Disease progression patterns in COPD

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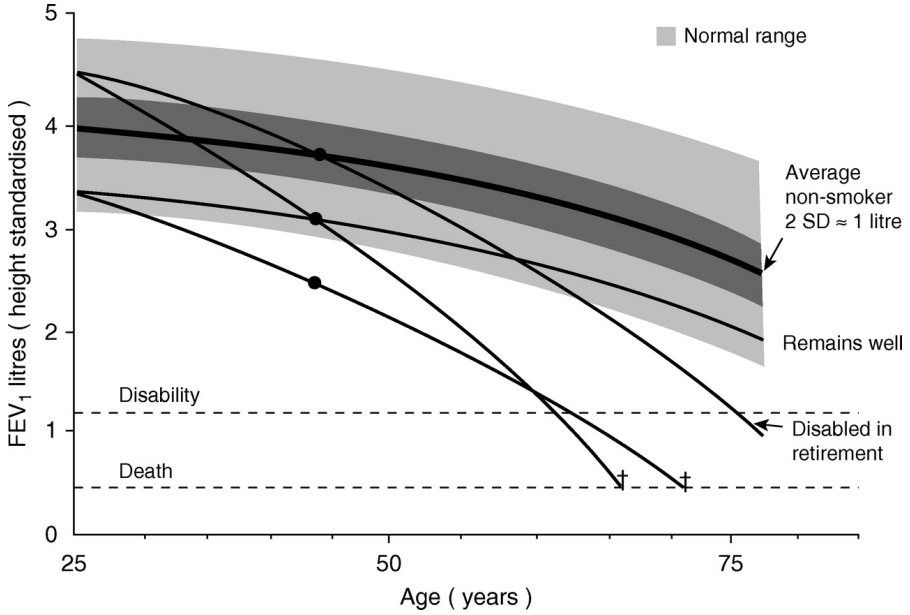
Centre for Medical Image Computing

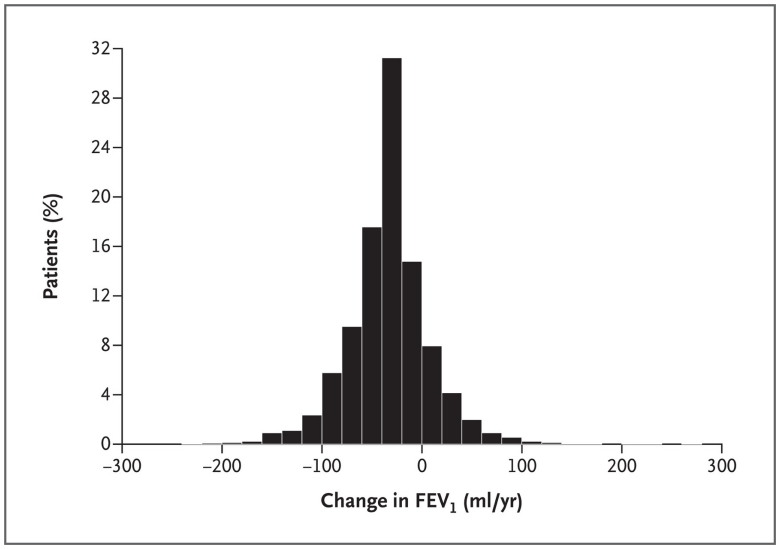
Progression Of Neurodegenerative Disease

No disclosures

COPD is heterogeneous and has a long-term progression that spans several decades

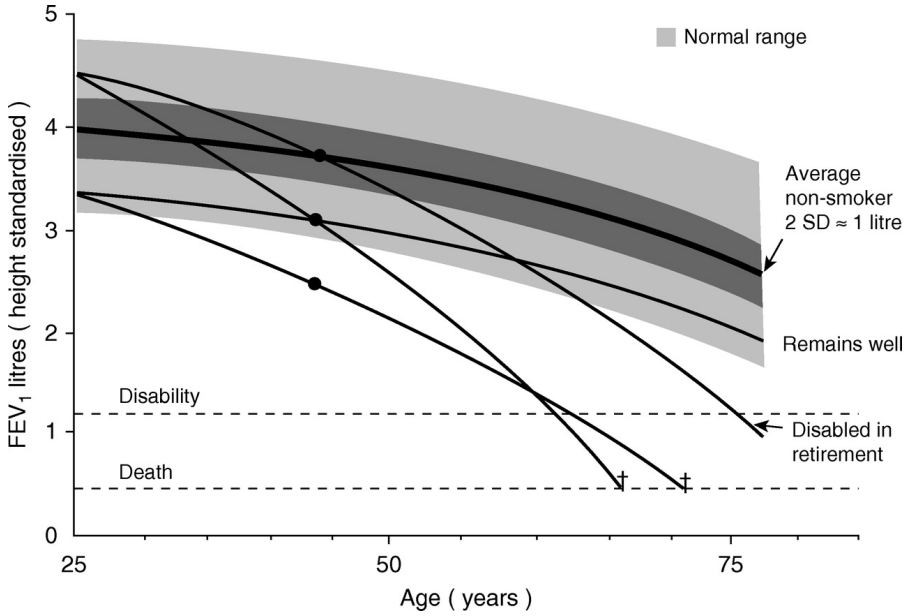


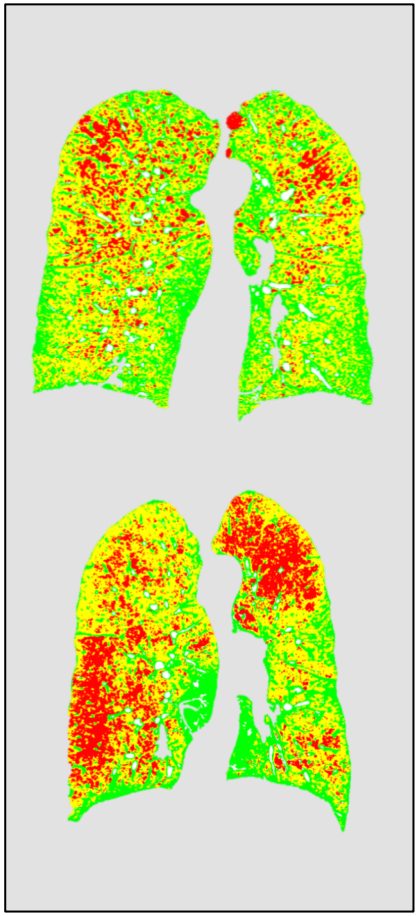
Fletcher-Peto,1977



Vestbo, 2011

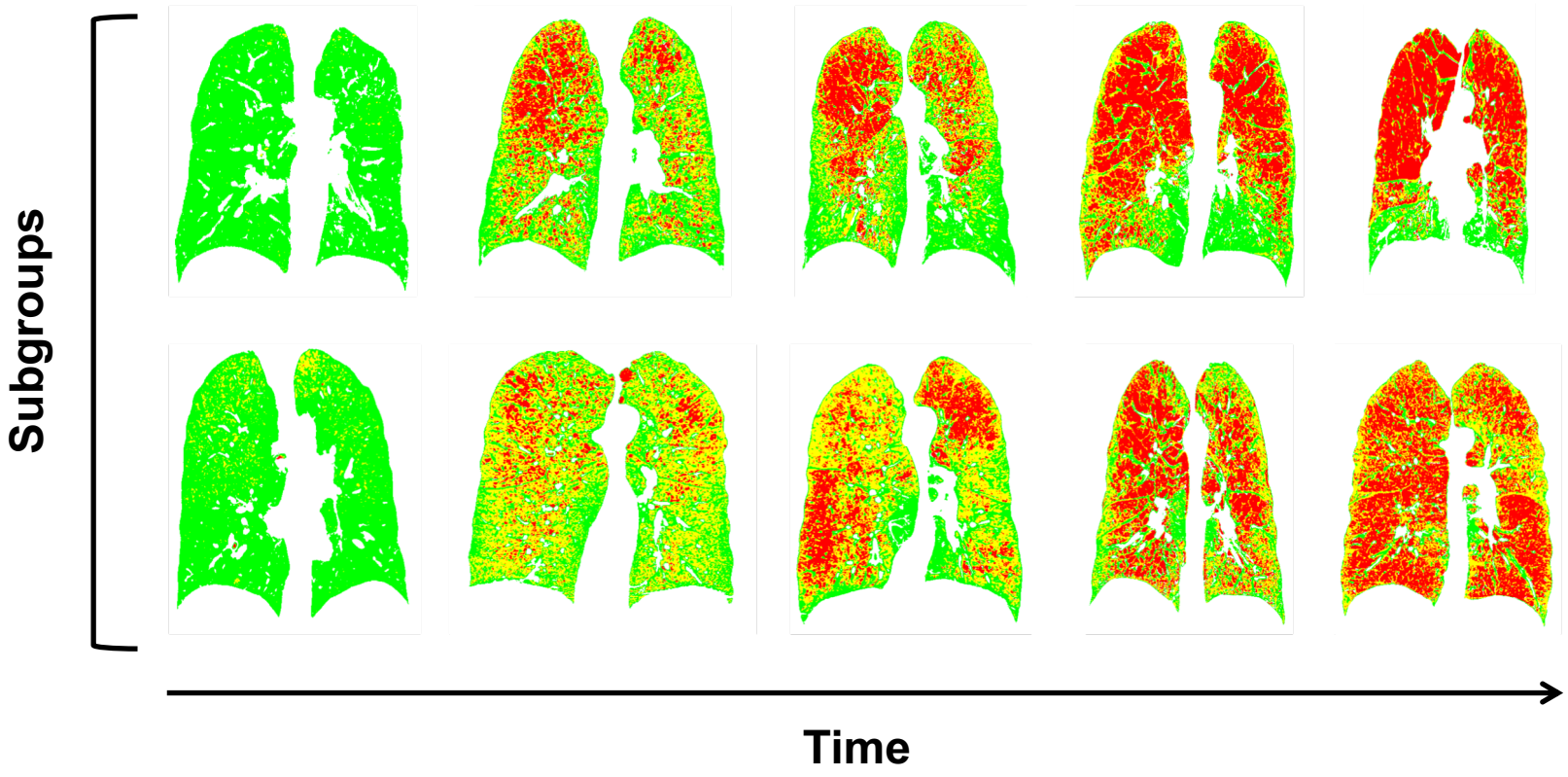
Lung function decline is a non-specific measure that can correspond to a range of underlying pathologies



