

QUANTITATIVE IMAGING A SYSTEMS TOOL

Lung cancer, COPD, cardiac & vascular disease

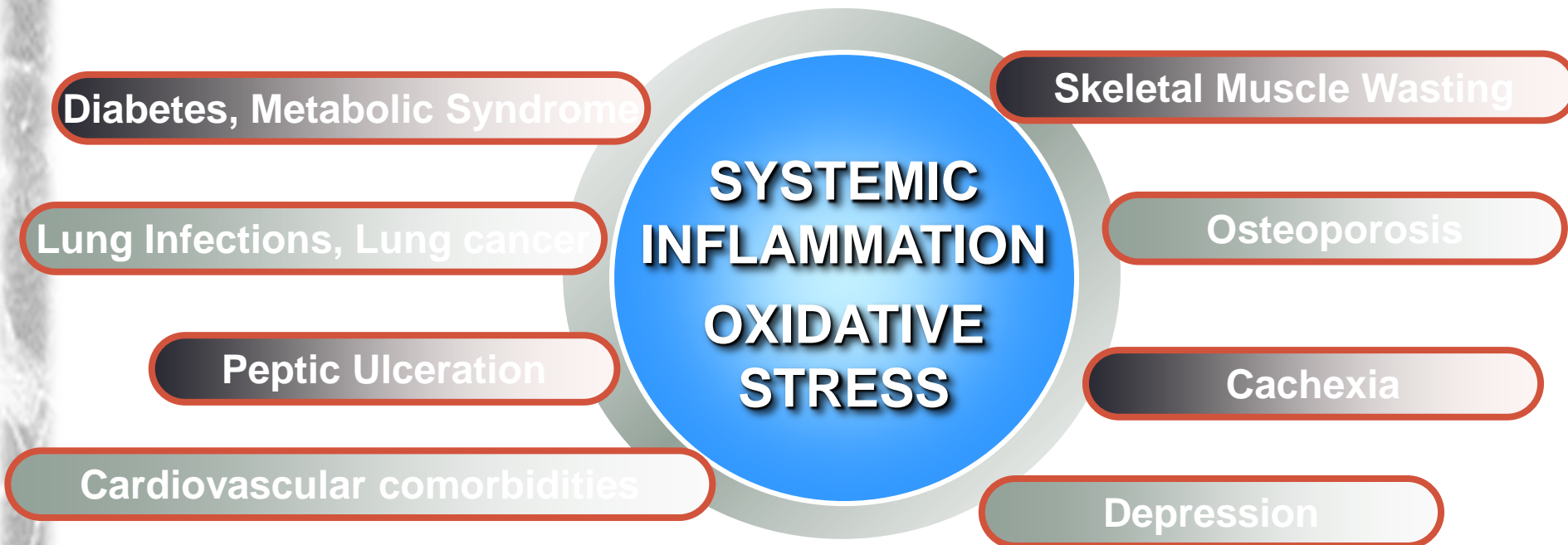
Raúl San José Estépar, Ph.D.

Brigham and Women's Hospital
Harvard Medical School



Adult aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years.

Systemic Effects





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[Home](#)
[Recommendations](#)
[Published Final
Recommendations](#)
[Recommendations in
Progress](#)
[Information for Health
Professionals](#)
[Information for
Consumers](#)
[Public Comments and
Nominations](#)
[Methods and Processes](#)
[About the USPSTF](#)

You are here: [Home](#) » [Recommendations for Primary Care Practice](#) » [Published Recommendations](#)

Lung Cancer: Screening

Release Date: December 2013

Recommendation Summary

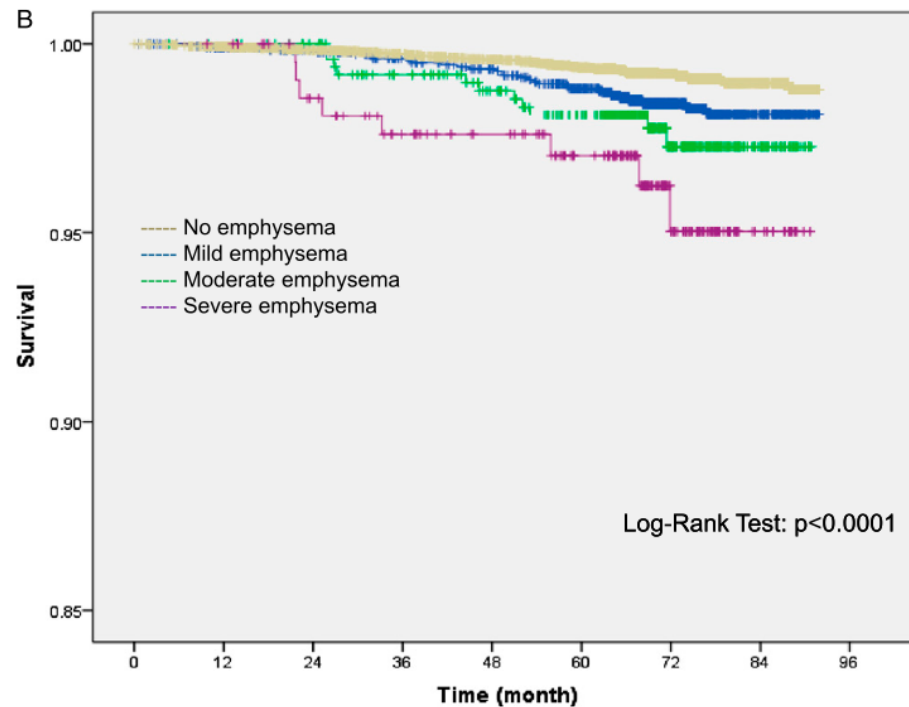
Summary of Recommendation and Evidence

Population	Recommendation	Grade (What's This?)
Adults Aged 55-80, with a History of Smoking	The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.	B

