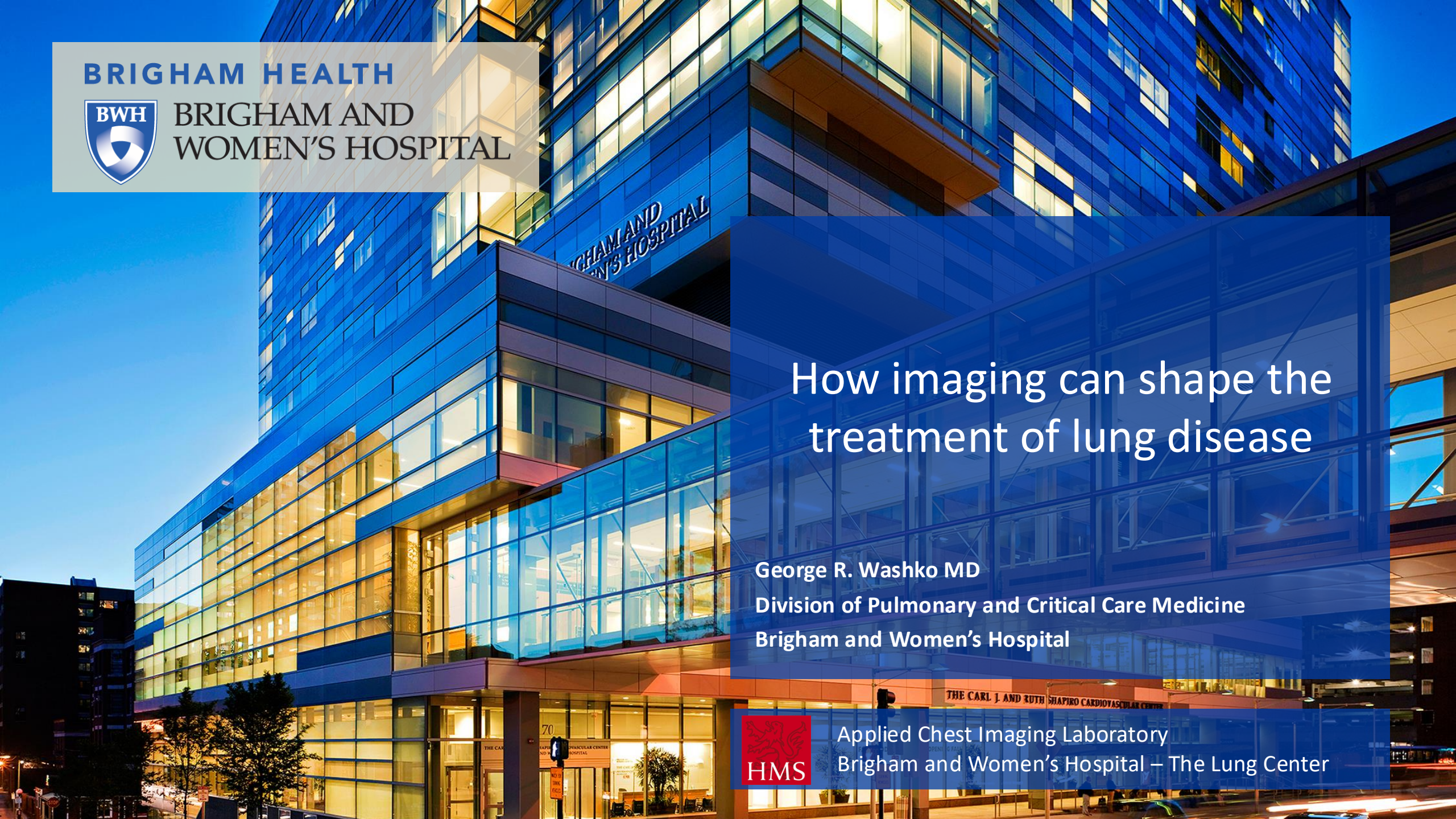
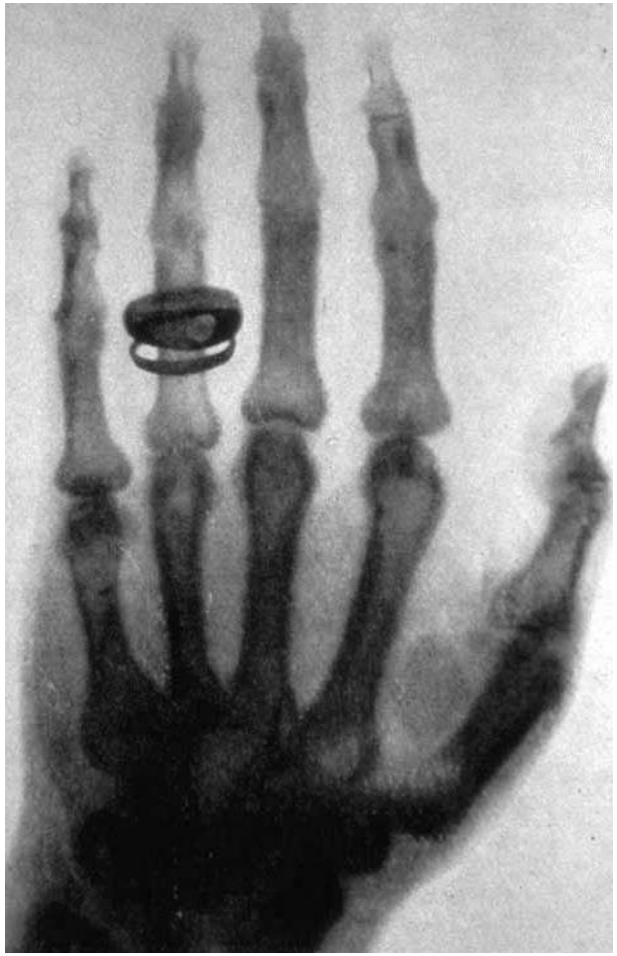

BRIGHAM HEALTH
BWH
BRIGHAM AND
WOMEN'S HOSPITAL
How imaging can shape the treatment of lung disease
George R. Washko MD
Division of Pulmonary and Critical Care Medicine
Brigham and Women's Hospital
HMS
Applied Chest Imaging Laboratory
Brigham and Women's Hospital – The Lung Center

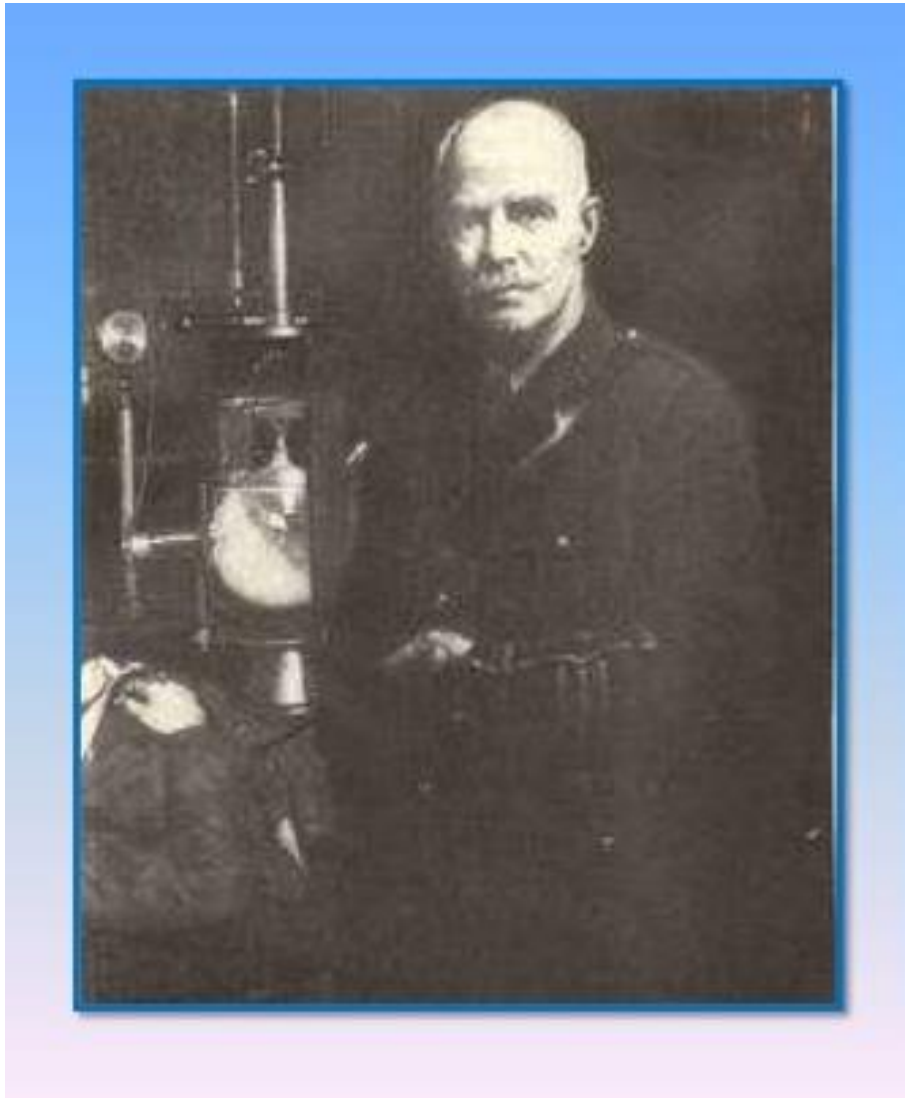
Disclosures

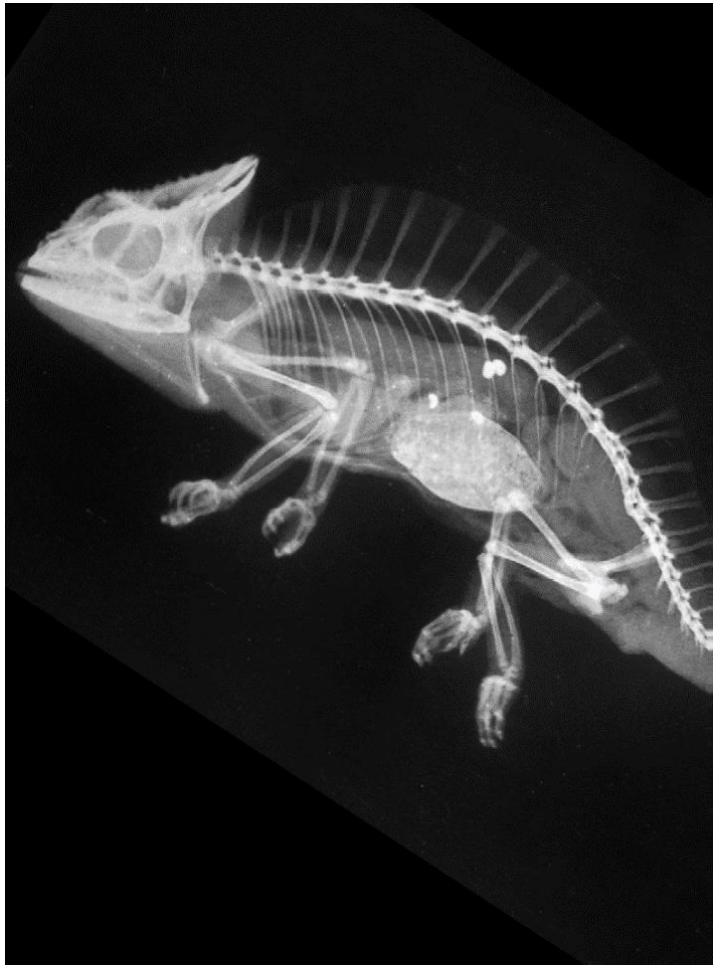
- Consultancies: Apogee, Astra Zeneca, Avalyn, Intellia Therapeutics, Pieris Pharmaceuticals, Regeneron, Sanofi, Verona Pharma, Vertex
- Quantitative Imaging Solutions: Co-founder of a consulting group and software development LLC for image analytics and data management
- Sponsors: Boehringer Ingelheim, DoD, Lung Biotechnology, NIH/NHLBI
- My wife works for Biogen

Wilhelm Rontgen: Nov 8 1895



Major John Hall Edwards

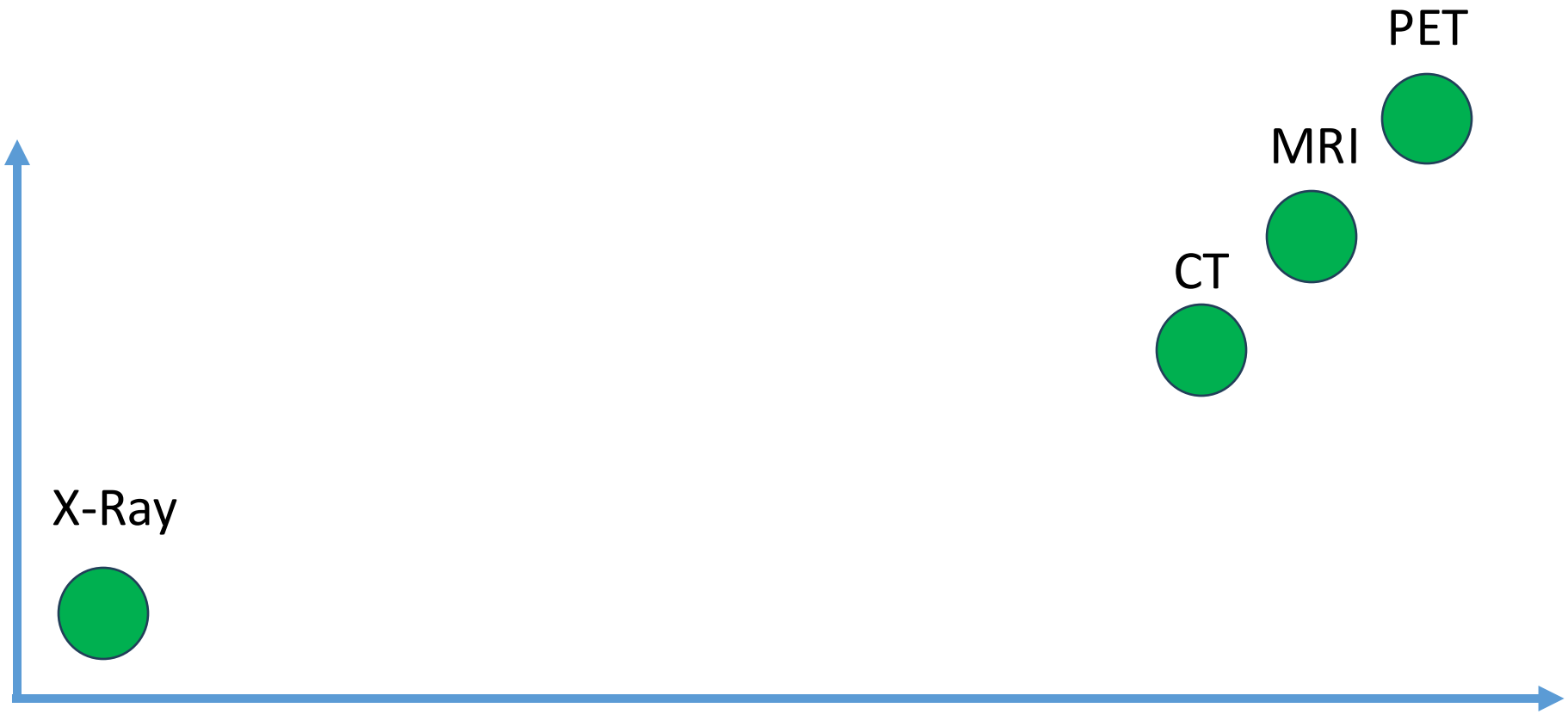




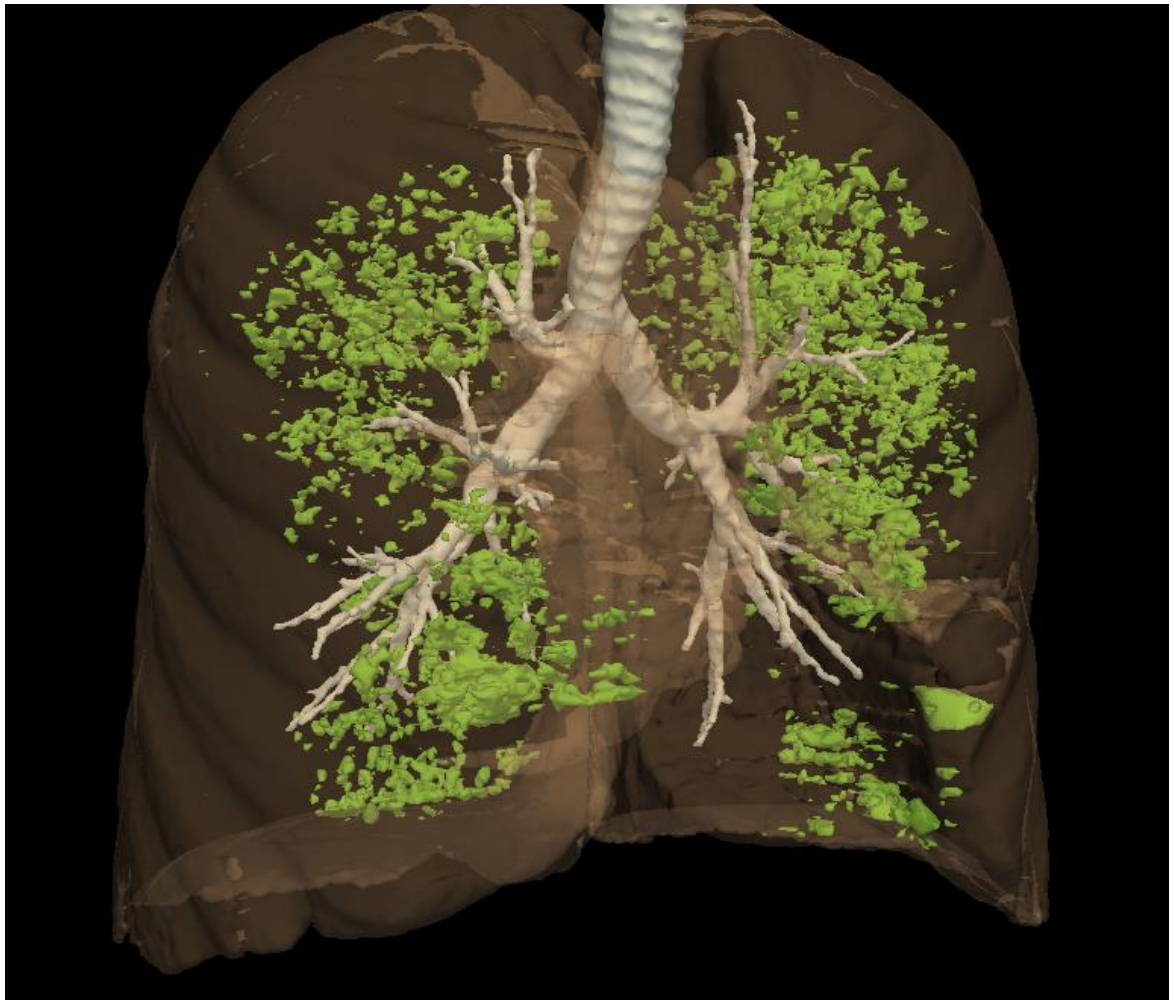
The Story of Radiology, Volume 2.
European Society of Radiology


01.1135.1

The exponential of imaging….

