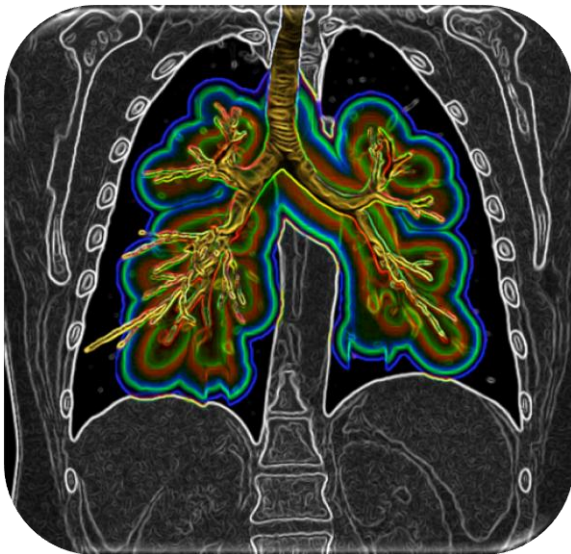


CHEST IMAGING PLATFORM TRAINING SESSION:

Quantification and Computer Assisted Diagnosis of Lung Diseases



Raúl San José Estépar, Ph.D.
Jorge Onieva Onieva M.S.

Applied Chest Imaging Lab
Brigham and Women's Hospital
Harvard Medical School



Today

1. Presentation
2. Agenda for this Week
3. Quantitative Imaging in Chest Diseases
 - Overview
 - Principles CT Scanning
 - COPD main challenges
 - Image-based biomarker development
4. Opportunities with Artificial Intelligence
 - Translation to patient care
5. Introduction to Chest Imaging Platform
6. Practicum: Emphysema Assessment

Search



Applied Chest Imaging Laboratory

Understanding of the lungs through image processing

(email)

[Home](#)[People](#) ▾[Projects](#) ▾[Education](#) ▾[Software](#)[Events](#) ▾[Publications](#)

About Us

The Applied Chest Imaging Laboratory is a multidisciplinary group to provide quantitative-based research on lung diseases. The primary focus on the lab is in Chronic Obstructive Pulmonary Disease, Pulmonary Vascular Disease and Interstitial Lung Disease. Our mission is to leverage the power of imaging to better understand and quantify disease processes by hypothesis driven modeling. Our group develops state-of-the-art imaging analysis and modeling algorithms to empower clinical and genetic research.

Our Projects

Projects

Active Projects

Airway Inspector: a chest imaging biomarker software platform for COPD

Recent Publications

Pulmonary artery enlargement is associated with right ventricular dysfunction and loss of blood volume in small pulmonary vessels in chronic obstructive pulmonary disease.

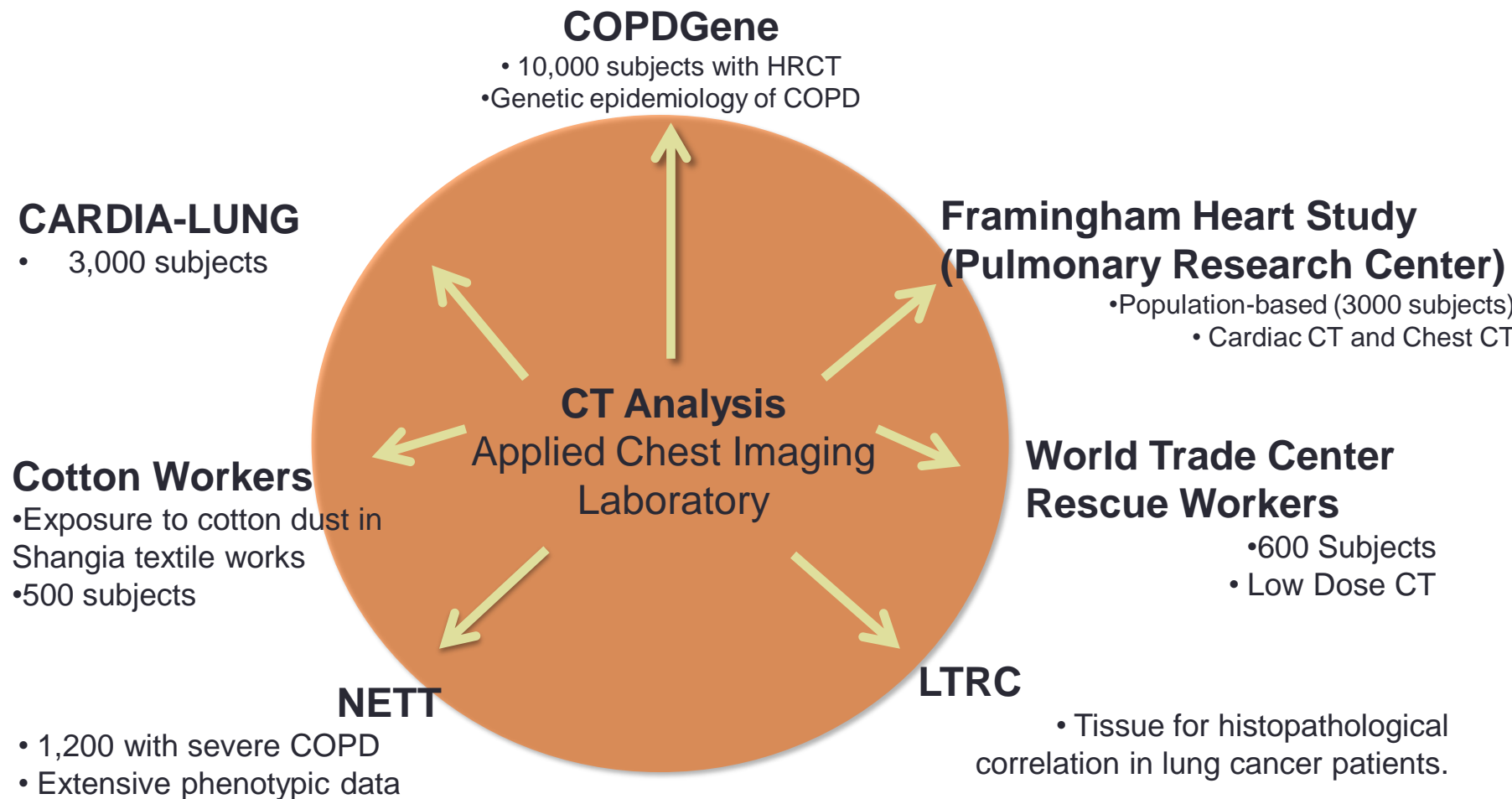
Lab Members

Farbod Nicholas Rahaghi

Christopher Dale

James Ross

ACIL Studies



Chest Imaging Platform: Open Source for quantitative Chest Imaging

www.chestimagingplatform.org

Chest Imaging Platform (CIP)

Home

Slicer CIP (Workstation)

CIP Library

About



Chest Imaging Platform (CIP)

- * A complete suite of tools
- * For Physicians and Researchers
- * Mainly oriented to lung phenotypes



The **Chest Imaging Platform (CIP)** offers both a software library and a clinical-oriented tool that can enable the development and translation of known and novel quantitative phenotypes in lung diseases, including COPD, ILD and ALI.

The Chest Imaging Platform is the evolution of the [Airway Inspector](#) program funded under the NIH award [R01HL116931](#)

[Workstation \(Slicer CIP\)](#)

Extension to the Slicer that integrates:

- CIP functionality as a Toolkit exposing of the CLIs.
- Slicer specific modules to provide user-friendly

[Library \(CIP\)](#)

CIP offers a Common library to perform:

- Lung and lobe automatic segmentation.
- Airway detection, sizing and labeling.

CIP also contains a python-based library for:

[Download and Install](#)

Learn how to download and install step by step the **CIP** tools:

- [Slicer CIP](#).
- [CIP Library](#).

Contact



Raul: rsanjose@bwh.harvard.edu

Jorge: jonieva@bwh.harvard.edu

Agenda

Tuesday

Common Track

9:00 - 10:30

Introduction to Quantitative CT
in chest diseases

Overview of CIP Modules

11:00 - 1:30

Emphysema: Basics and Module
tutorial

Practicum: Emphysema

Wednesday

Clinical Track

Raul

9:00-10:30

Airway Disease: Basics and
Module tutorial

Lung Cancer: Intro and Module
tutorial

11:00-1:30

Practicum: Airway Disease and
Lung Cancer

Technical Track

Jorge

CIP Intro: Architecture and
Building

Using CIP: Emphysema Pipeline
Example

Agenda

Thursday

Clinical Track

Raul

9:00-10:30

Assessment of Other Chest
Diseases: Pulmonary
Hypertension, Bronchiectasis
and Pulmonary Embolism