A System-based Analysis has Real Implications

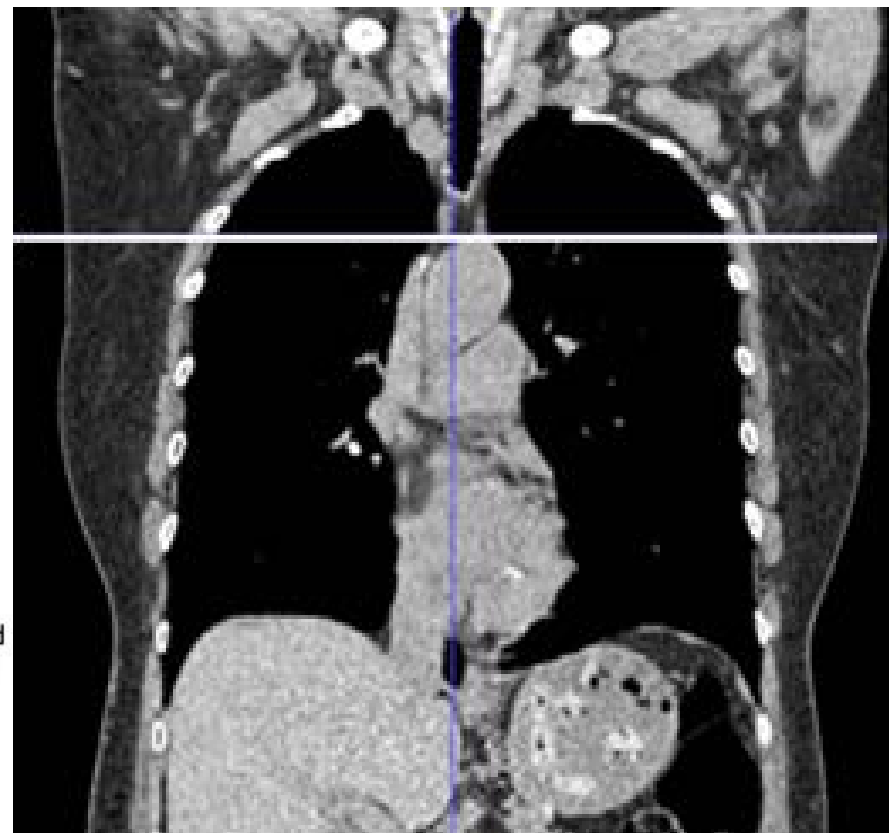
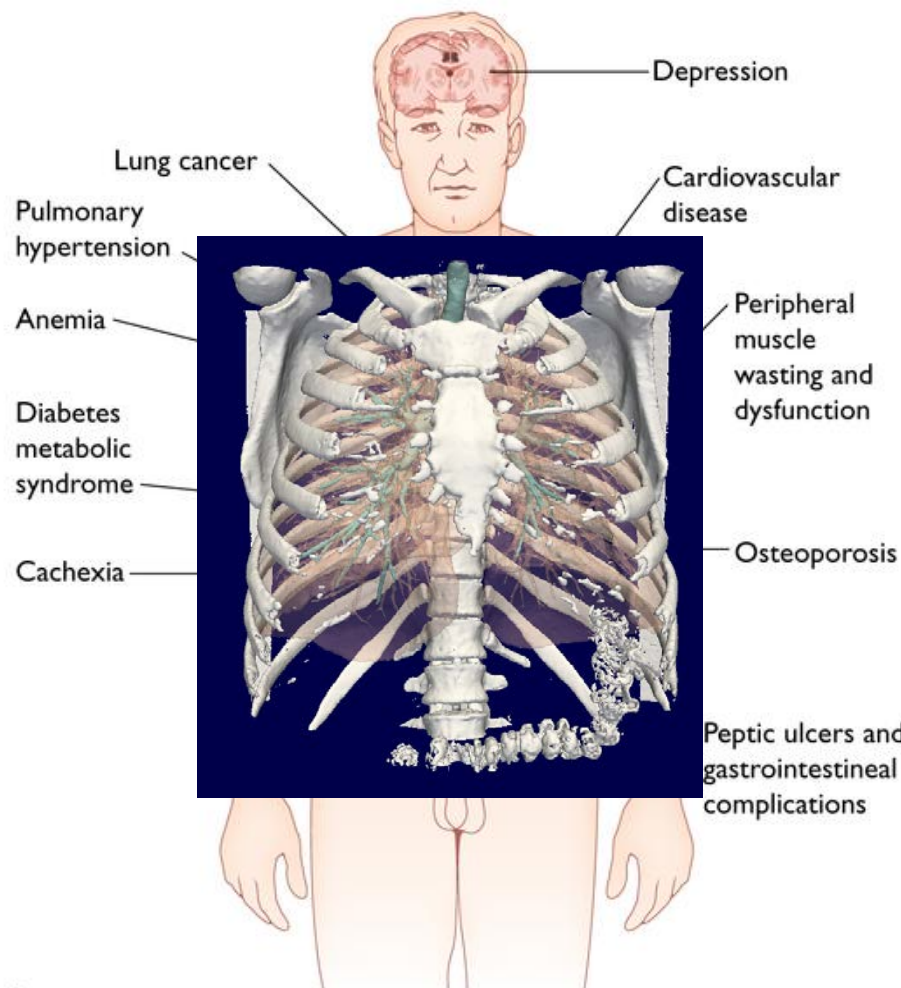
COPD

Lung Cancer



COPD and Lung Cancer: Common Molecular-Genetic Pathways

A Holistic Tool to Smoking Related Disease



A

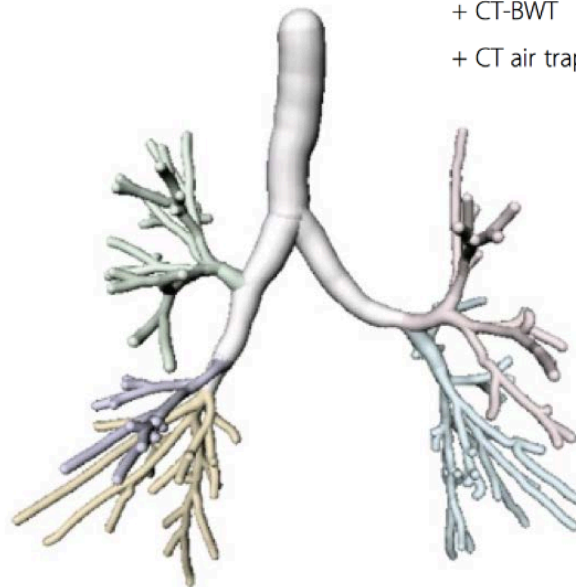
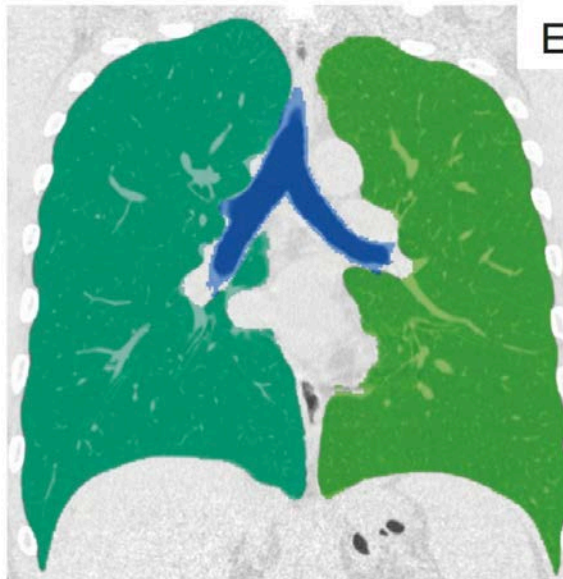
Atlas of COPD, Springer Science. 2008

© Current Medicine

COPD Evaluation is Possible in Low Dose CT

Diagnosis of chronic obstructive pulmonary disease in lung cancer screening Computed Tomography scans: independent contribution of emphysema, air trapping and bronchial wall thickening

Onno M Mets¹, Michael Schmidt^{2,3}, Constantinus F Buckens⁴, Martijn J Gondrie¹, Ivana Isgum⁵, Matthijs Oudkerk⁶, Rozemarijn Vliegenthart⁶, Harry J de Koning⁷, Carlijn M van der Aalst⁷, Mathias Prokop⁸, Jan-Willem J Lammers⁹, Pieter Zanen⁹, Firdaus A Mohamed Hoesein¹, Willem PThM Mali¹, Bram van Ginneken^{3,5}, Eva M van Rikxoort^{3†} and Pim A de Jong^{1*†}