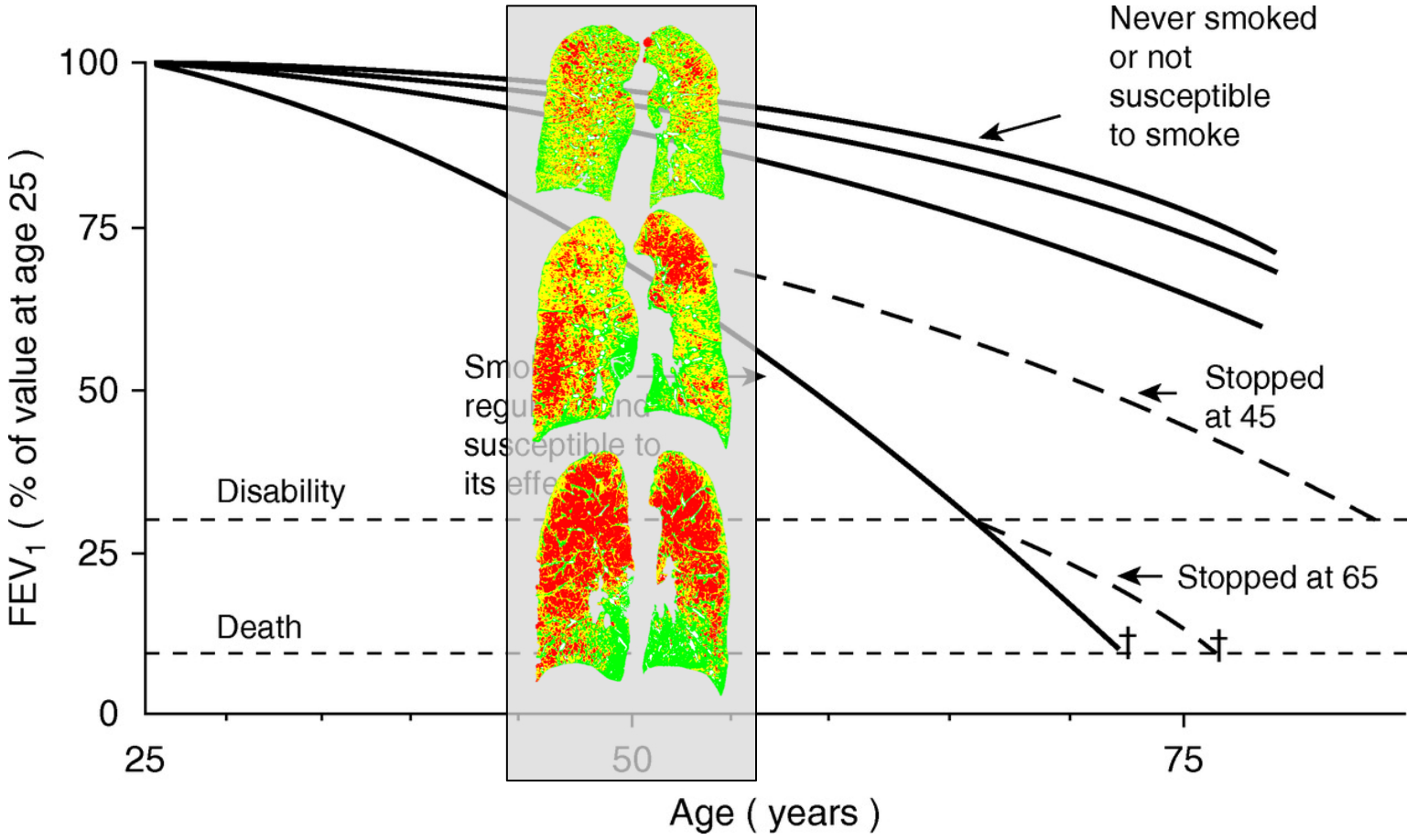


Fletcher-Peto,1977

Hypothetical description of COPD progression



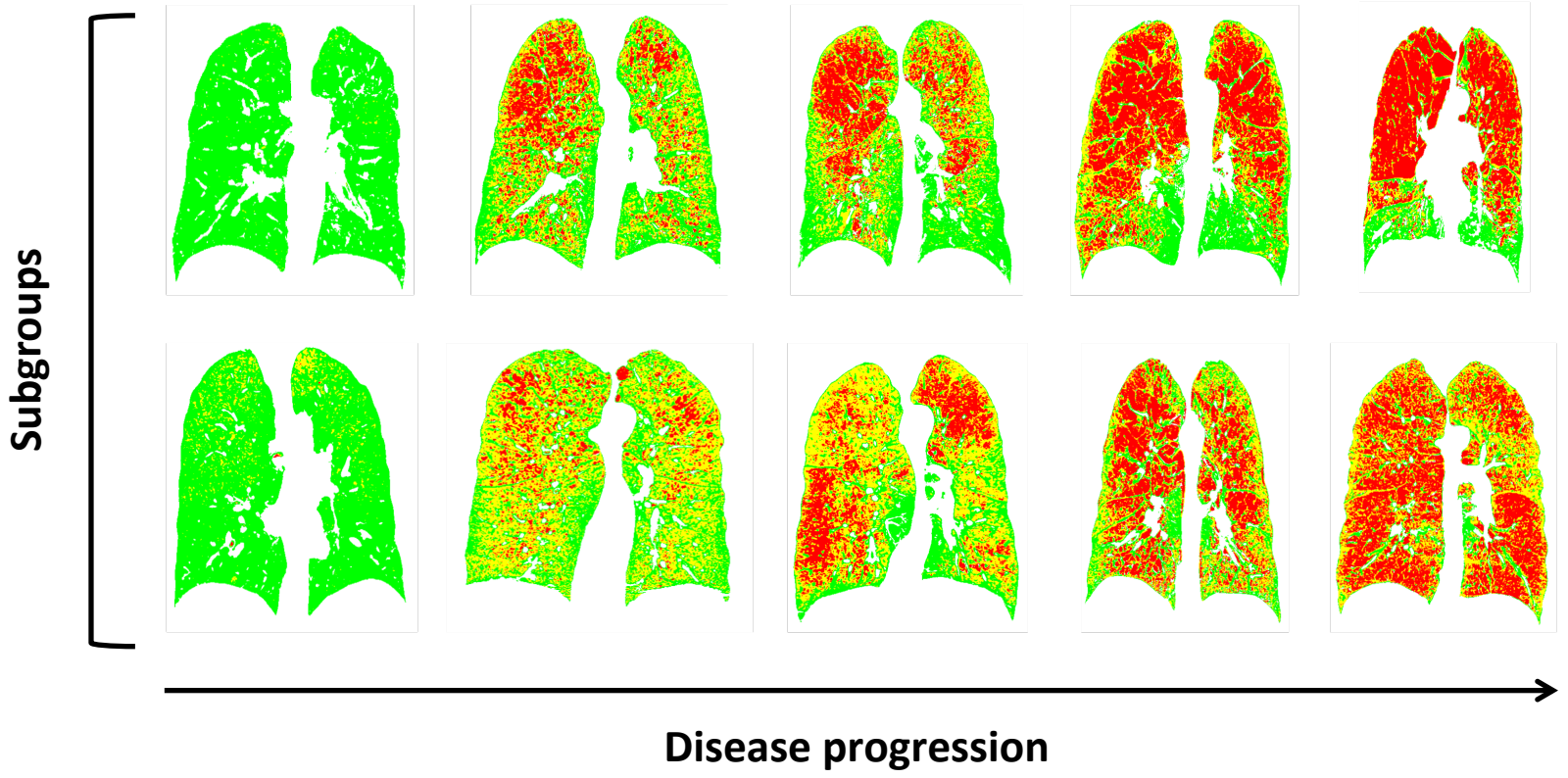
Disentangling imaging trajectories is complicated by long-term natural history of COPD



Fletcher-Peto,1977

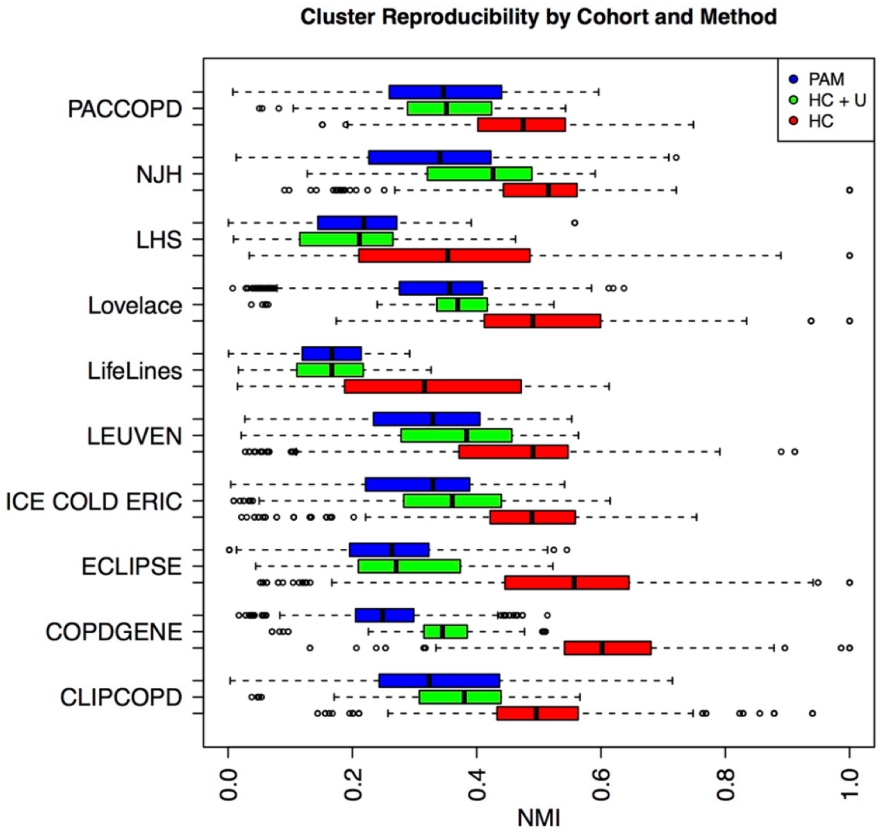
Objectives

- Demonstrate use of a novel machine learning technique to identify subgroups of COPD with distinct progression patterns
- Apply technique to image-based markers from COPDGene study

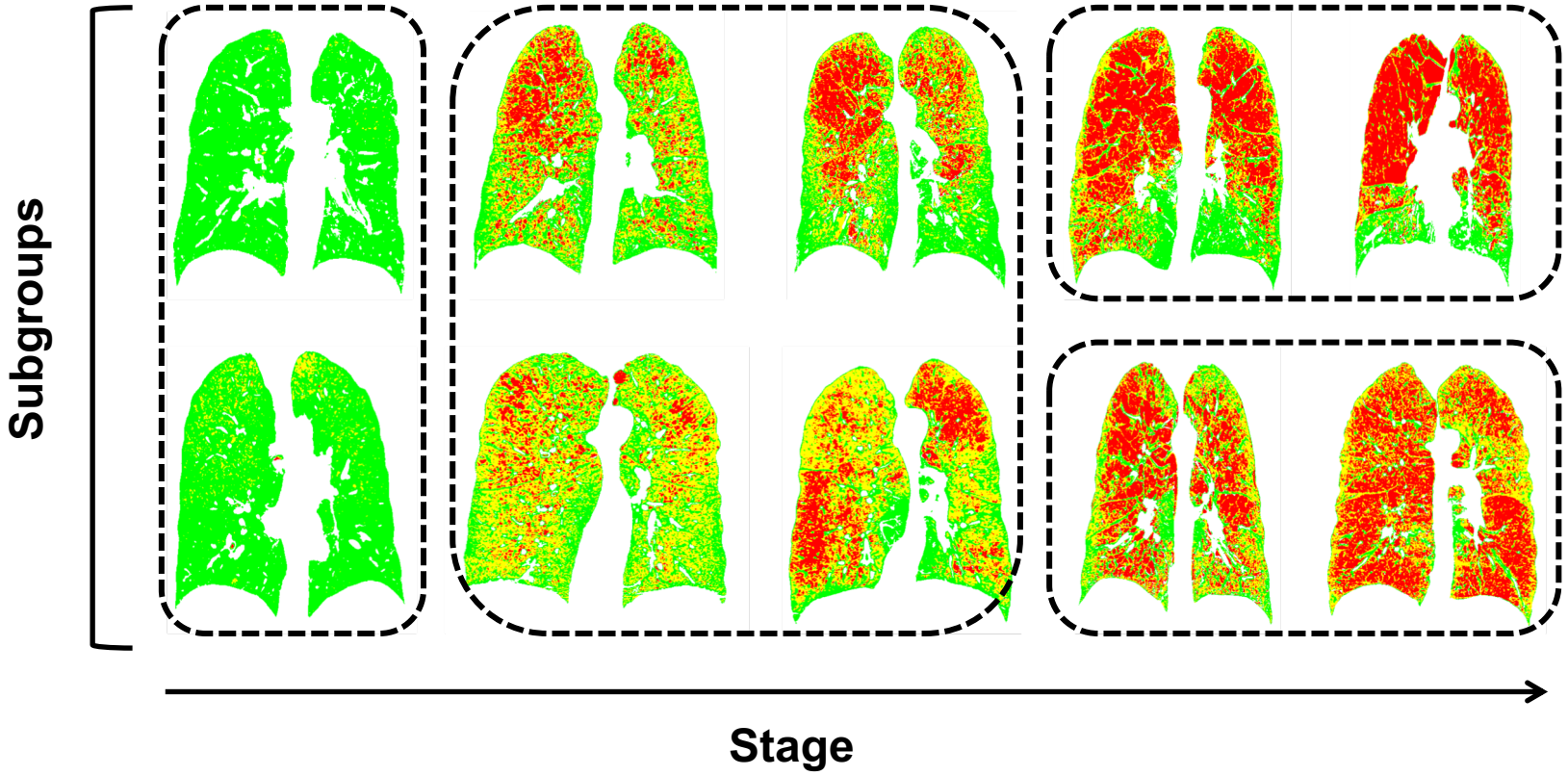


Previous studies investigating heterogeneity use clustering

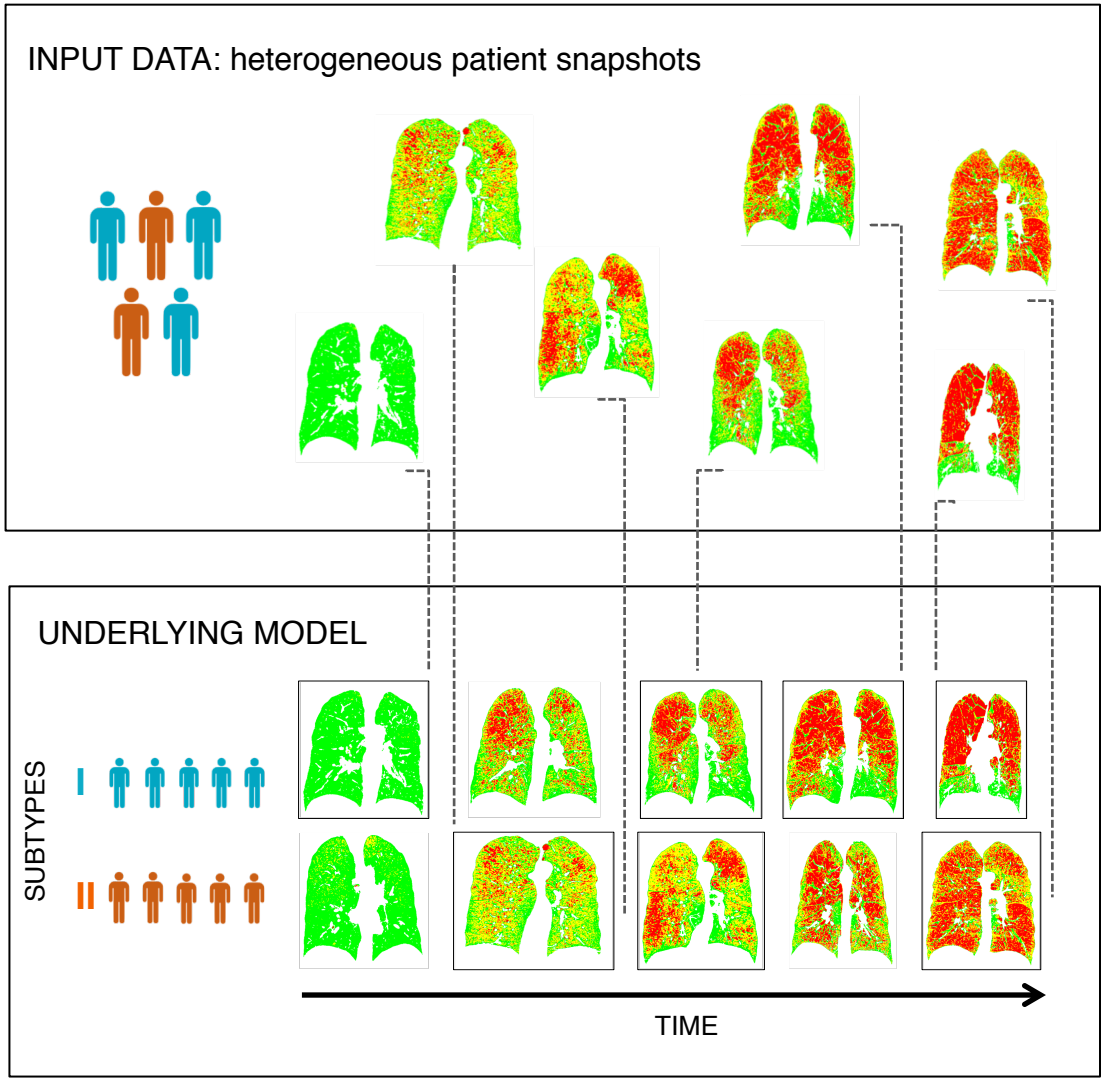
- Clustering associates individuals with similar biomarker profiles
- Doesn't describe the progression of the disease
- Results highly variable (Castaldi et al. 2017)