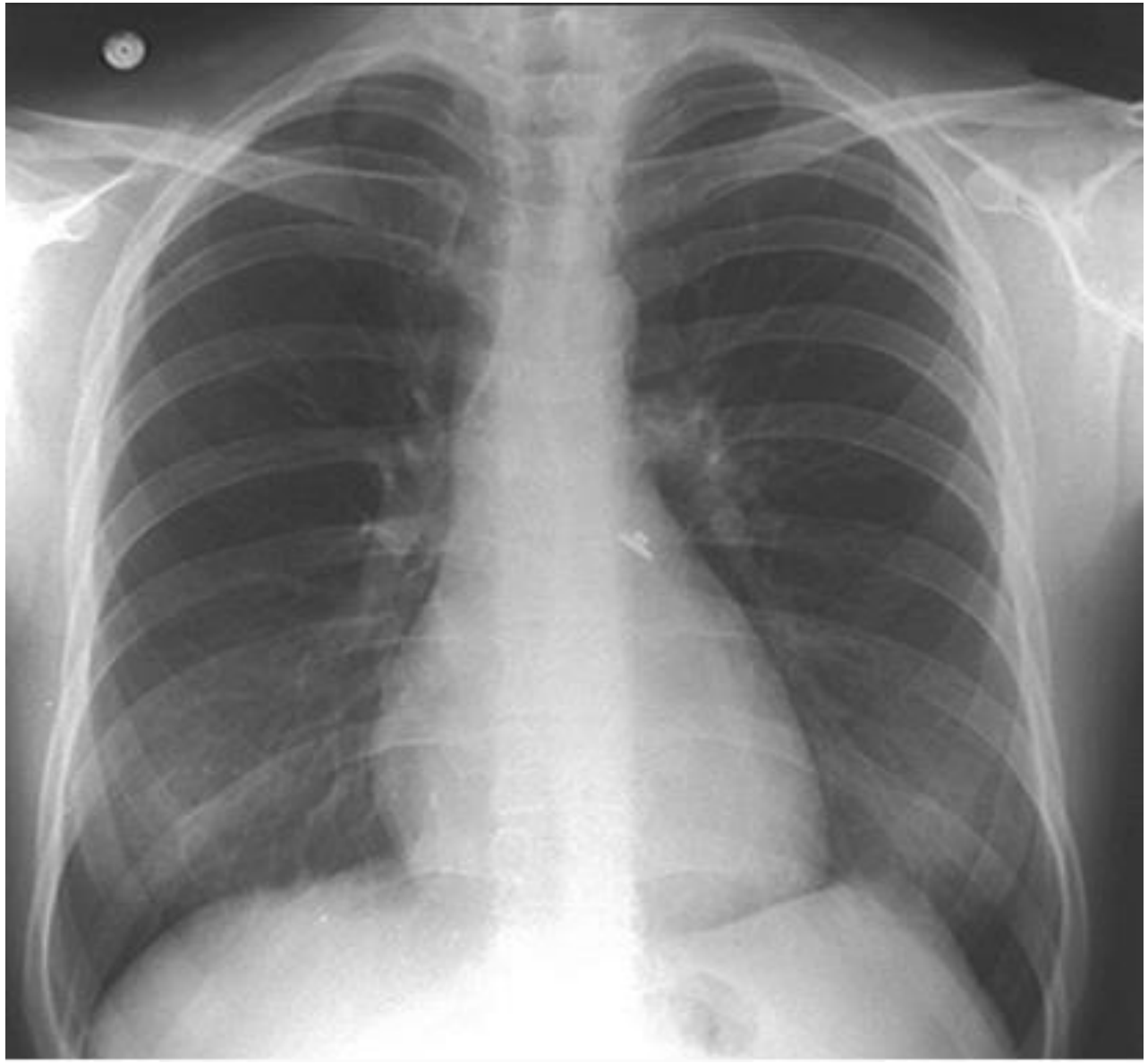


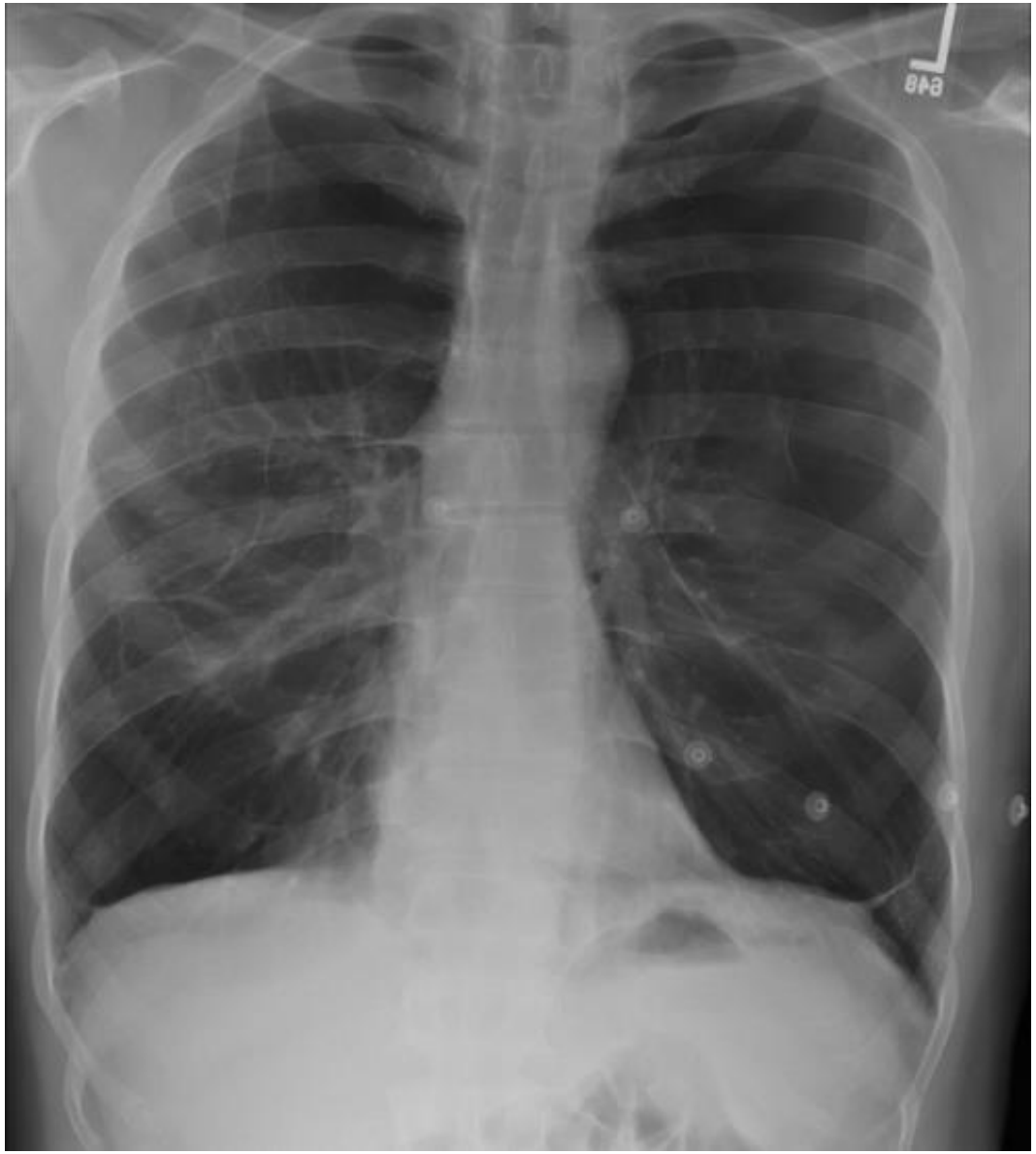
Past/Present/Future



- Parenchyma
  - Emphysema
  - ILD
- Vasculature
  - Pulmonary embolism
  - Vasculopathy
- Airways
  - Mucus Plugs
  - Bronchiectasis
- Lung Cancer
- Body Composition
- Intrinsic Susceptibility

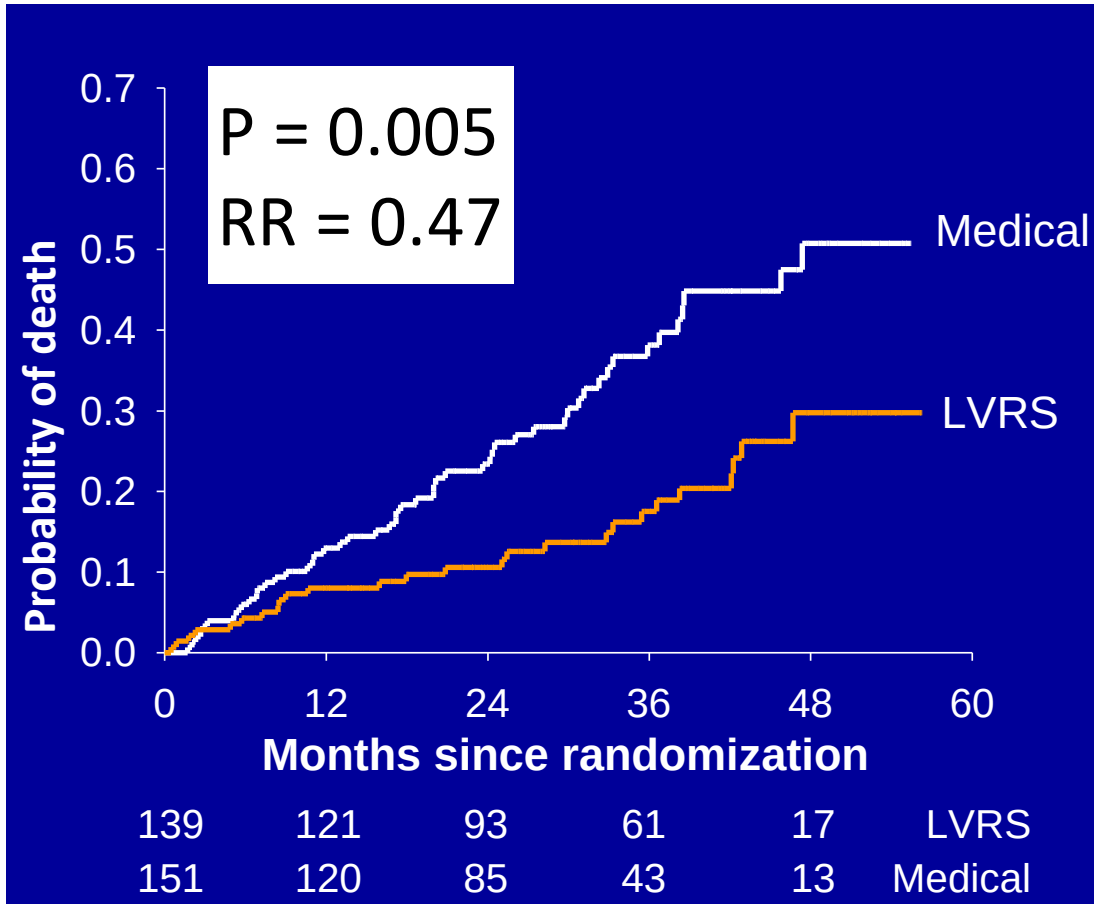
Emphysema

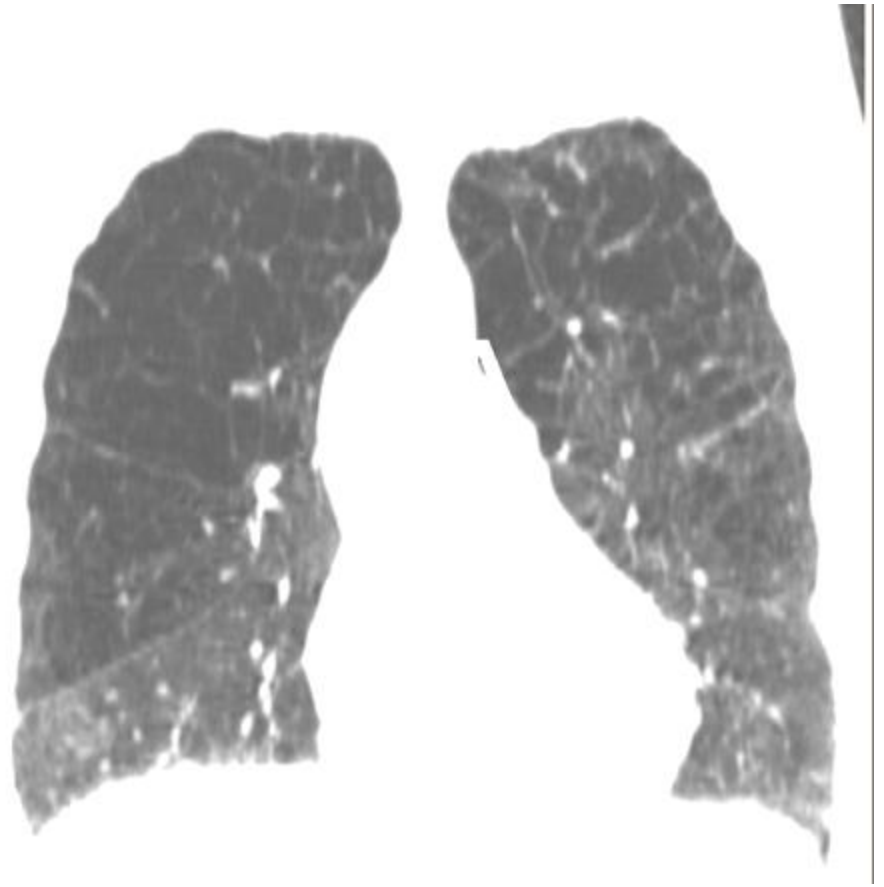




NETT Results: Mortality

Upper-lobe disease and low exercise capacity





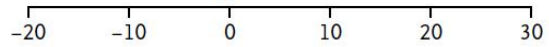
High-risk patients excluded

NEJM 2003;348:2059-73.

Endobronchial Valves

A

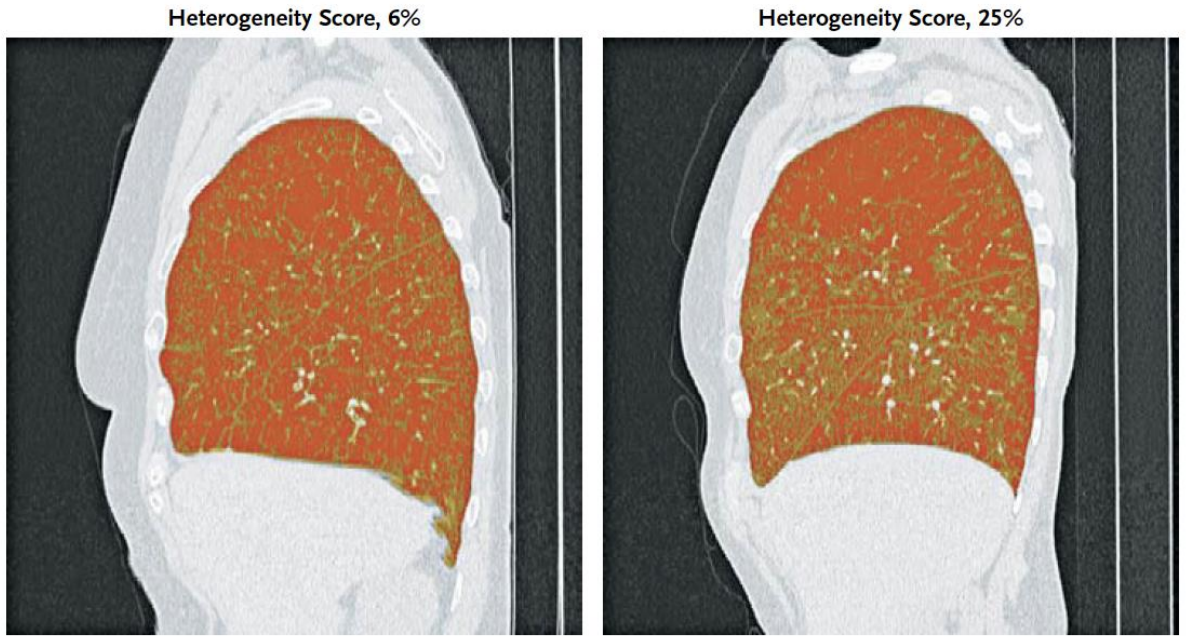
Degree of Heterogeneity	Percent Change in FEV_1 (Treatment–Control)	Point Estimate (95% CI)	P Value
≥25%		15.3 (5.3 to 25.3)	0.003
≥15% to <25%		5.8 (–4.5 to 16.1)	0.27
≥6% to <15%		5.9 (–1.4 to 13.1)	0.12
<6%		–0.4 (–8.8 to 8.1)	0.93



B

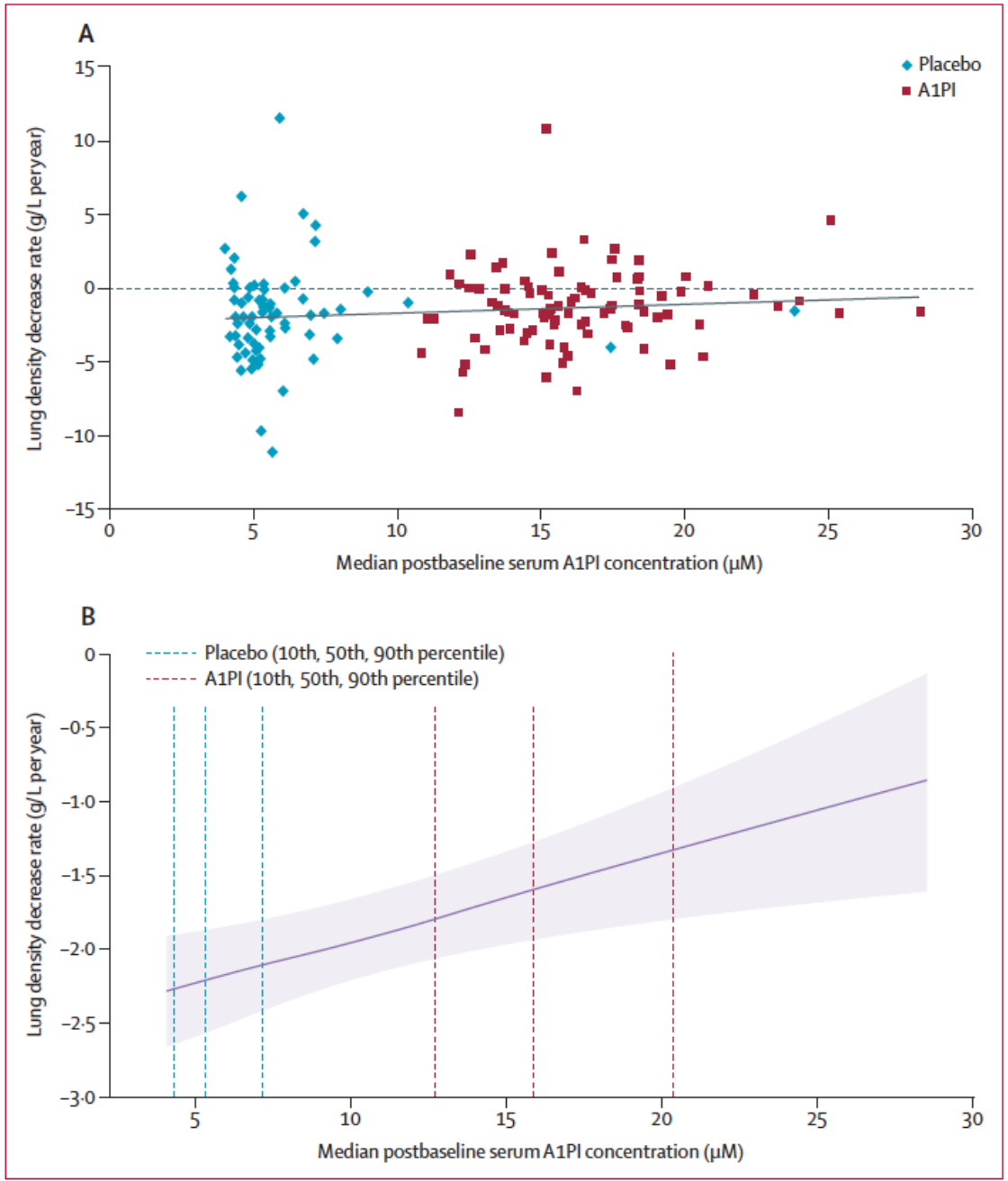
Degree of Heterogeneity	Percent Change in 6MWT (Treatment–Control)	Point Estimate (95% CI)	P Value
≥25%		16.2 (3.8 to 28.5)	0.009
≥15% to <25%		8.1 (–1.6 to 17.8)	0.10
≥6% to <15%		–2.7 (–16 to 10.6)	0.67
<6%		0.7 (–7.8 to 9.2)	0.89

C



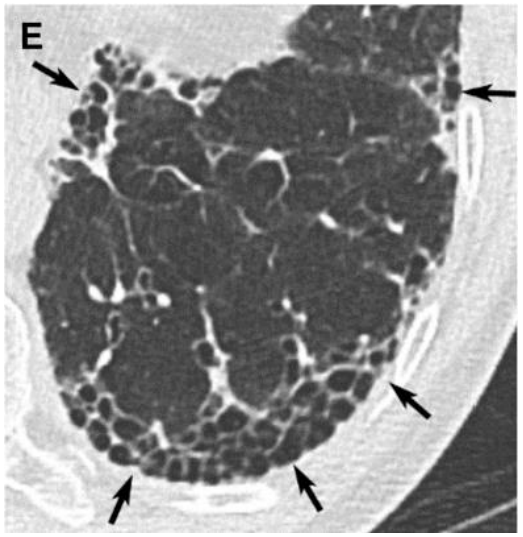
NEJM 2010;363:1233-44.

