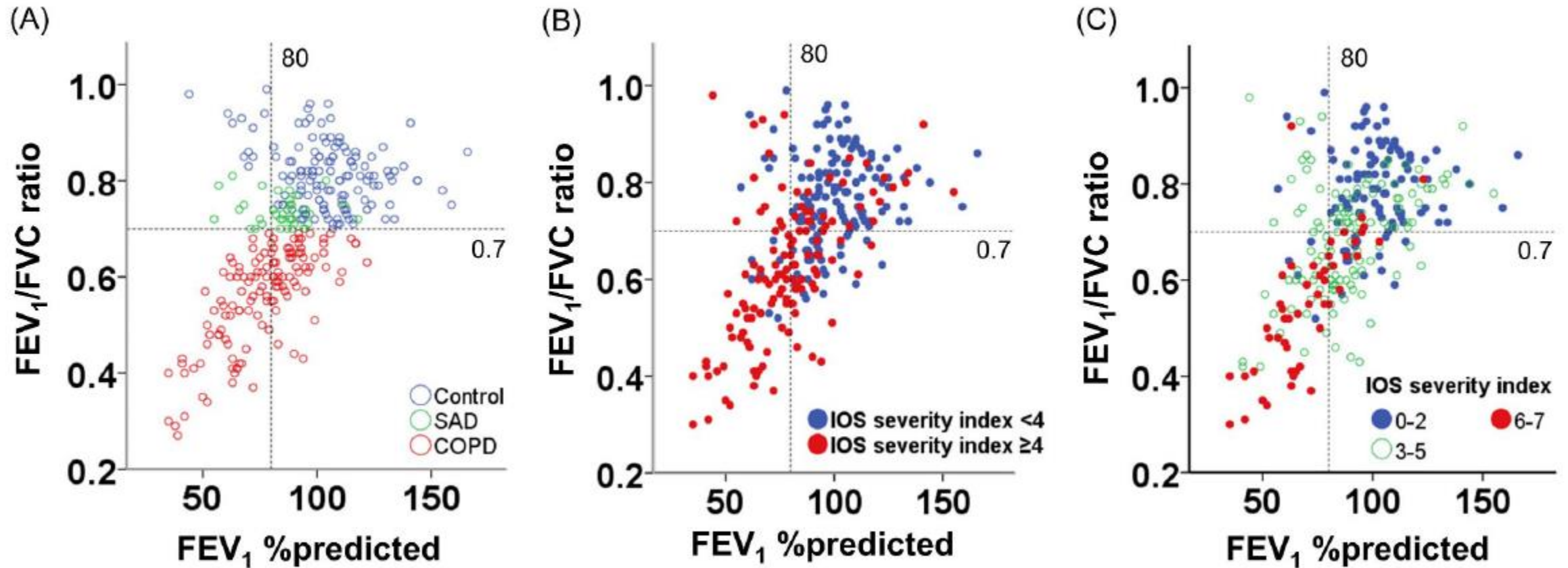
Adjusted				
PRM _{emph}	FVC change	<i>P</i>	FEV ₁ change	<i>P</i>
All (n = 106)	22.9 (-16.1, 61.9)	0.247	-6.7 (-29.1, 15.7)	0.553
GOLD 1 (n = 63)	-3.6 (-68.9, 61.8)	0.913	-1.5 (-15.1, 42.1)	0.944
GOLD 2 (n = 43)	39.5 (-18.1, 97.0)	0.172	-1.9 (-30.7, 26.9)	0.895
PRM _{fSAD}	FVC change	<i>P</i>	FEV ₁ change	<i>P</i>
All (n = 106)	-8.0 (-14.5, -1.6)	0.016	-6.0 (-9.6, -2.4)	0.001
GOLD 1 (n = 63)	-5.6 (-12.7, 1.5)	0.119	-4.2 (-8.9, 0.4)	0.074
GOLD 2 (n = 43)	-26.6 (-40.8, -12.4)	<0.001	-11.8 (-18.9, -4.7)	0.002