11:00-1:30

Practicum: Other Chest
Diseases

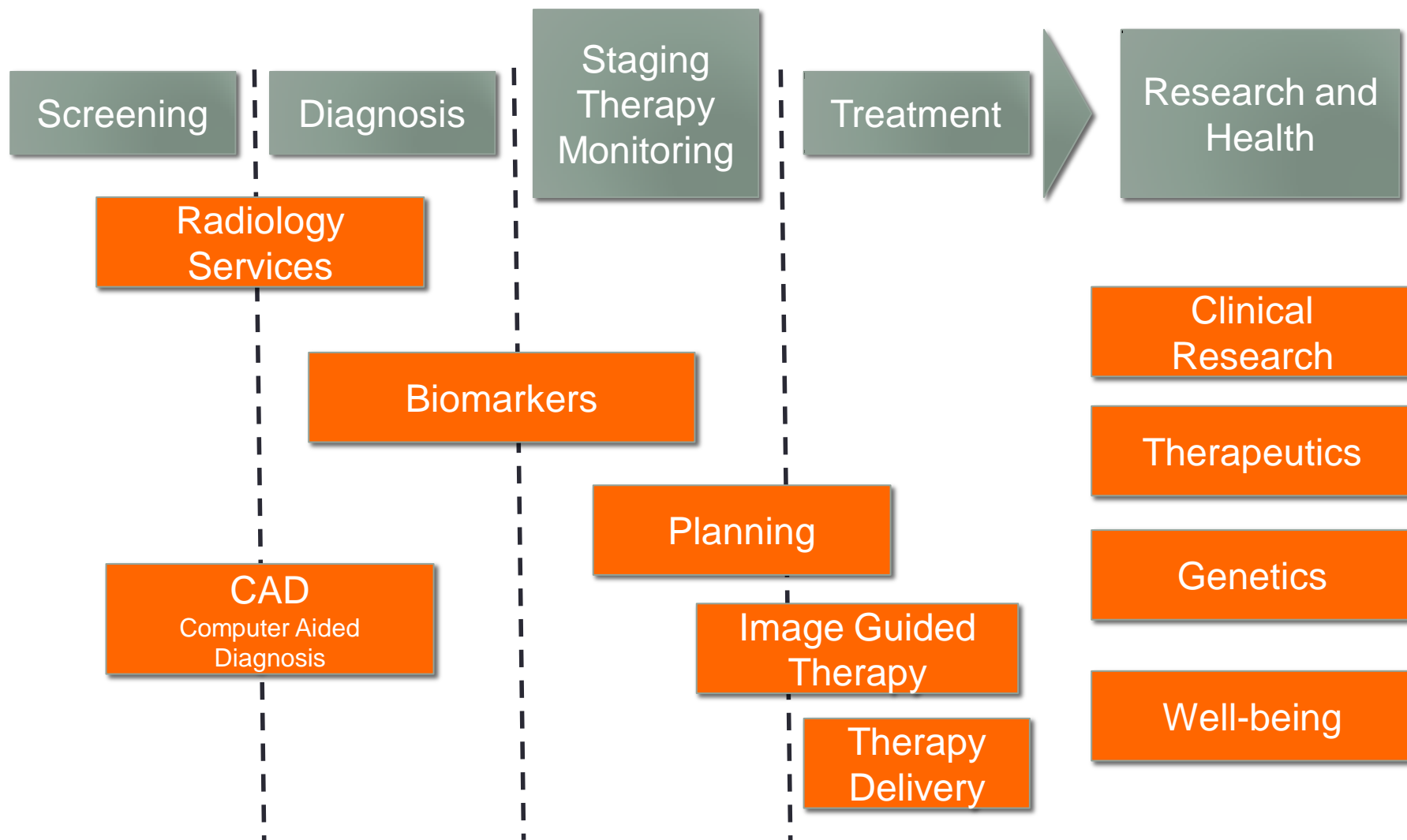
Technical Track

Jorge

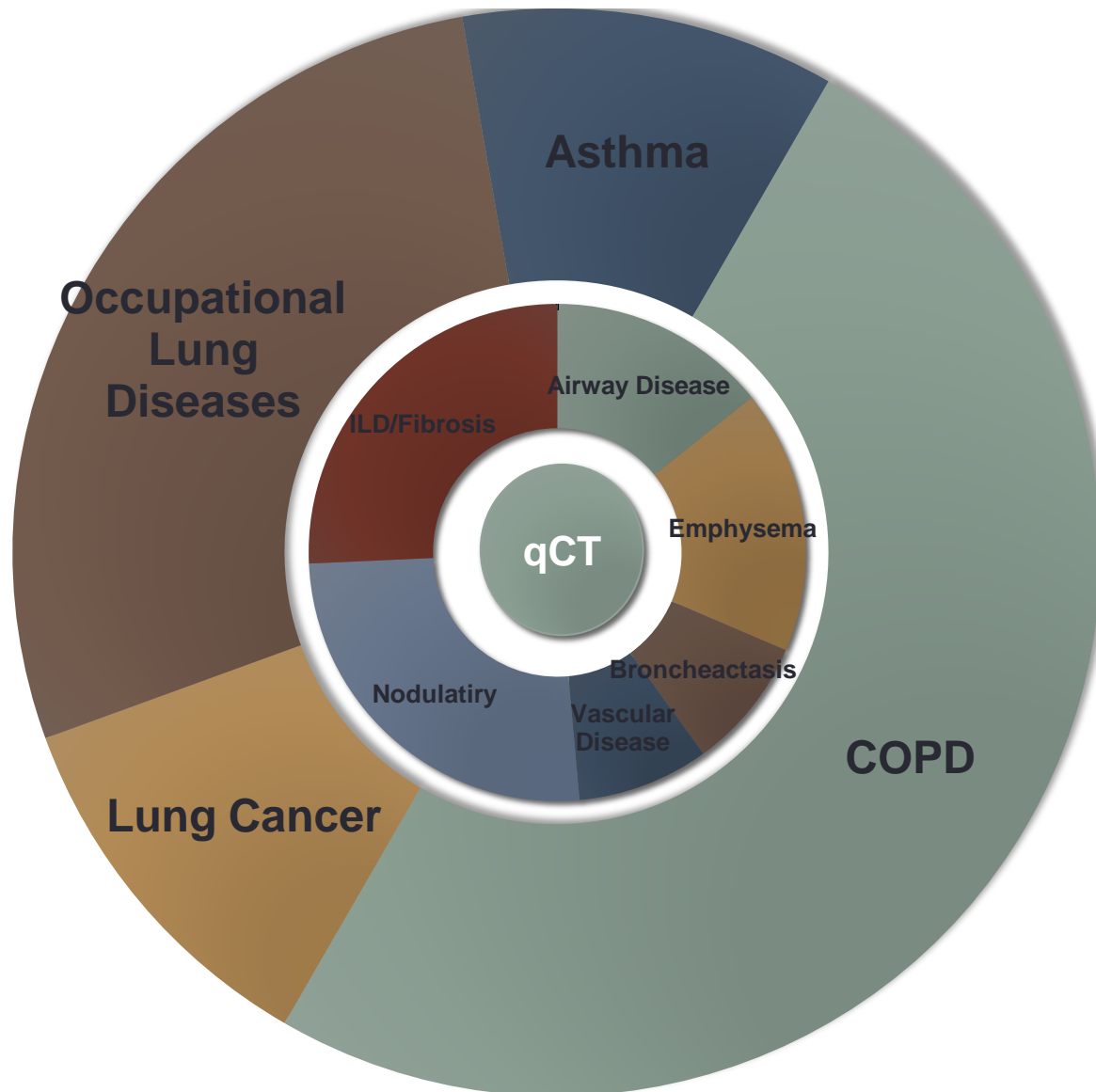
Developing with CIP (Part I):
C++ and Python

Developing with CIP (Part II):
Writing a SlicerCIP module

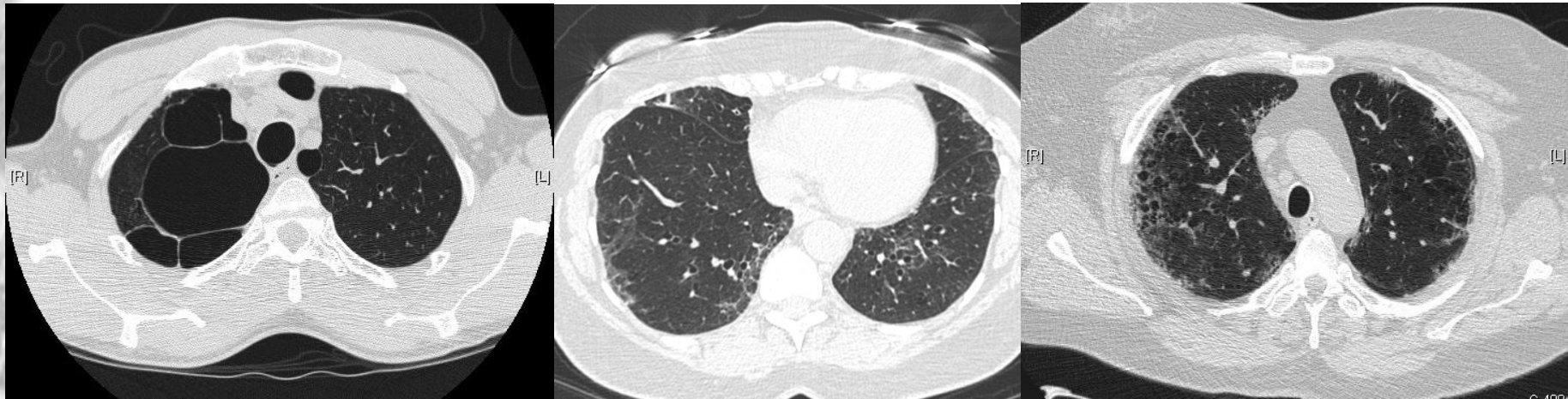
Imaging in Healthcare Today



The *Lung Disease Spectrum*



Smoking Related Lung Disease



Emphysema/COPD
Fibrosis



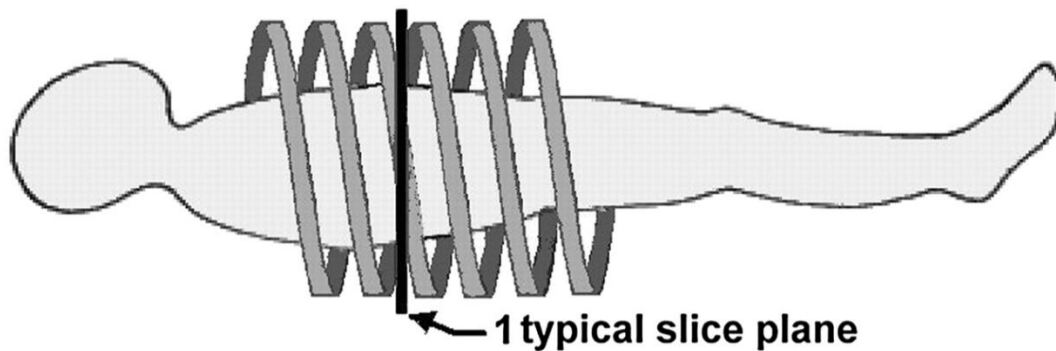
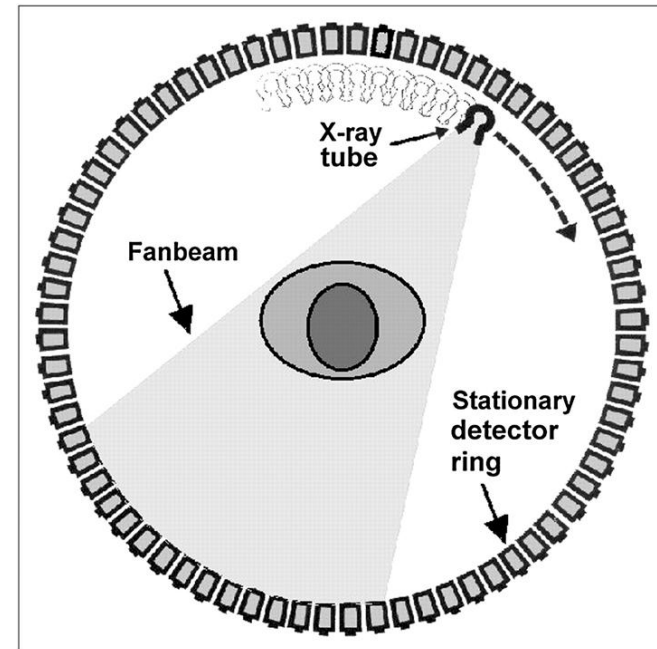
Overlap



Pulmonary

CT SCANNING

Principles of CT Scanning

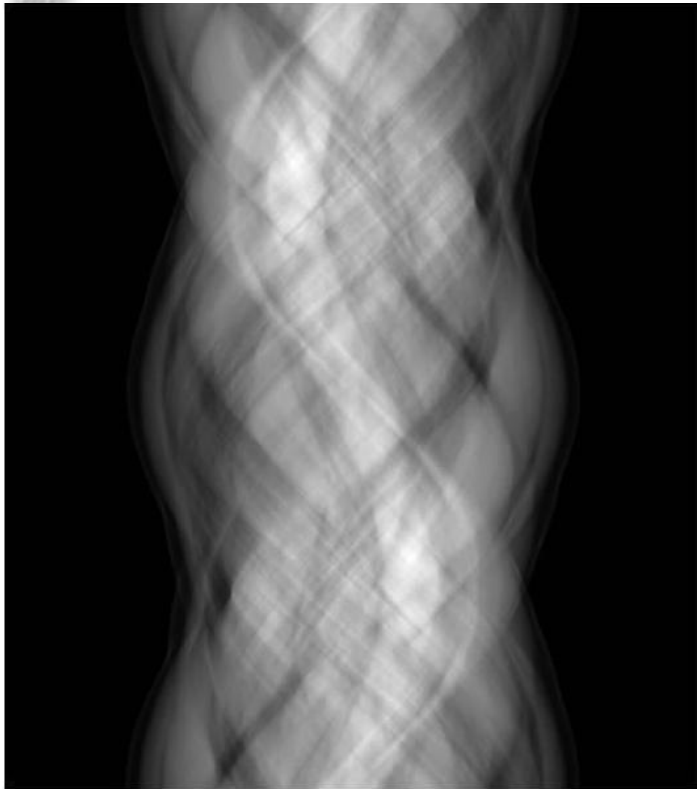


Principles of CT Scanning

- **All materials attenuate (absorb/deflect) radiation to a varying degree**
- **Rotating X-ray beam produces a “sinogram” of attenuations (i.e. difference between delivered and received)**
- **Moving patient through gantry converts plane/grid to volume**
- **The rotating beam signal (“sinogram”) is converted to a spatial signal (the image) through reconstruction.**

Principles of CT Scanning

Sinogram



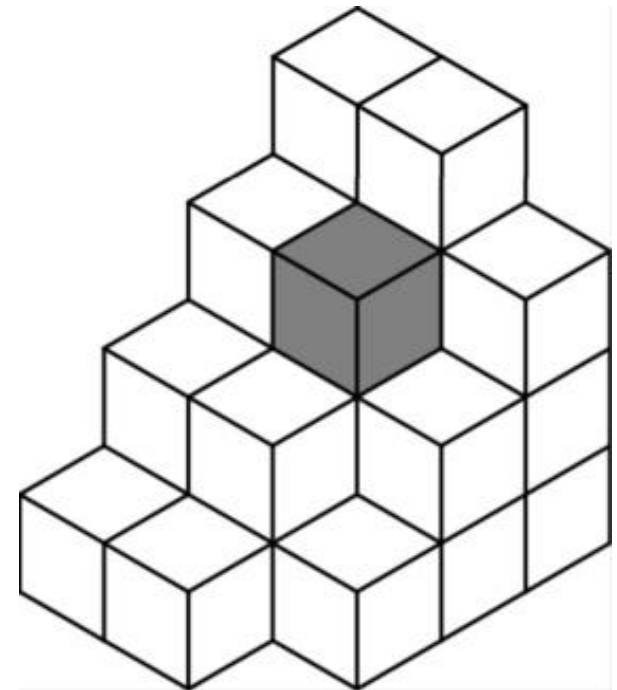
Reconstruction

Image



Principles of CT Scanning

- **Volumated pixels = Voxels**
- **Voxels have an attenuation number**
- **Each attenuation number is assigned a shade of gray**



Principles of CT Scanning

- Attenuation number = Hounsfield Unit (HU)