Model	C-index (95% CI)	
	Asymptomatics	Symptomatics
1 Baseline model *	0.674 (0.625 - 0.722)	0.634 (0.589 - 0.679)
2 + CT-BWT	0.739 (0.695 - 0.783)	0.764 (0.725 - 0.803)
3 + CT air trapping	0.737 (0.693 - 0.780)	0.794 (0.759 - 0.829)
4 + CT emphysema	0.753 (0.707 - 0.800)	0.806 (0.771 - 0.841)
5 + CT-BWT + CT air trapping	0.771 (0.730 - 0.813)	0.821 (0.788 - 0.855)
6 + CT emphysema + CT air trapping	0.782 (0.740 - 0.824)	0.872 (0.844 - 0.899)
7 + CT emphysema + CT-BWT	0.828 (0.790 - 0.866)	0.886 (0.859 - 0.912)
8 + CT emphysema + CT-BWT + CT air trapping	0.832 (0.795 - 0.869)	0.905 (0.881 - 0.929)

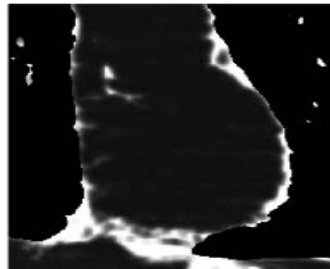
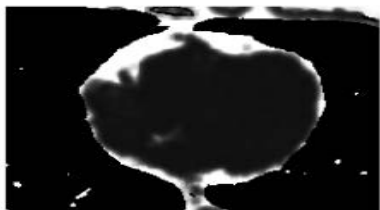
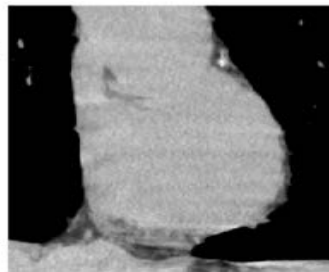
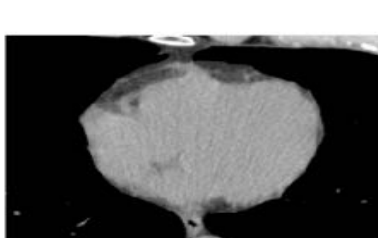
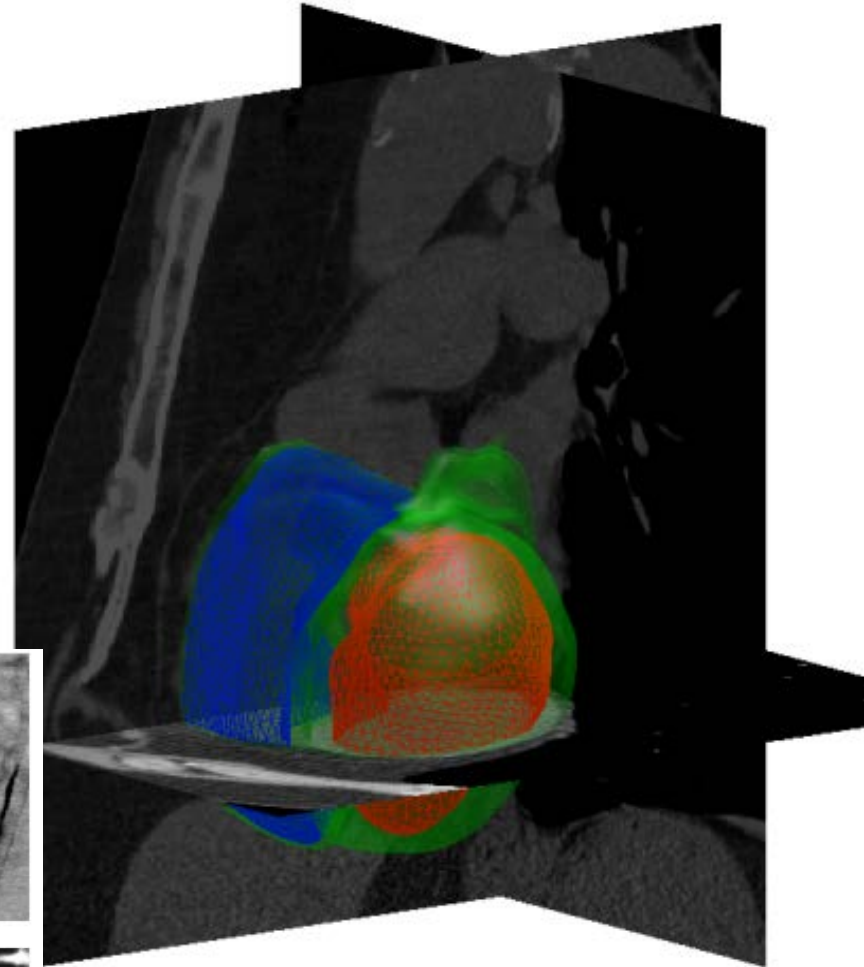
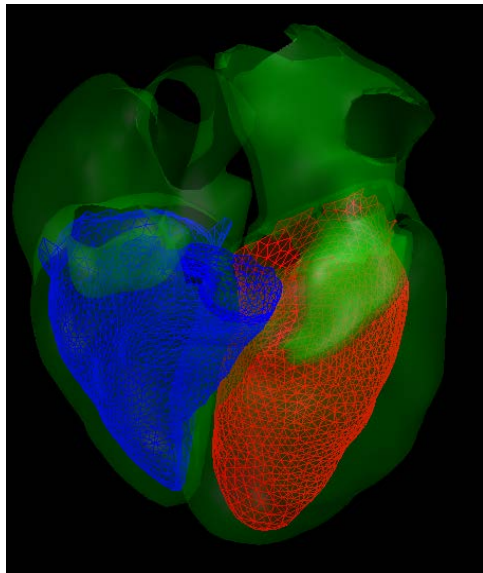
Coronary Calcium Scoring in LCS

- Calcification increases the risk of death among smokers screened for lung cancer
 - Agatston scores 400 and higher increased the risk of death by a factor of 12 [Takx,2015].
- Visual assessment of lung cancer screening scans, even without Agatston scoring, was sufficient to assess cardiac risk.
 - Hazard ratios for visual assessment of mild, moderate were 2.09 to 3.8 [Chiles,2015]

R. A. P. Takx, et al, *J Cardiovasc Comput Tomogr*, vol. 9, no. 1, pp. 50–57, Jan. 2015

C. Chiles, et al, *Radiology*, vol. 276, no. 1, pp. 82–90, Jul. 2015.

Assessing Cardiac Dysfunction in Low Dose CTs



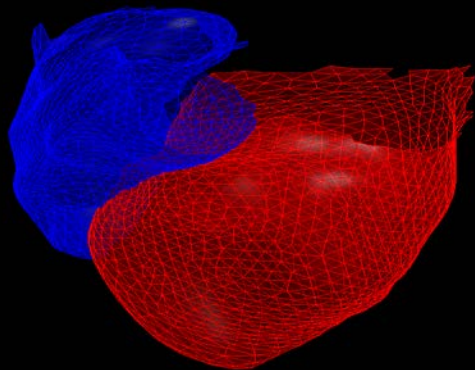
Correlation with cMRI Measures of Ventricular Geometry

n=24

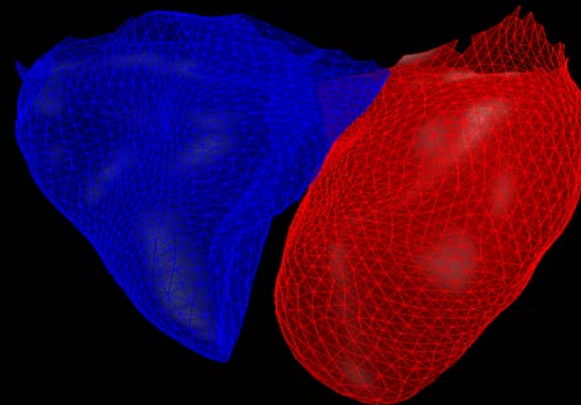
Correlation with Echo Measures of Ventricular Geometry