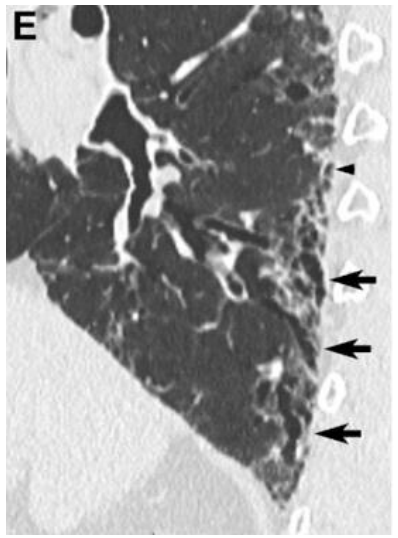
Response to Therapy

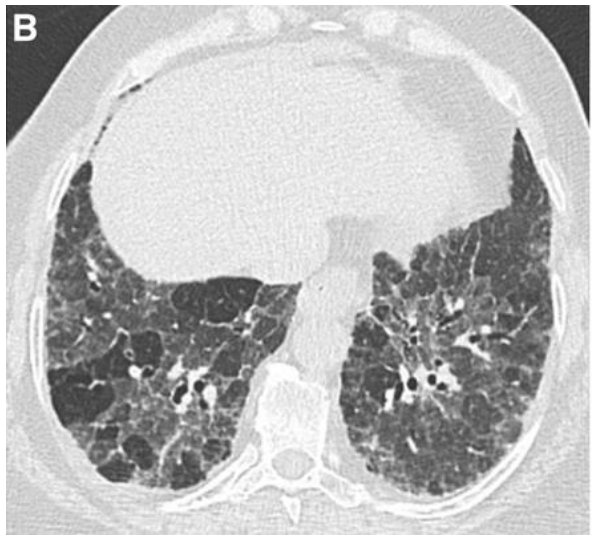


Lancet 2015;386(9991):360-8.

Interstitial Lung Disease







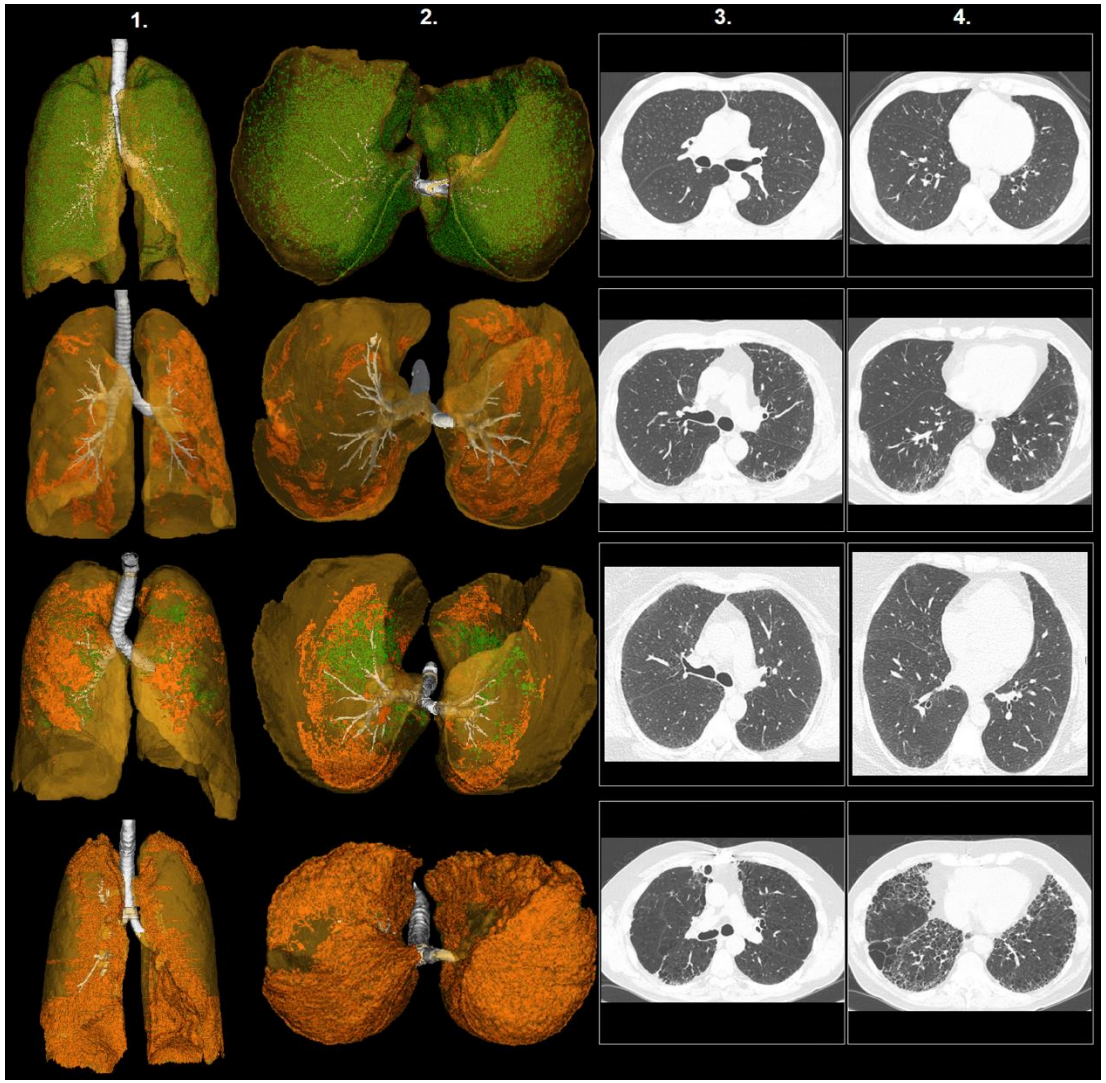
IPF suspected*		Histopathology pattern			
		UIP	Probable UIP	Indeterminate for UIP	Alternative diagnosis
HRCT pattern	UIP	IPF	IPF	IPF	Non-IPF dx
	Probable UIP	IPF	IPF	IPF (Likely)**	Non-IPF dx
	Indeterminate for UIP	IPF	IPF (Likely)**	Indeterminate for IPF***	Non-IPF dx
	Alternative diagnosis	IPF (Likely)** /non-IPF dx	Non-IPF dx	Non-IPF dx	Non-IPF dx

AJRCCM 2018;198(5):e44-e68.

Interstitial Lung Abnormalities

Interstitial Lung Abnormalities (ILA)

- 3-7% of adults over 50
- Subtypes are progressive
- Associated with MUC5B
- Associated with adverse outcomes
  - All cause and respiratory mortality



NEJM 2013;368:2192-2200.

JAMA 2016;315:672-681.

NEJM 2011;364:897-906.

Interstitial Lung Abnormalities

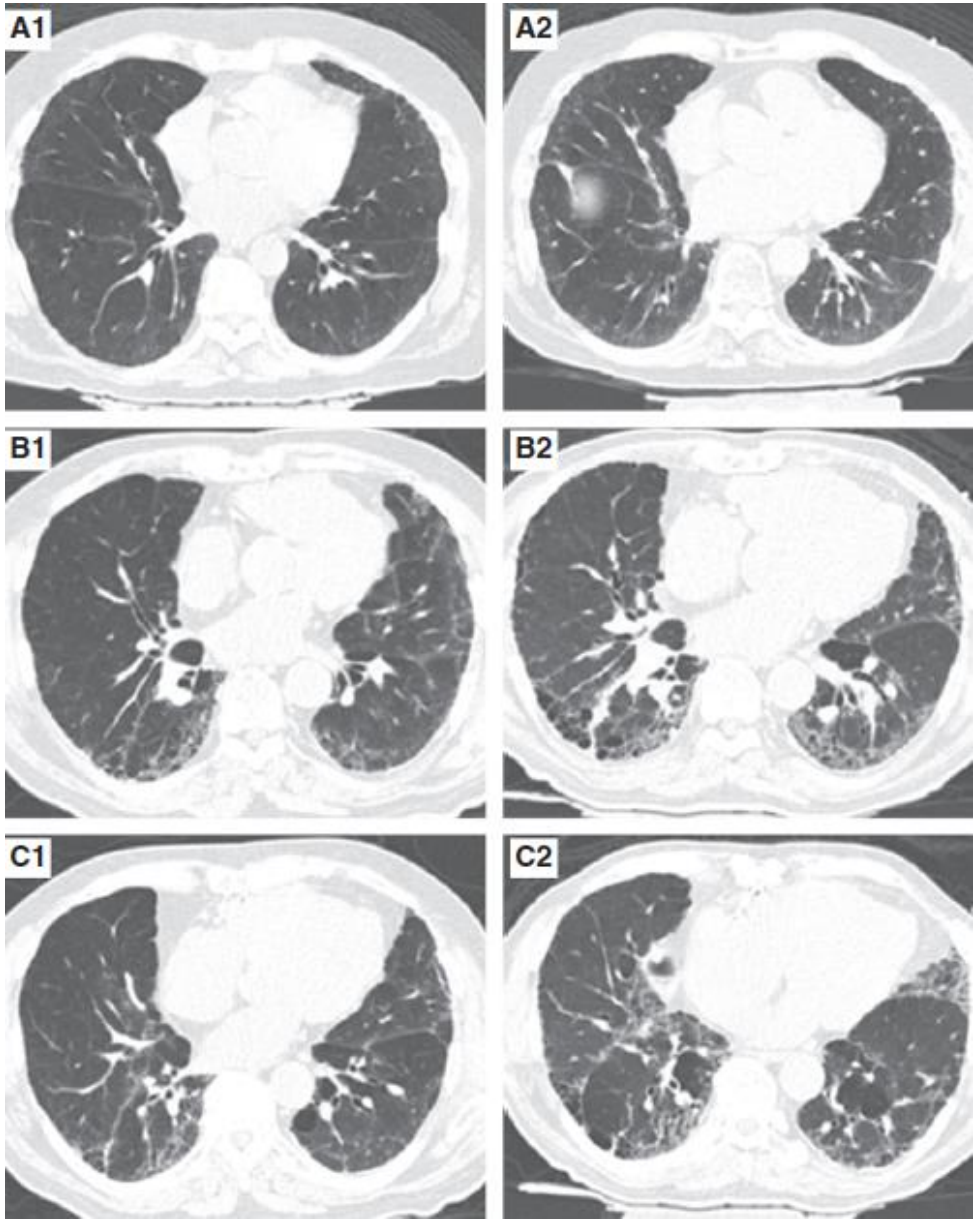


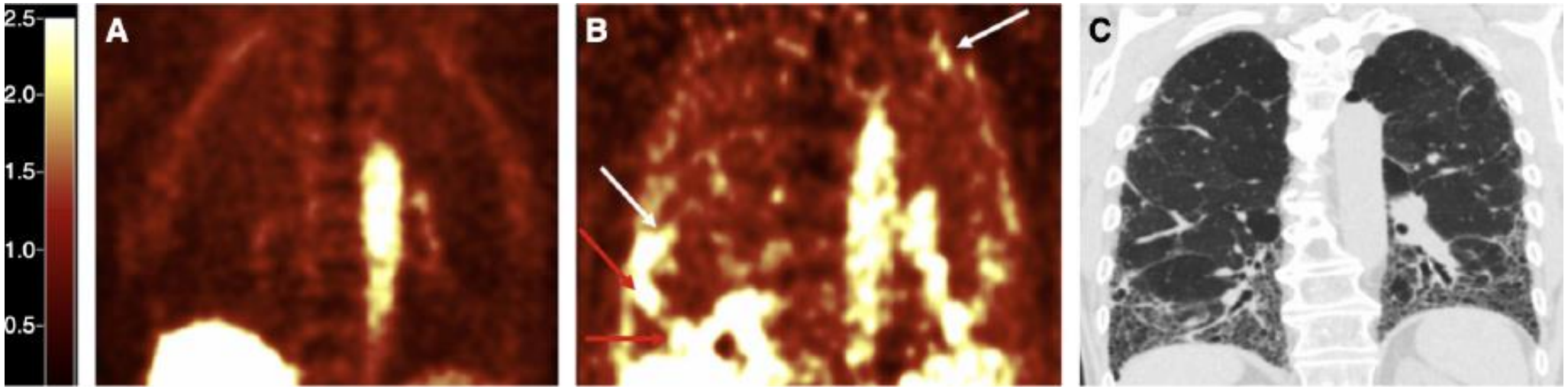
Table 3. Association between Imaging Features and ILA Progression

	Unadjusted Analysis		Adjusted Analysis*	
	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Centrilobular nodules	0.2 (0.1–0.4)	<0.0001	0.2 (0.1–0.5)	0.0002
Ground glass†	—	—	—	—
Subpleural reticular markings	5.9 (2.3–15)	0.0002	6.6 (2.3–19)	0.0004
Nonemphysematous cysts	3.1 (1.6–5.9)	0.0005	2.5 (1.3–5.1)	0.009
Lower lobe predominant changes	5.2 (1.8–15)	0.002	6.7 (1.8–25)	0.004
Traction bronchiectasis	5.9 (2.3–14.9)	0.0002	6.6 (2.3–19)	0.0004
Honeycombing‡	—	—	—	—

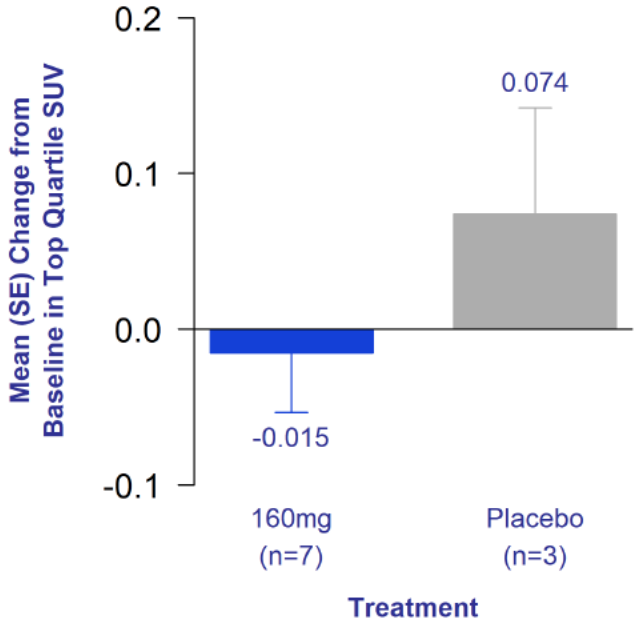
For definition of abbreviations, *see* Table 2.
*Adjusted for age, sex, body mass index, pack-years smoking, current smoking status, and *MUC5B* genotype.
†Odds of progression cannot be calculated for ground glass because all participants with ILA had ground glass on computed tomography scan.
‡Odds of progression cannot be calculated because all participants with honeycombing had evidence of imaging progression.

AJRCCM 2019;200:175-183.

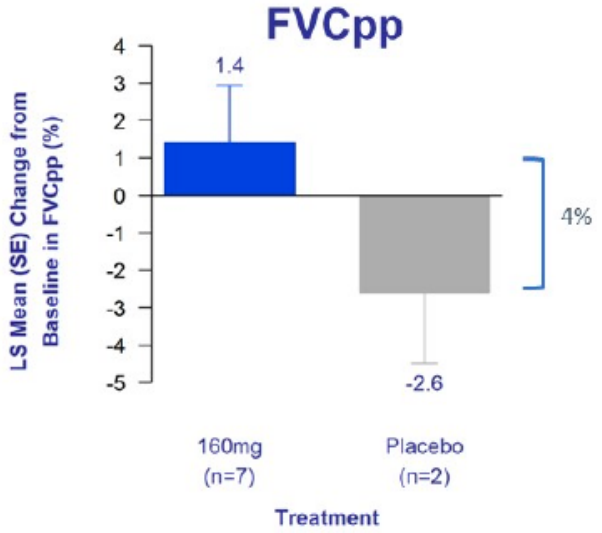
Collagen-Targeted PET



AJRCCM 2019;200(2):28-261.