-1000



0



+1000

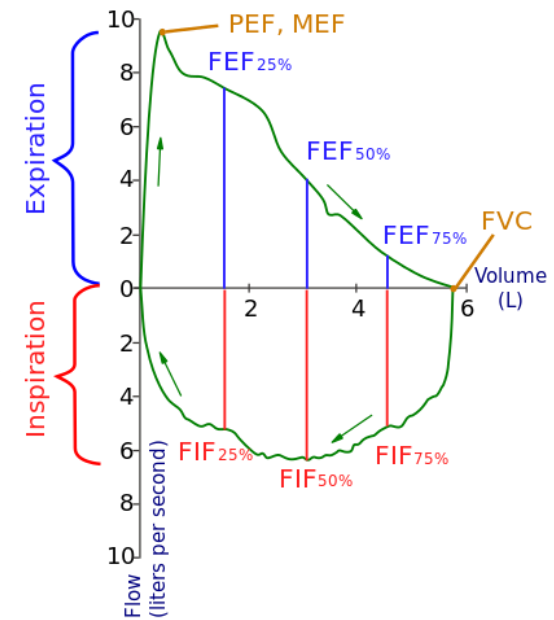
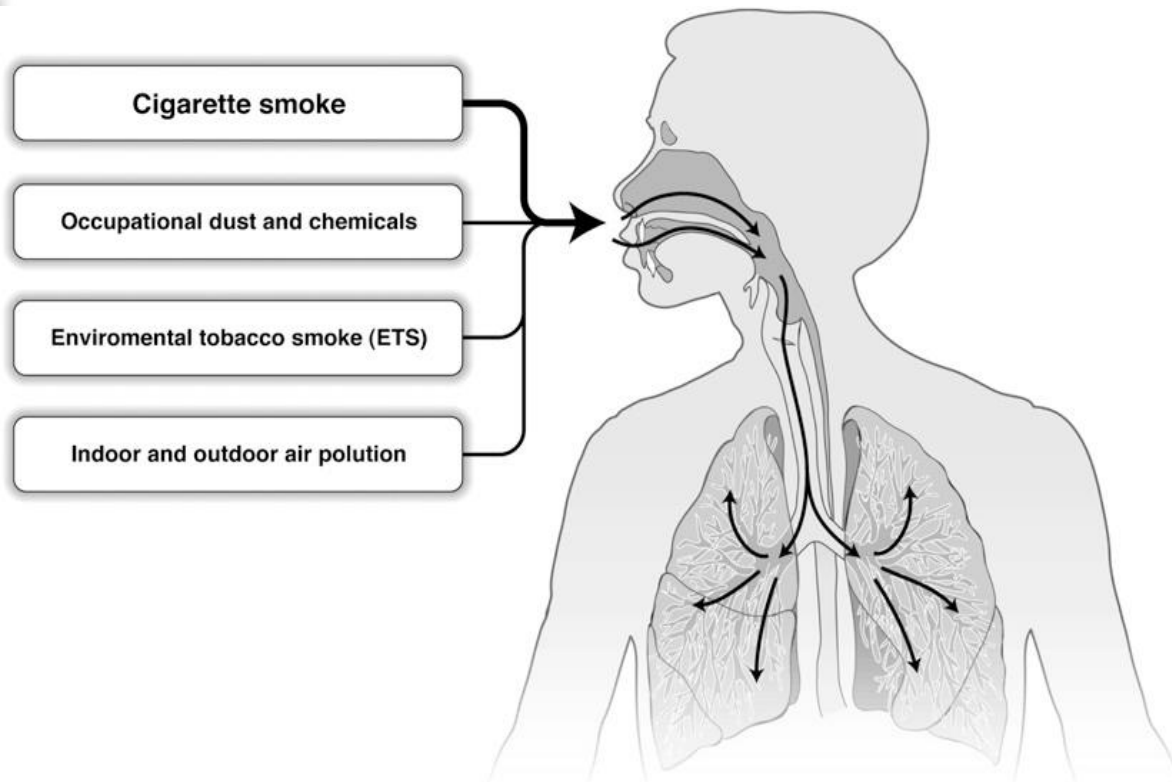


- Lung tissue threshold < -400 HU

COPD

Chronic Obstructive Pulmonary Disease (COPD)

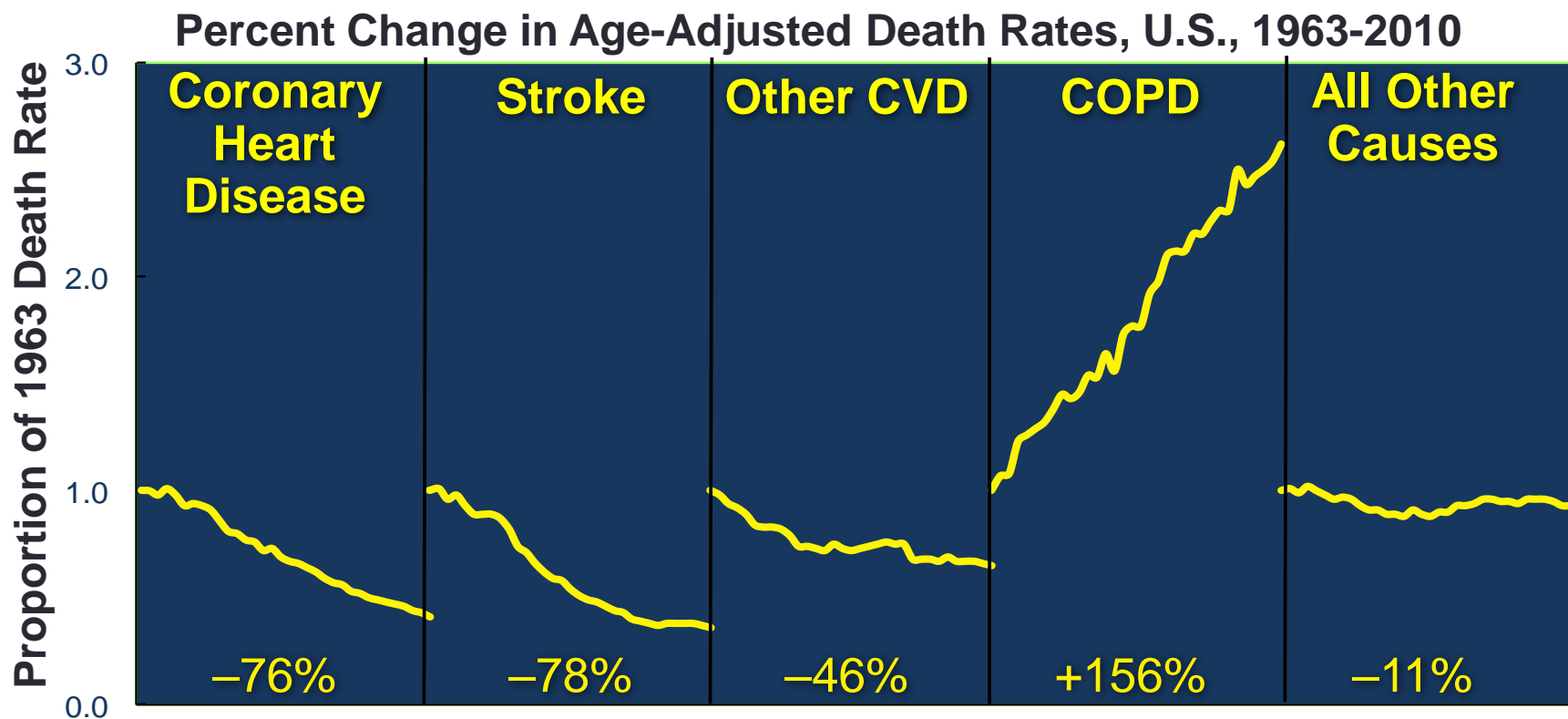
- Definition: “**Airflow limitation** that is **not fully reversible**. The airflow limitation is usually **progressive** and associated with an **abnormal inflammatory response** of the lung to noxious particles or gases.”
- Causes:



COPD: A Growing Public Health Concern

64 million people affected by COPD in World wide
24 million in US, 21 million in EU, 1.5 million in Spain

Projected to be the third-leading cause of death by 2020

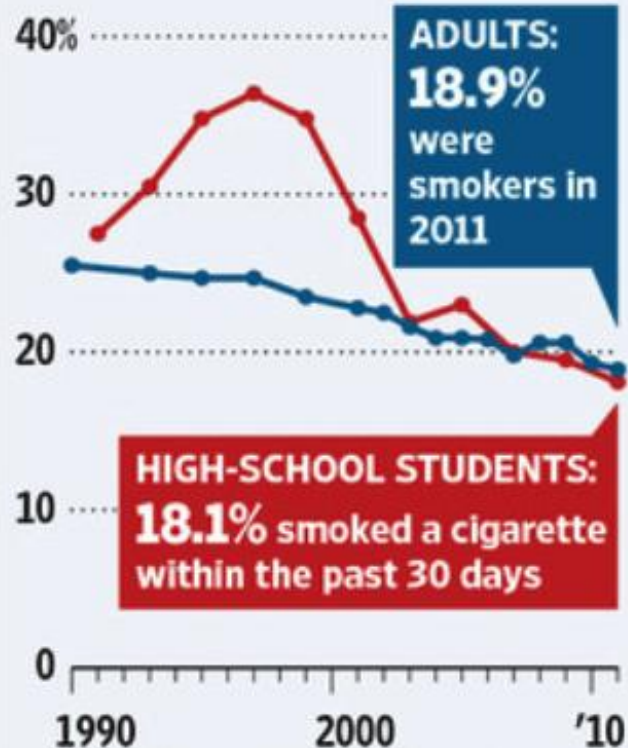


COPD: A Growing Disease



Stubbing Out

Reported cigarette use in the U.S. since 1990

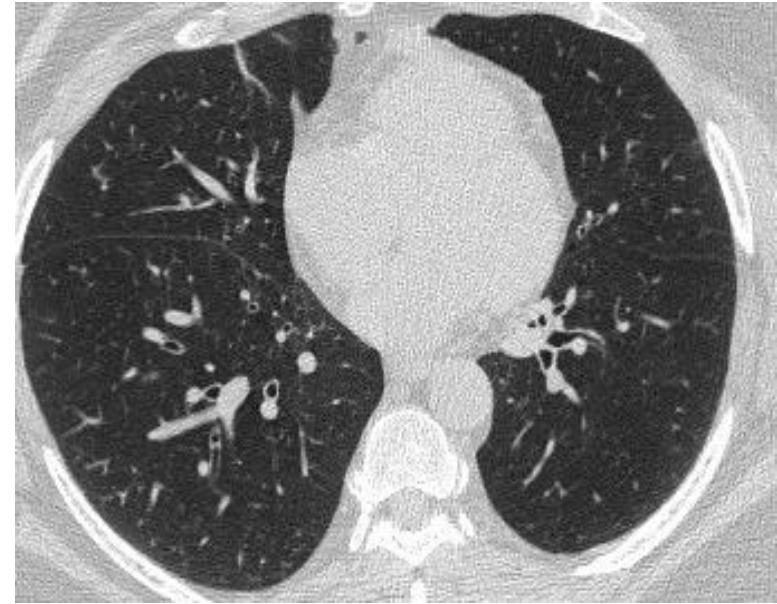
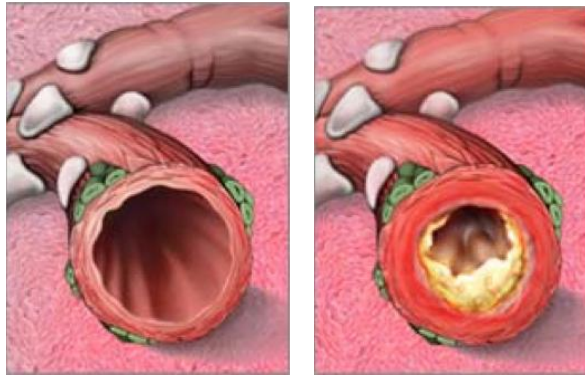
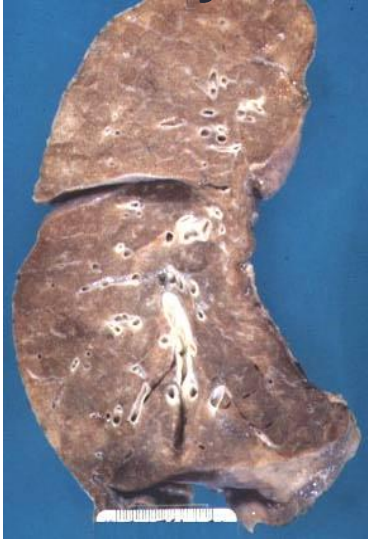


Source: Centers for Disease Control and Prevention

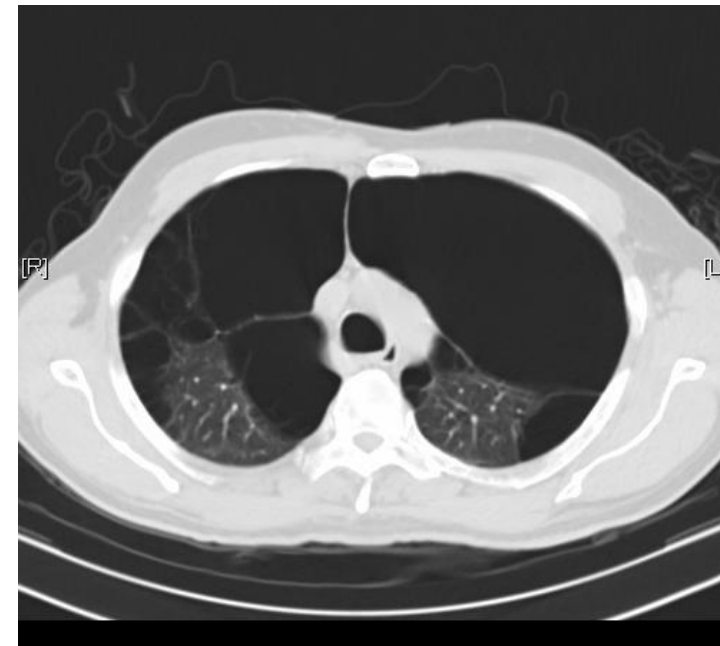
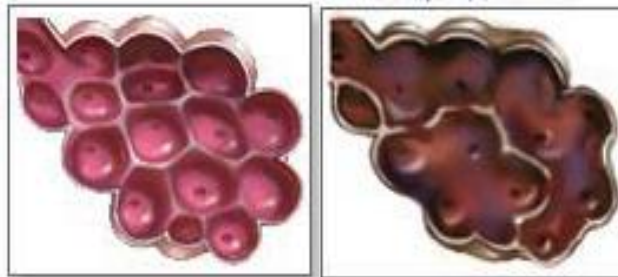
The Wall Street Journal