Associations with Ventricular Dysfunction

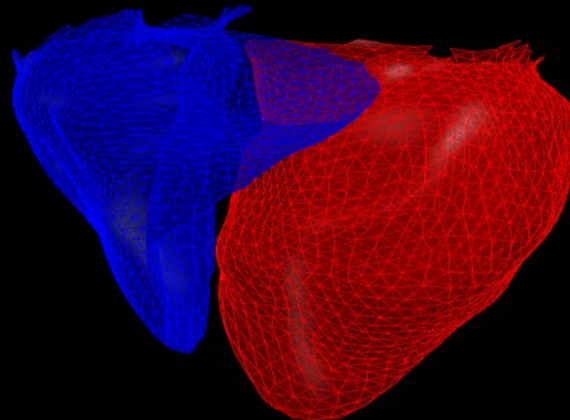
GOLD 3, RV/LV=0.8, RVSP=47



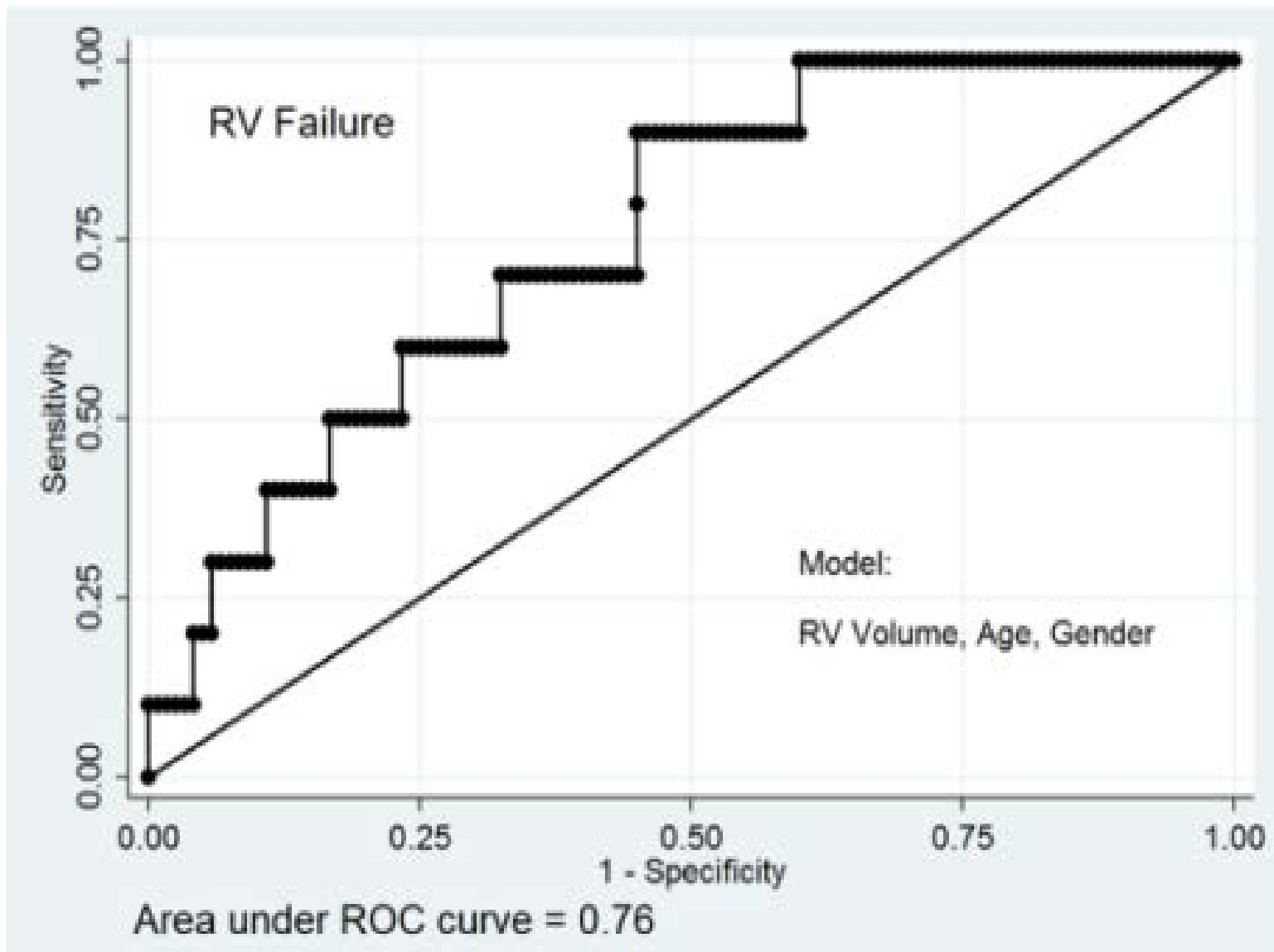
GOLD 2, EF=35%



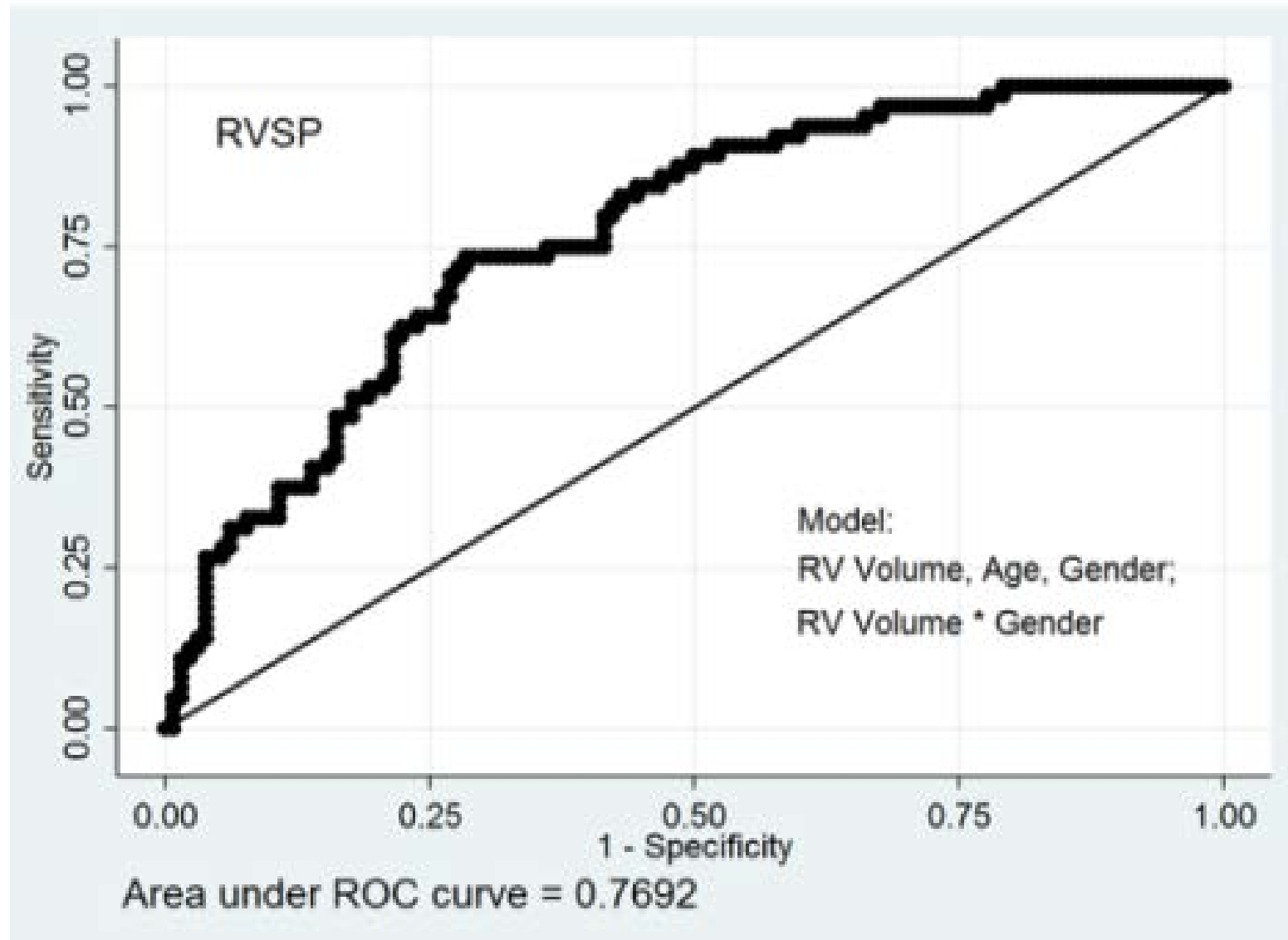