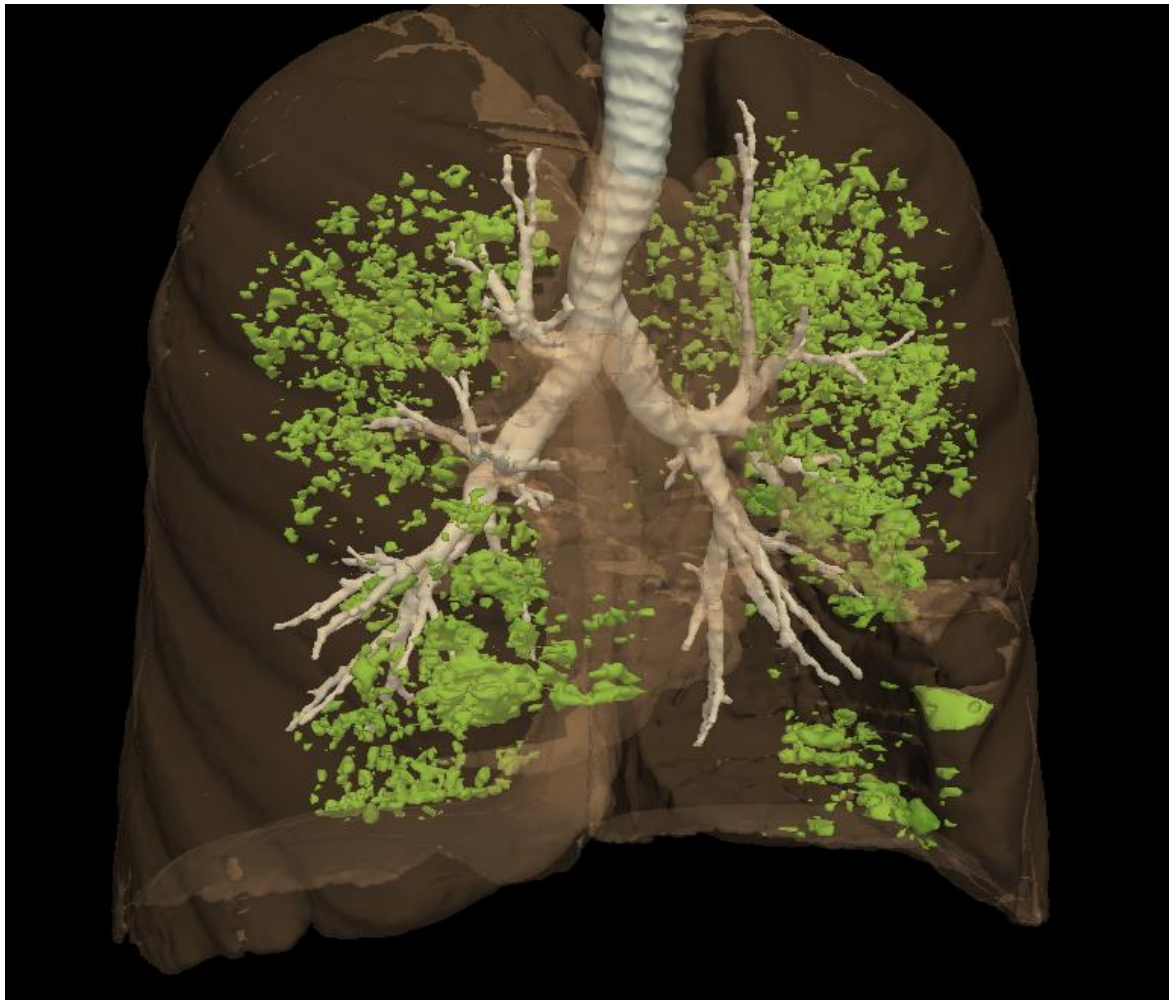


Mean Change from Baseline in Uptake of Collagen PET Tracer After 12 Weeks



Pliant Press Release, May 2024

Past/Present/Future



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  - ILD
- Vasculature
  - Pulmonary embolism
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  - Mucus Plugs
  - Bronchiectasis
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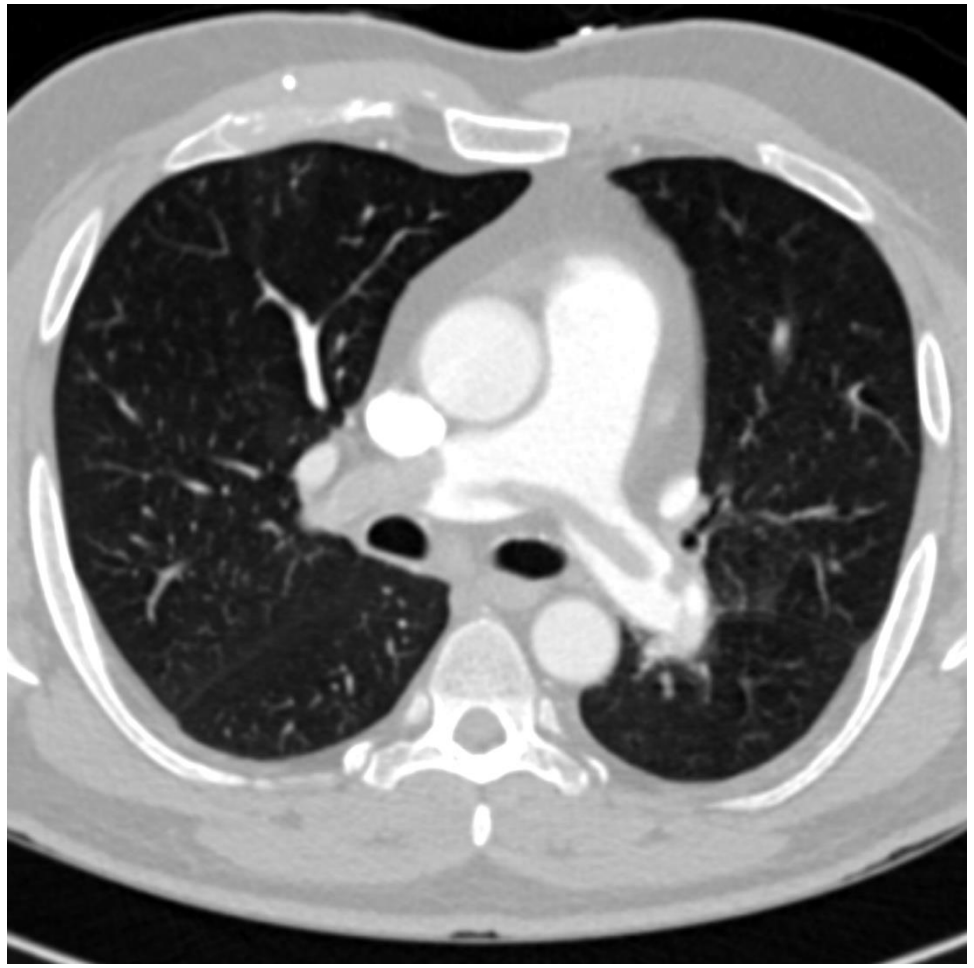
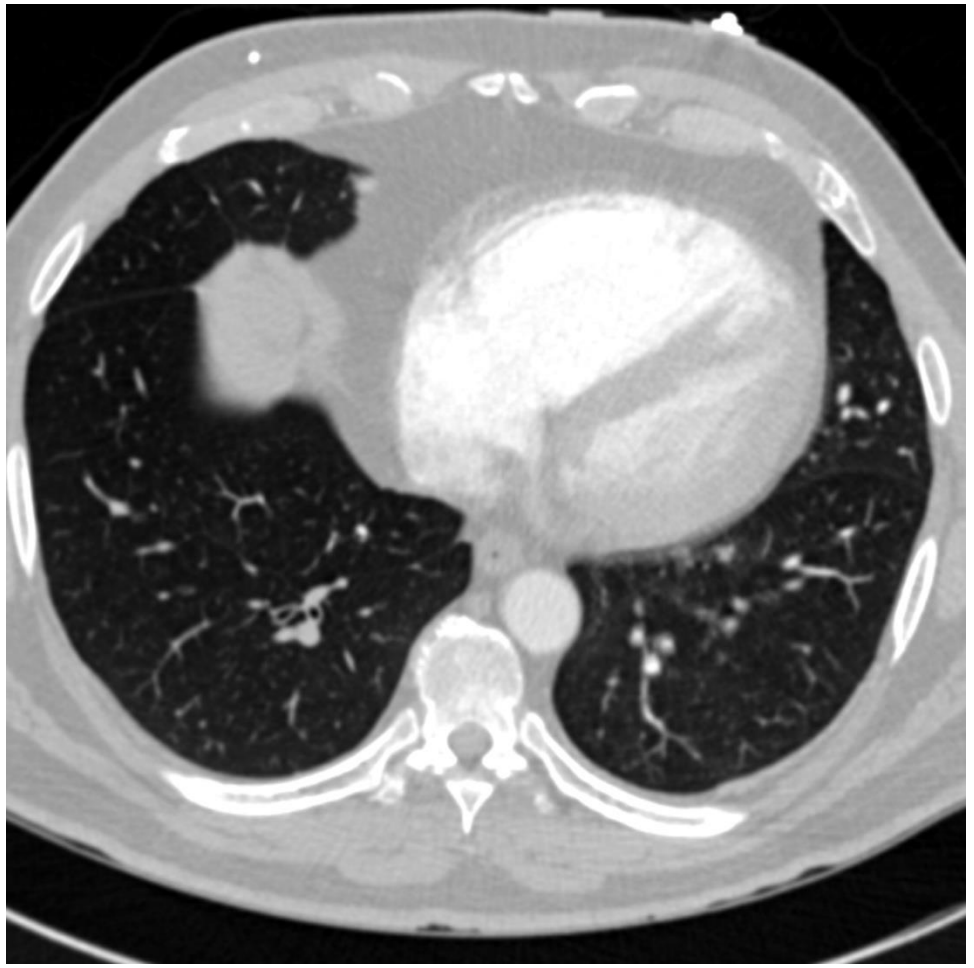
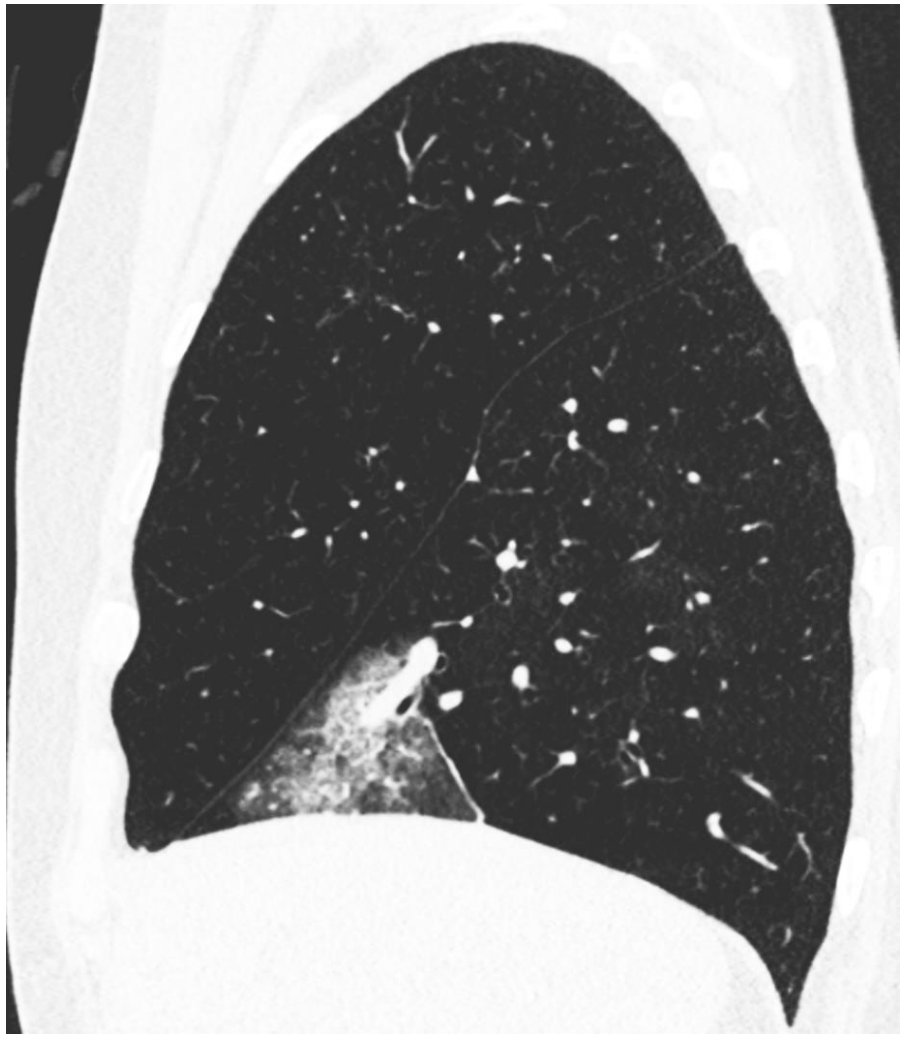
Pulmonary Embolism