Clustering conflates disease subtypes and stages



Subtype and Stage Inference (SuStaIn)



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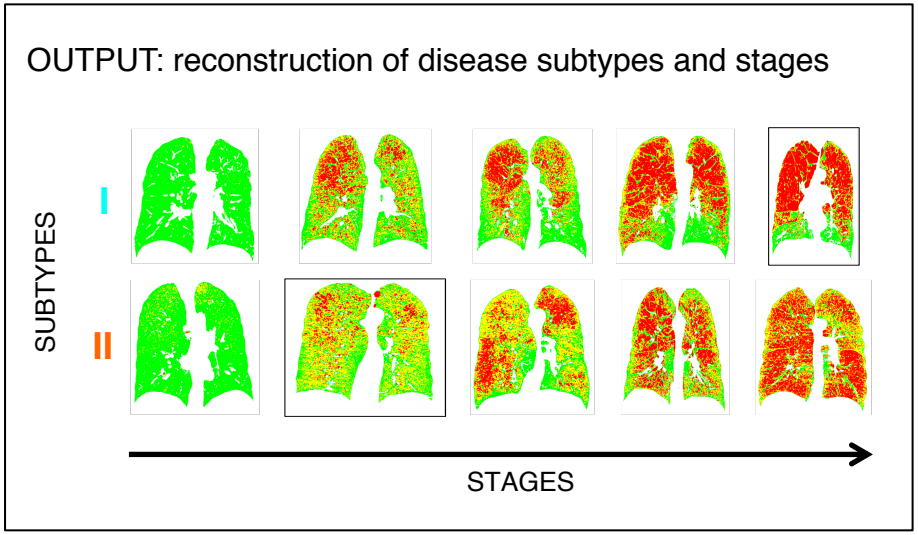
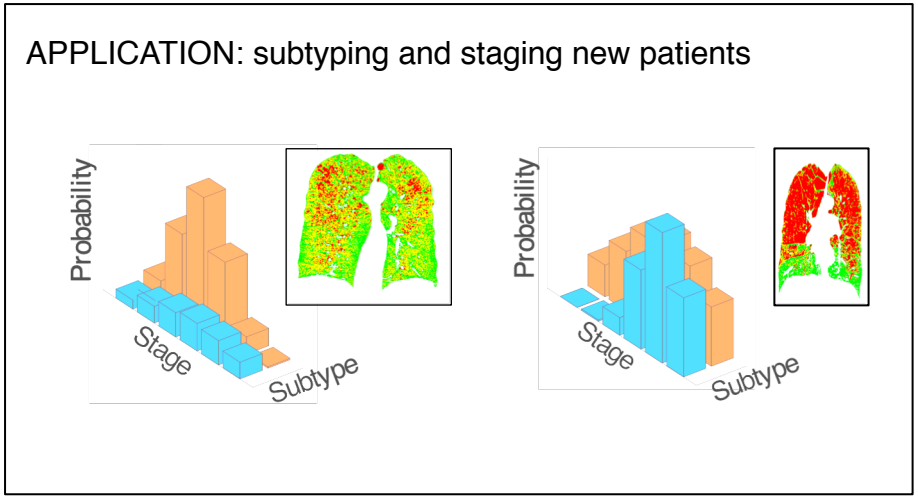
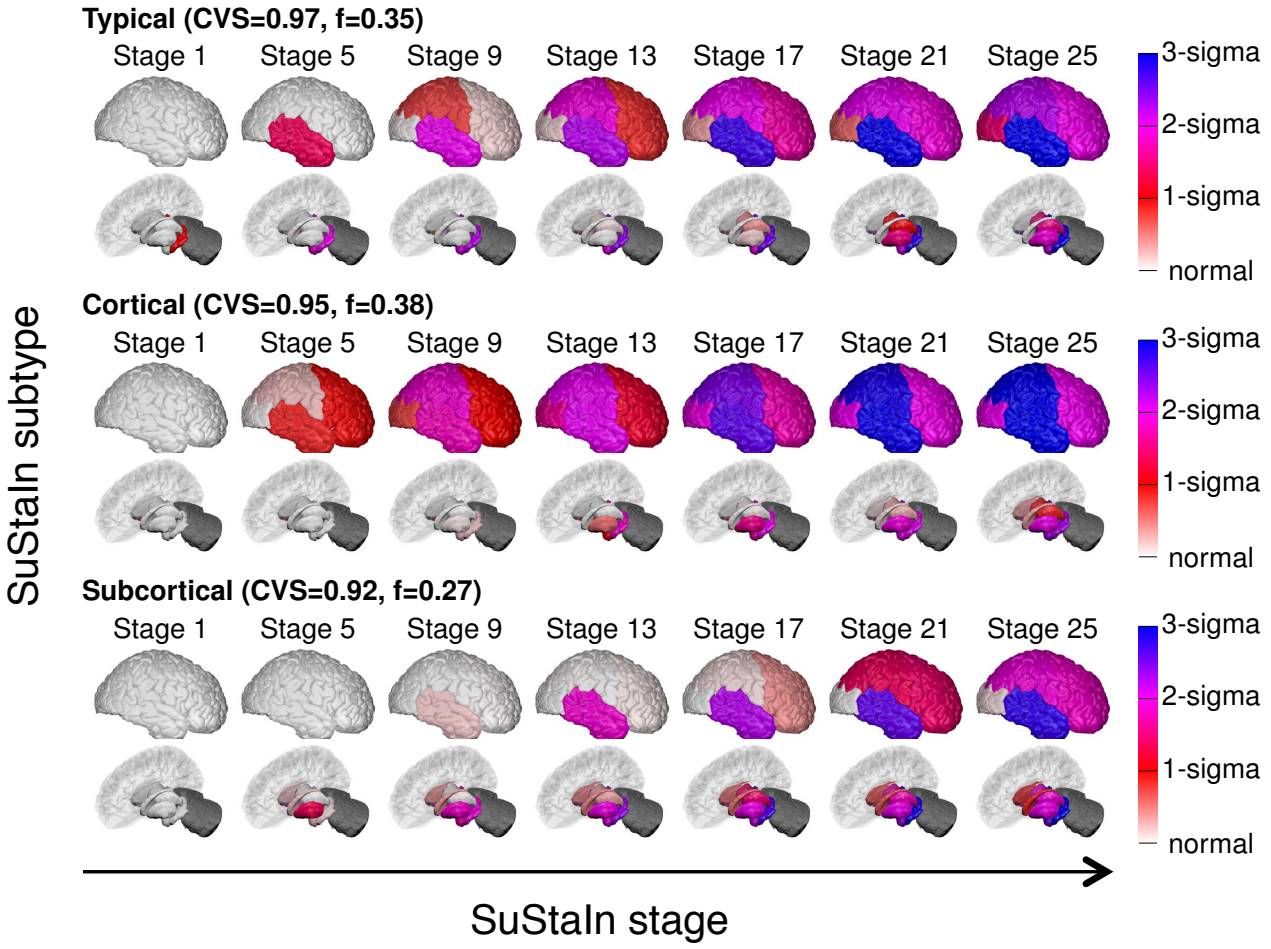




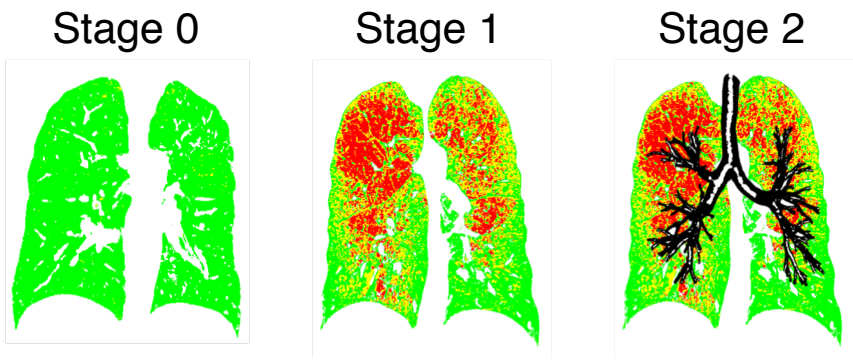
SuStaIn initially developed for Alzheimer's disease, but naturally extends to COPD



Young et al., Nature Communications, 2018 (In press)

Reconstructing temporal progression from cross-sectional data

A



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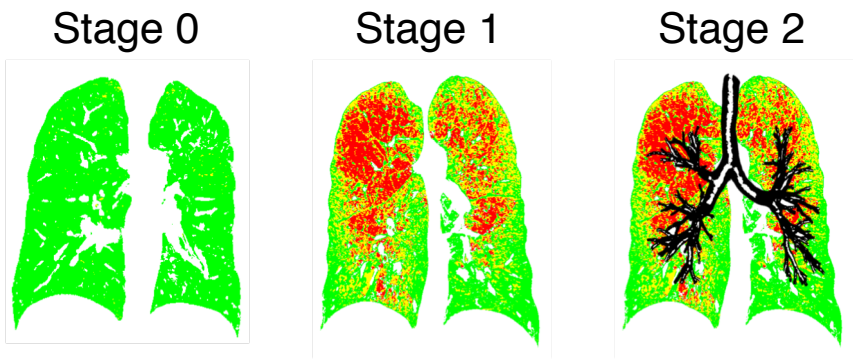
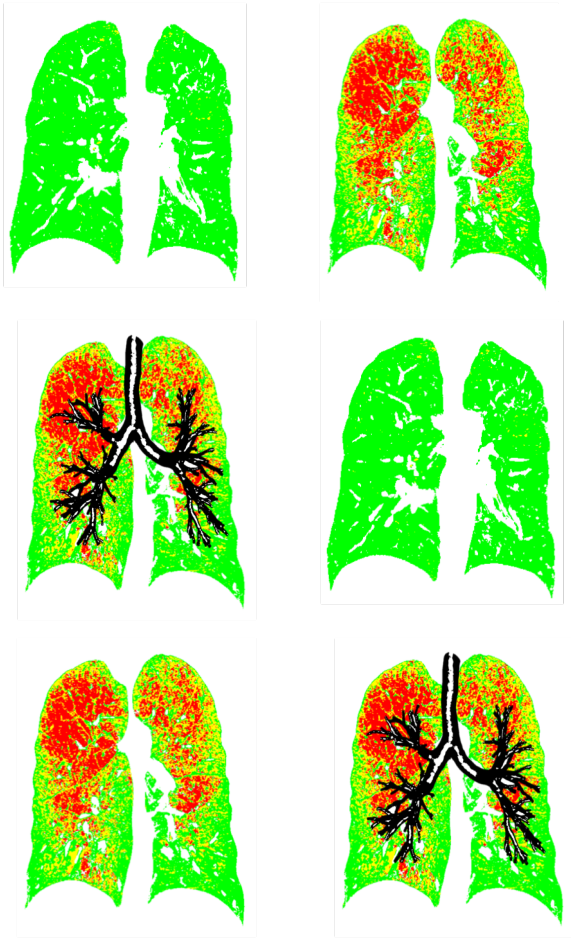


Cross-sectional samples



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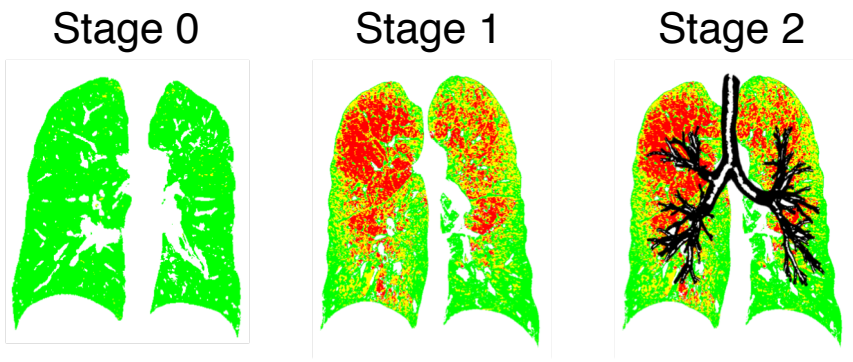