GOLD 0, RV/LV=0.5, no dys.



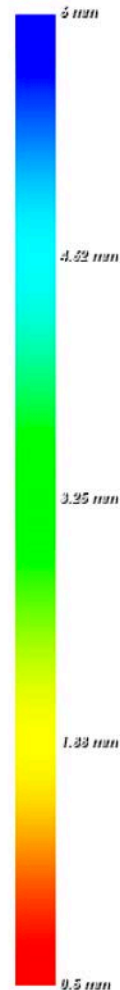
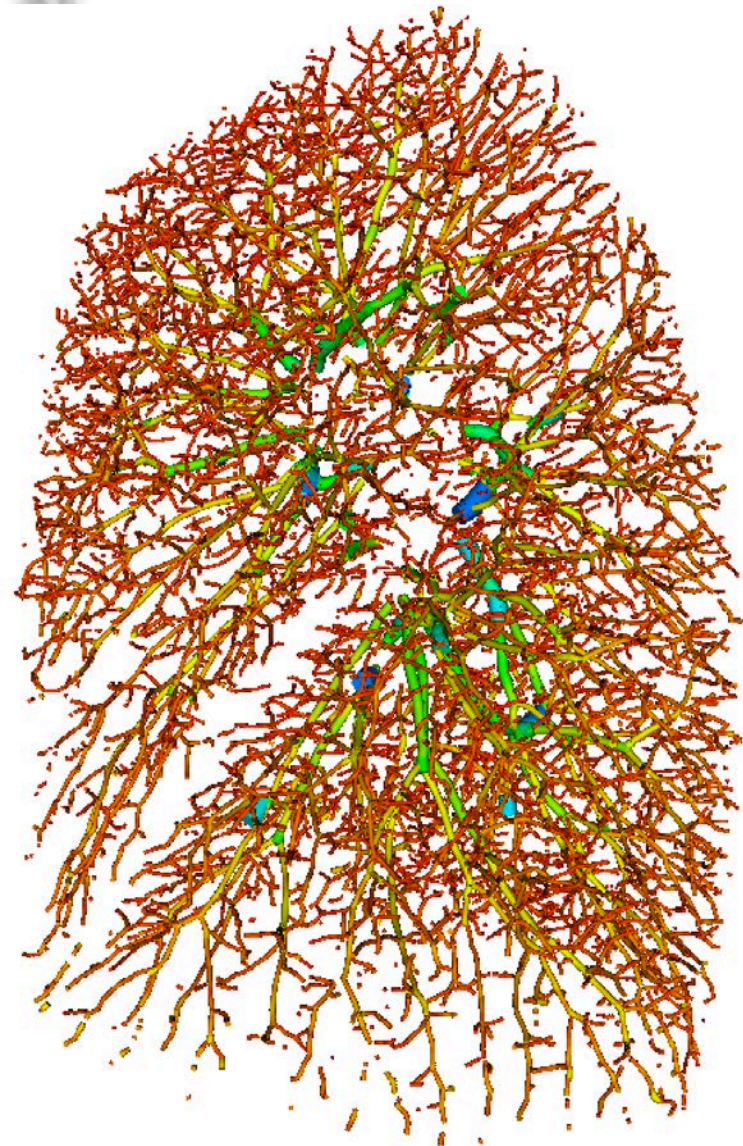
Predicting RV Failure



Predicting Elevated RVSP (> 40 mmHg)