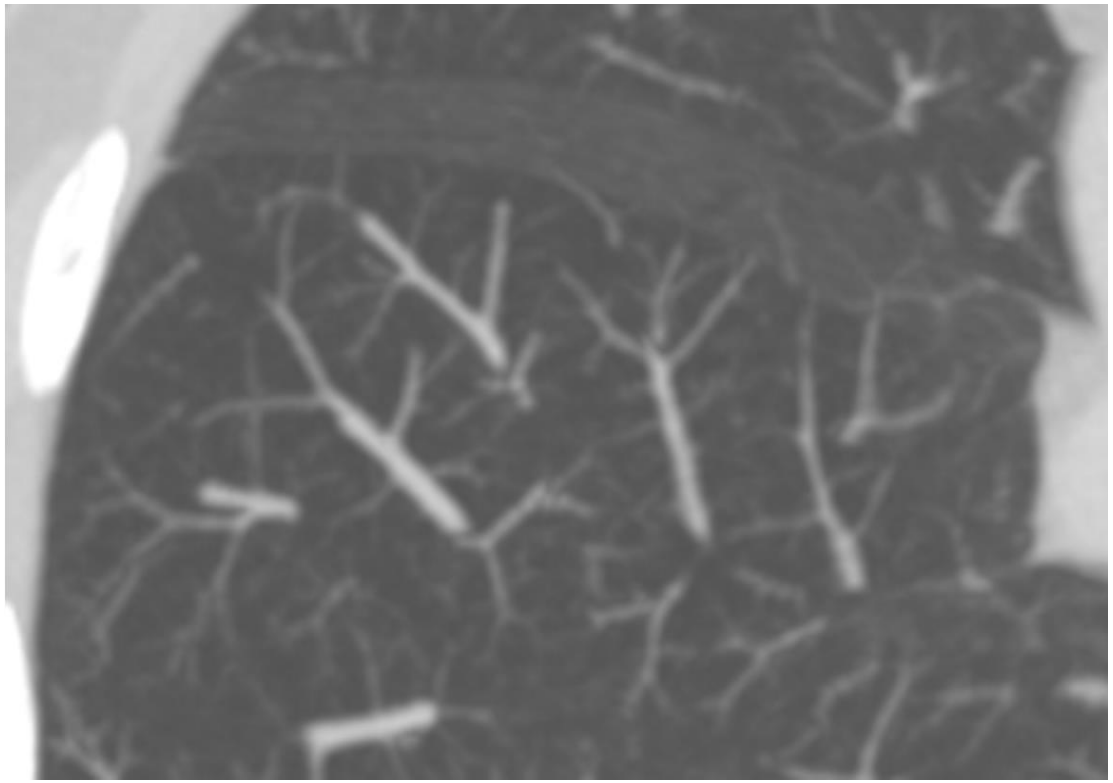


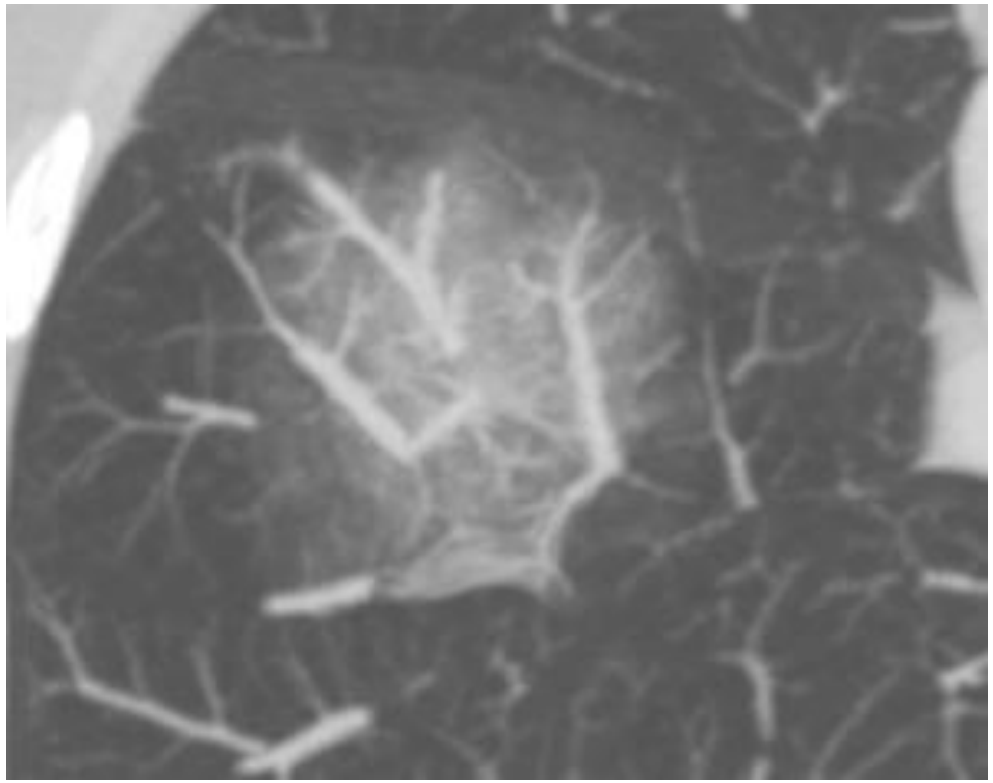


CTEPH – Balloon Therapy

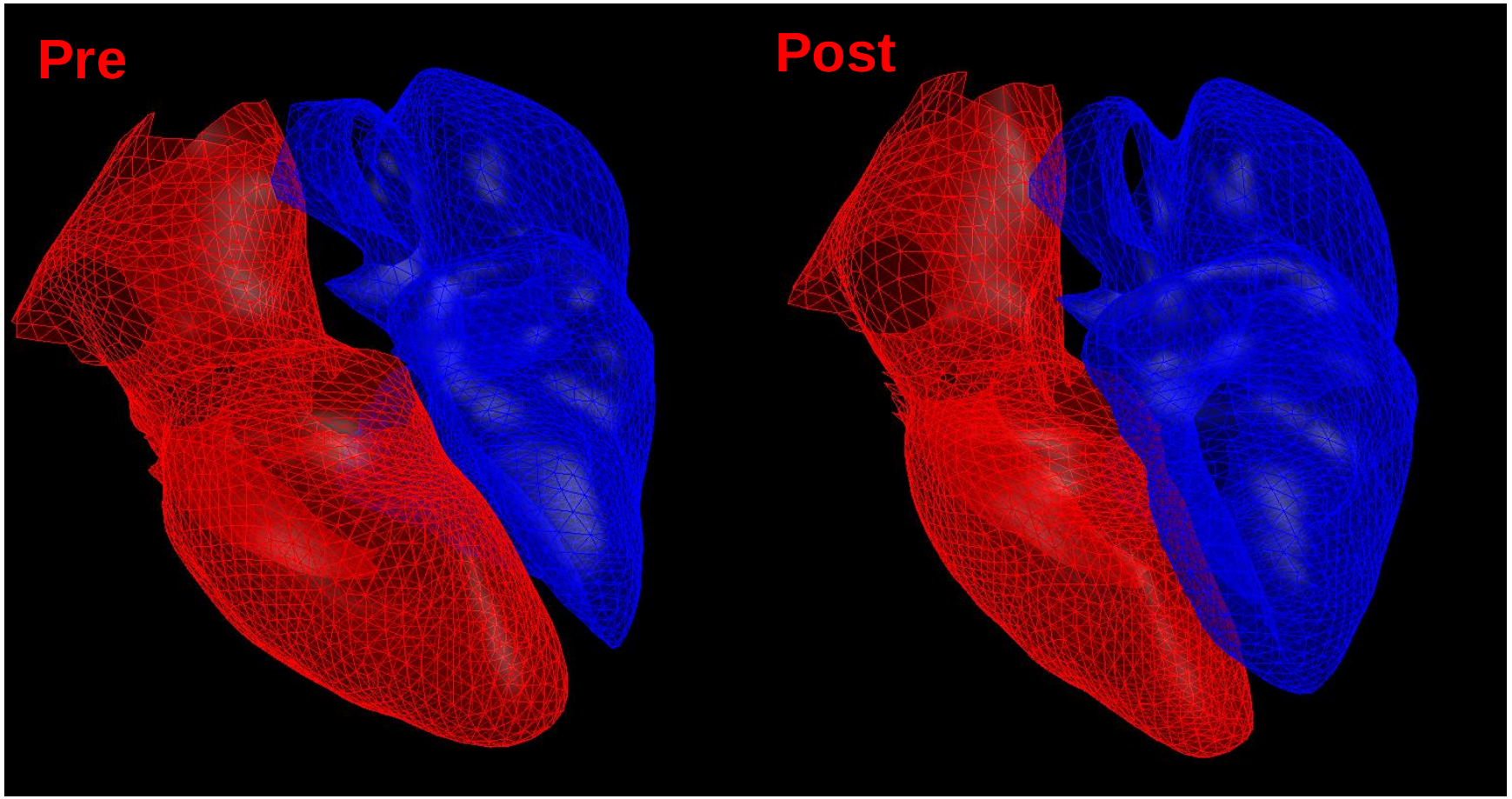


CTEPH – Balloon Therapy





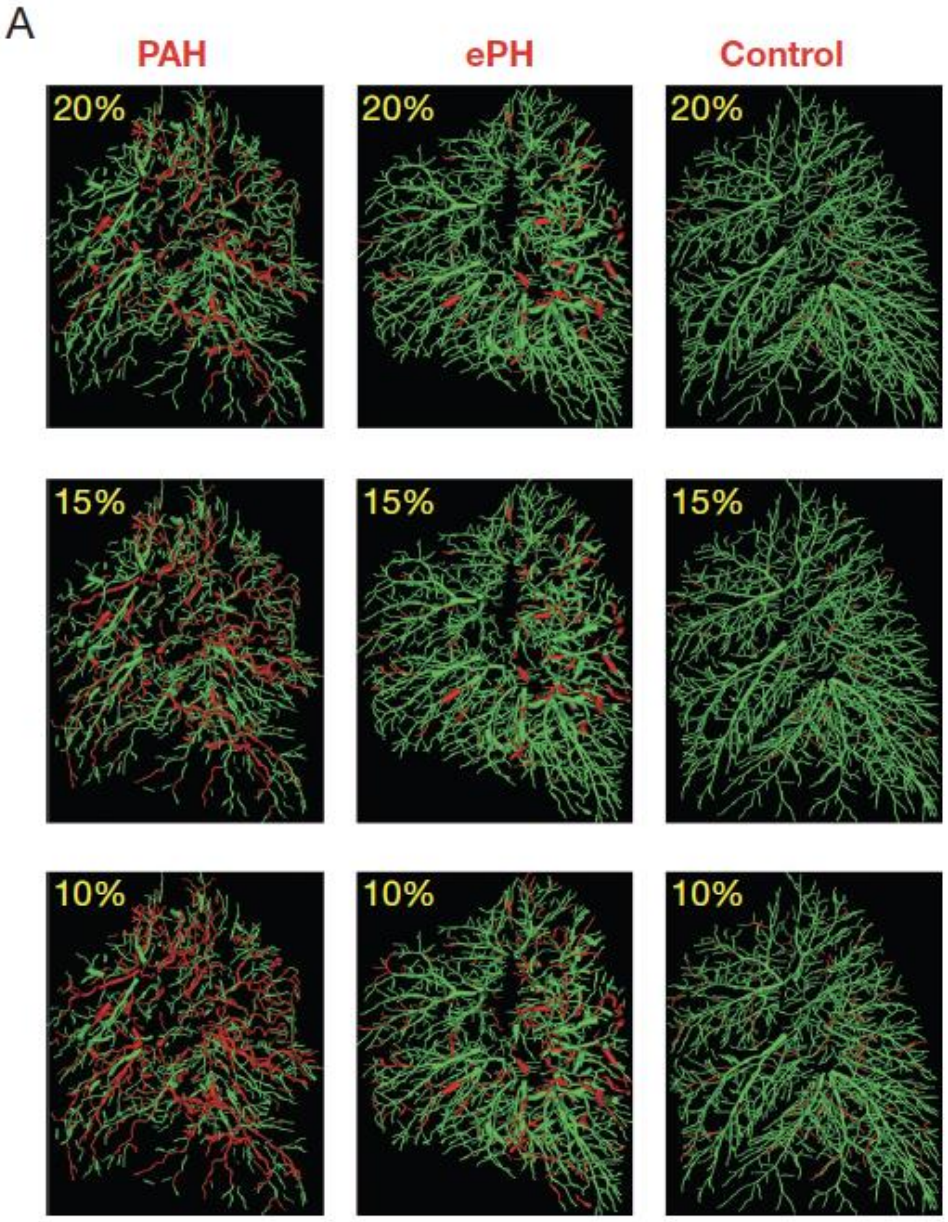
Response to Ultrasound Assisted Catheter Based PE Therapy (EKOS) SEATTLE II



RV: 167ml
LV: 119ml

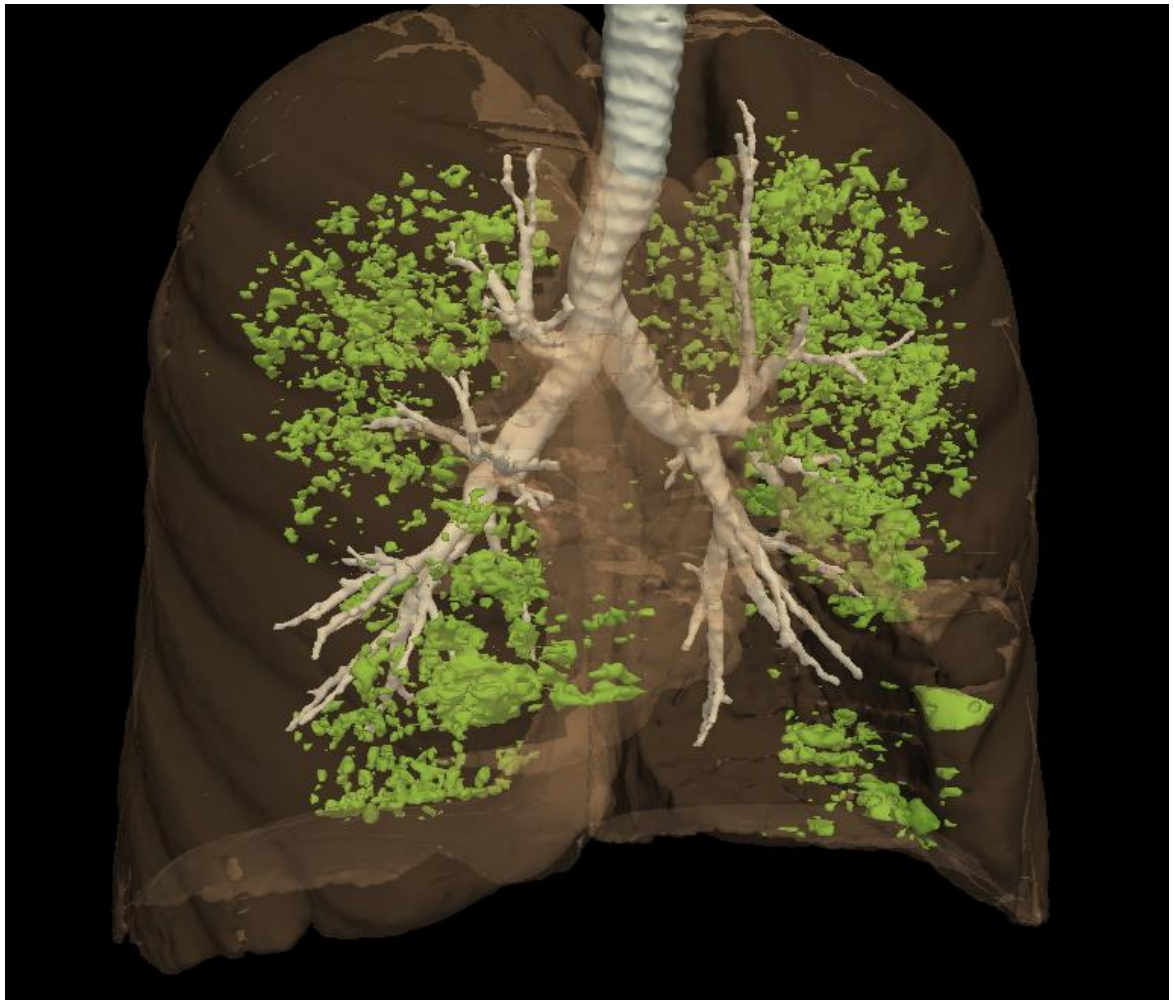
RV: 134ml
LV: 165ml

At Risk for PAH?



Chest 2021;160(6):2220-2231.

Past/Present/Future



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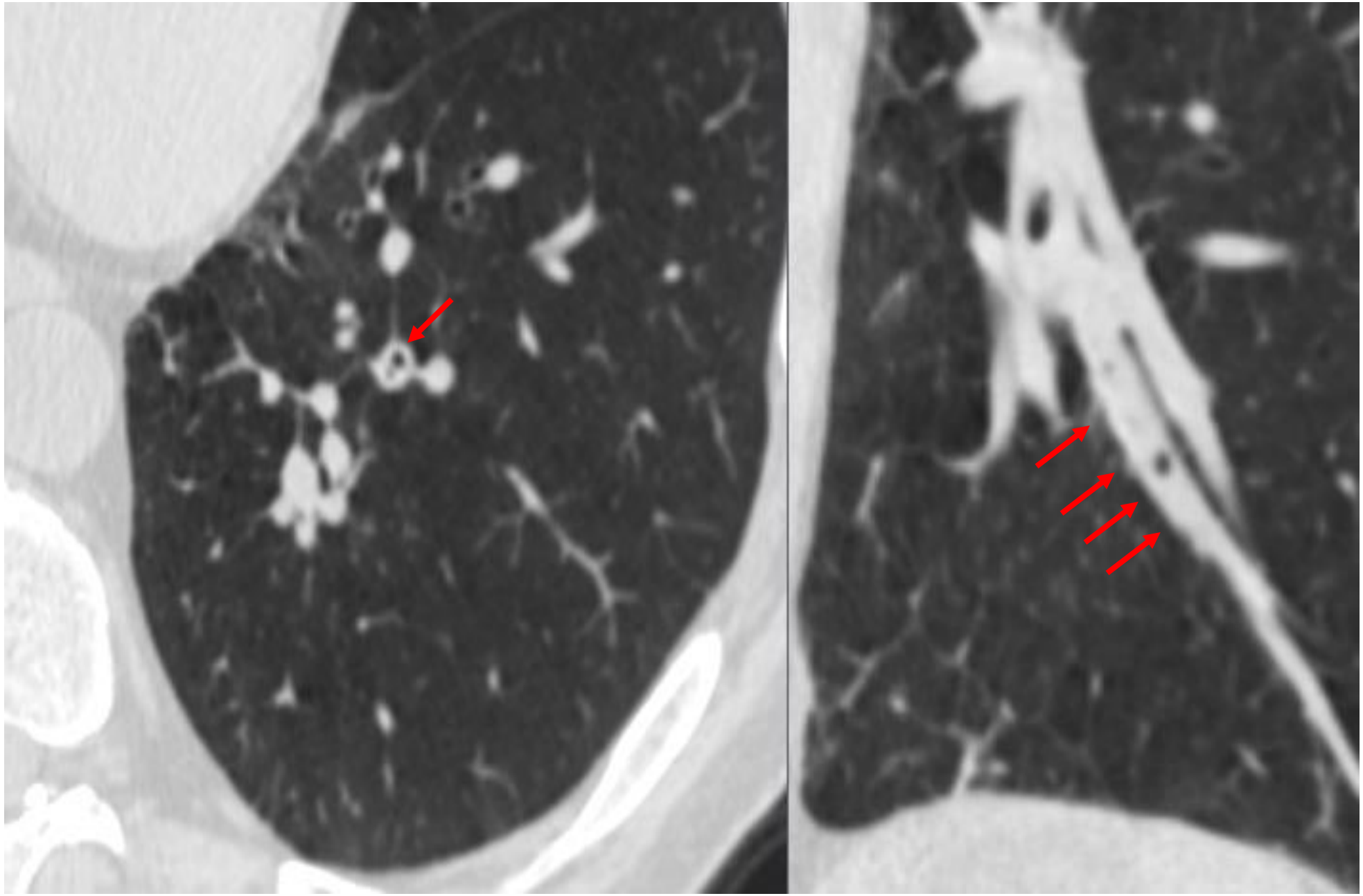
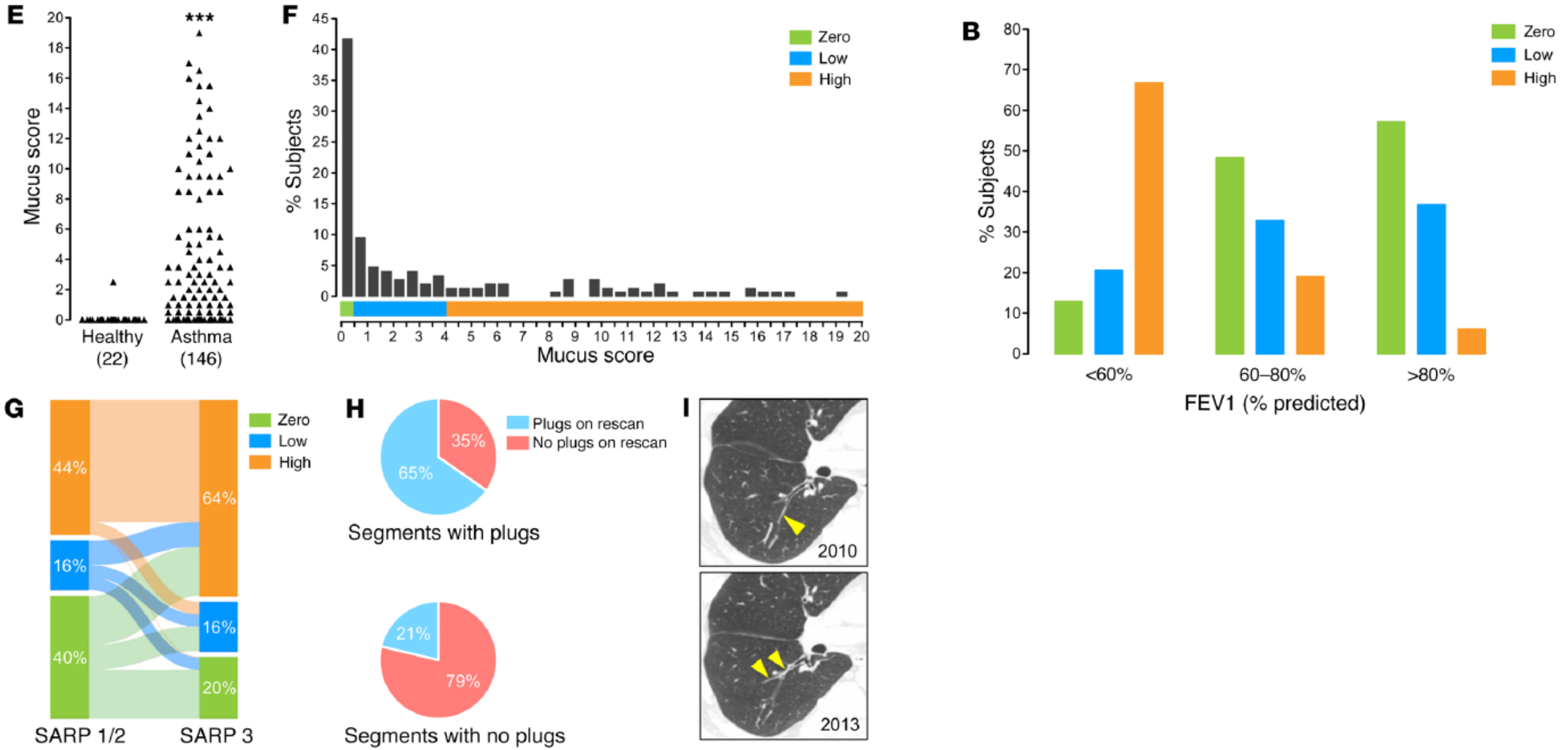
Mucus Dysfunction

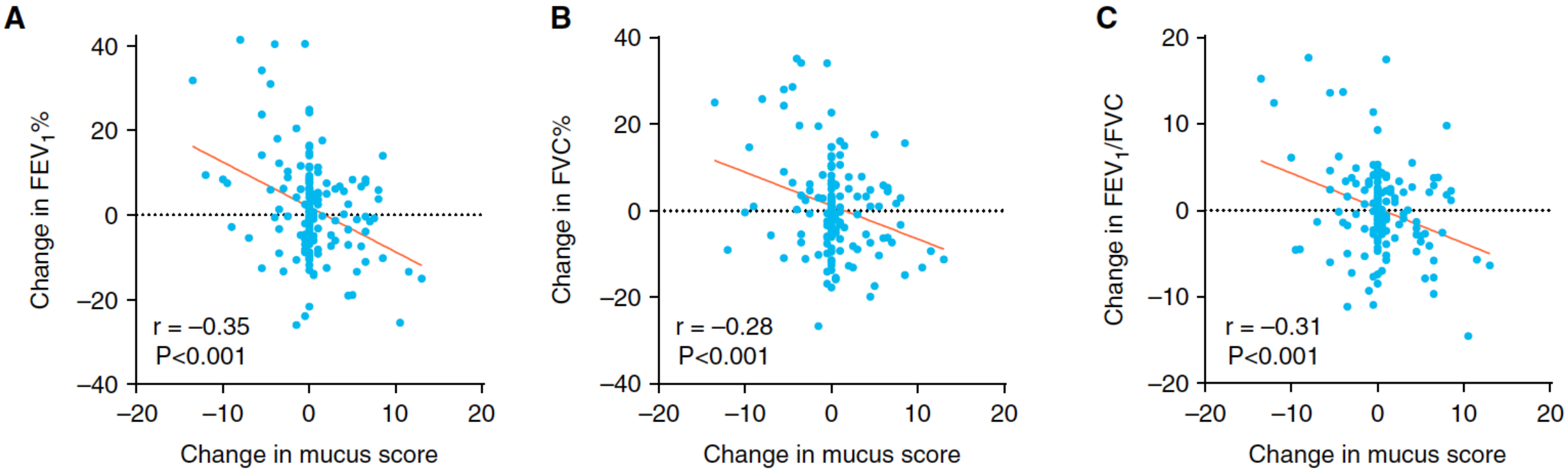


Mucus Plugs - Asthma



JCI 2018;128(3):997-1009.

Mucus Plugs - Asthma

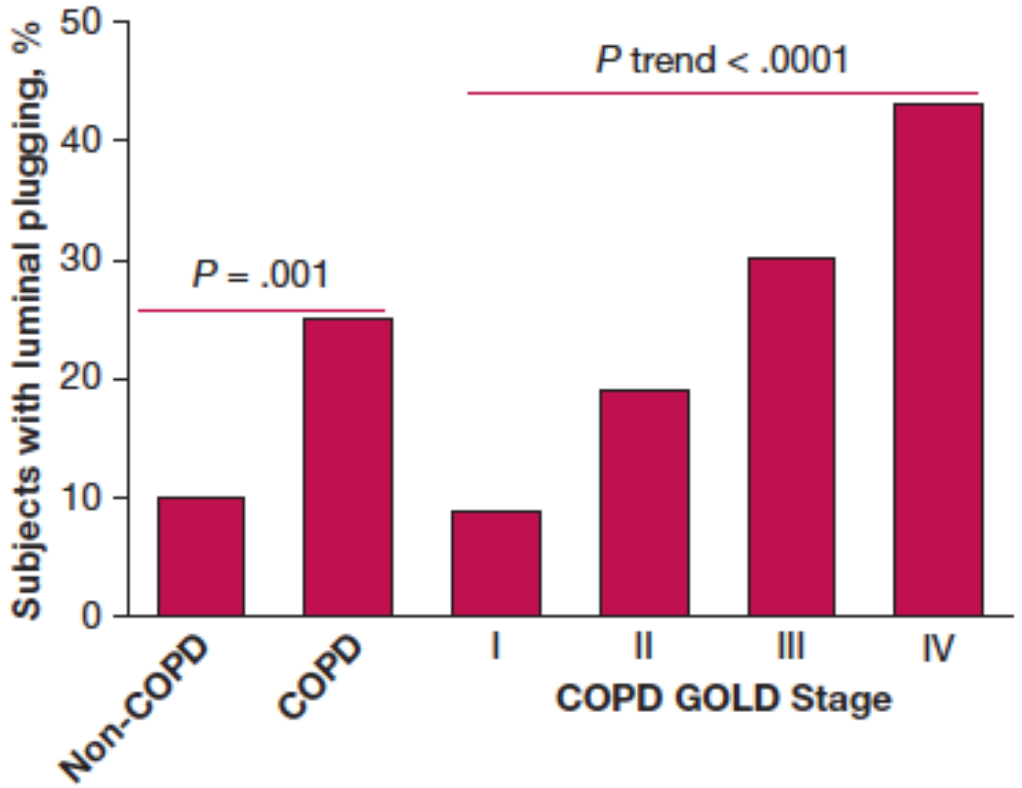


AJRCCM 2022;205(9):1036-1045.