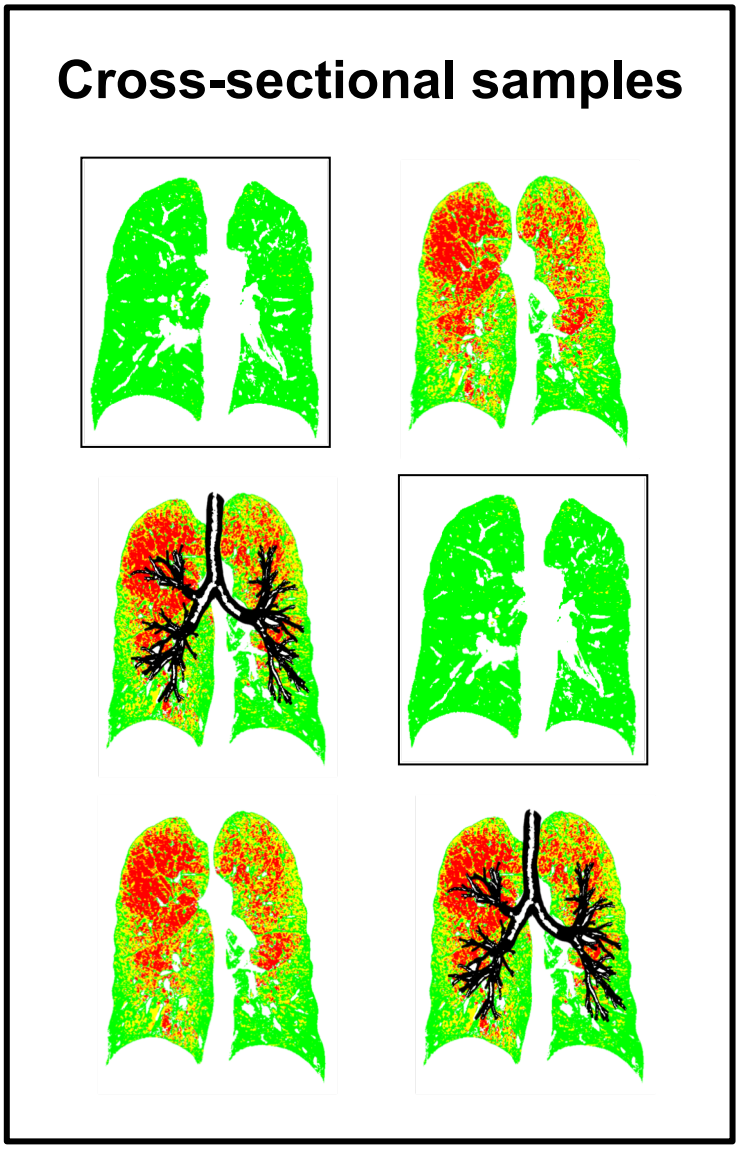

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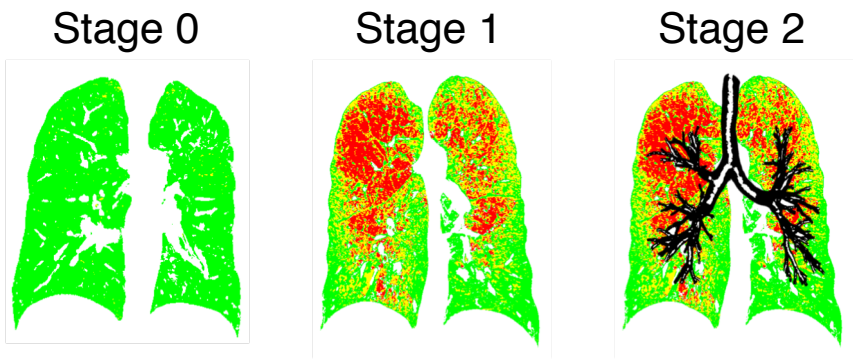

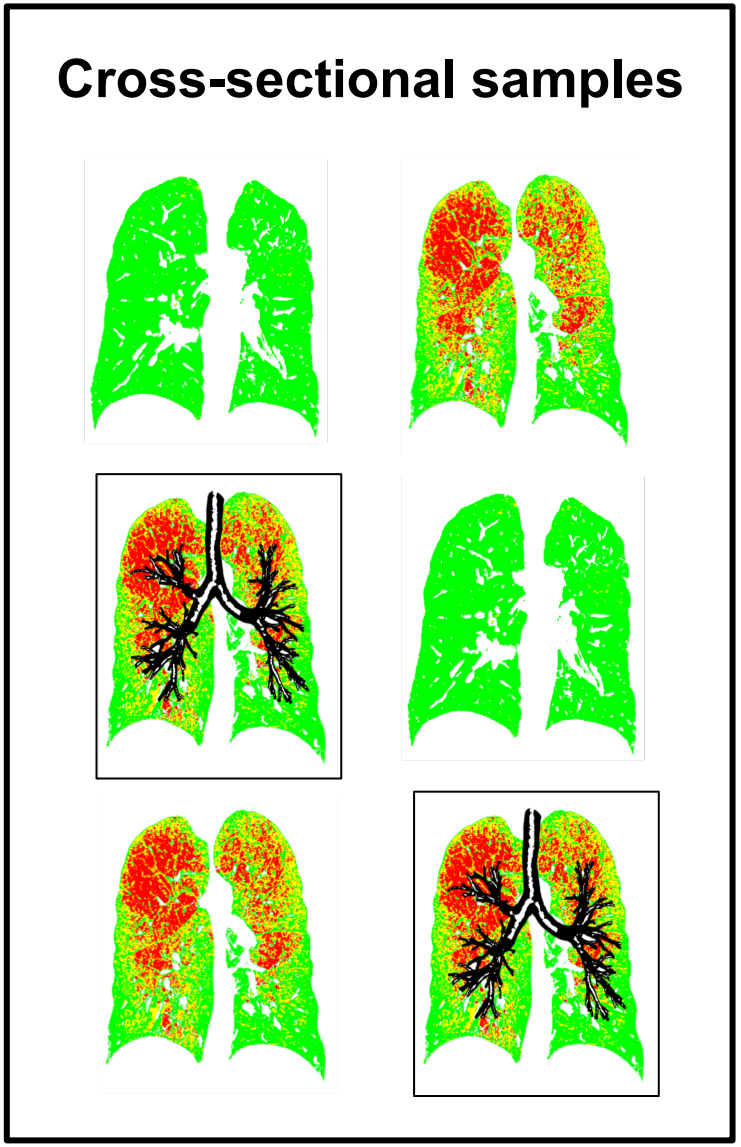

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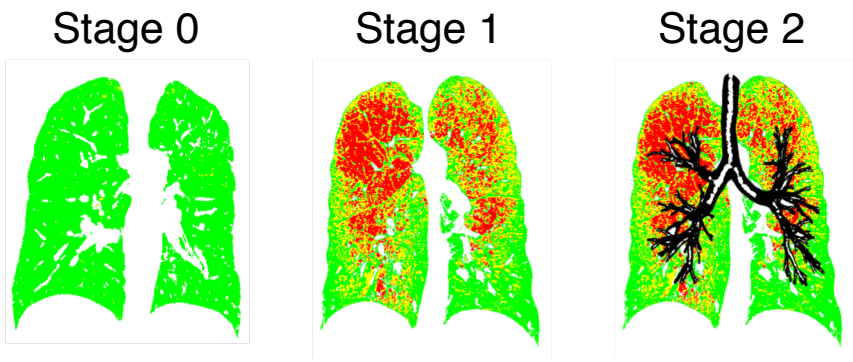

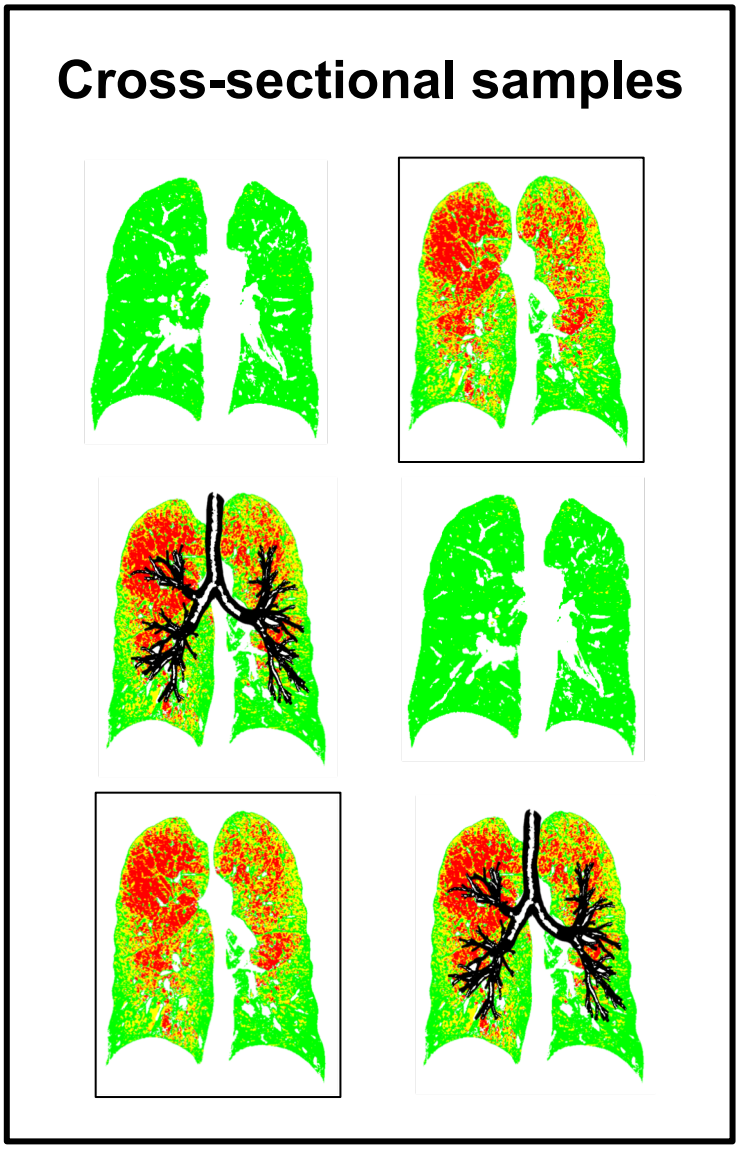

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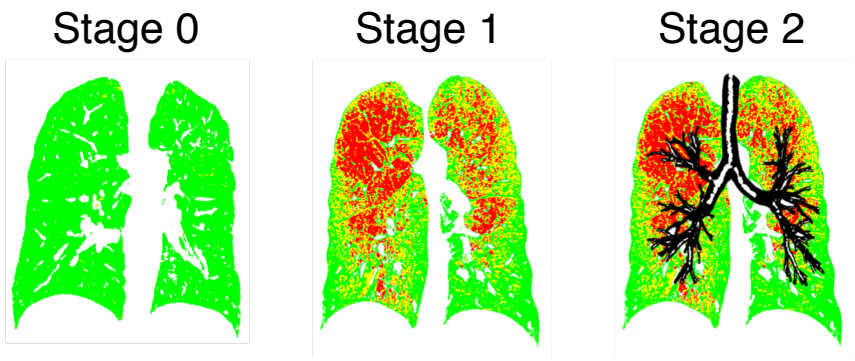