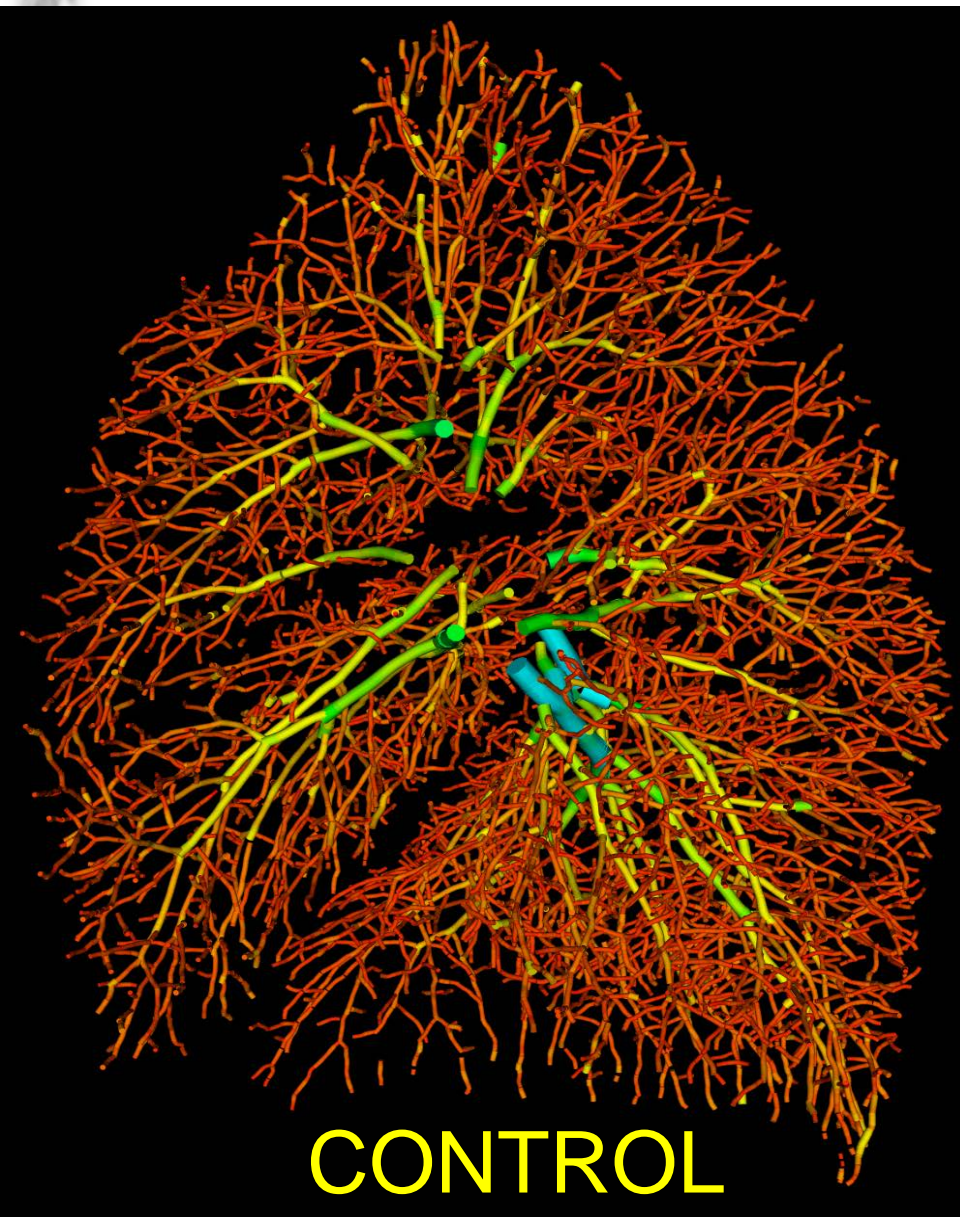
Next Frontier: Pulmonary Vasculature



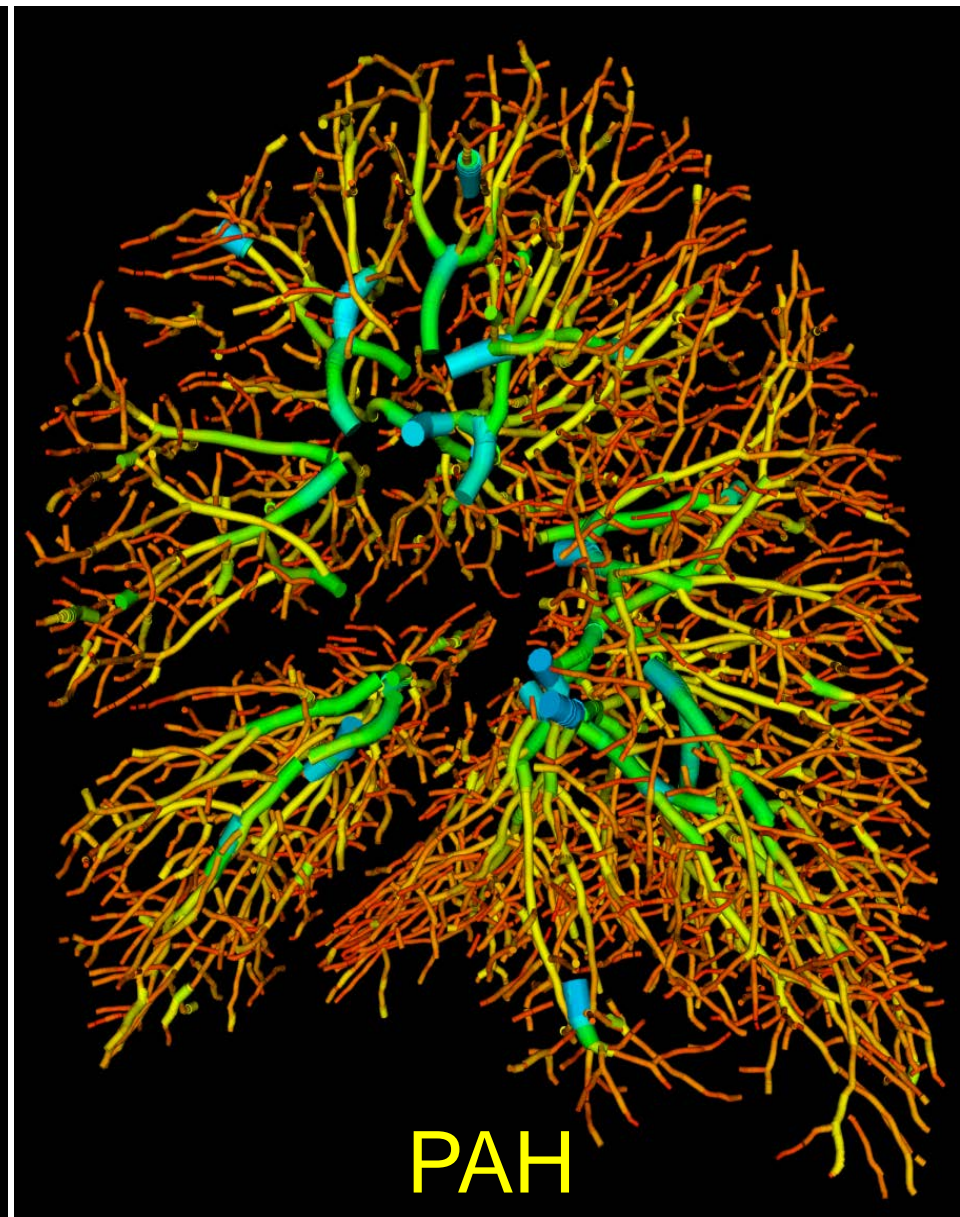
- Consistent evidences show that pulmonary vascular change markers are early biomarkers of disease progression
- Assessment of small vessels enable Pulmonary Hypertension evaluation.