Evaluation of small airway disease and COPD using iOS

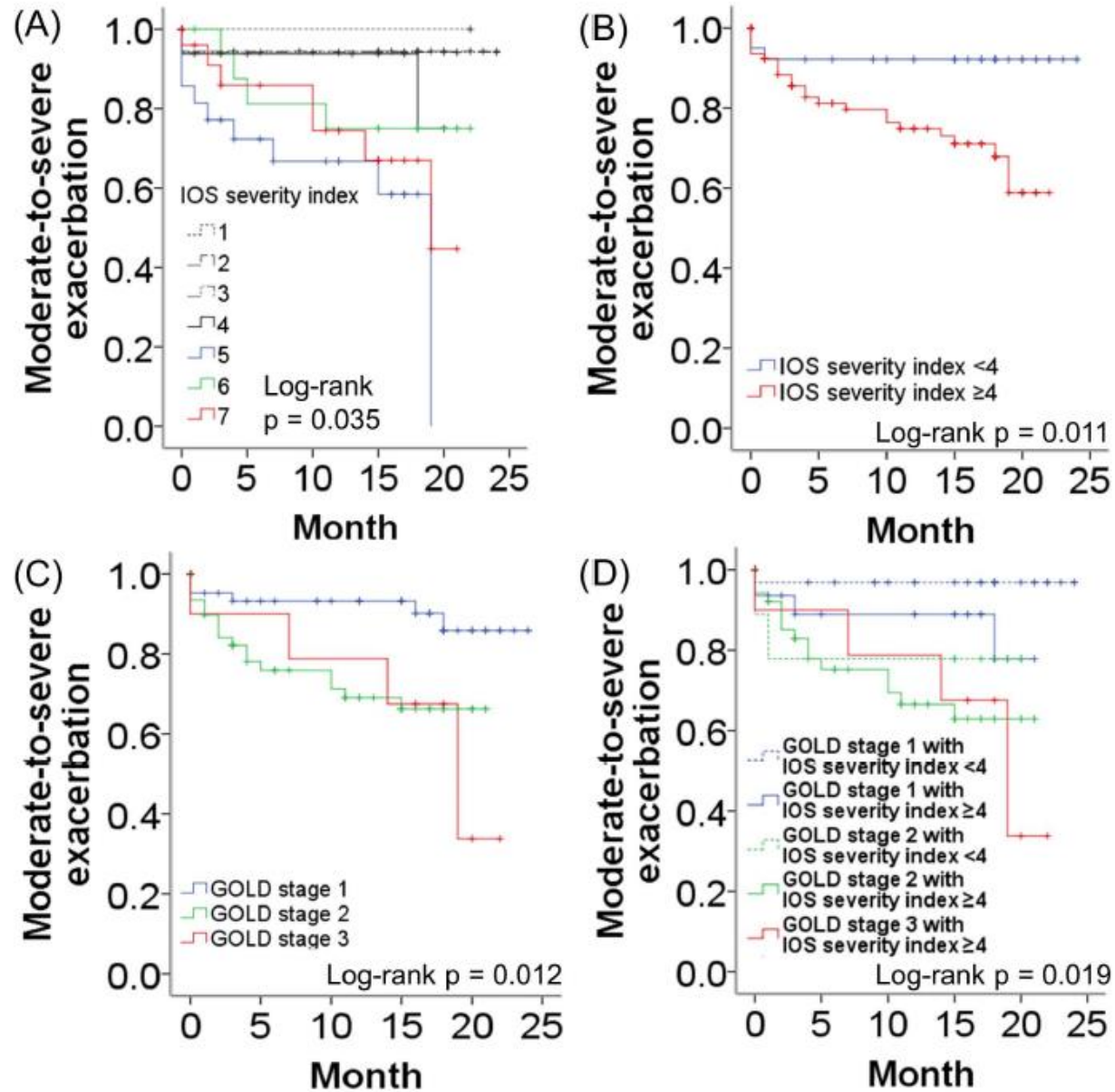
- Small airways, defined as terminal or respiratory bronchioles with an internal diameter < 2 mm, are the major site of airflow obstruction in COPD.
- Small airway disease (SAD) is one of the key pathological features that can occur before the progression of emphysema resulting from parenchymal destruction.
- Impulse oscillometry (IOS) is easily performed even in patients in whom conventional pulmonary function tests (PFTs) are challenging, such as in elderly patients with COPD.
- SAD was diagnosed when more than two of the following three spirometry parameters were $< 65\%$ of the predicted value: forced expiratory flow between 25% and 75% of vital capacity ($FEF_{25-75\%}$), $FEF_{50\%}$, and $FEF_{75\%}$.
- The study population was divided into three groups: (1) COPD, (2) SAD without COPD, and (3) control (without COPD and/or SAD).