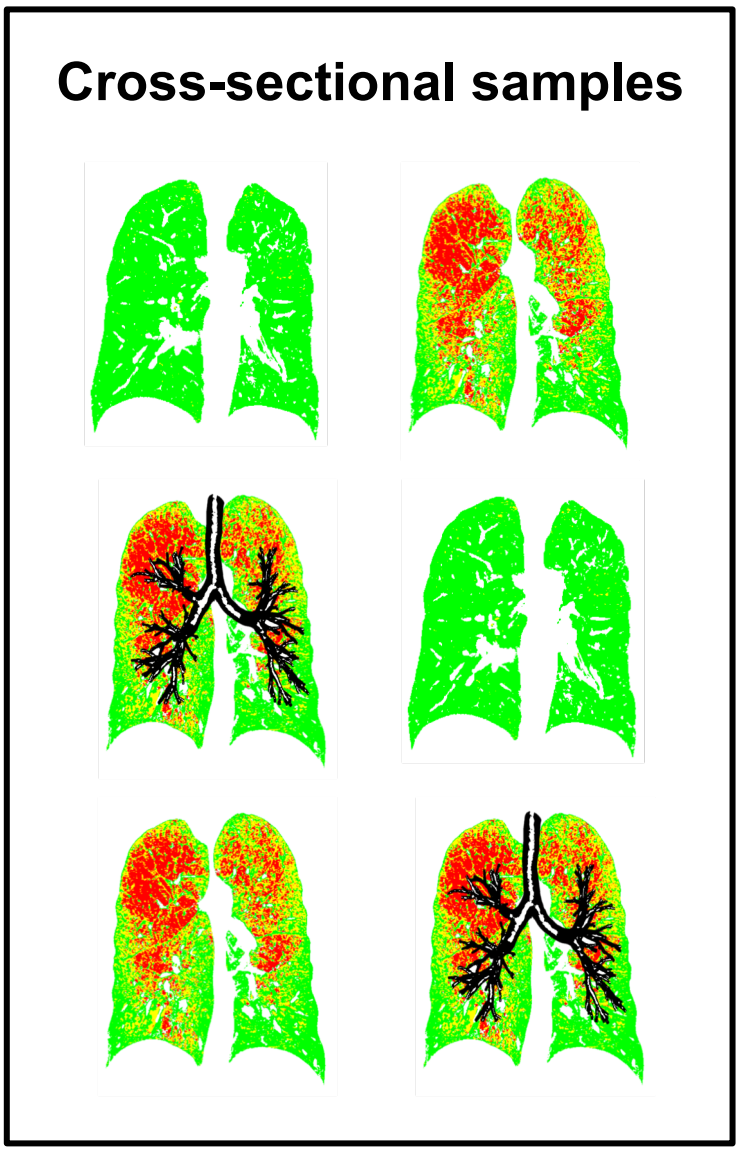

Reconstructing temporal progression from cross-sectional data

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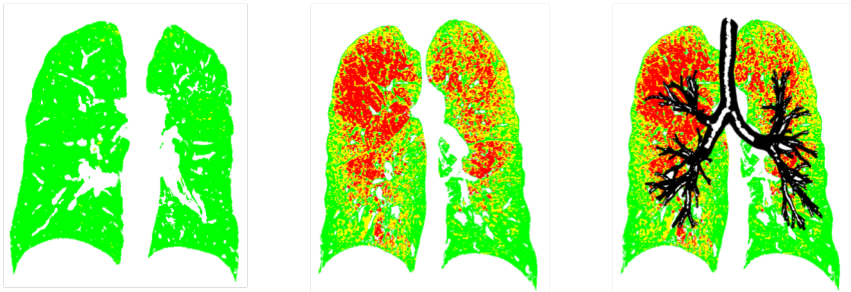
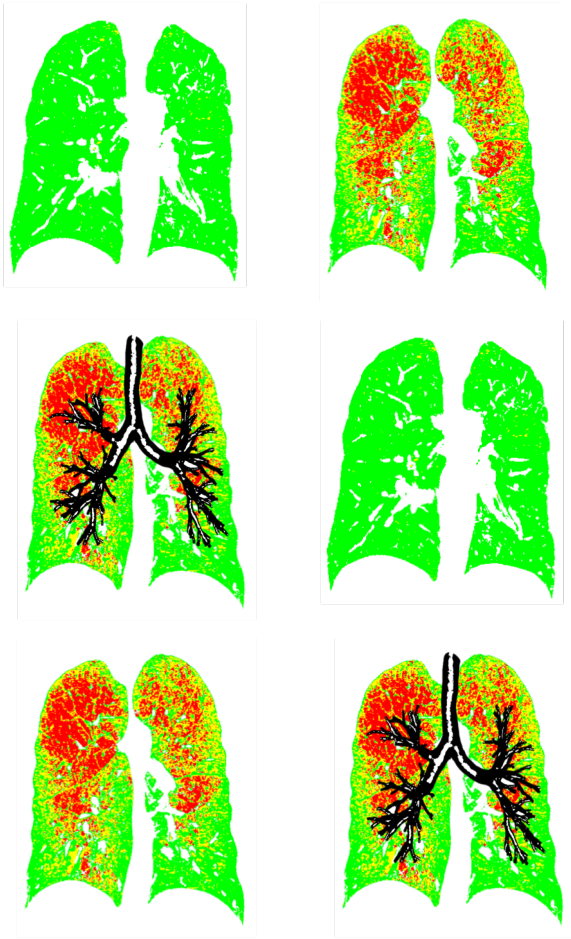
Stage 0 Stage 1 Stage 2



Emphysema precedes airway wall thickening

Cross-sectional samples



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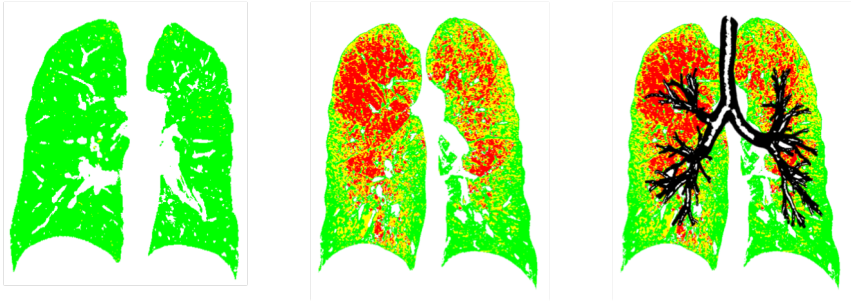
Stage 0 | Stage 1 | Stage 2



B

Stage 0 | Stage 1 | Stage 2

Reconstructing temporal progression from cross-sectional data

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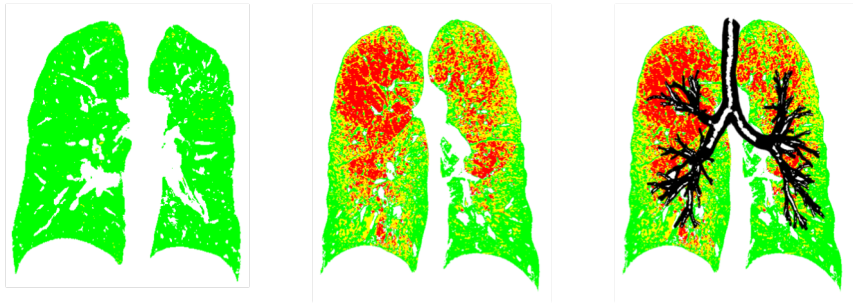
Stage 0 | Stage 1 | Stage 2



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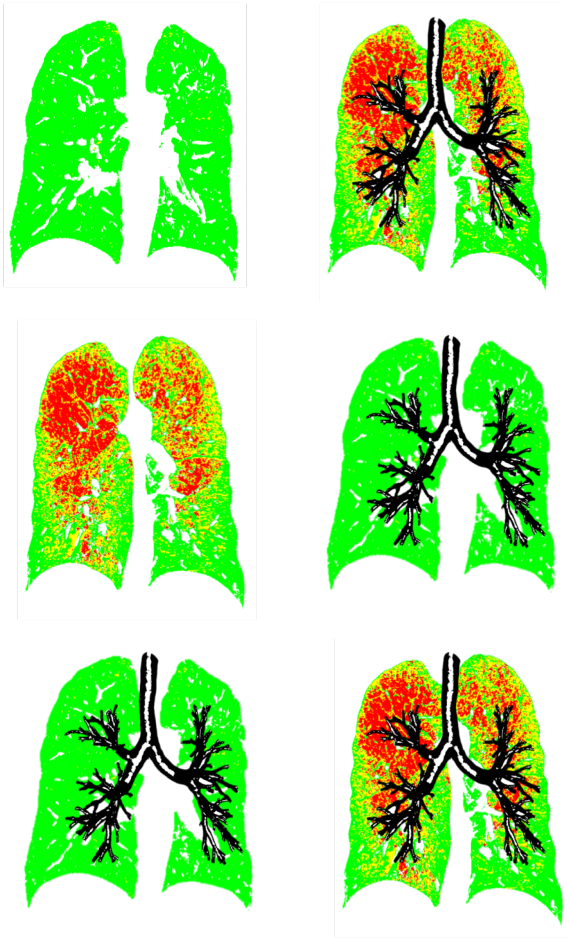

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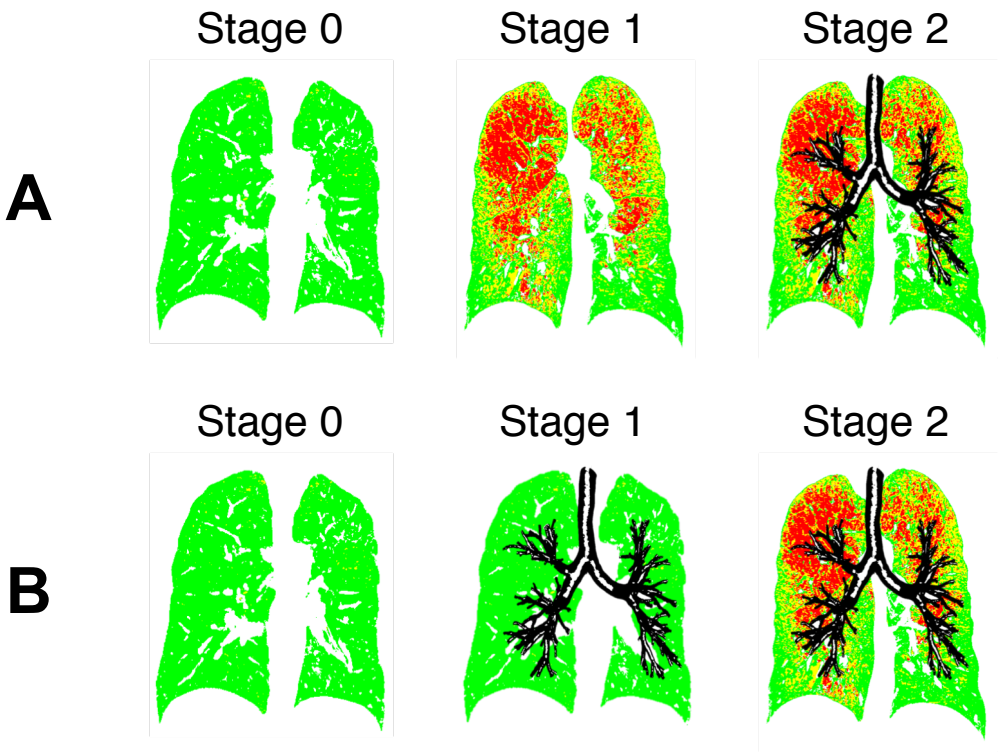

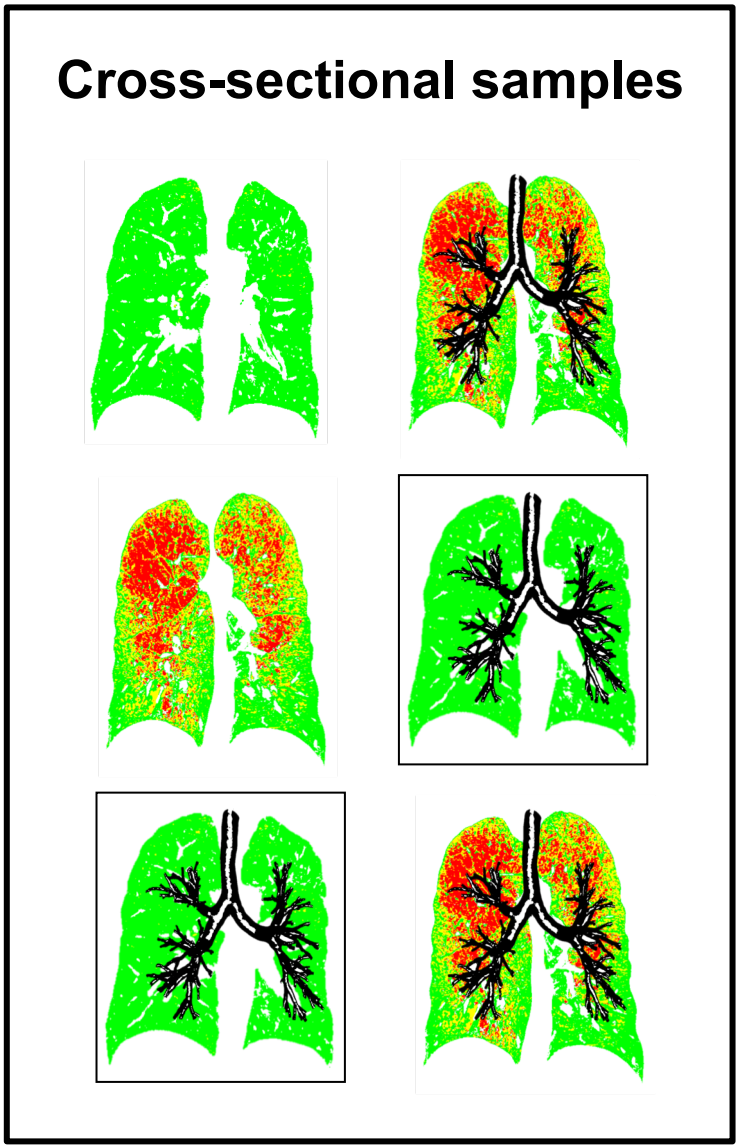

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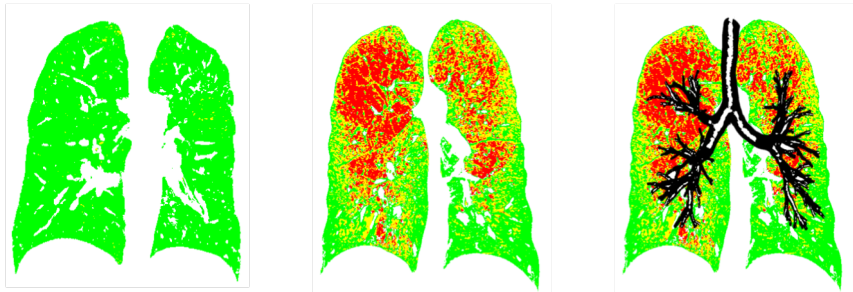

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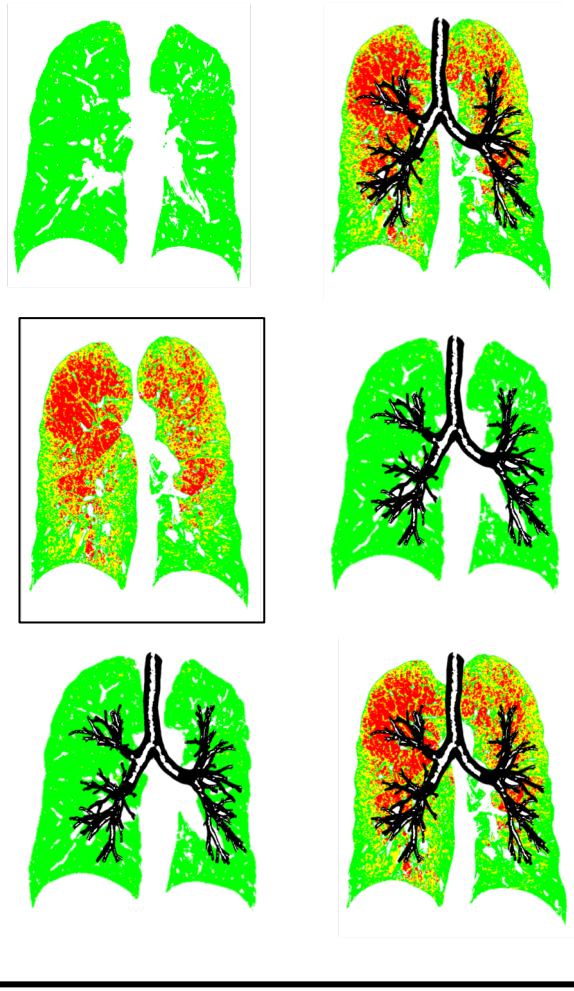