Luminal Plugging on Chest CT Scan

Association With Lung Function, Quality of Life, and COPD Clinical Phenotypes

Yuka Okajima, MD, MPH; Carolyn E. Come, MD, MPH; Pietro Nardelli, PhD; Sushil K. Sonavane, MD; Andrew Yen, MD; Hrudaya P. Nath, MD; Nina Terry, MD; Scott A. Grumley, MD; Asmaa Ahmed, MD; Seth Kligerman, MD; Kathleen Jacobs, MD; David A. Lynch, MD; Barry J. Make, MD; Edwin K. Silverman, MD, PhD; George R. Washko, MD; Raúl San José Estépar, PhD; and Alejandro A. Diaz, MD, MPH



Prevalence of mucus plugging in COPD 25%-67%

Clinical Impact

↓ FEV1 % pred (-6%)

↓ HRQL (-4.9)

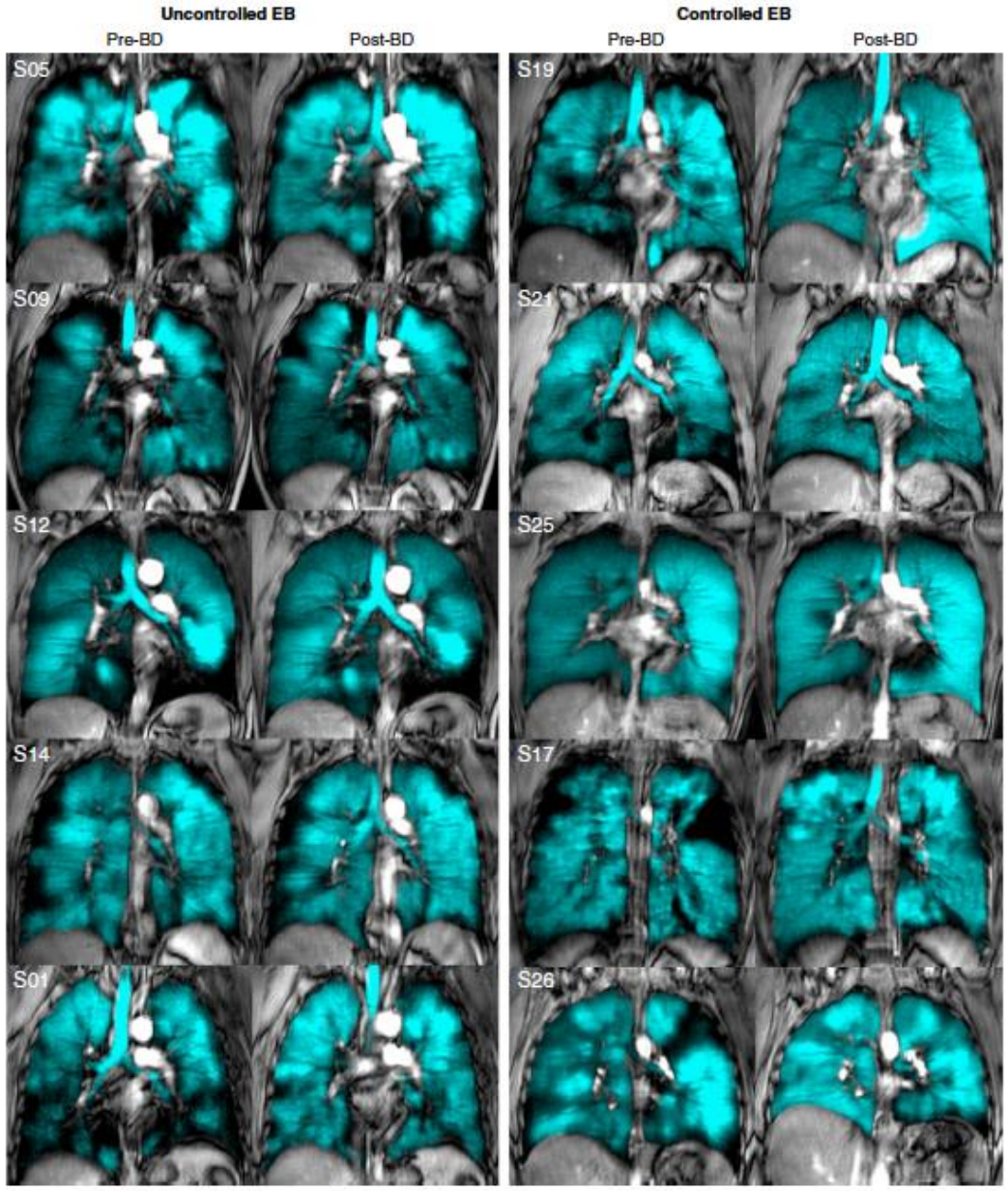
↑ Emphysema (OR=2.6)

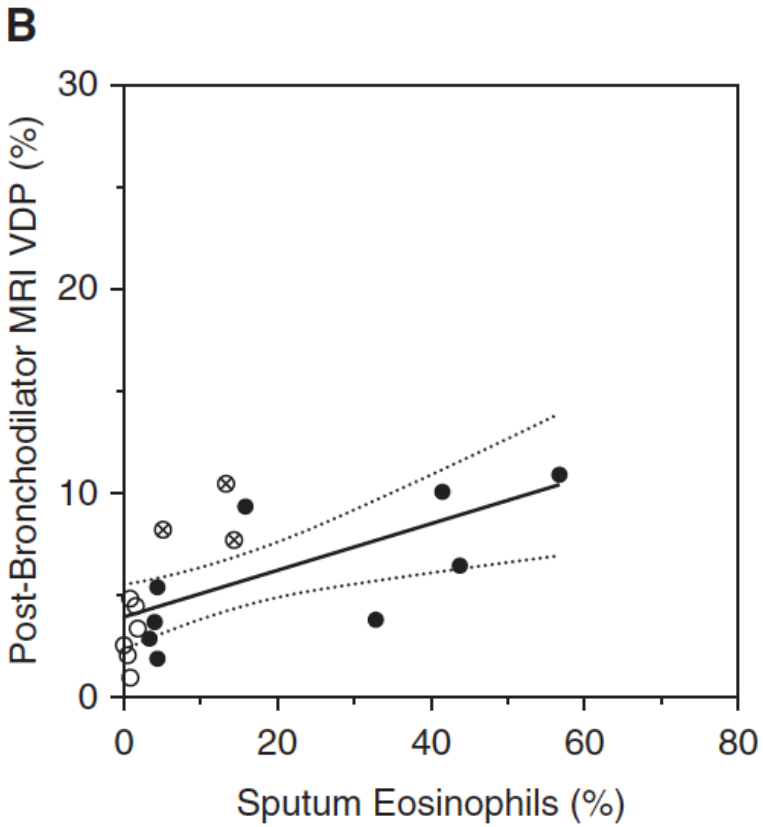
Persistence of mucus plugs

-67% at 1 year

Okajima, Chest 2020; Dunican, AJRCCM 2021

Airway Disease - Asthma





AJRCCM 2018;197:878-884.

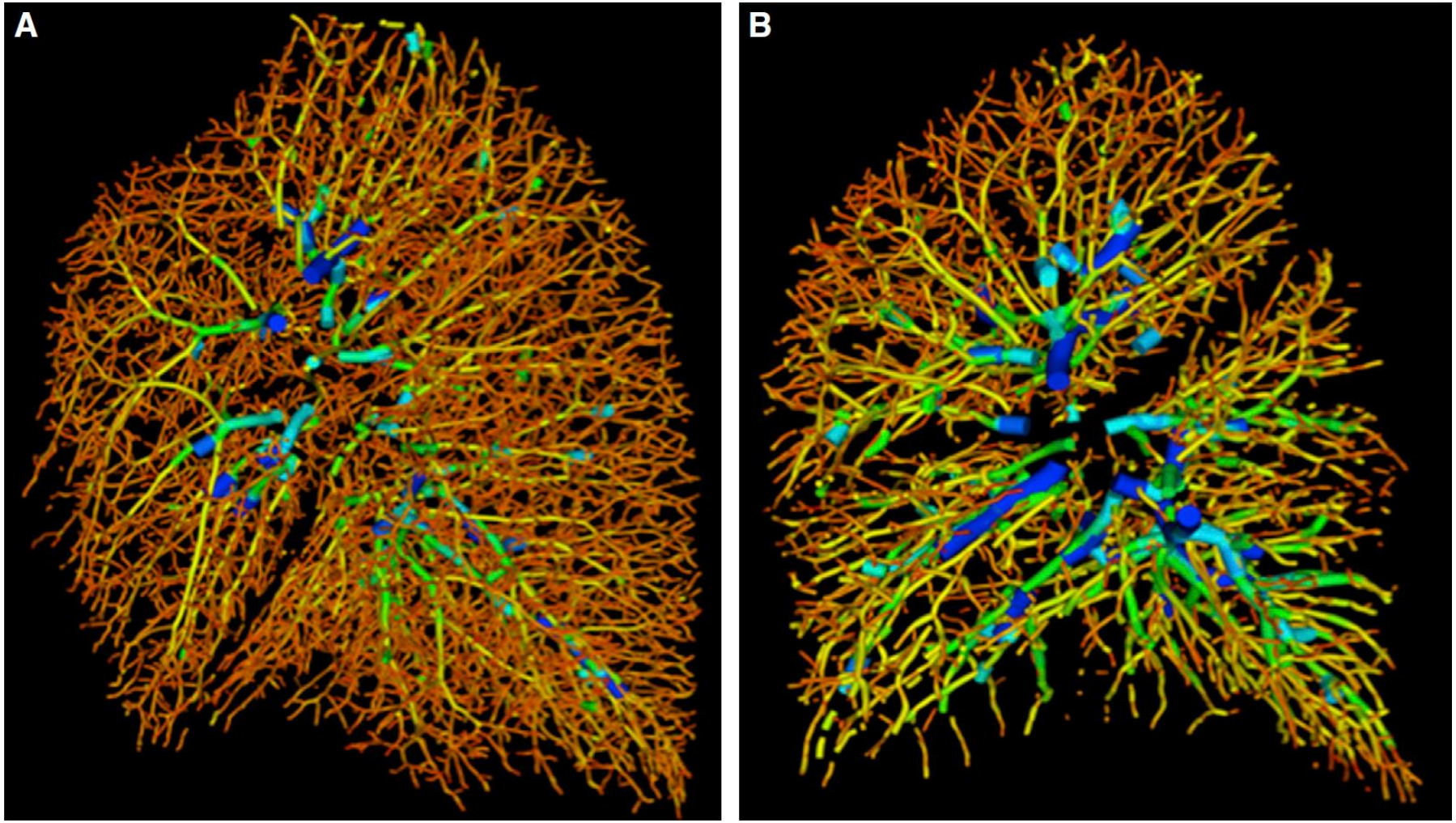
BRIGHAM HEALTH
BRIGHAM AND WOMEN'S HOSPITAL

Pruning of the Pulmonary Vasculature in Asthma

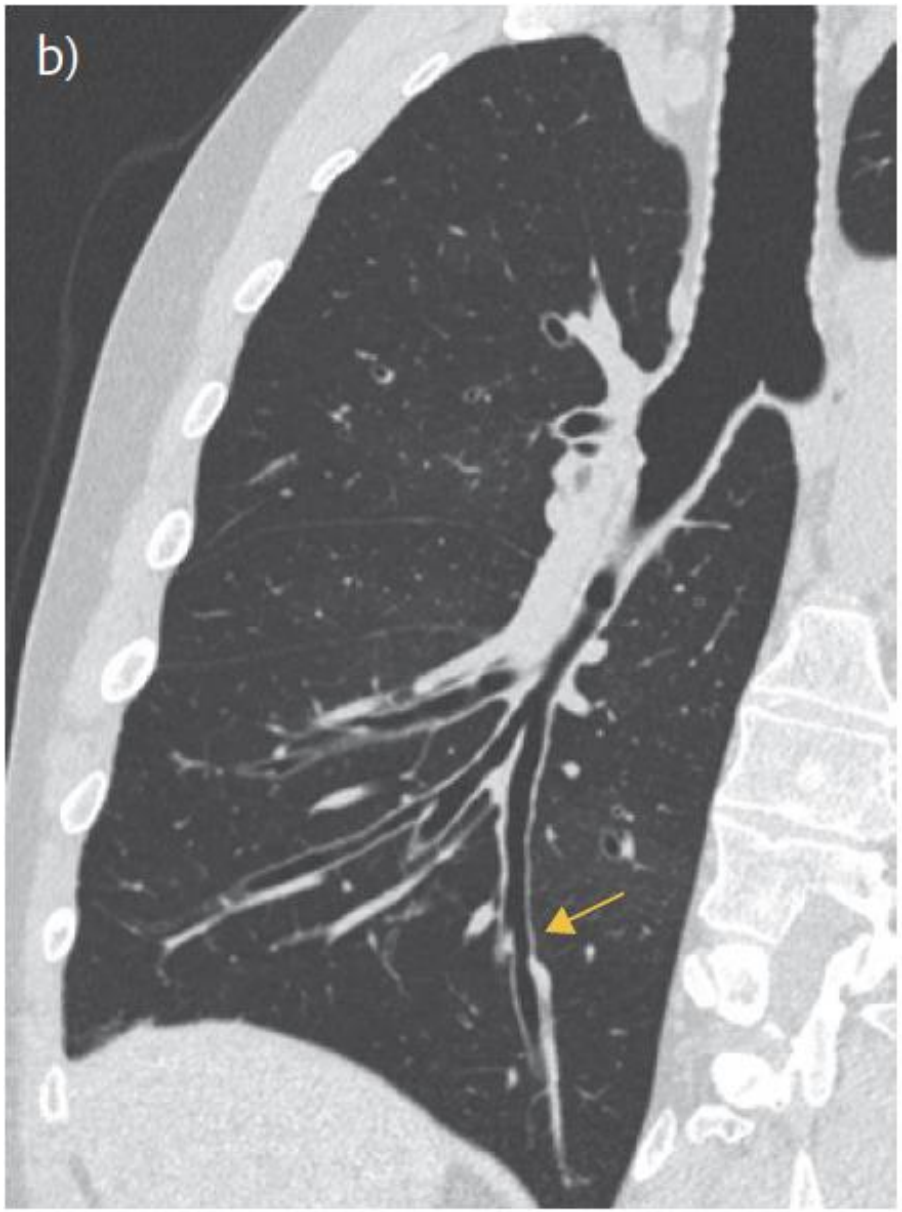
The Severe Asthma Research Program (SARP) Cohort

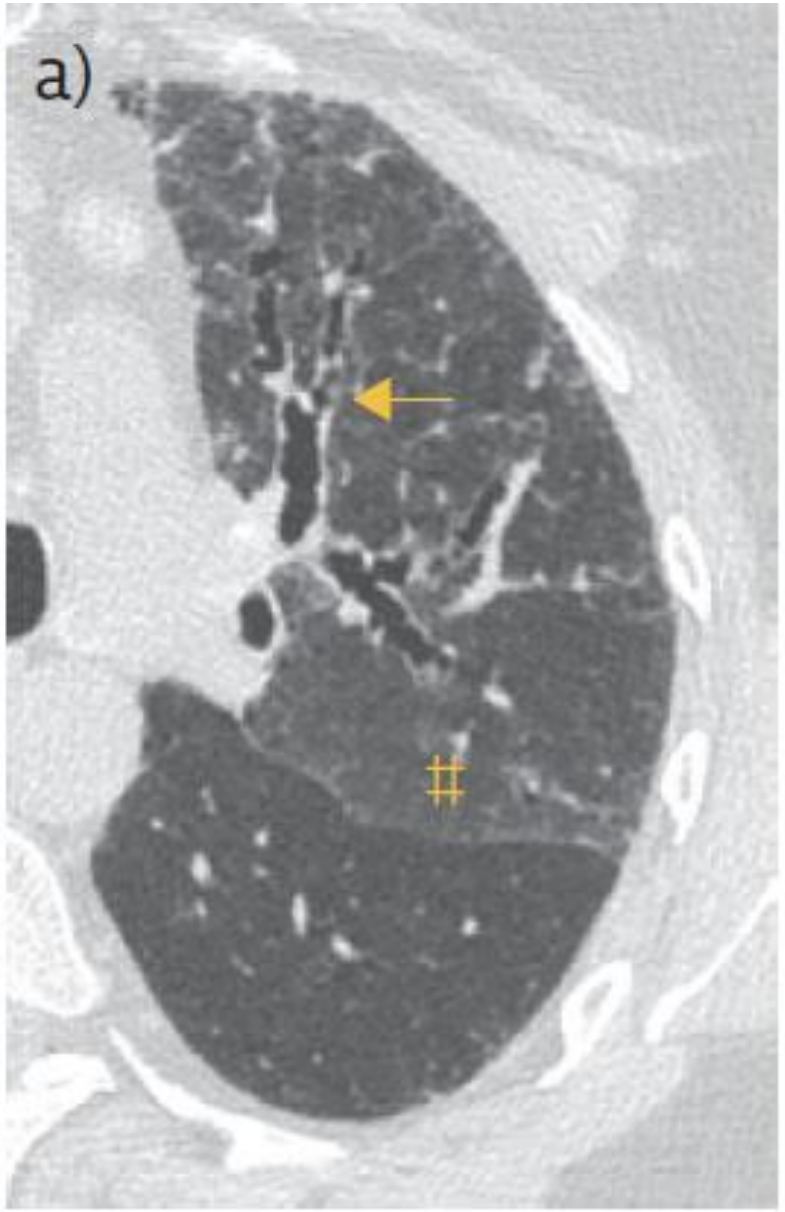
HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

Samuel Y. Ash[1,2*], Farbod N. Rahaghi[1,2*], Carolyn E. Come[1,2], James C. Ross[2], Alysha G. Colon[3], Juan Carlos Cardet-Guisasola[4], Eleanor M. Dunican[5], Eugene R. Bleecker[6], Mario Castro[7], John V. Fahy[8], Sean B. Fain[9,10,11], Benjamin M. Gaston[12,13], Eric A. Hoffman[14,15,16], Nizar N. Jarjour[17], David T. Mauger[18], Sally E. Wenzel[19], Bruce D. Levy[1], Raul San Jose Estepar[2], Elliot Israel[1,‡], and George R. Washko[1,2‡]; for the SARP Investigators