Understanding COPD

Airway Disease



Emphysema



Disease Onset

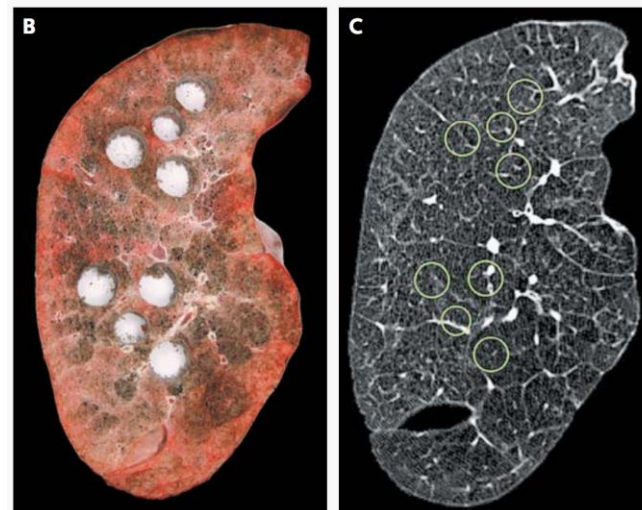
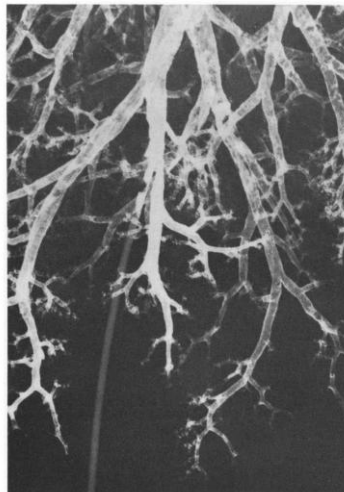
The New England Journal of Medicine

Copyright, 1968, by the Massachusetts Medical Society

Volume 278 JUNE 20, 1968 Number 25

SITE AND NATURE OF AIRWAY OBSTRUCTION IN CHRONIC OBSTRUCTIVE LUNG DISEASE*

JAMES C. HOGG, M.D., M.Sc., PETER T. MACKLEM, M.D., C.M., F.R.C.P. (C),
AND W. M. THURLBECK, M.B., CH.B., M.C.PATH.

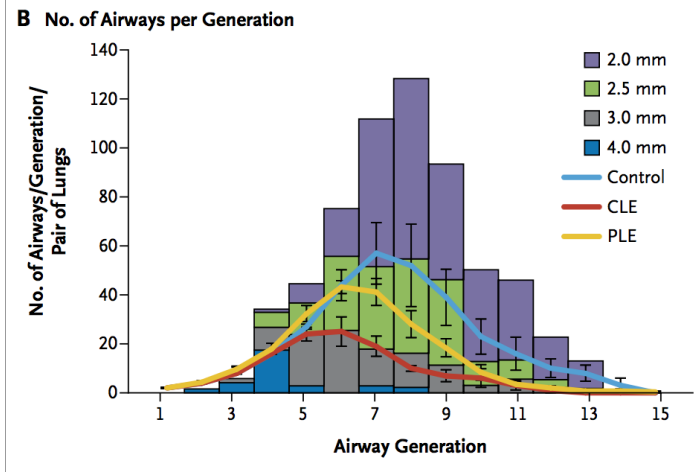


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 27, 2011 VOL. 365 NO. 17

Small-Airway Obstruction and Emphysema in Chronic Obstructive Pulmonary Disease

John E. McDonough, M.Sc., Ren Yuan, M.D., Ph.D., Masaru Suzuki, M.D., Ph.D., Nazgol Seyednejad, B.Sc., W. Mark Elliott, Ph.D., Pablo G. Sanchez, M.D., Alexander C. Wright, Ph.D., Warren B. Gefter, M.D., Leslie Litzky, M.D., Harvey O. Coxson, Ph.D., Peter D. Paré, M.D., Don D. Sin, M.D., Richard A. Pierce, Ph.D., Jason C. Woods, Ph.D., Annette M. McWilliams, M.D., John R. Mayo, M.D., Stephen C. Lam, M.D., Joel D. Cooper, M.D., and James C. Hogg, M.D., Ph.D.



Disease Pathogenesis

The NEW ENGLAND JOURNAL *of* MEDICINE

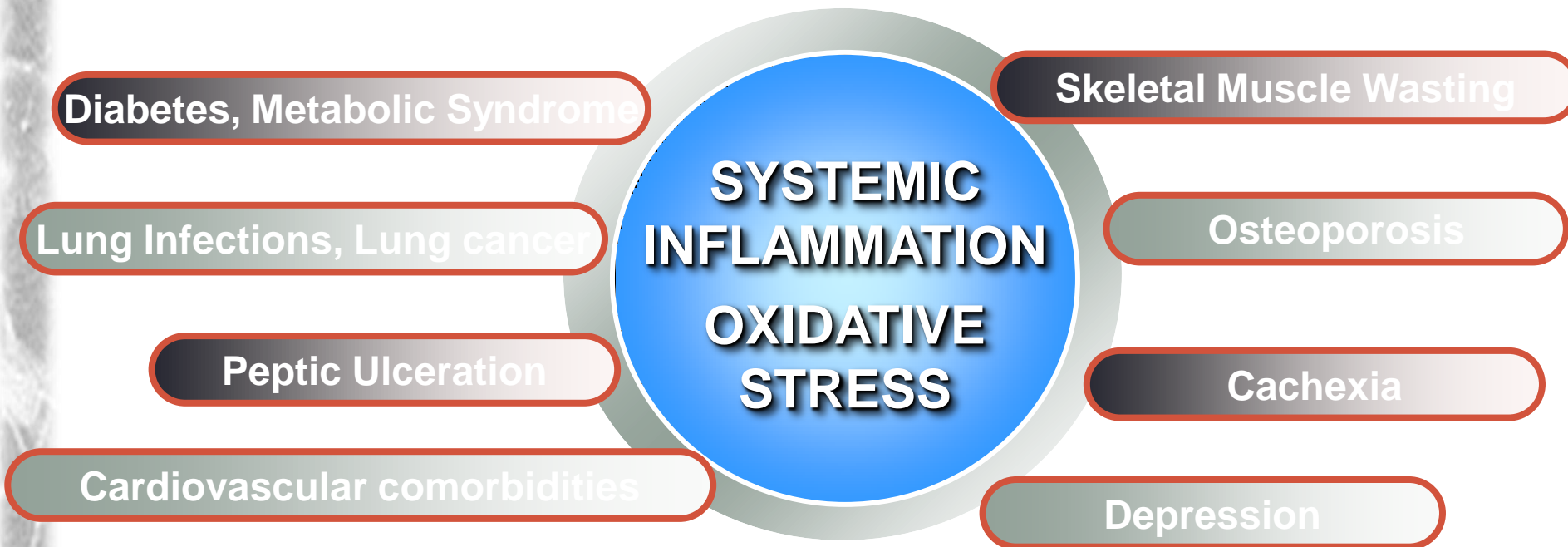
REVIEW ARTICLE

MECHANISMS OF DISEASE

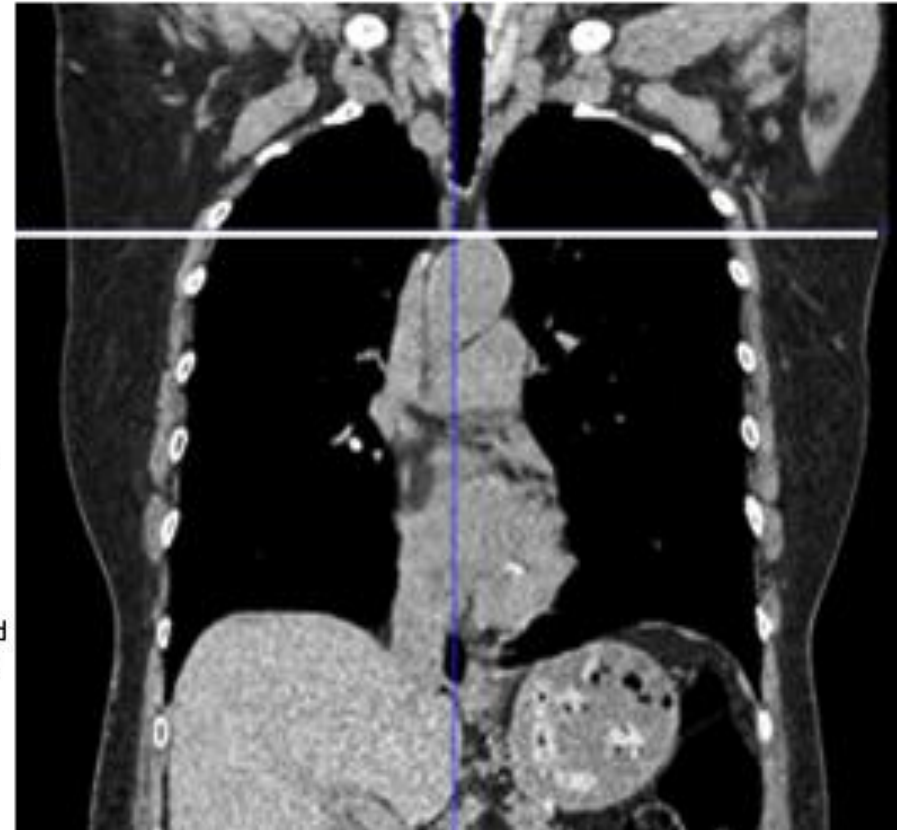
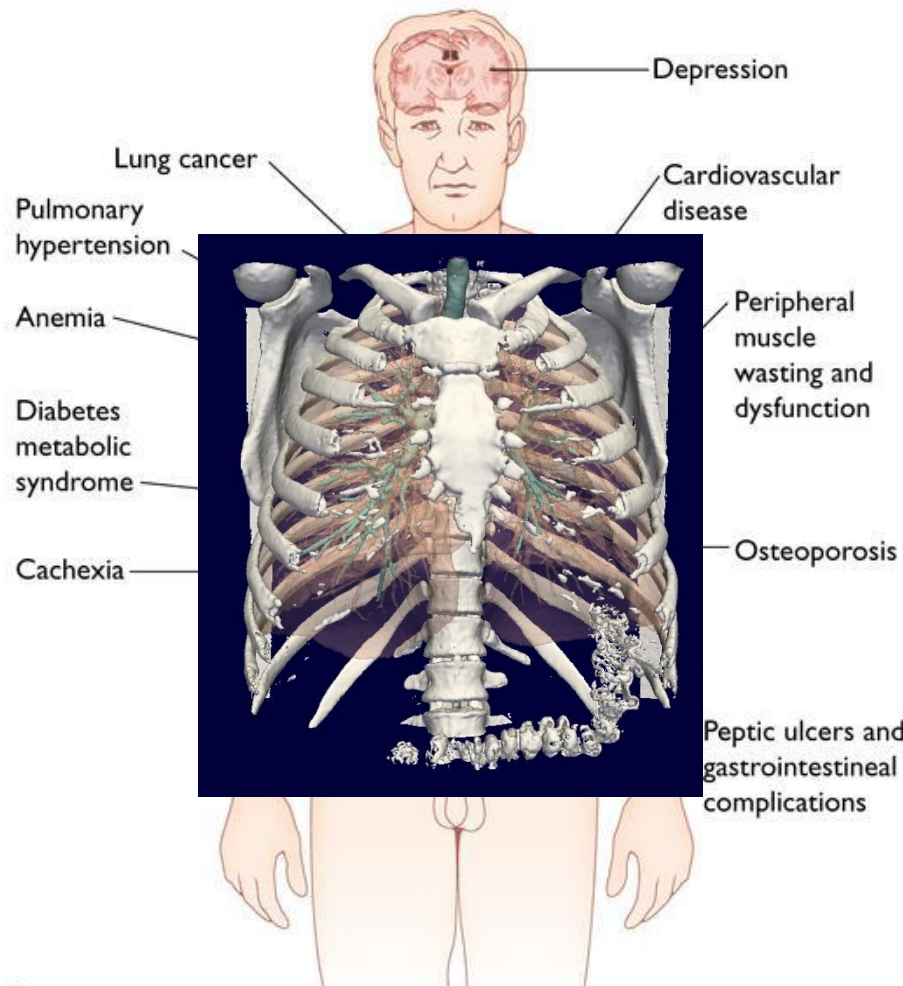
Immunologic Aspects of Chronic Obstructive Pulmonary Disease

Manuel G. **Cosio**, M.D., Marina Saetta, M.D., and Alvar Agusti, M.D.