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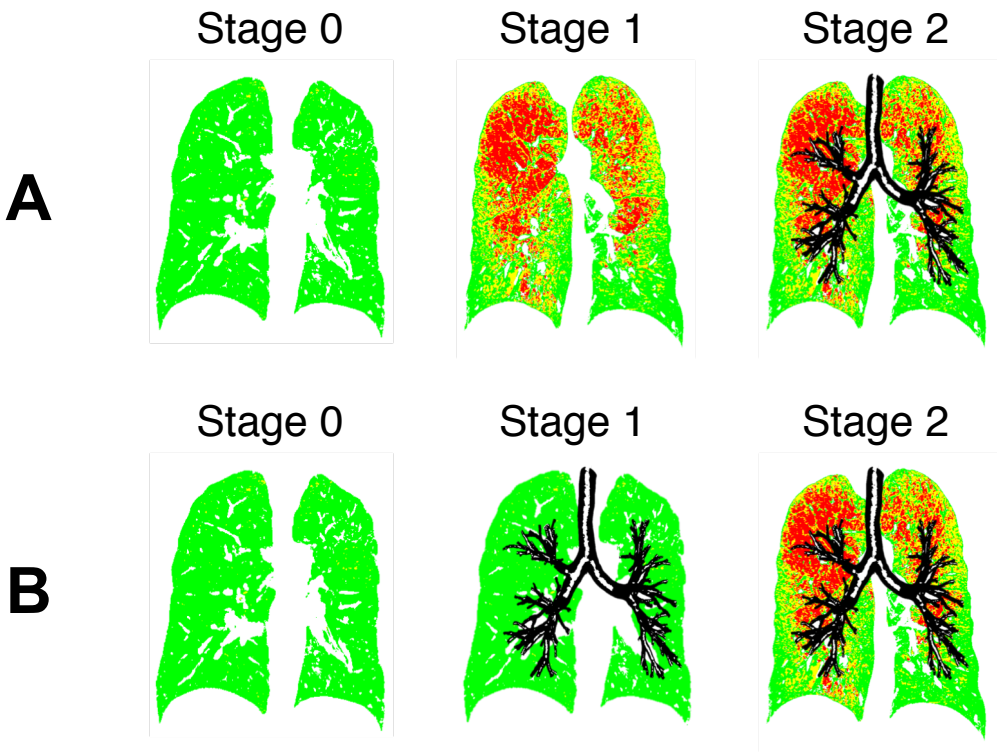
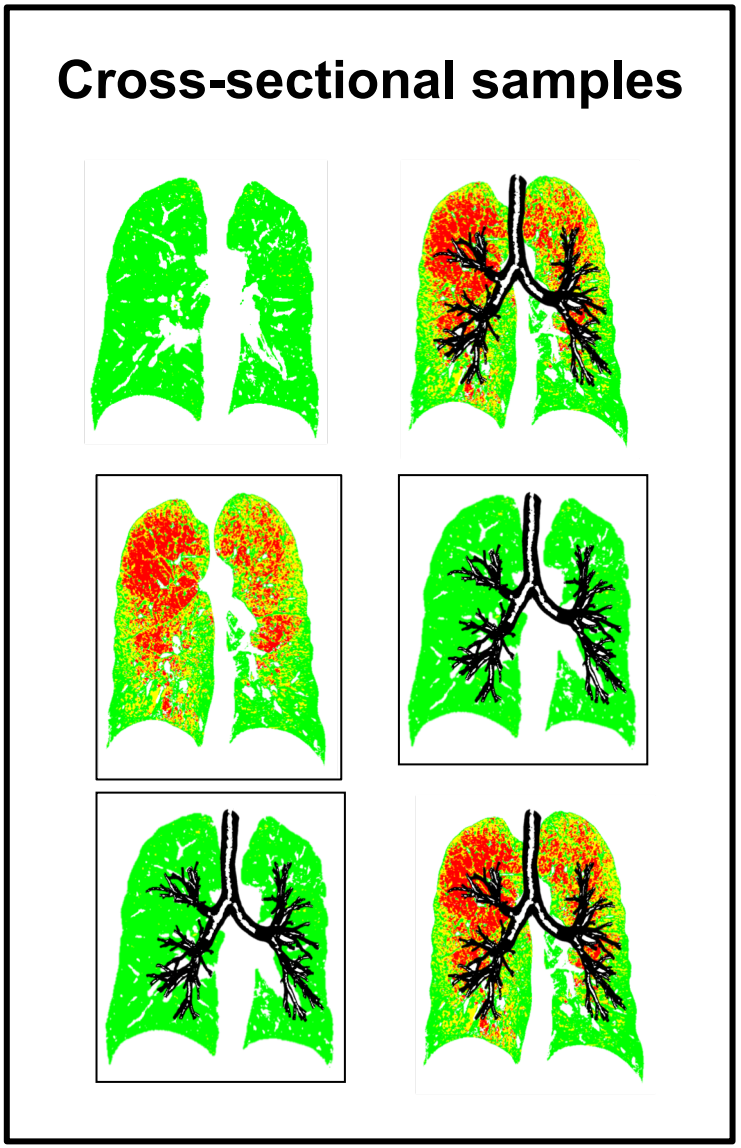
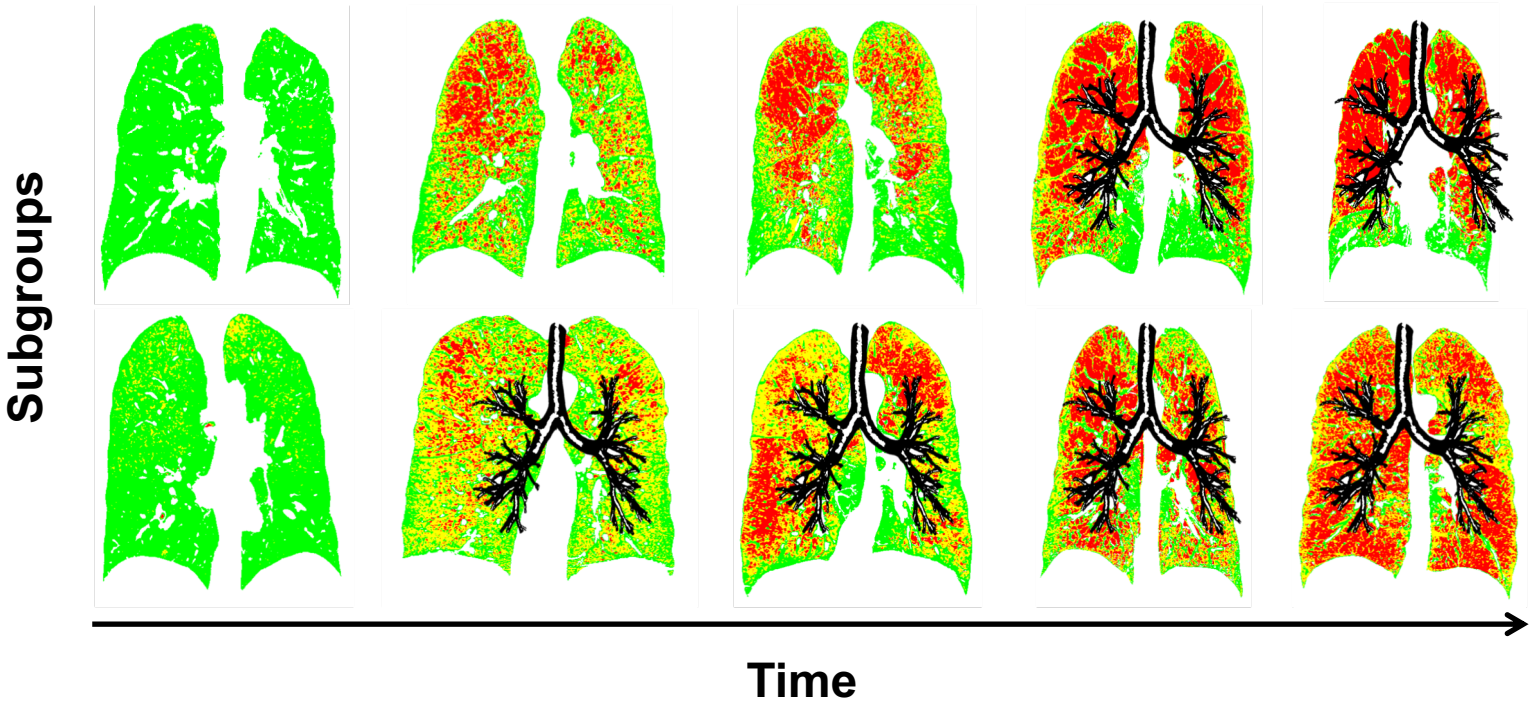


Two subtype progression patterns:
Emphysema precedes airway wall thickening
Airway wall thickening precedes emphysema



SuStaIn formulates this idea mathematically and generalises it to multiple subtypes and biomarkers



- Stages are indexed as a biomarker reaching a new z-score relative to a control population
- SuStaIn estimates the optimal number of subtypes

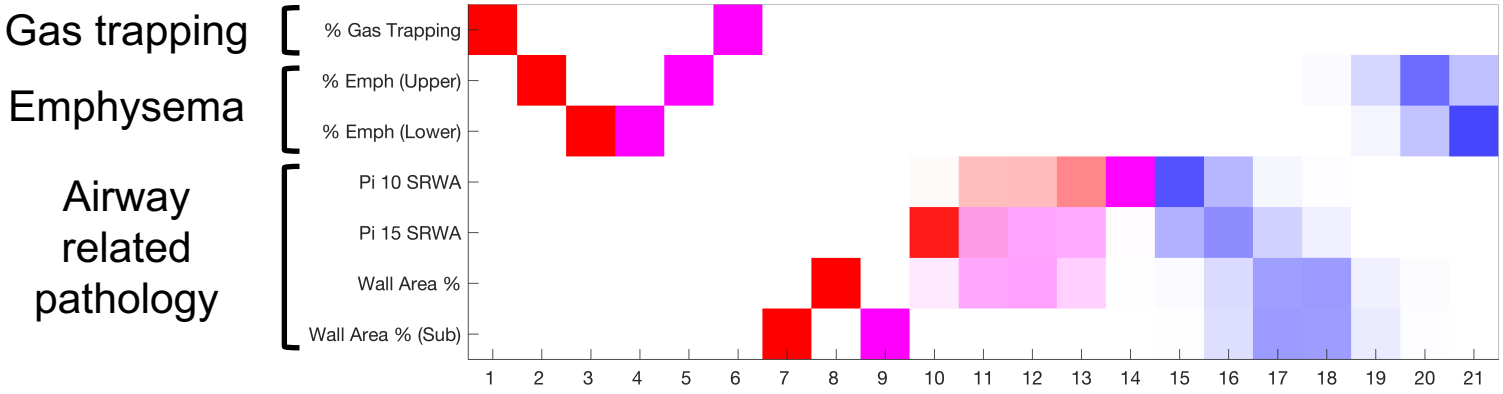
Application of SuStaIn to COPDgene dataset

- Selected a set of 1349 patients (GOLD stage 1-4) with cross-sectional CT imaging measures available
- Seven image based-markers
- Measured relative to a set of 1151 smoking controls

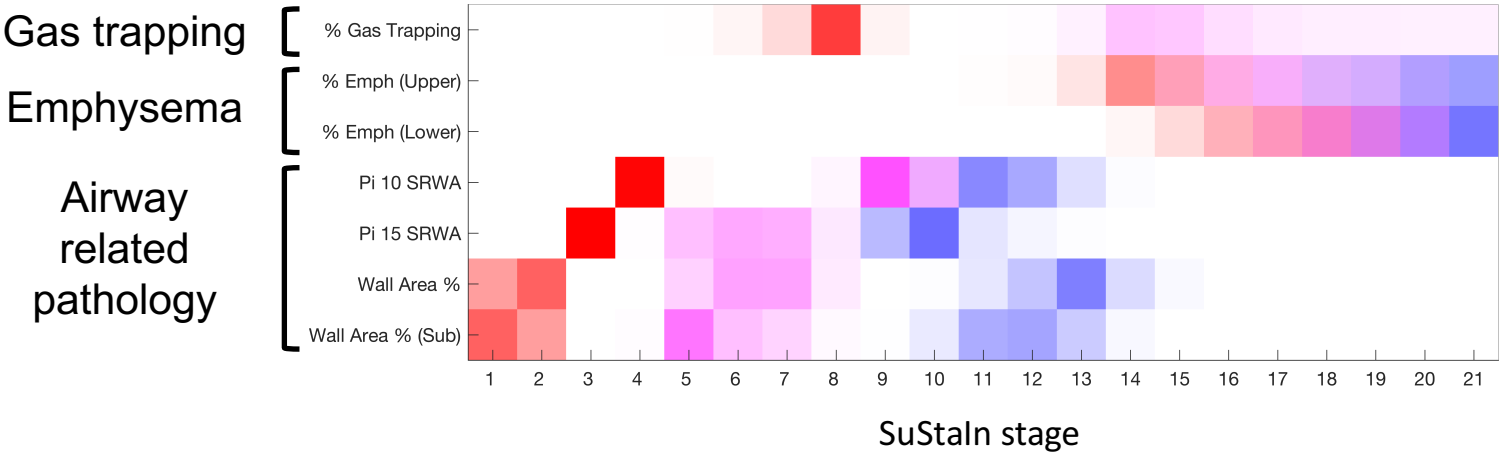
Tissue		Airway
Gas trapping	Emphysema	Airway related pathology
• % Gas trapping	• % Upper lobe emphysema • % Lower lobe emphysema	• Pi10 square root airway wall area • Pi15 square root airway wall area • % Segmental wall area • % Sub-segmental wall area