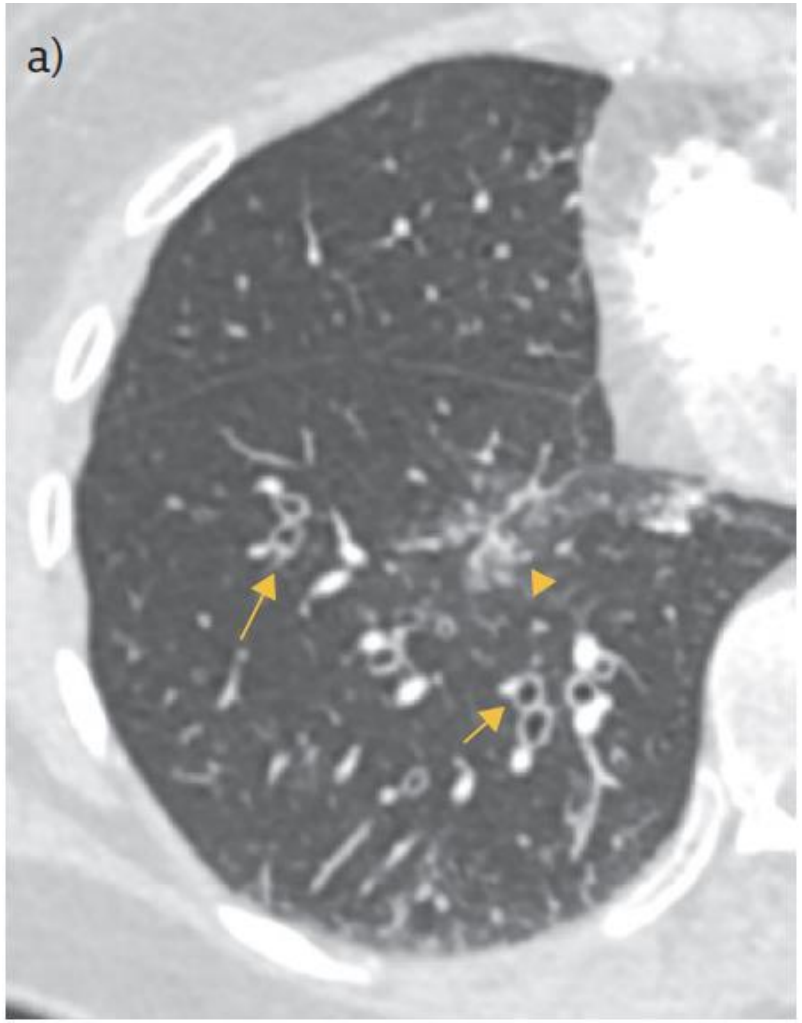
Bronchiectasis





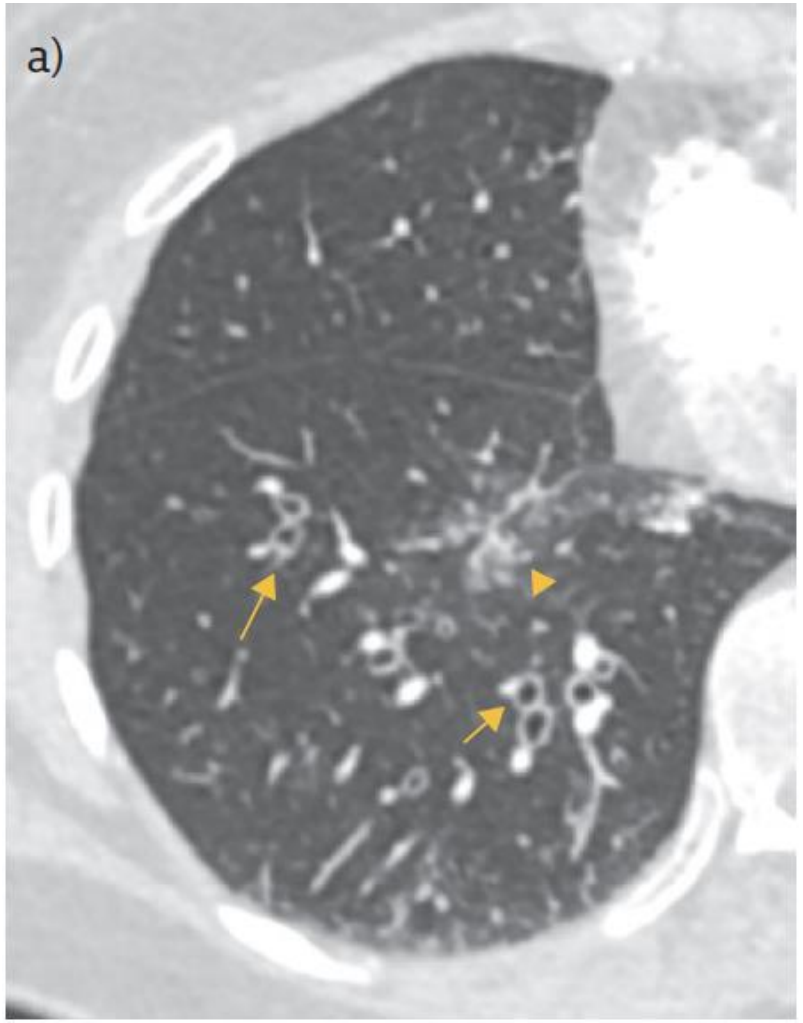
Breathe; 15:190-197.

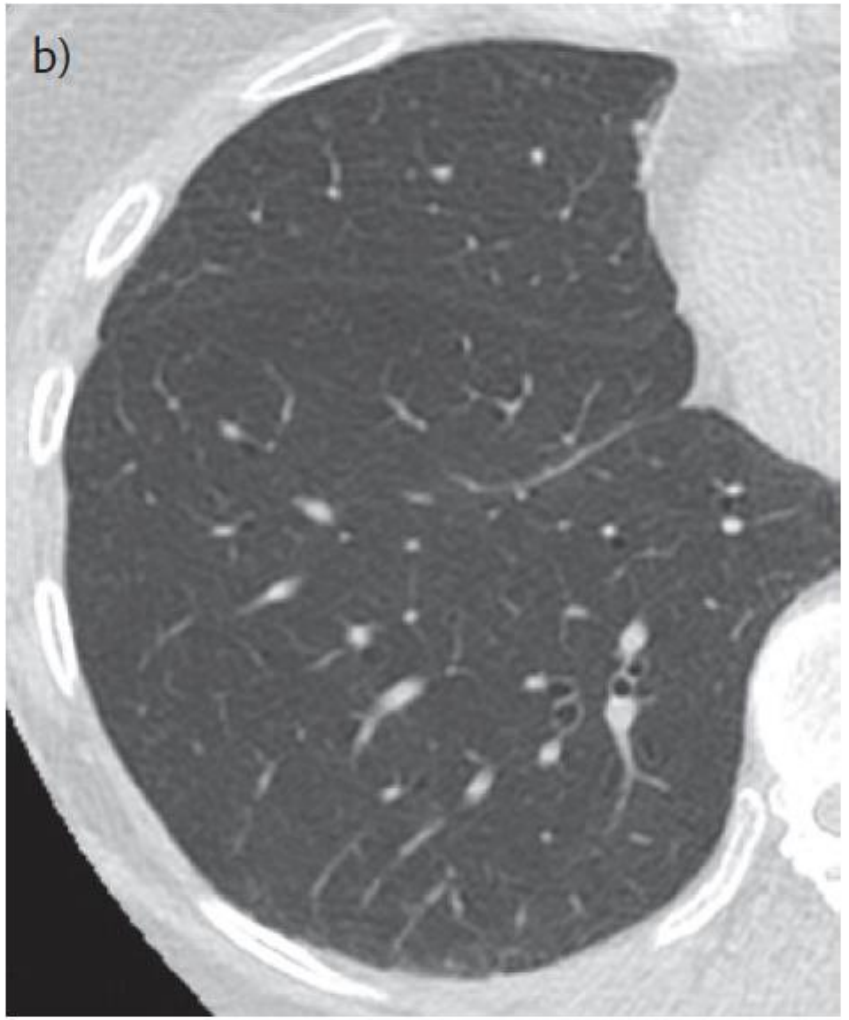
Bronchiectasis



Breathe; 15:190-197.

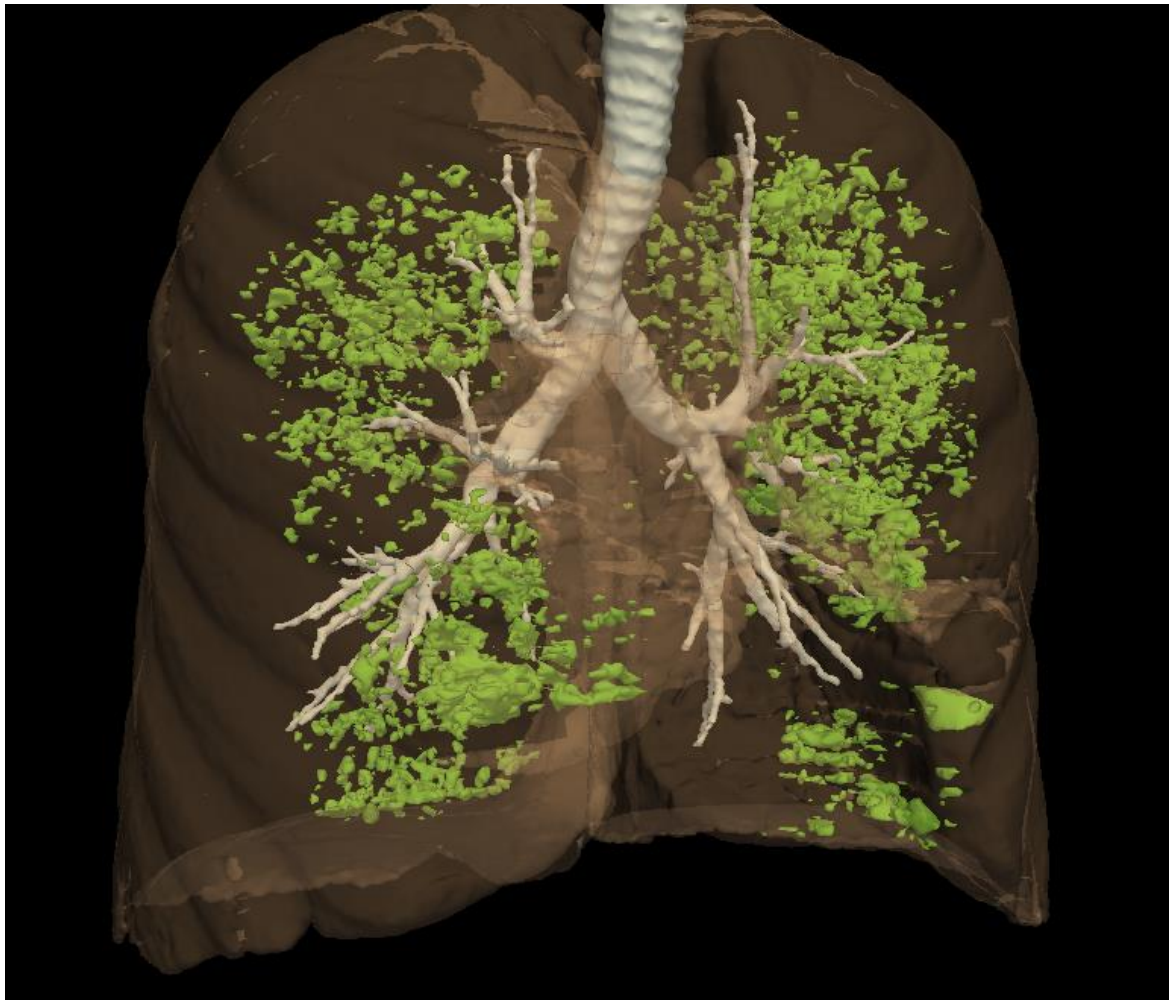
Bronchiectasis





Breathe; 15:190-197.

Past/Present/Future



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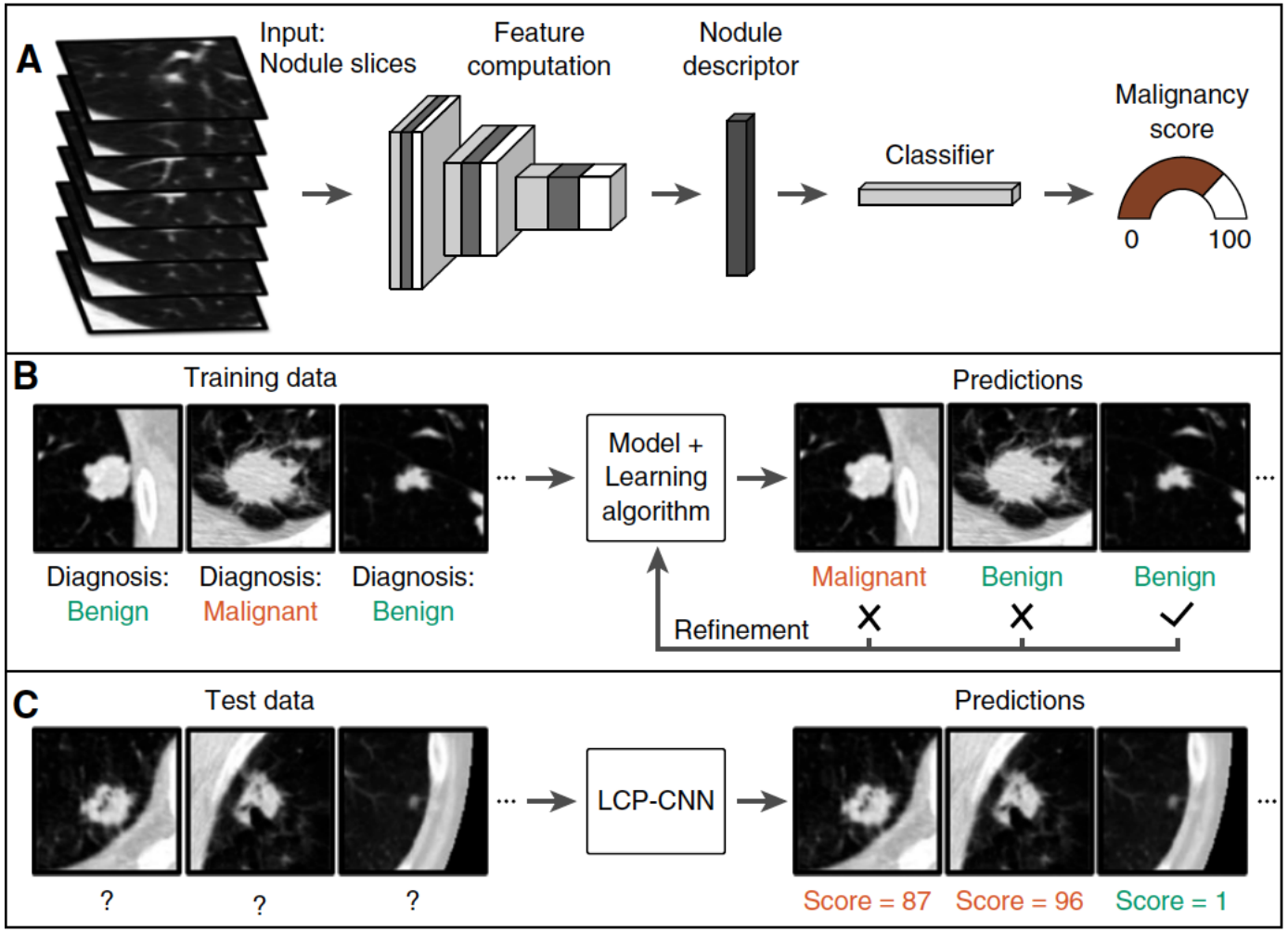
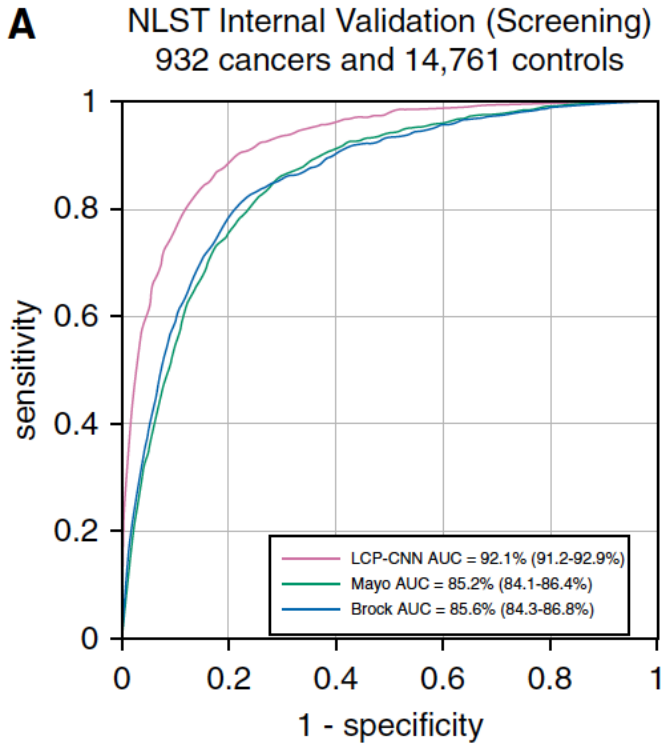
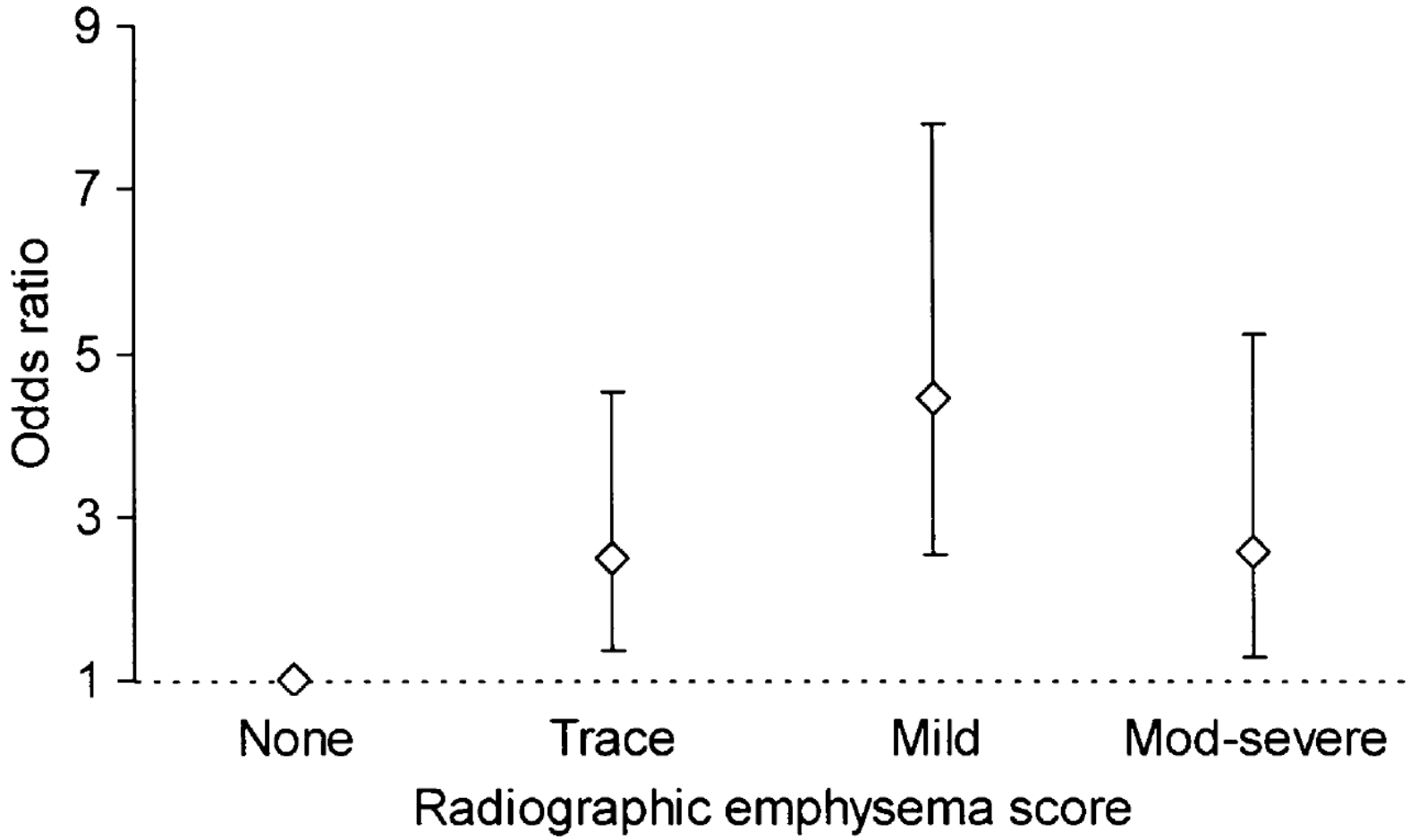
Lung Cancer