Systemic Effects



A Holistic Tool to Smoking Related Disease

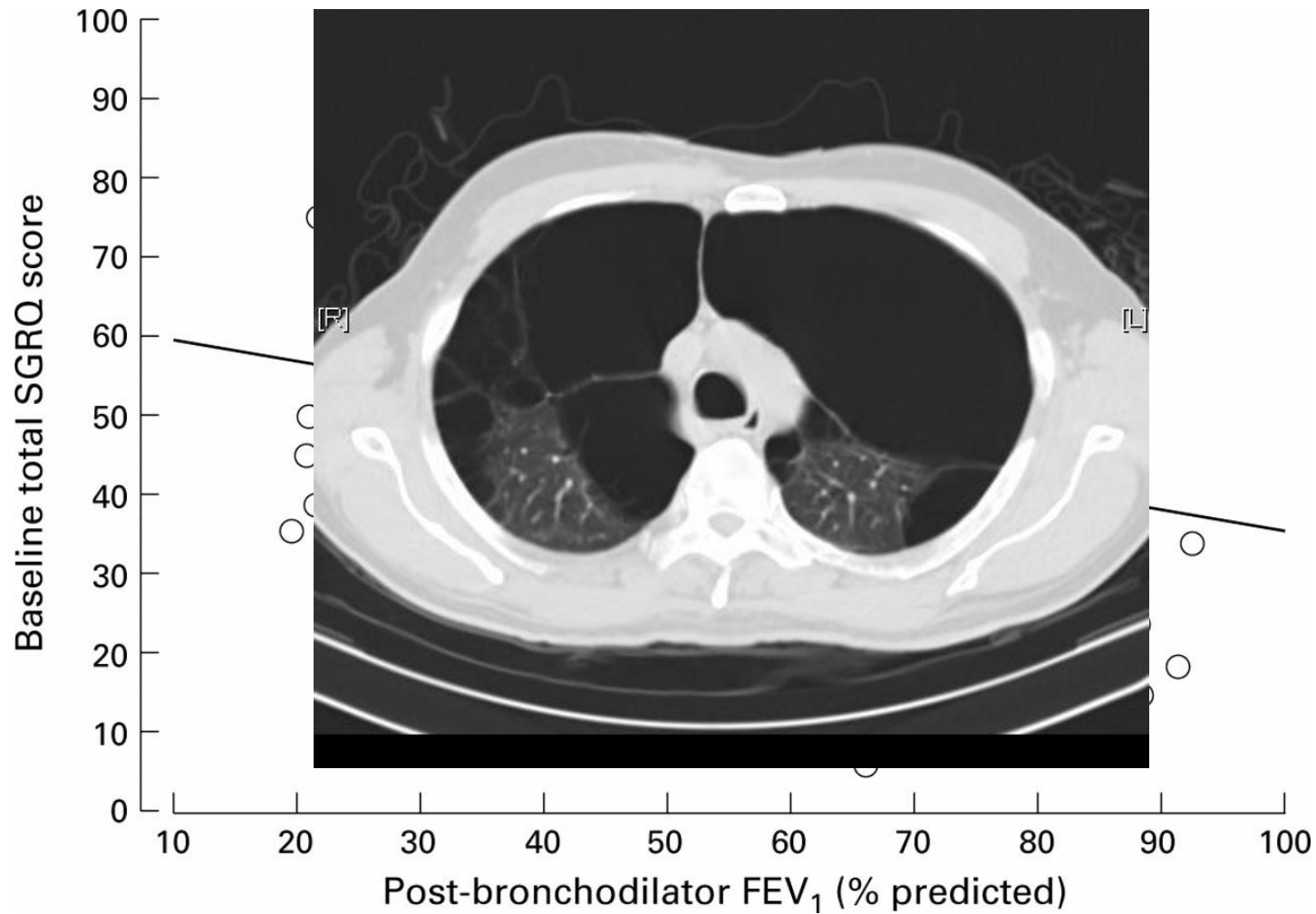


A

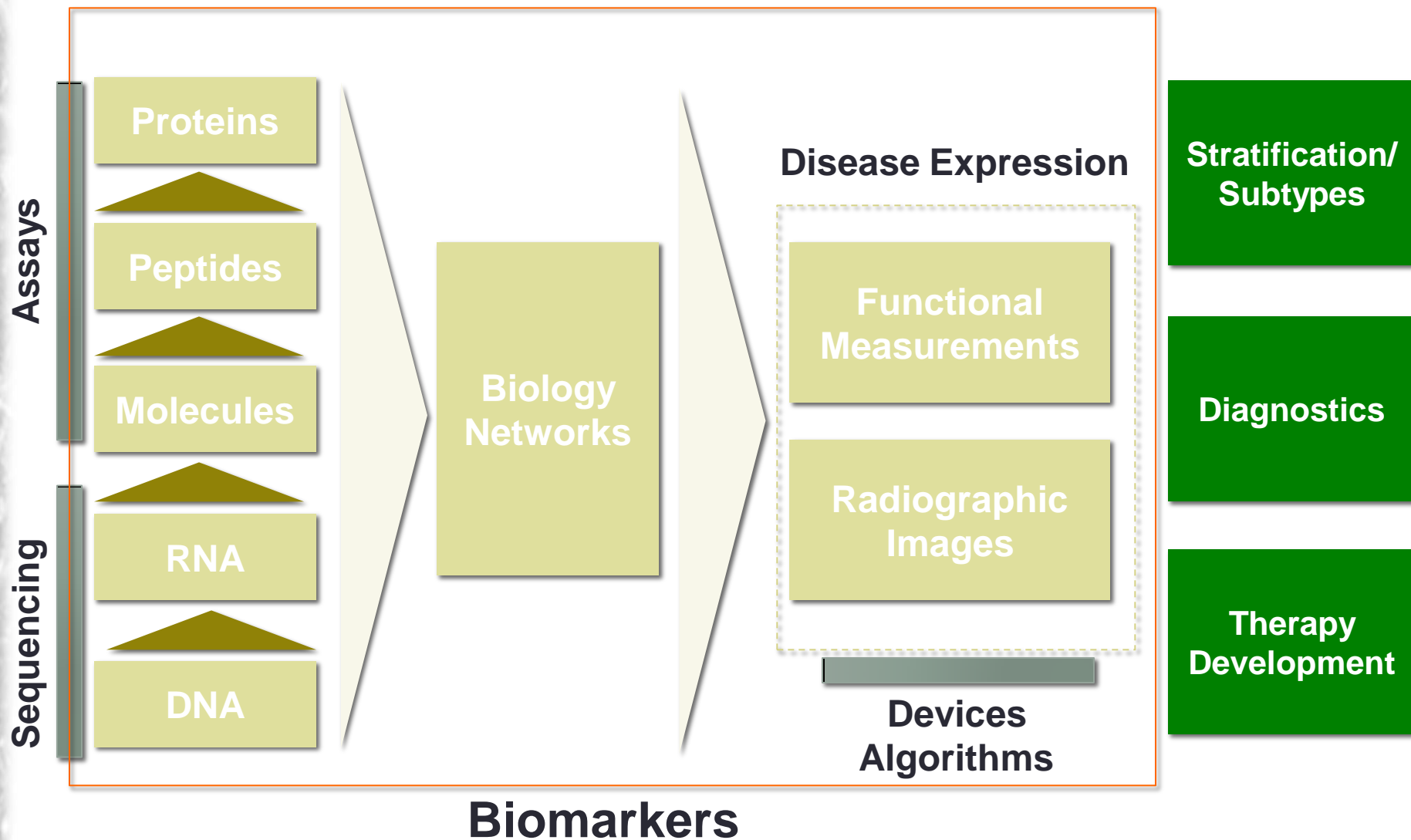
Atlas of COPD, Springer Science. 2008

© Current Medicine

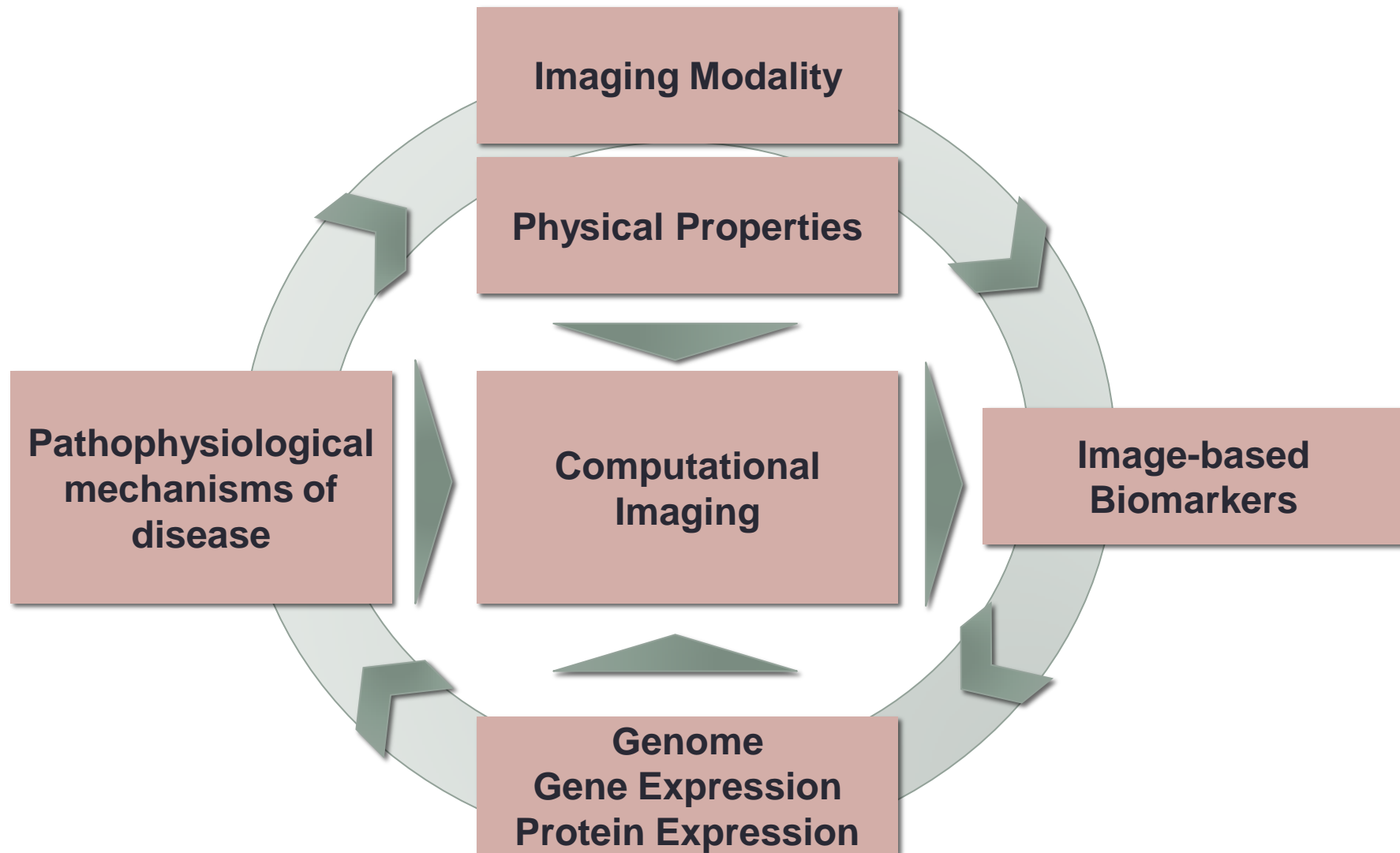
Why do we need new Biomarkers in COPD?