Variable	Control (n = 134)	SAD (n = 38)	COPD (n = 134)	P-value
Age, years	60.0 ± 17.6	65.4 ± 12.6	69.5 ± 10.9	< 0.001
Male sex, n (%)	67 (50.0)	16 (42.1)	112 (83.6)	< 0.001
Body mass index, kg/m ²	24.3 ± 0.3	24.6 ± 0.7	24.1 ± 0.3	0.779
Smoking history, n (%)				< 0.001
Never smoker	68 (53.1)	18 (50.0)	27 (21.1)	
Ex-smoker	30 (23.4)	8 (22.2)	61 (47.7)	
Current smoker	30 (23.4)	10 (27.8)	40 (31.3)	
Smoking intensity, pack-year	14.8 ± 2.1	12.9 ± 3.0	30.7 ± 2.3	< 0.001
Chronic respiratory symptom, n (%)	48 (35.8)	17 (44.7)	59 (45.4)	0.255
Cough	27 (20.1)	3 (7.9)	5 (3.8)	< 0.001
Sputum	7 (5.2)	3 (7.9)	8 (6.1)	0.748
Dyspnea	21 (15.7)	13 (34.2)	52 (40.0)	< 0.001
Inhaler use, n (%)	8 (6.0)	10 (26.3)	63 (47.0)	< 0.001
Charlson Comorbidity Index	0.83 ± 0.1	1.0 ± 0.2	2.0 ± 0.1	< 0.001
Severity of IOS results, n (%)				< 0.001
Normal	111 (82.8)	20 (52.6)	60 (44.8)	
Mild	12 (9.0)	6 (15.8)	24 (17.9)	
Moderate	5 (3.7)	6 (15.8)	25 (18.7)	
Severe	4 (3.0)	3 (7.9)	8 (6.0)	
Very severe	2 (1.5)	3 (7.9)	17 (12.7)	

Relationship between IOS severity and clinical variables



Relationship between IOS severity and exacerbation



Combination of CT and iOS in COPD

- The prospective data from Konkuk University Medical Center
- 36 patients, divided into three groups: 21 with COPD, 6 with PRISM, and 9 ever-smokers with normal lung function.
- iOS parameter
 - resistance (R), reactance(X), Fres (resonance frequency), Reactance area (AX), R5-R20 (indicate small airway disease)
- Dh (luminal diameter), WT (airway wall thickness), ADI (deformation index), Jacobian, PRM_{emph} , PRM_{fSAD}

Comparison of COPD vs. non-COPD

	COPD	Non-COPD	p-value
R5- R20	12.241	27.930	0.003
AX	0.424	1.748	0.013
Fres	13.469	21.341	0.001
WT in trachea	3.877	3.544	0.026
Dh in trachea	17.542	17.949	0.302
Jacobian in total	1.613	1.821	0.035
PRM _{emph}	0.148	0.123	0.211
PRM _{fSAD}	0.074	0.201	<0.001

- Emph

Emph_LLL	0.00	-0.05	-0.05	-0.05	-0.09	-0.07	-0.09	-0.03	0.09	0.08	0.13
Emph_LUL	0.00	-0.05	-0.06	-0.07	-0.12	-0.09	-0.11	-0.05	0.11	0.10	0.17
Emph_RLL	-0.00	-0.08	-0.10	-0.12	-0.09	-0.08	-0.09	-0.05	0.08	0.08	0.07
Emph_RML	-0.04	-0.14	-0.12	-0.11	0.01	0.00	0.02	0.09	-0.03	-0.01	0.01
Emph_RUL	0.05	-0.06	-0.06	-0.07	-0.11	-0.11	-0.11	-0.05	0.12	0.12	0.10
Emph_Total	0.02	-0.06	-0.08	-0.09	-0.13	-0.12	-0.14	-0.08	0.13	0.13	0.18
	R5Hz_Pre	R10Hz_Pre	R15Hz_Pre	R20Hz_Pre	X5Hz_Pre	X10Hz_Pre	X15Hz_Pre	X20Hz_Pre	Fres_Pre	AX_Pre	Di5-20_Pre

- fSAD

fSAD_LLL	0.27	0.29	0.22	0.17	-0.41	-0.38	-0.41	-0.38	0.41	0.40	0.30
fSAD_LUL	0.13	0.14	0.07	0.03	-0.28	-0.21	-0.25	-0.22	0.27	0.23	0.13
fSAD_RLL	0.37	0.36	0.28	0.21	-0.43	-0.42	-0.46	-0.46	0.45	0.44	0.30
fSAD_RML	0.08	0.06	0.00	-0.05	-0.15	-0.12	-0.18	-0.18	0.19	0.15	0.03
fSAD_RUL	0.17	0.18	0.10	0.05	-0.19	-0.19	-0.23	-0.23	0.26	0.22	0.10
fSAD_Total	0.18	0.19	0.11	0.06	-0.28	-0.24	-0.29	-0.27	0.29	0.27	0.15
	R5Hz_Pre	R10Hz_Pre	R15Hz_Pre	R20Hz_Pre	X5Hz_Pre	X10Hz_Pre	X15Hz_Pre	X20Hz_Pre	Fres_Pre	AX_Pre	Di5-20_Pre

Summary

- Quantification of CT imaging in COPD
 - Emphysema -> kernel conversion in multi center cohort
 - Direct airway measurement -> limitation in assessment of small airway
 - Small airway measurement -> Quantification of air trapping
 - > PRM analysis
- Impulse oscillometry for small airway disease
- Combination IOS parameters with variable of chest CT