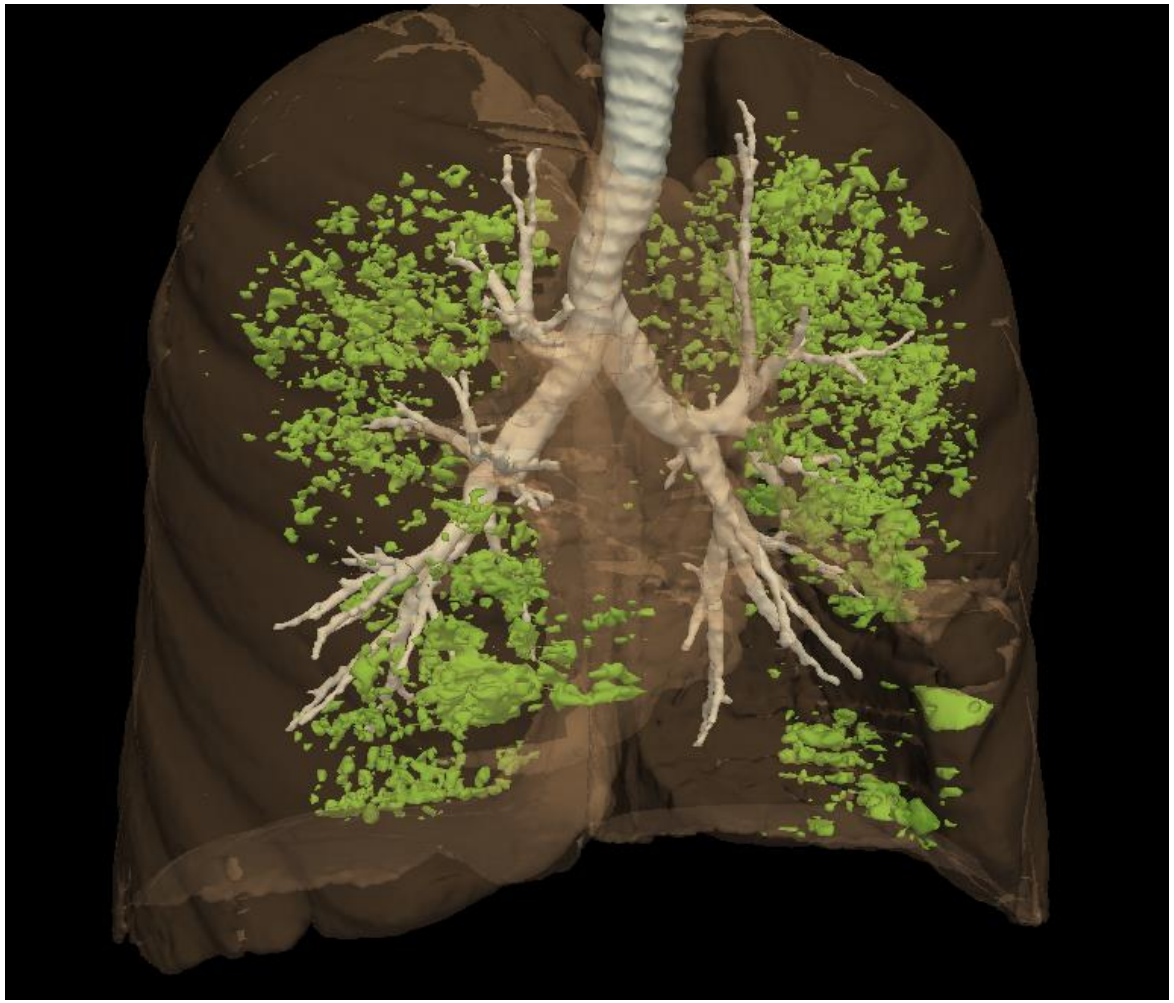
AJRCCM 2020;202:241-249.

Lung Cancer



AJRCCM 2008;178:738-744.

Past/Present/Future



- Parenchyma
  - Emphysema
  - ILD
- Vasculature
  - Pulmonary embolism
  - Vasculopathy
- Airways
  - Mucus Plugs
  - Bronchiectasis
- Lung Cancer
- Body Composition
- Intrinsic Susceptibility

Bone Mineral Density

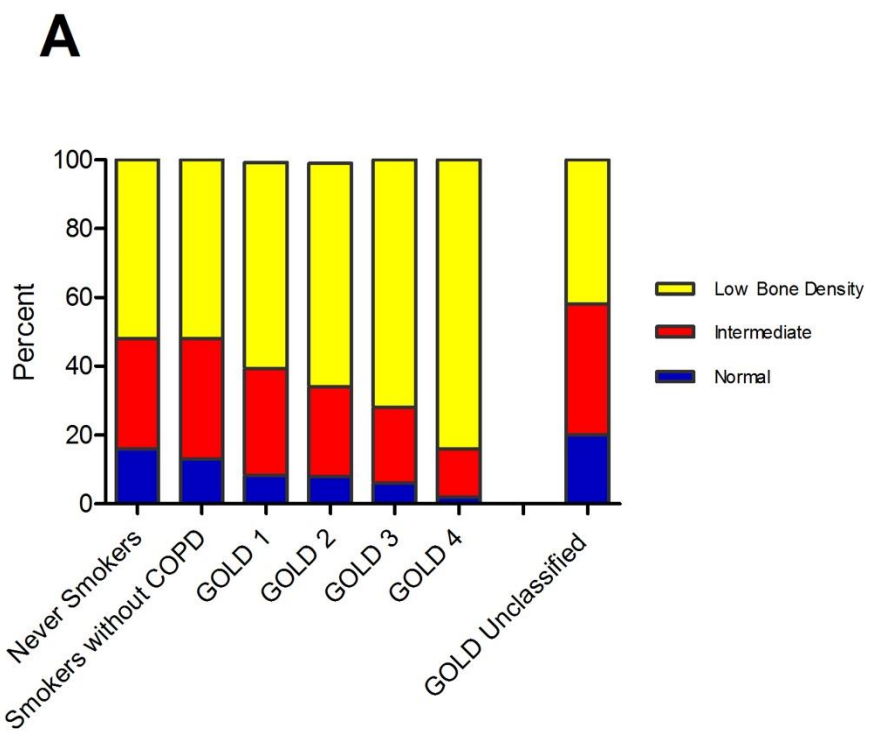
N=3321 current and ex-smokers in COPDGene

Low volumetric bone mineral density (vBMD)

- 58% of all subjects
- 84% of subjects with very severe COPD

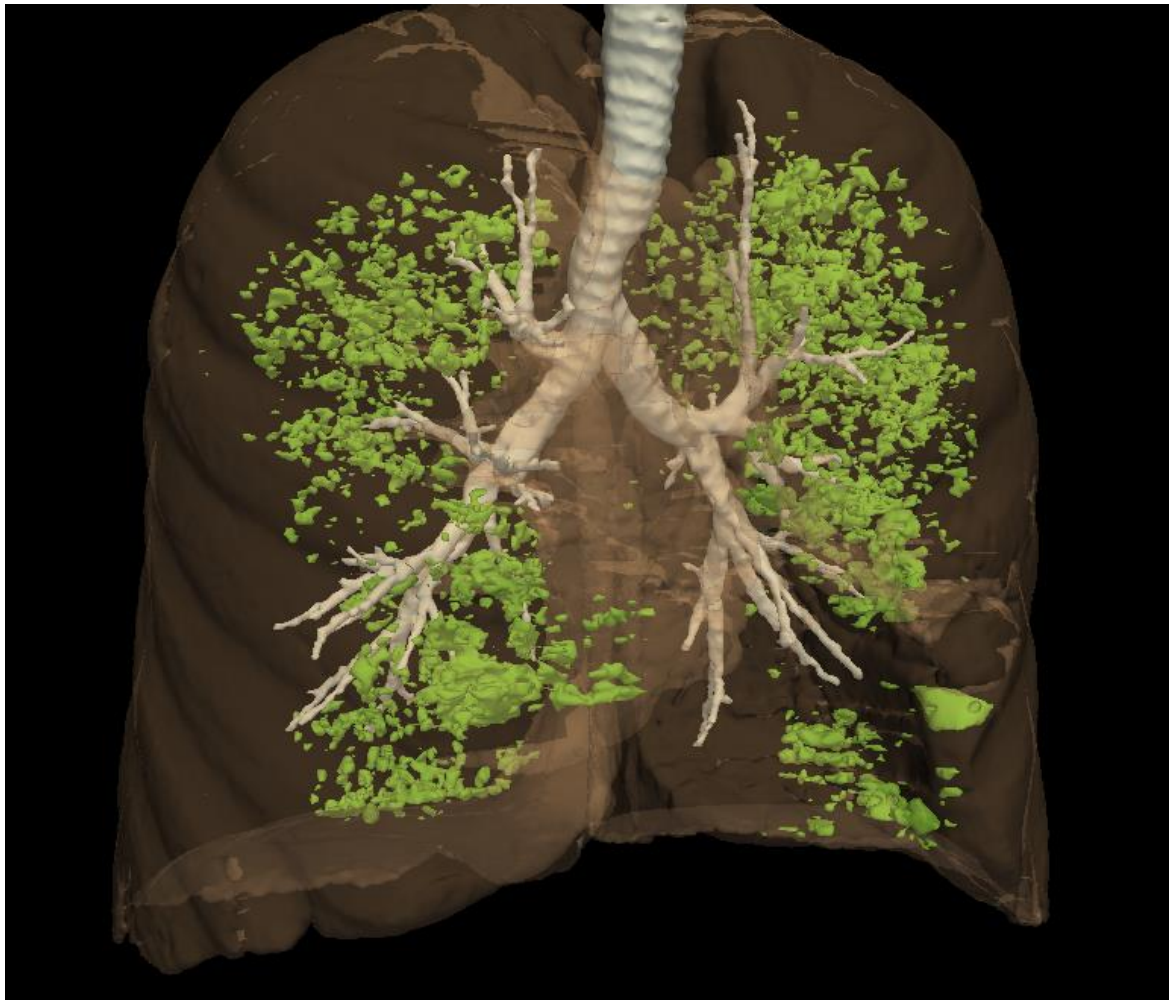
Males had greater risk of low vBMD (-2.5 SD below young adult mean by QCT)

Males with more vertebral fractures



Jaramillo et al. Annals of ATS 2015

Past/Present/Future



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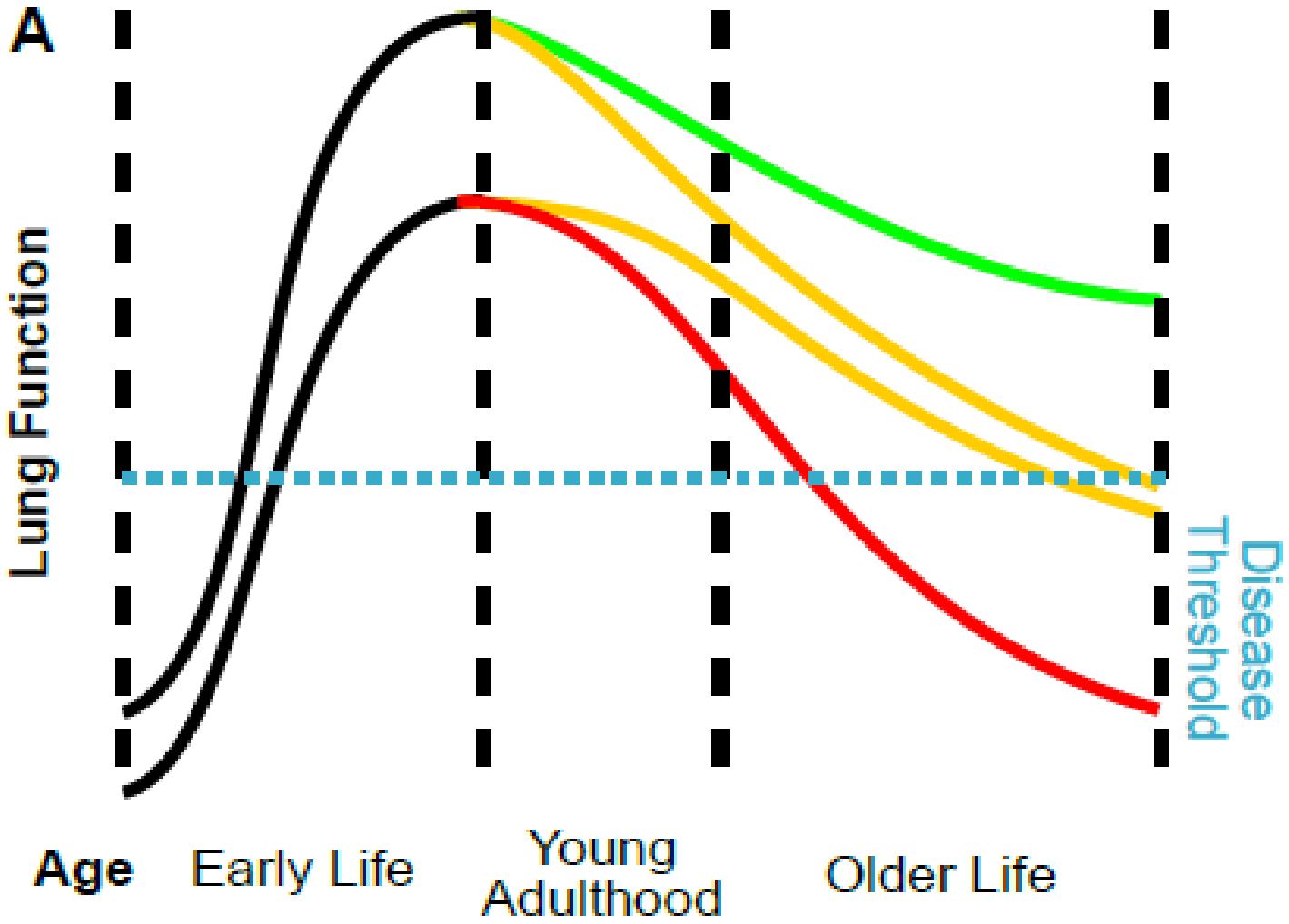
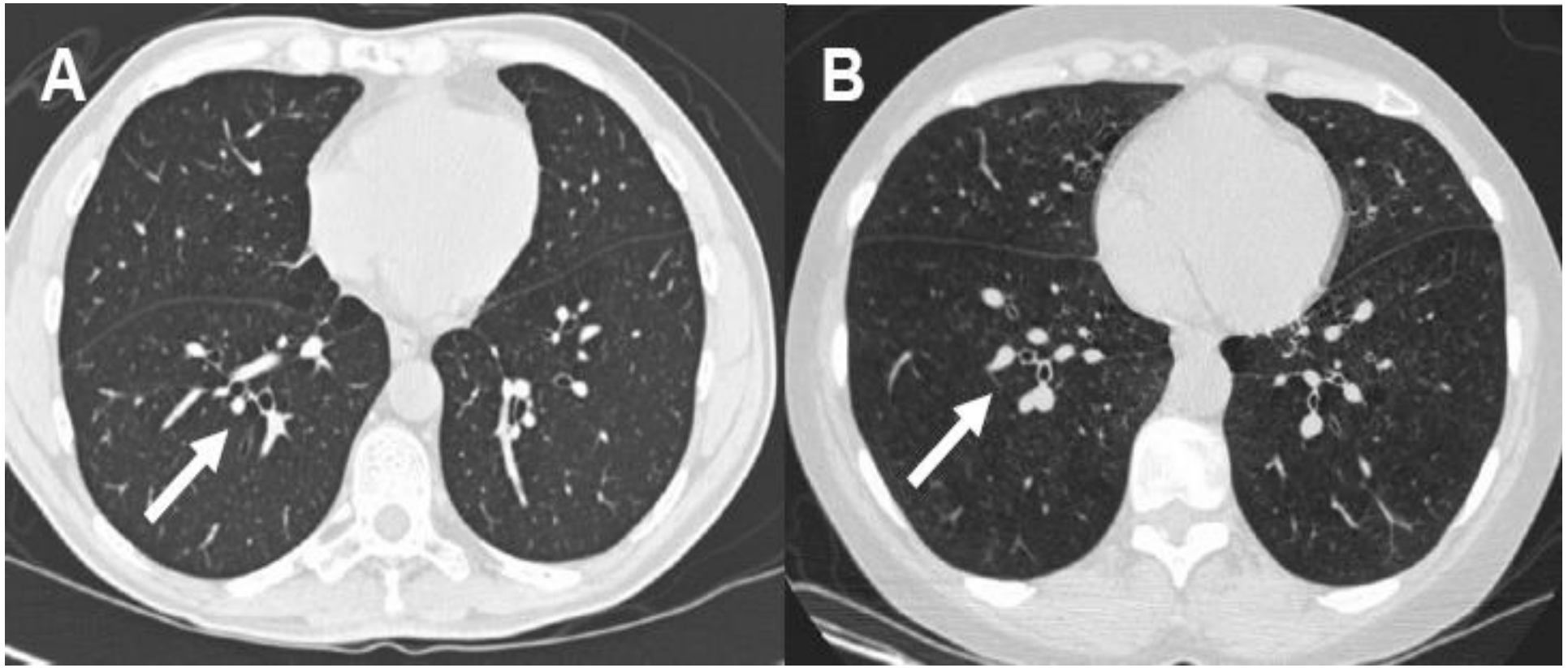
Trajectories of Lung Function



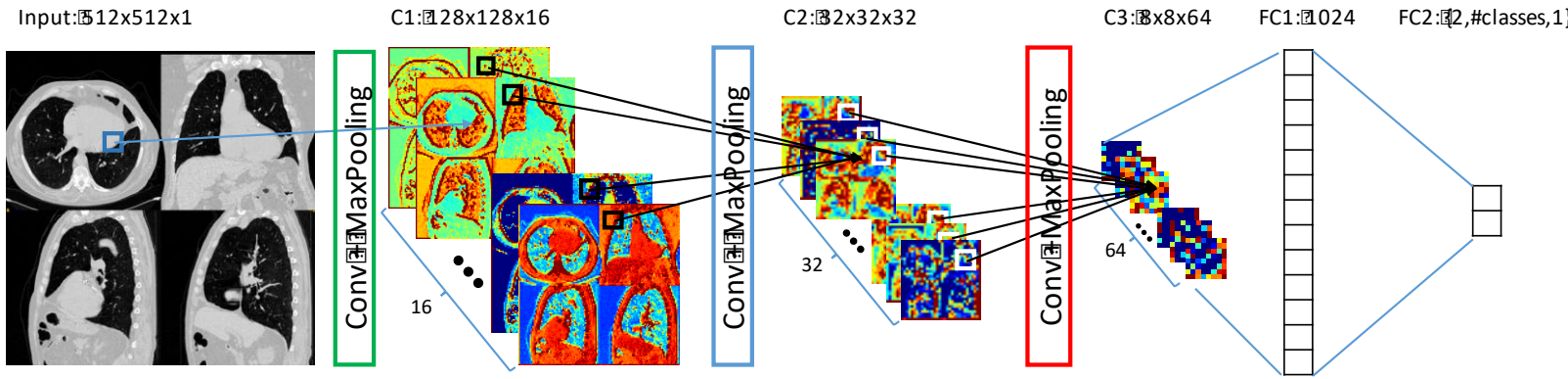
AJRCCM 2018;198(4): 440-446.

Innate Lung Structure?



J. App. Physio. 2014

"Featureless" Image Analysis



Outcome \ Clinical Phenotype

Am J Respir Crit Care Med, 2018

Thank you!