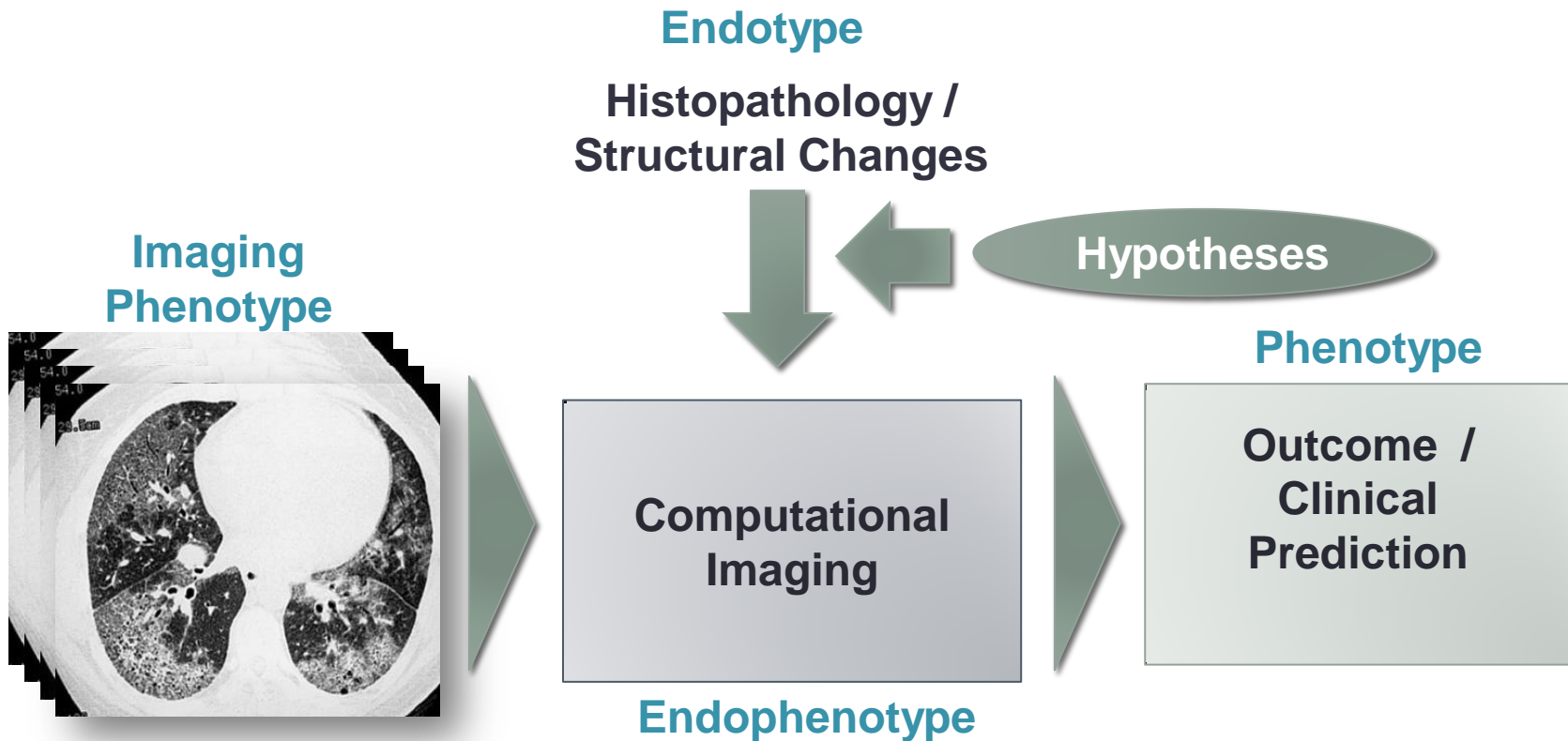
Biomarkers Landscape



Developing Imaging Biomarkers

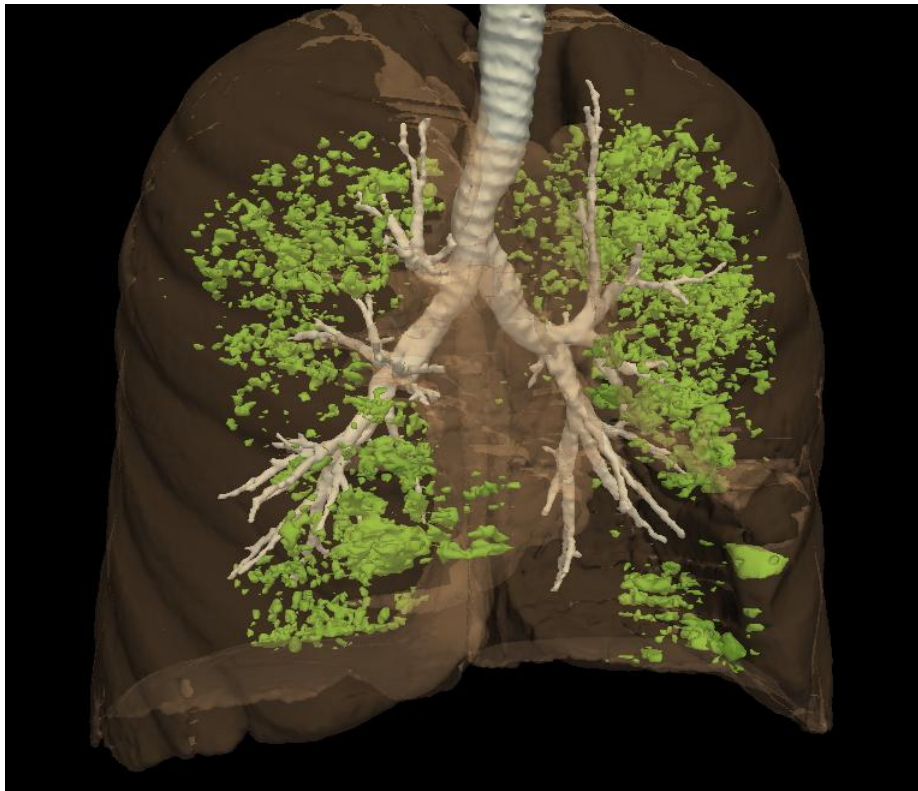


Computational Imaging in COPD



What are the *imaging endophenotypes* that are linked to the clinical manifestation and the prognostication of COPD?

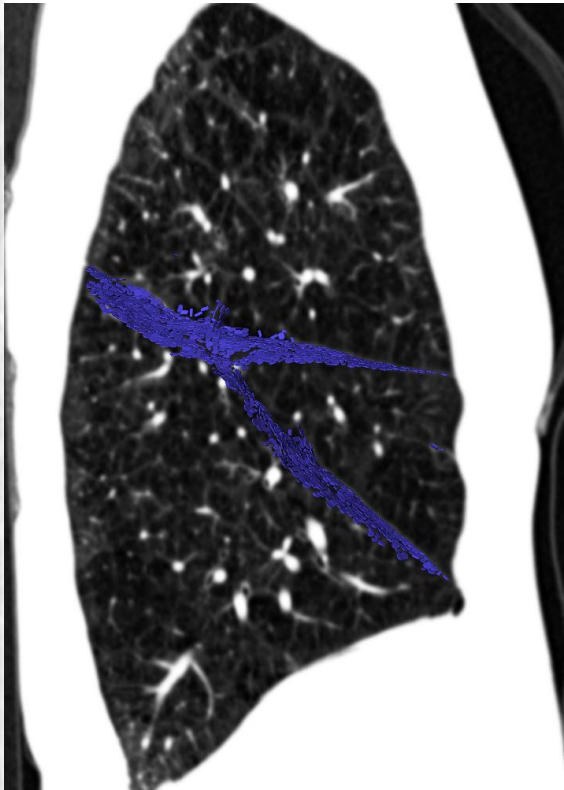
In-vivo Measurements of Disease



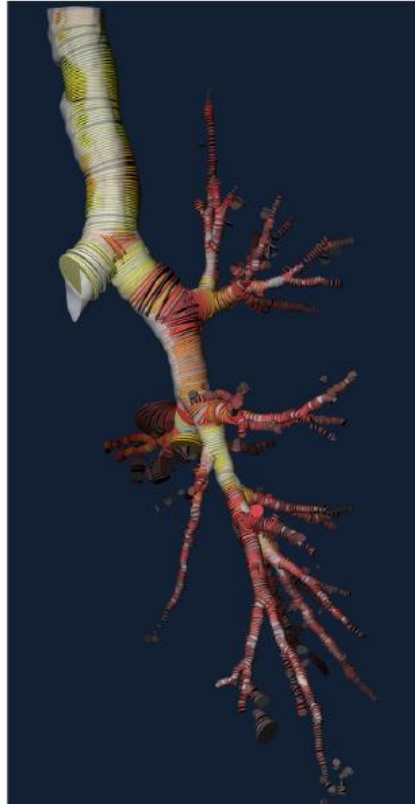
- Parenchyma
- Airways
- Vasculature
- Extra-pulmonary

Computational Imaging by Image Analysis

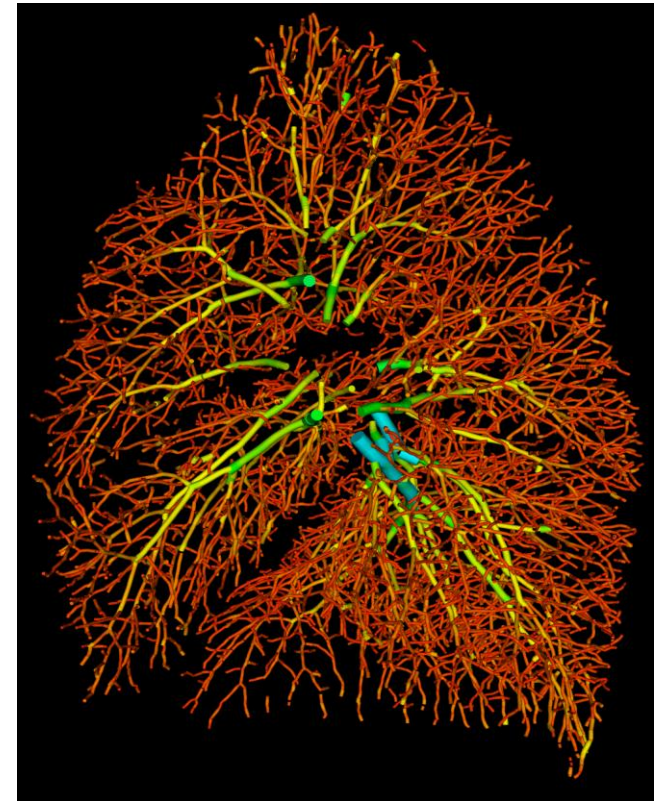
Pulmonary Fissures



Airways

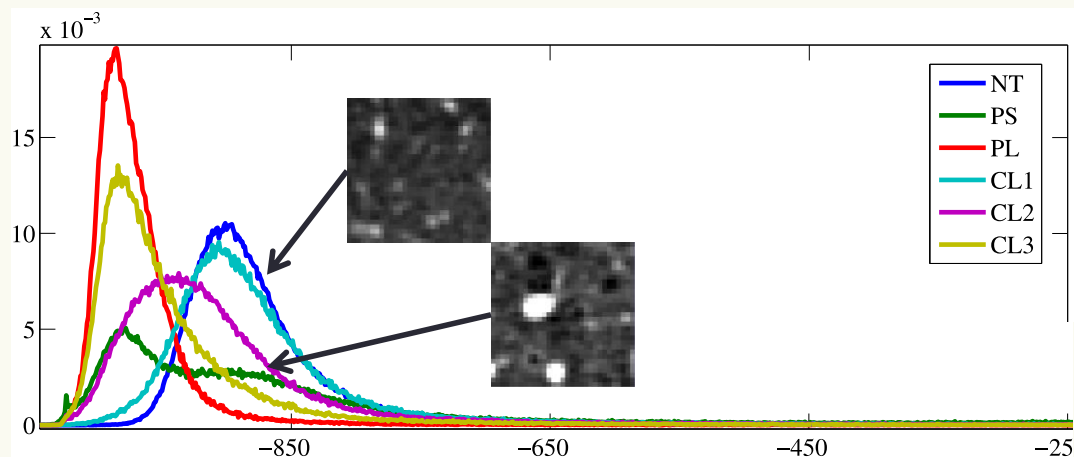


Vasculature



Emphysema Subtyping via Local Histogram

Mean Local Histogram for Emphysema Patterns



NT: Normal (non emphysema)