Dougherty, ATS, 2015

K. S. Iyer, *Am. J. Respir. Crit. Care Med.*, 2015.

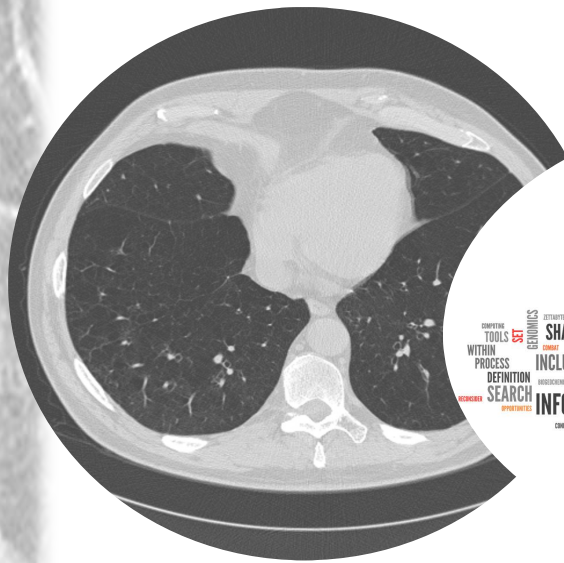


CONTROL



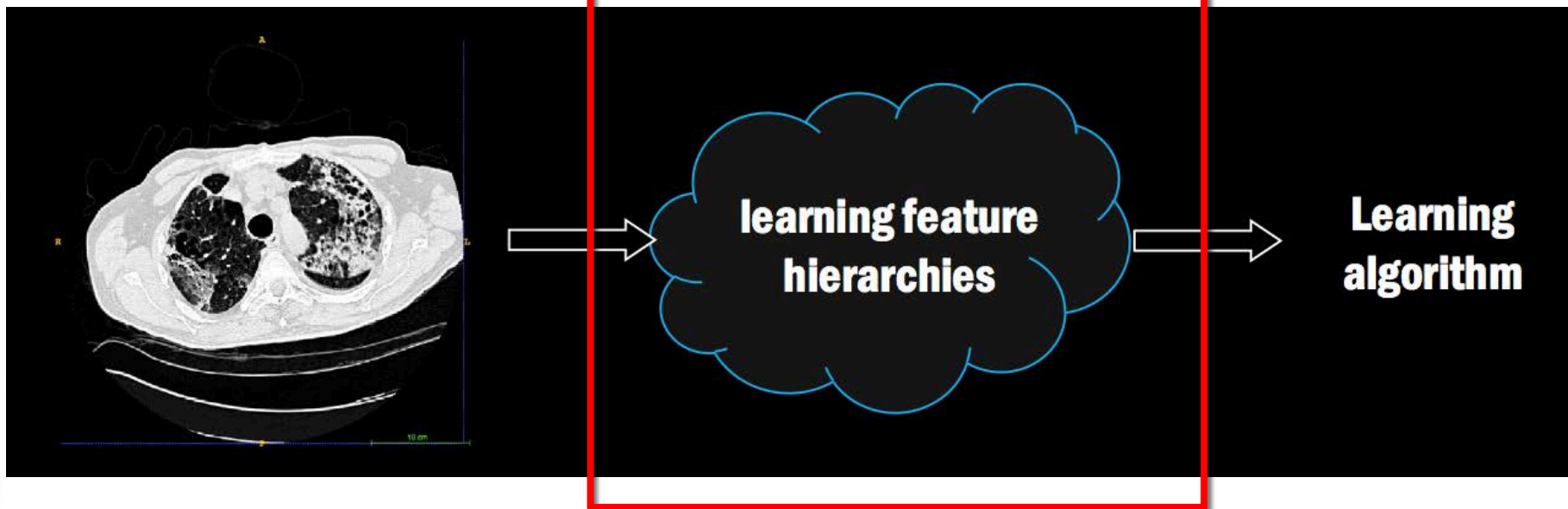
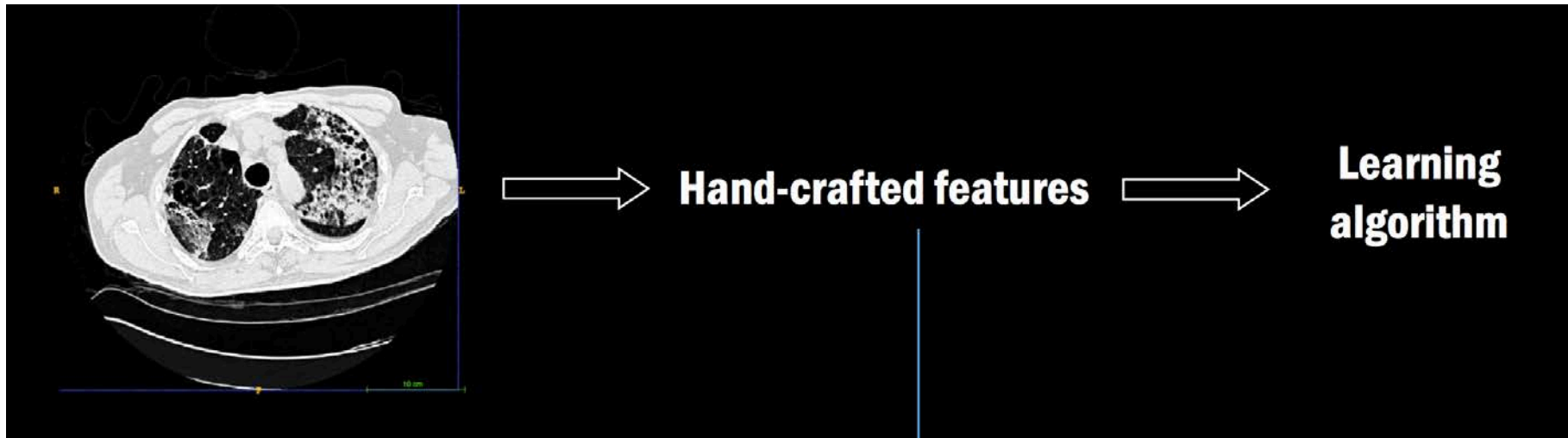
PAH

Automated Diagnosis: Deep Learning



Deep learning is one of the most disruptive technology radiology has seen since the advent of digital imaging

What is the magic behind?