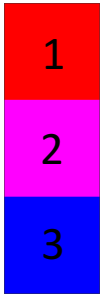
SuStaIn identifies a Tissue-Airway and an Airway-Tissue group

Tissue-Airway 76.3%



Airway-Tissue 23.7%





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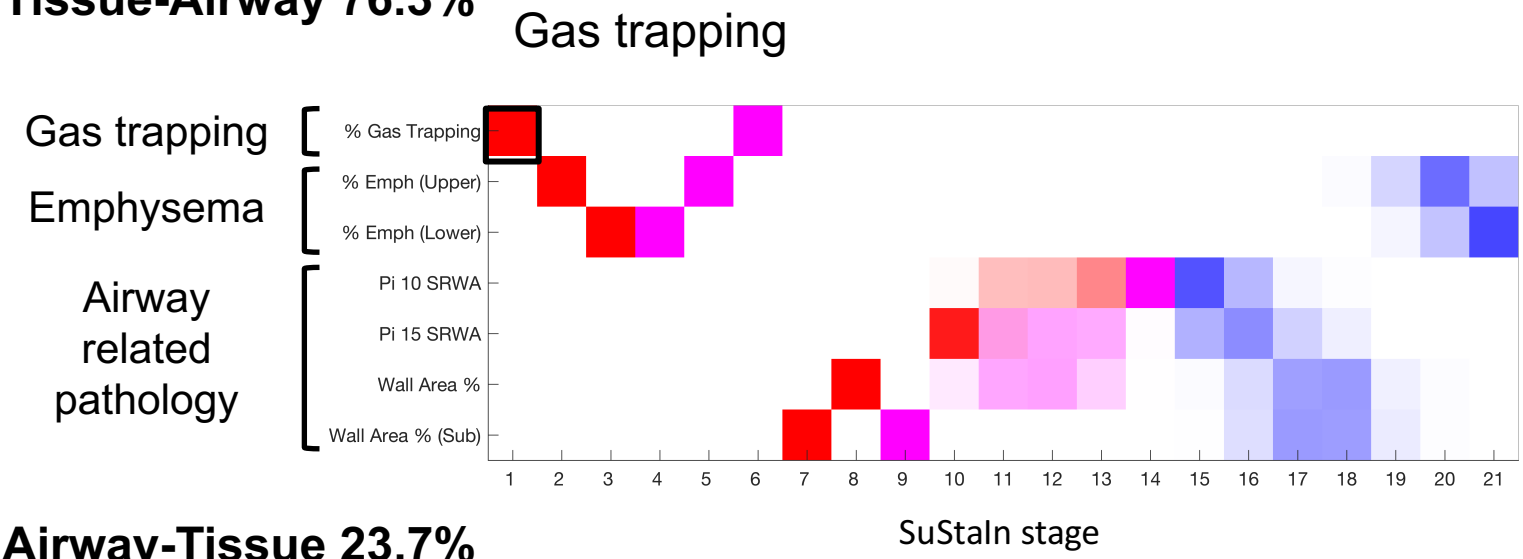

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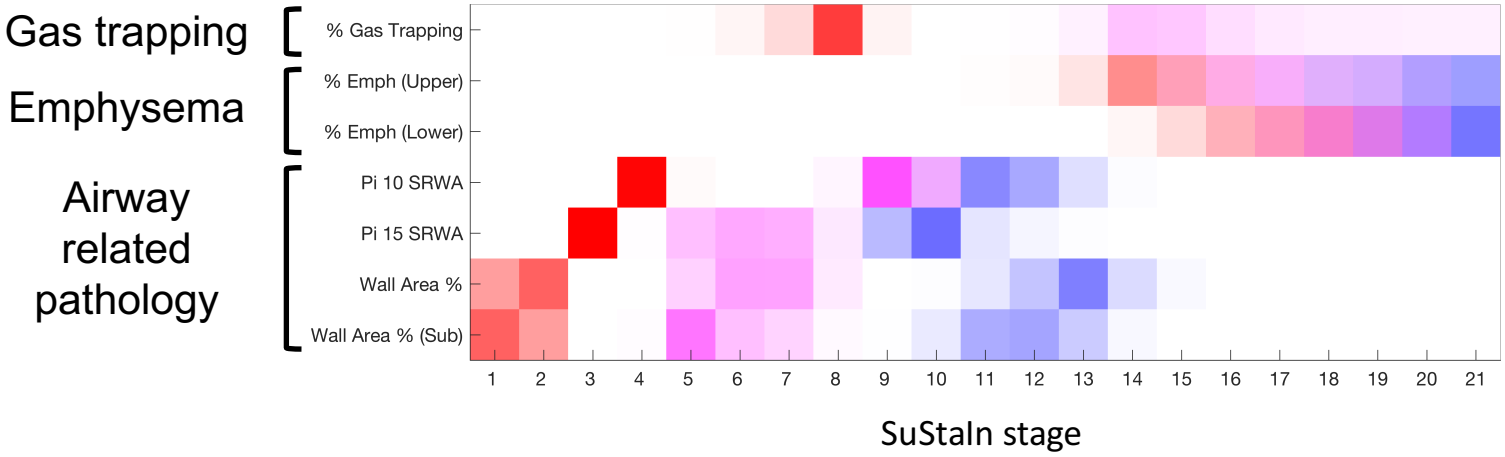

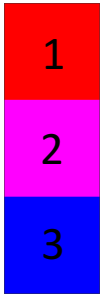

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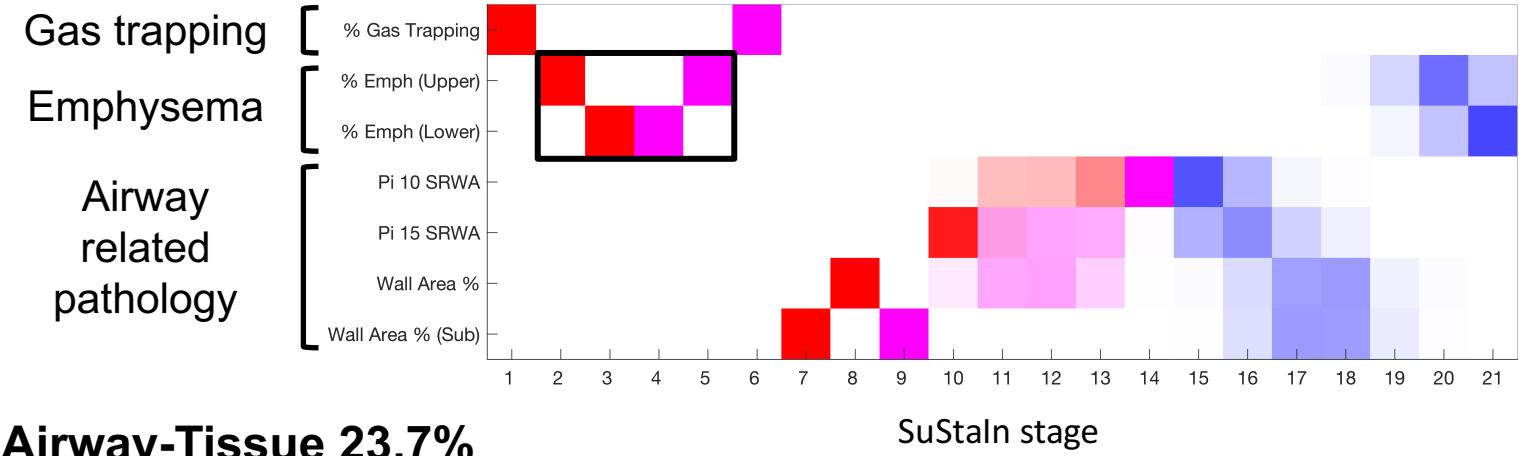
Gas trapping → Emphysema



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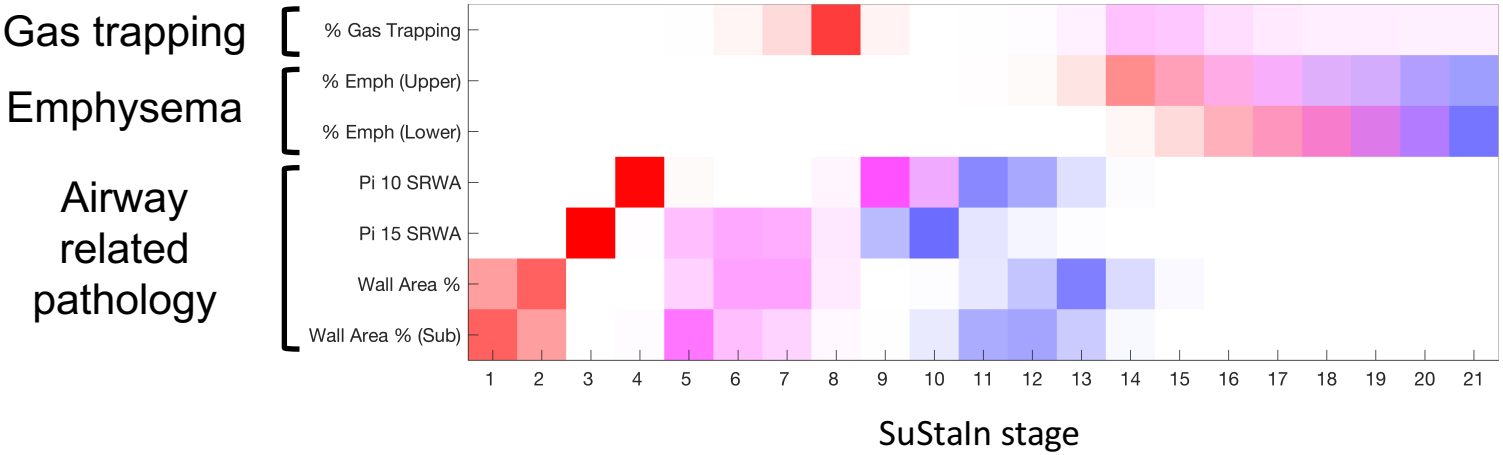

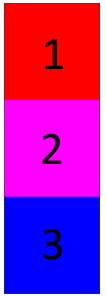

SuStaIn identifies a Tissue-Airway and an Airway-Tissue group

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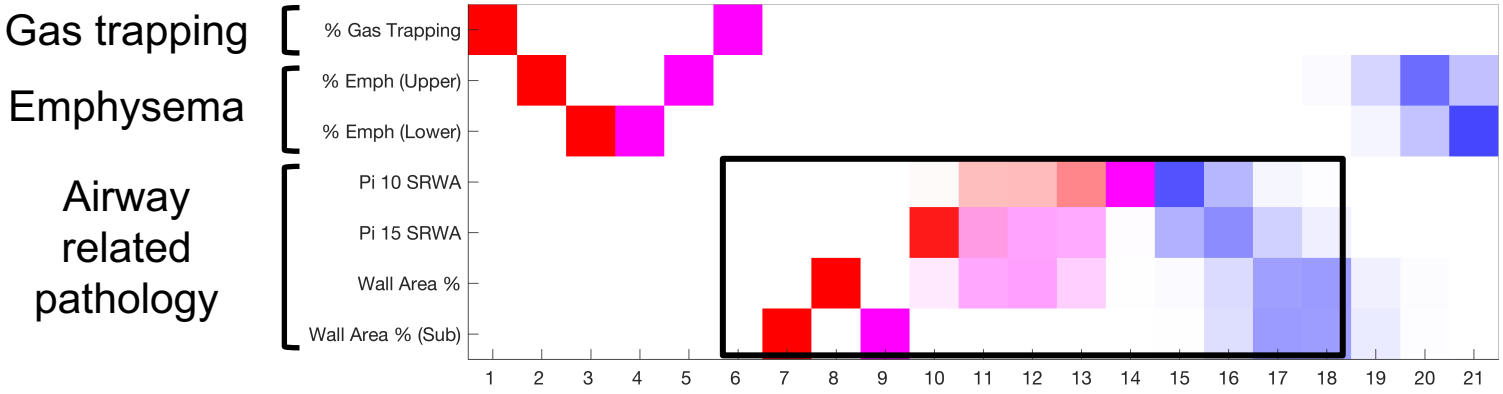
Gas trapping → Emphysema → Airway related pathology