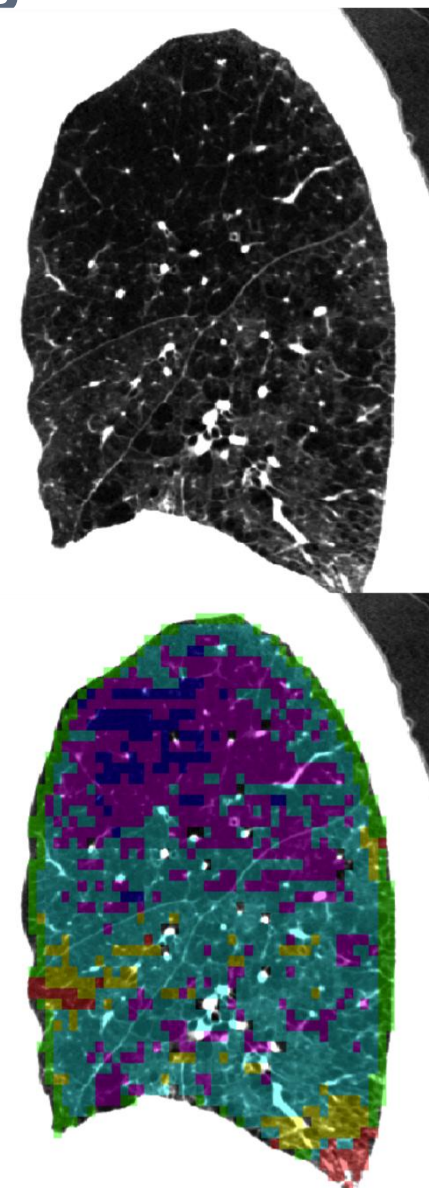
PS: Paraseptal

PL: Panlobular

CL1: Mild Centrilobular

CL2: Moderate Centrilobular

CL3: Severe Centrilobular

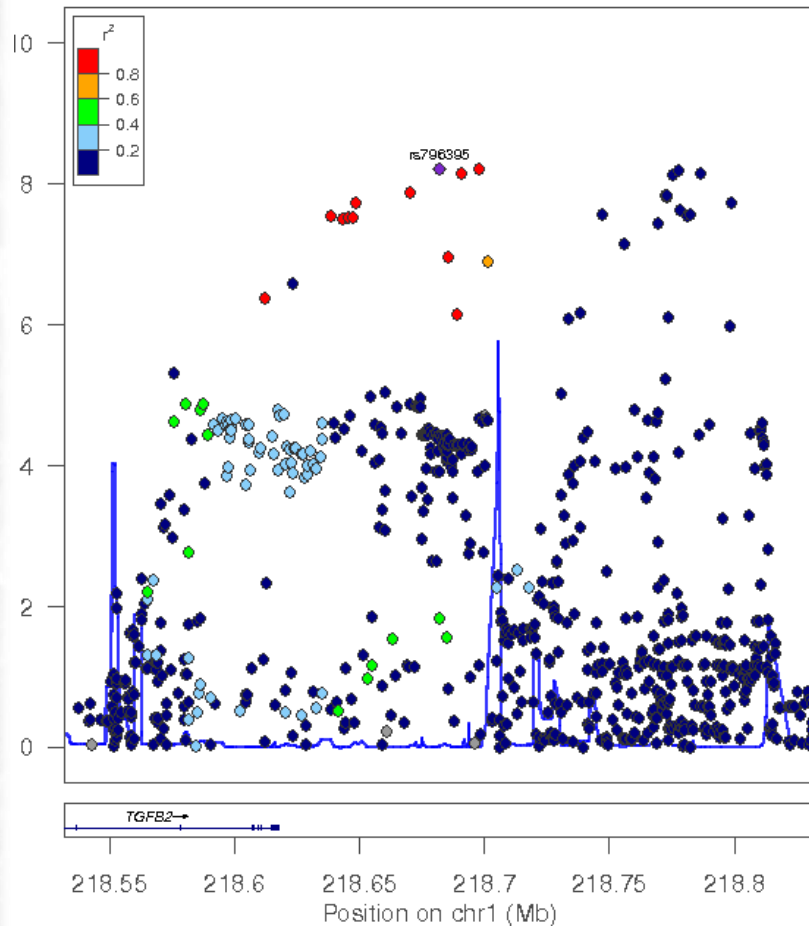


Genome-wide Significant Associations with Emphysema Subtypes in COPD Gene

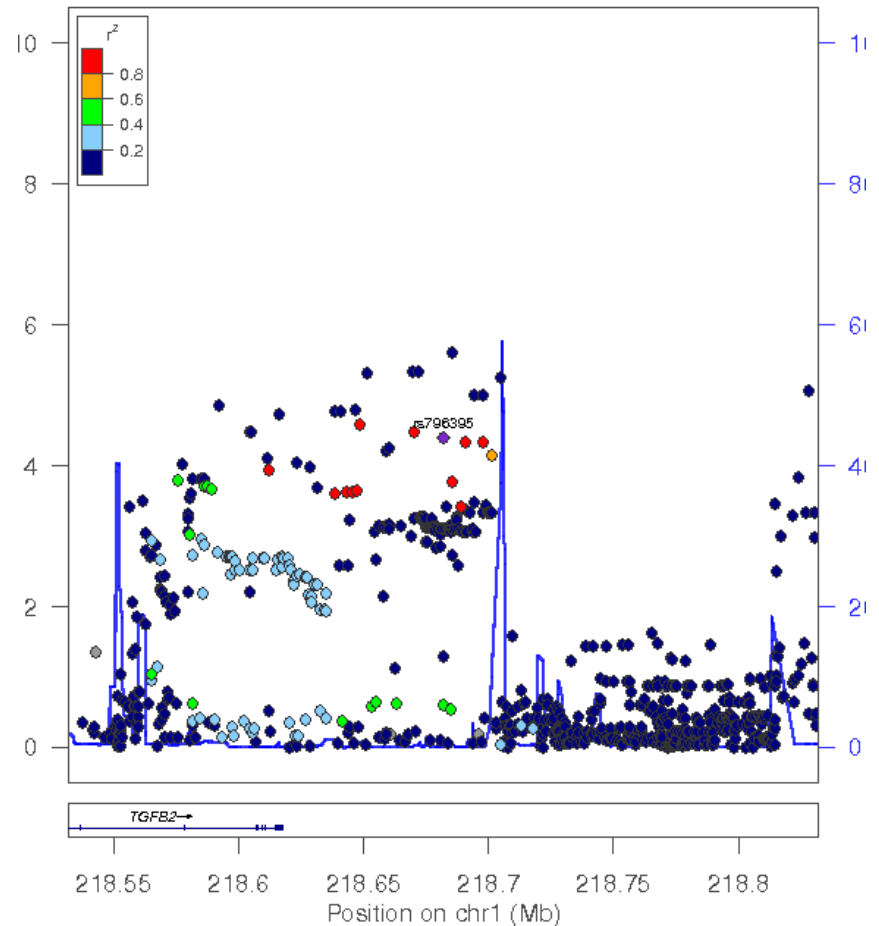
LHE Pattern	Lead SNP	Nearest Gene	Locus	Position (BP)	Effect Allele	P Value Meta
Normal	rs17486278	<i>CHRNA5</i>	15q25	78867482	A	8.3×10^{-13}
	rs138641402	<i>HHIP</i>	4q31	145445779	A	1.7×10^{-9}
	rs1690789	<i>TGFB2</i>	1q41	218698027	C	2.9×10^{-8}
	rs17368659	<i>MMP12</i>	11q22	102742761	G	1.1×10^{-8}
Moderate centrilobular	rs114205691	<i>CHRNA3</i>	15q25	78901113	C	3.1×10^{-13}
	rs56113850	<i>CYP2A6</i>	19q13	41353107	T	1.3×10^{-9}
	rs17368582	<i>MMP12</i>	11q22	102738075	G	2.7×10^{-9}
	rs1690789	<i>TGFB2</i>	1q41	218698027	C	7.9×10^{-9}
Severe centrilobular	rs9788721	<i>AGPHD1</i>	15q25	78802869	T	1.8×10^{-13}
	rs379123	<i>MYO1D</i>	17q11	30891814	T	1.5×10^{-8}
Panlobular	rs11852372	<i>AGPHD1</i>	15q25	78801394	A	1.5×10^{-10}
	rs9590614	<i>VWA8</i>	13q14	42175588	G	1.1×10^{-8}

- Novel associations within genes associated with cell migration (*MYO1D*) and cell signaling (*VWA8*).
- Genome-wide significant associations were observed at previously established COPD-associated loci at 4q31 (nearby gene *HHIP*), 15q25(*CHRNA3/5/IREB2*), 11q22 (*MMP12*), and 19q13 (*CYP2D6*).

Co-localization Evidence for TGFBR2



**GWAS – Moderate
Centrilobular Emphysema**



eQTL – GTEx Fibroblasts

ARTIFICIAL INTELLIGENCE

What is this all about?

LETTER

doi:10.1038/nature21056

Dermatologist-level classification of skin cancer with deep neural networks

Andre Esteva^{1*}, Brett Kuprel^{1*}, Roberto A. Novoa^{2,3}, Justin Ko², Susan M. Swetter^{2,4}, Helen M. Blau⁵ & Sebastian Thrun⁶

Research

JAMA | **Original Investigation** | INNOVATIONS IN HEALTH CARE DELIVERY

Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs

Varun Gulshan, PhD; Lily Peng, MD, PhD; Marc Coram, PhD; Martin C. Stumpe, PhD; Derek Wu, BS; Arunachalam Narayanaswamy, PhD; Subhashini Venugopalan, MS; Kasumi Widner, MS; Tom Madams, MEng; Jorge Cuadros, OD, PhD; Ramasamy Kim, OD, DNB; Rajiv Raman, MS, DNB; Philip C. Nelson, BS; Jessica L. Mega, MD, MPH; Dale R. Webster, PhD

Editorials in Main Medical Journals

Predicting the Future — Big Data, Machine Learning, and Clinical Medicine

Opinion

EDITORIAL

Translating Artificial Intelligence Into Clinical Care

Andrew L. Beam, PhD; Isaac S. Kohane, MD, PhD

Opinion



VIEWPOINT

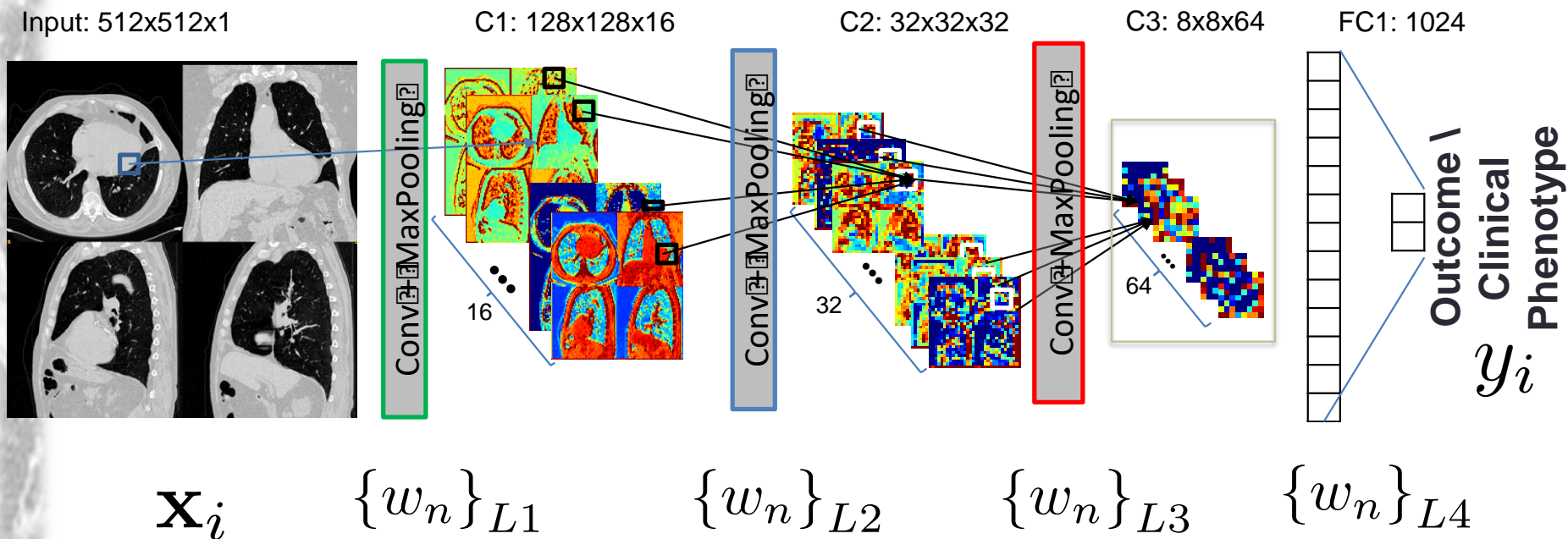
INNOVATIONS IN HEALTH CARE DELIVERY

Adapting to Artificial Intelligence Radiologists and Pathologists as Information Specialists