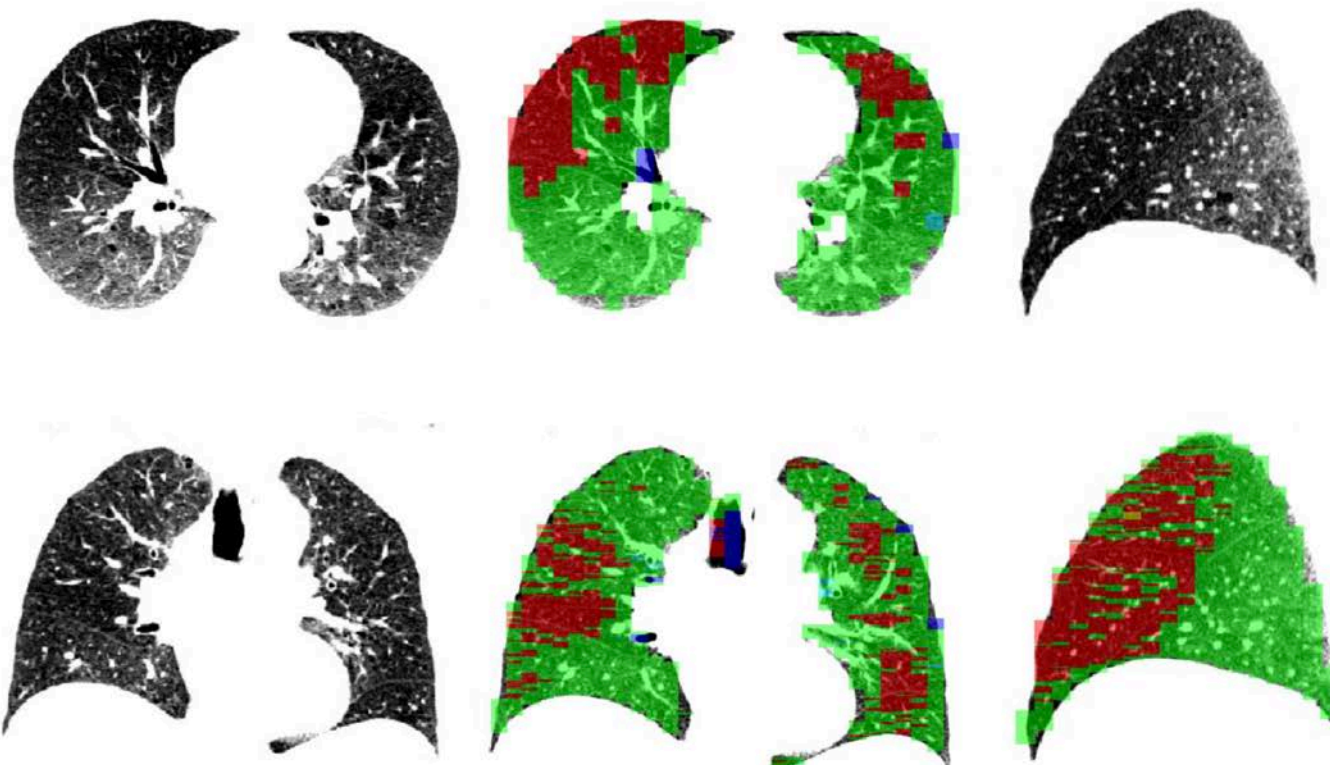
Healthy

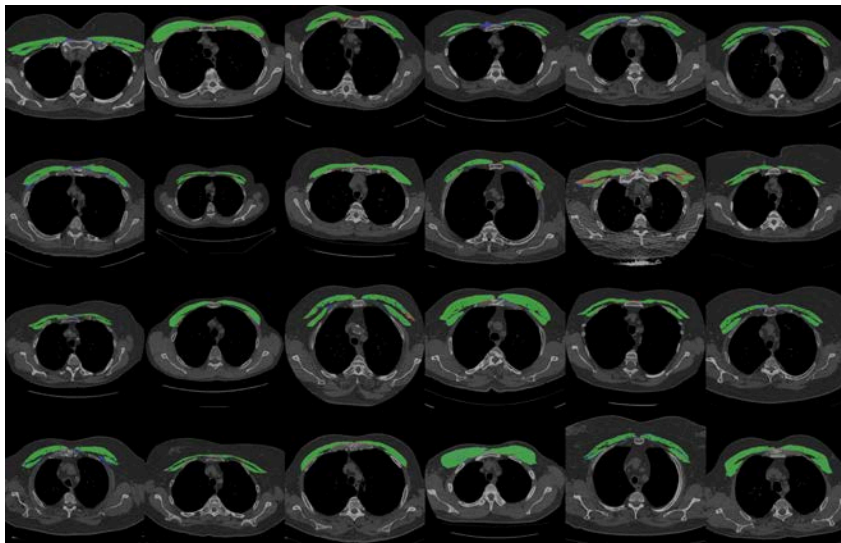
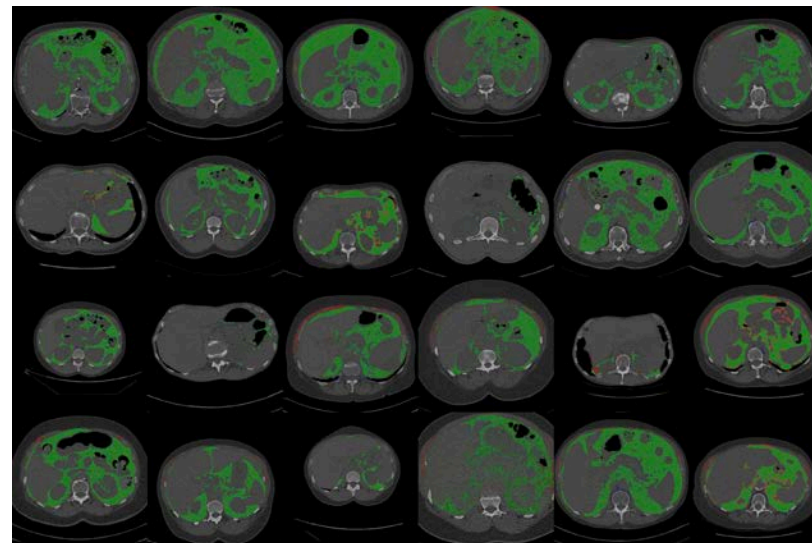
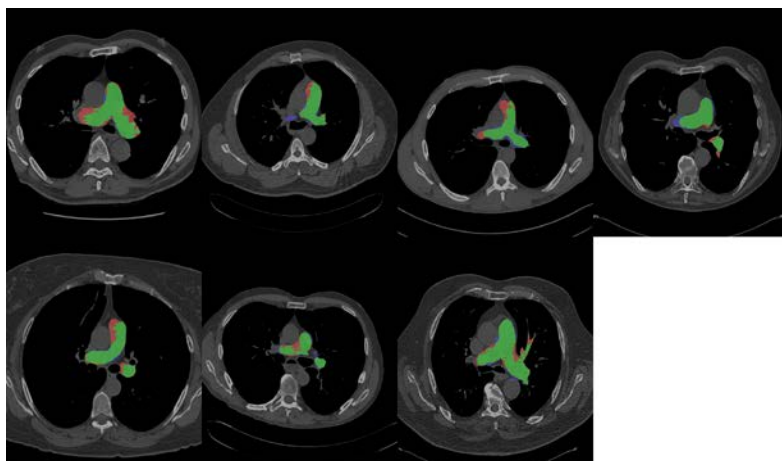
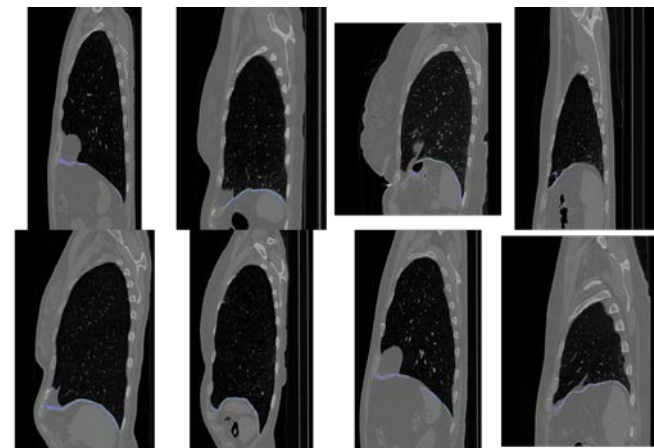
Reticular

**Paraseptal
Emphysema**

**Centrilobular
Emphysema**

**Subpleural
Line**



Pec Muscles**Visceral Fat****Pulmonary Artery and Aorta****Diaphragm**

A “Brave New World”?

Sex

	G+	G-
Pos	468	023
Neg	035	474
P(P T)	0.930	0.046
Odds ratio: 275.568		

Race

	G+	G-
Pos	049	018
Neg	061	872
P(P T)	0.445	0.020
Odds ratio: 38.914		

Severe_Exacerbations

	G+	G-
Pos	046	078
Neg	151	725
P(P T)	0.234	0.097
Odds ratio: 2.832		

BronchAttack

	G+	G-
Pos	389	164
Neg	227	220
P(P T)	0.631	0.427
Odds ratio: 2.299		

ReportedER

	G+	G-
Pos	061	103
Neg	270	566
P(P T)	0.184	0.154
Odds ratio: 1.241		

ReportedHospital

	G+	G-
Pos	039	094
Neg	221	646
P(P T)	0.150	0.127
Odds ratio: 1.213		

Conclusions

- Integrated analysis of chest CT scans are key to perform early disease detection.
- Registries can empower data scientist to deliver an integrated understanding of disease under an integrated screening framework.
- Variability has to be harnessed but it should not stop us.