VIEWPOINT

Unintended Consequences of Machine Learning in Medicine

Convolutional Neural Network to Predict COPD Outcomes



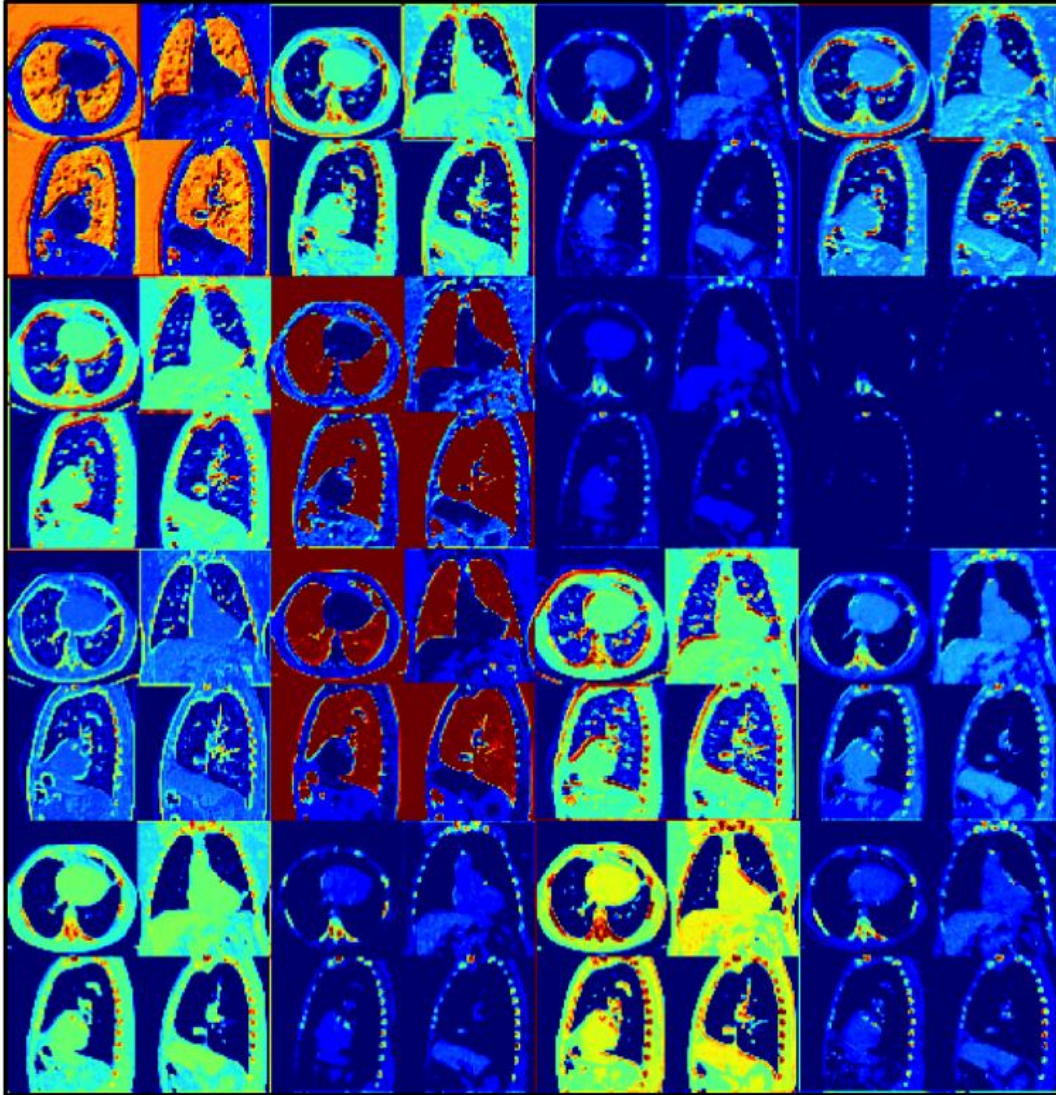
Deep Learning Regressor Performance

Testing Cohort

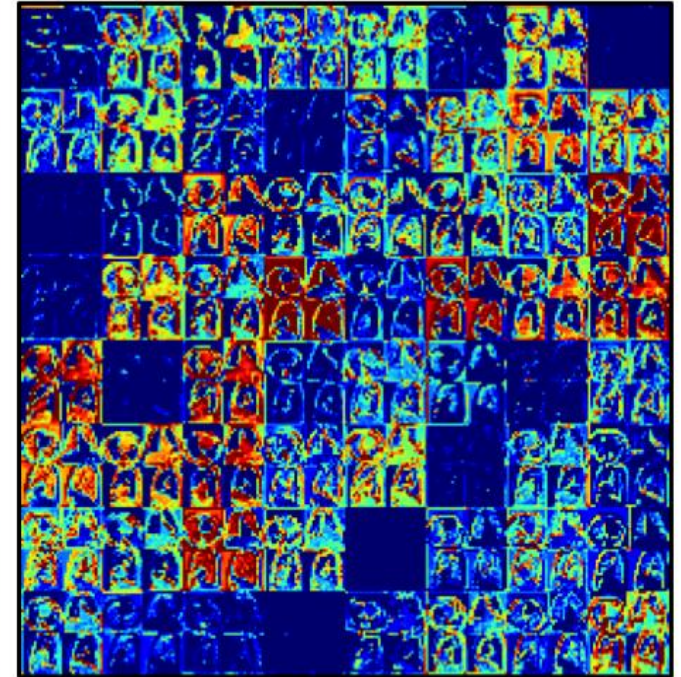
	COPDGene (n=1,000) Reconstruction Kernel		Replication ECLIPSE (n=1,547)
	STD	SHARP	
FEV1 (r)	0.735 [0.705 - 0.762]	0.735 [0.705 - 0.762]	0.64 [0.542 - 0.756]
GOLD Stage (Accuracy)	51.2% / 74.7%	52.0% / 73.8%	29.4% / 74.6%
ARD AUC	0.633 [0.602 - 0.663]	0.627 [0.597 - 0.658]	0.55 [0.51 - 0.62]
Mortality AUC	0.72 [0.6 - 0.78]	0.709 [0.58 - 0.737]	0.6 [0.52 - 0.71]

Interpretation of Network

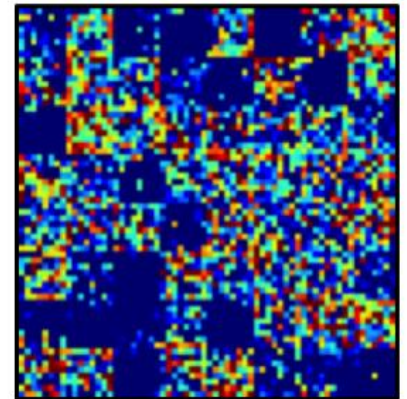
LAYER 1



LAYER 2

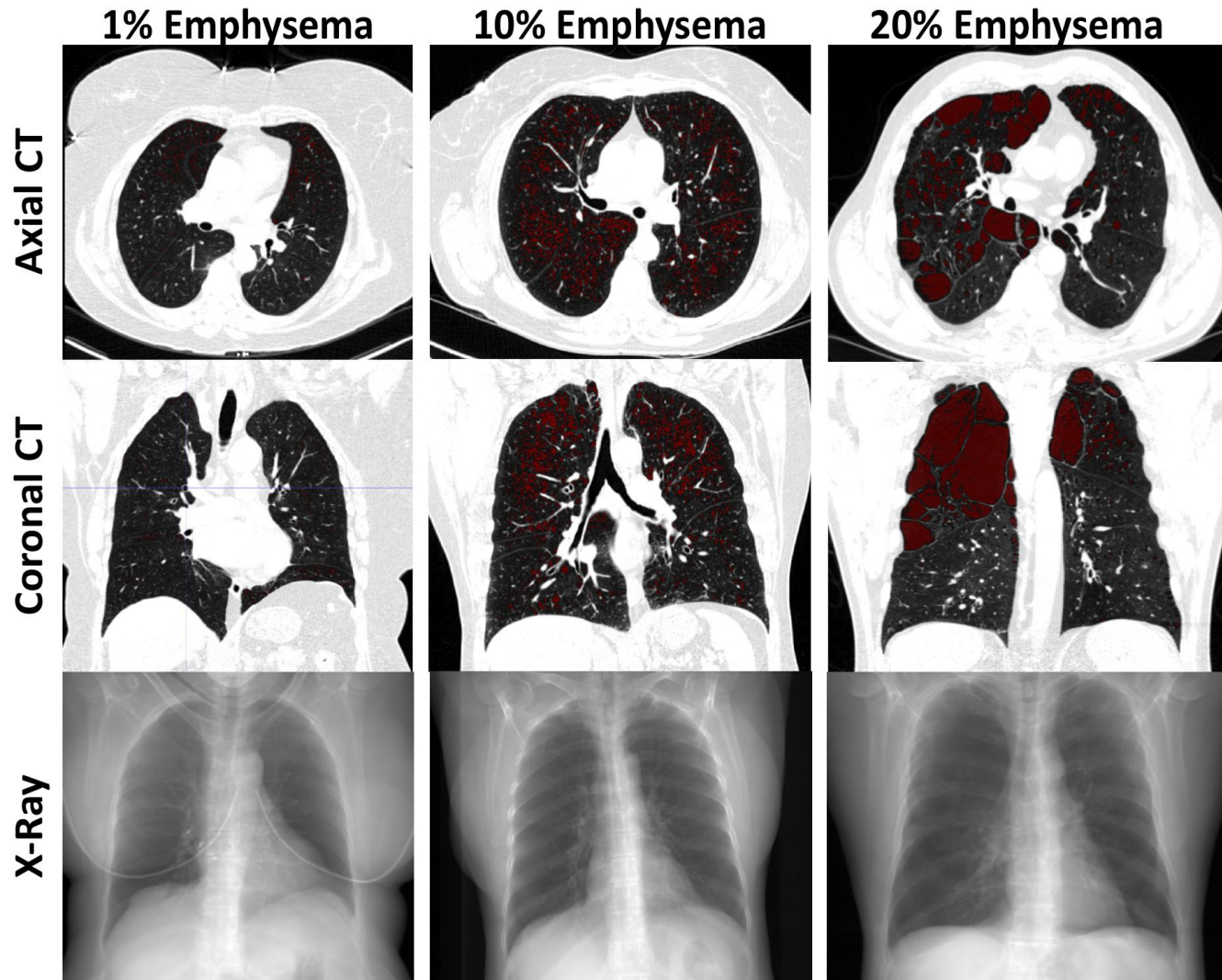


LAYER 3



What is the Clinical Translation?

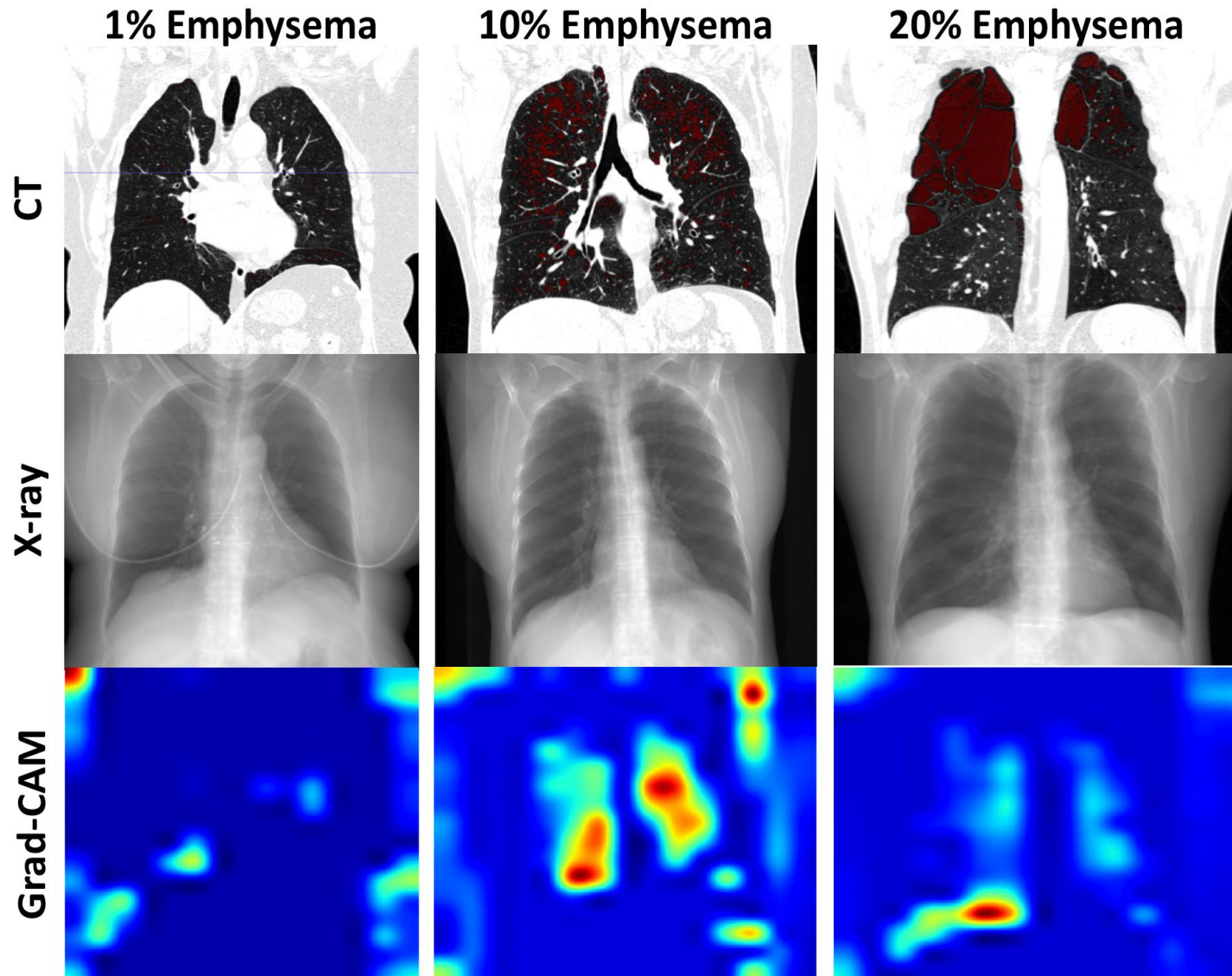
- Prediction of Emphysema Scoring from X-Ray



Emphysema Diagnosis on X-ray

Disease threshold (%emphysema)	Sensitivity [95%CI]	Specificity [95%CI]	AUC (%)
≥ 3	67.96 [65.89 – 70.03]	80.18 [78.68 – 81.68]	82.48
≥ 5	78.36 [76.22 – 80.50]	76.90 [75.45 – 78.35]	85.91
≥ 7.5	78.56 [76.13 – 80.99]	82.10 [80.84 – 83.36]	88.39
≥ 10	85.68 [83.37 – 87.99]	80.42 [79.16 – 81.68]	90.73

What is the network learning?



Acknowledgements

Applied Chest Imaging Laboratory

- Samuel Ash
- Carolyn Come
- Alejandro Diaz
- Ruben San Jose Estepar
- Rola Harmouche
- Stefanie Mason
- Pietro Nardelli
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- Jorge Onieva
- Nick Rahagi
- James Ross
- Gonzalo Vegas Sanchez-Ferrero
- German Gonzalez Serrano
- George Washko
- Tom Young

• NHLBI

- R01HL116931
 - R01HL116473
 - COPDGene Study
-
- Boehringer Ingelheim
 - BTG
 - Janssen Pharmaceuticals

Muchas Gracias



rsanjose@bwh.harvard.edu