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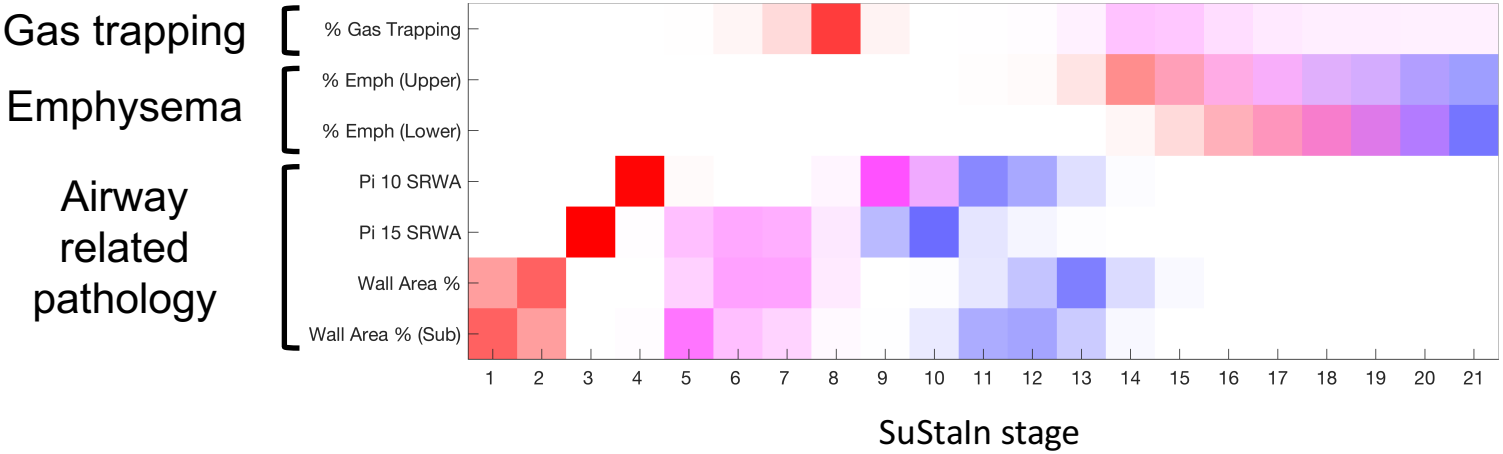

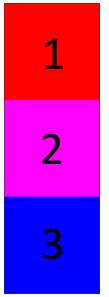

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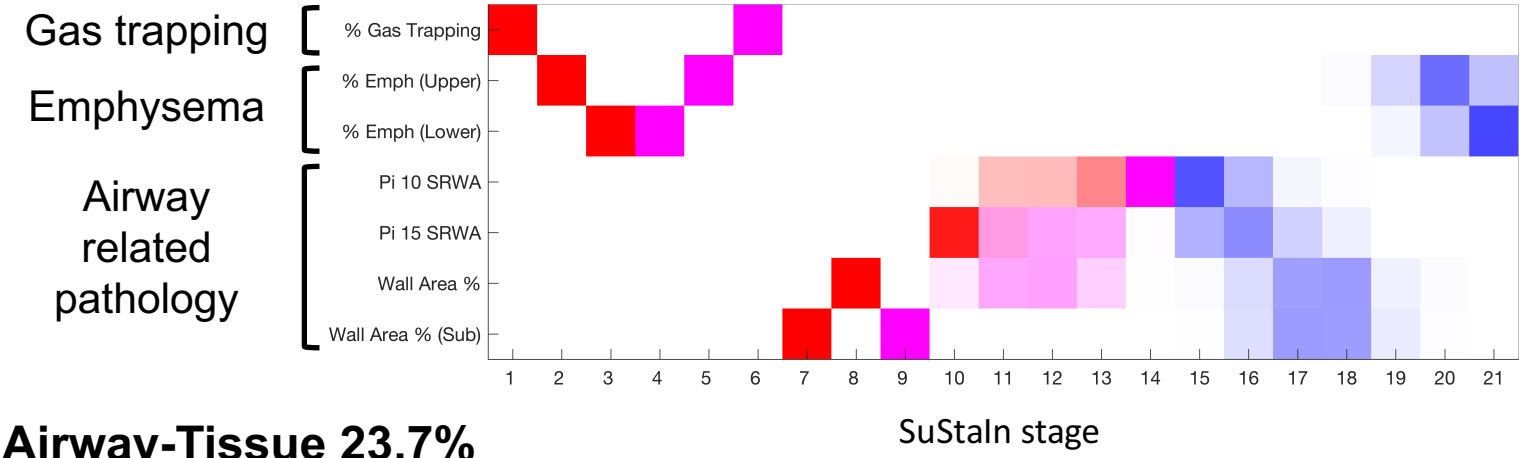
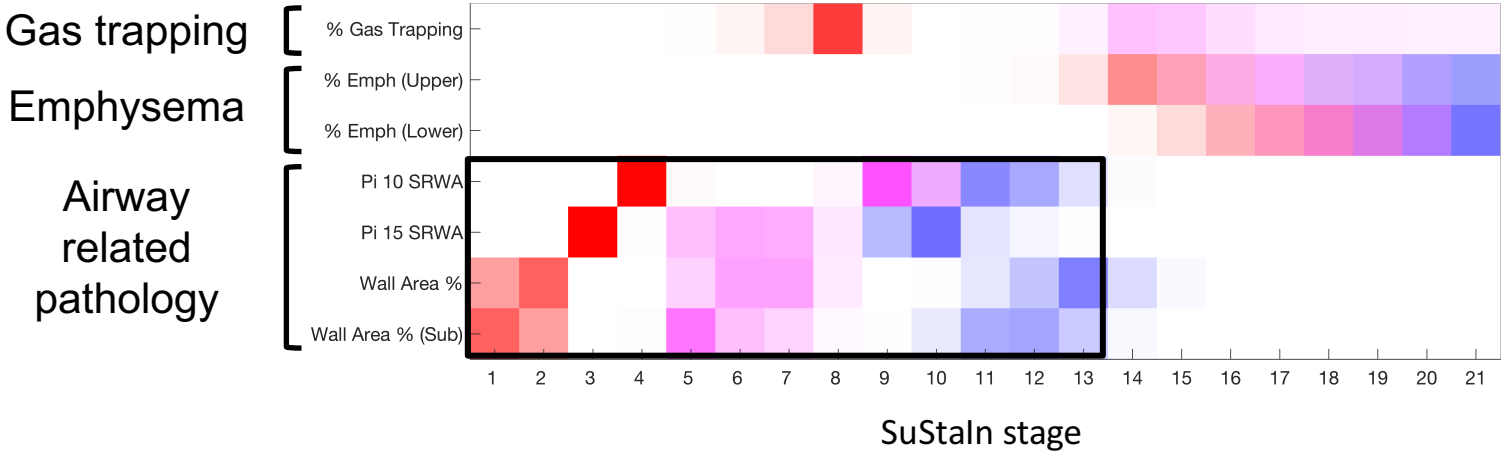
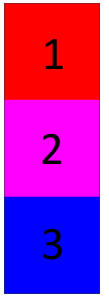


Airway-Tissue 23.7%

Airway related pathology

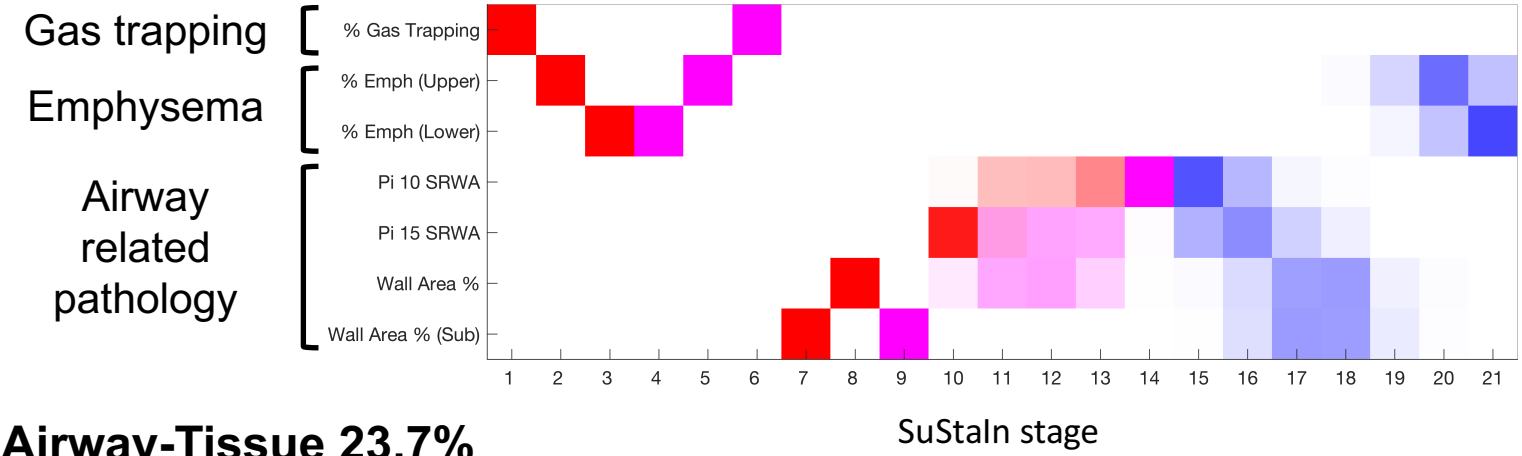




SuStaIn identifies a Tissue-Airway and an Airway-Tissue group

Tissue-Airway 76.3%

Gas trapping → Emphysema → Airway related pathology



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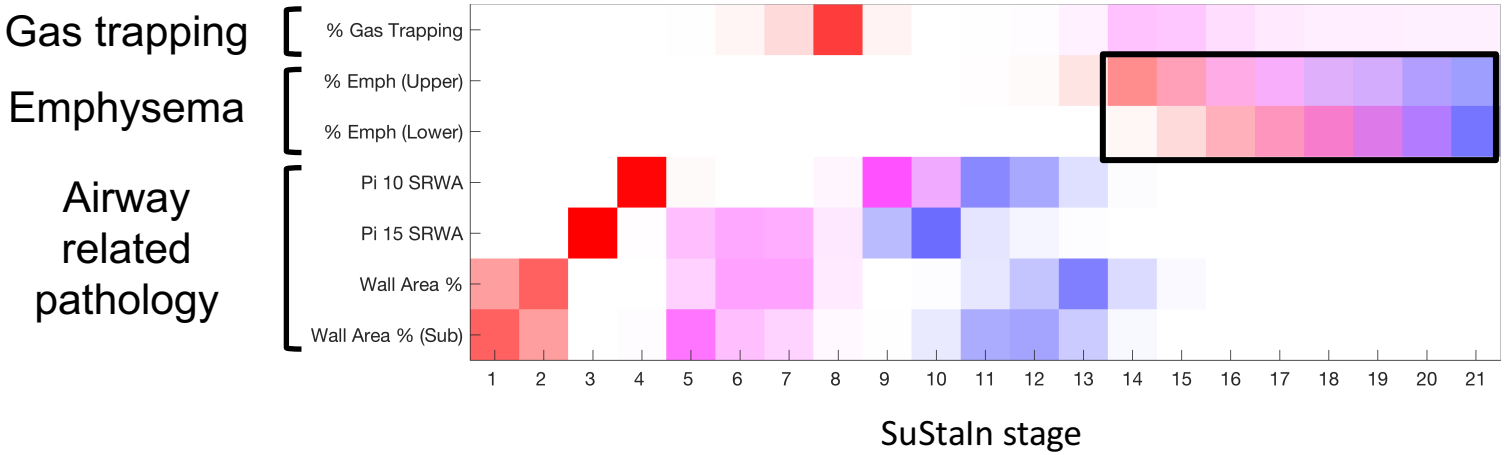
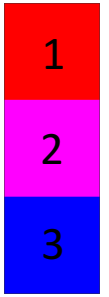
Airway related pathology → Emphysema





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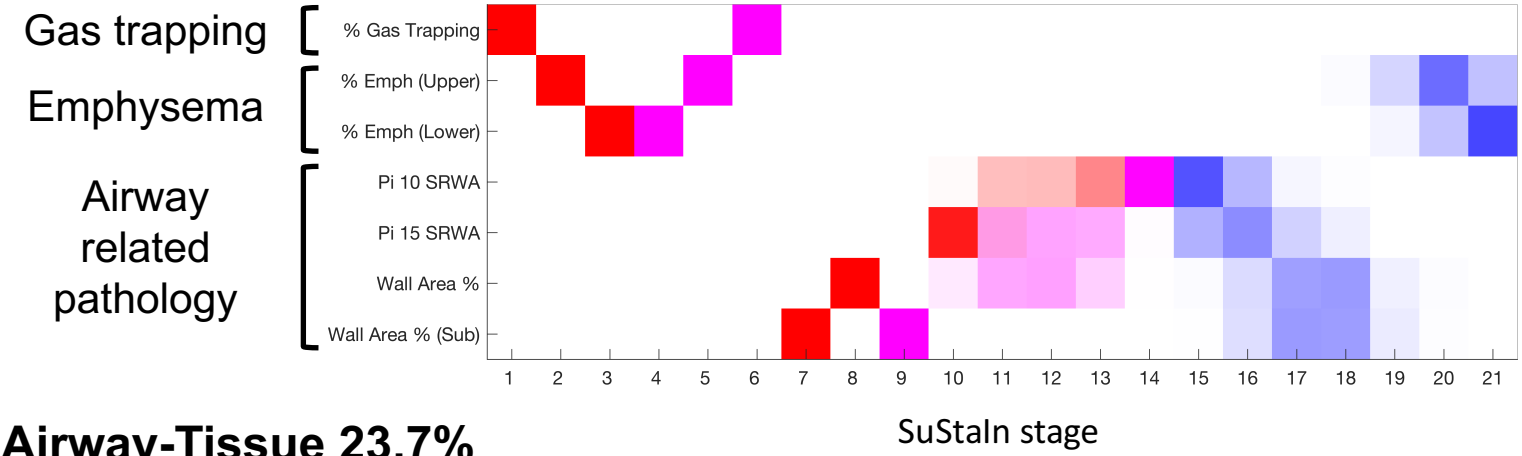
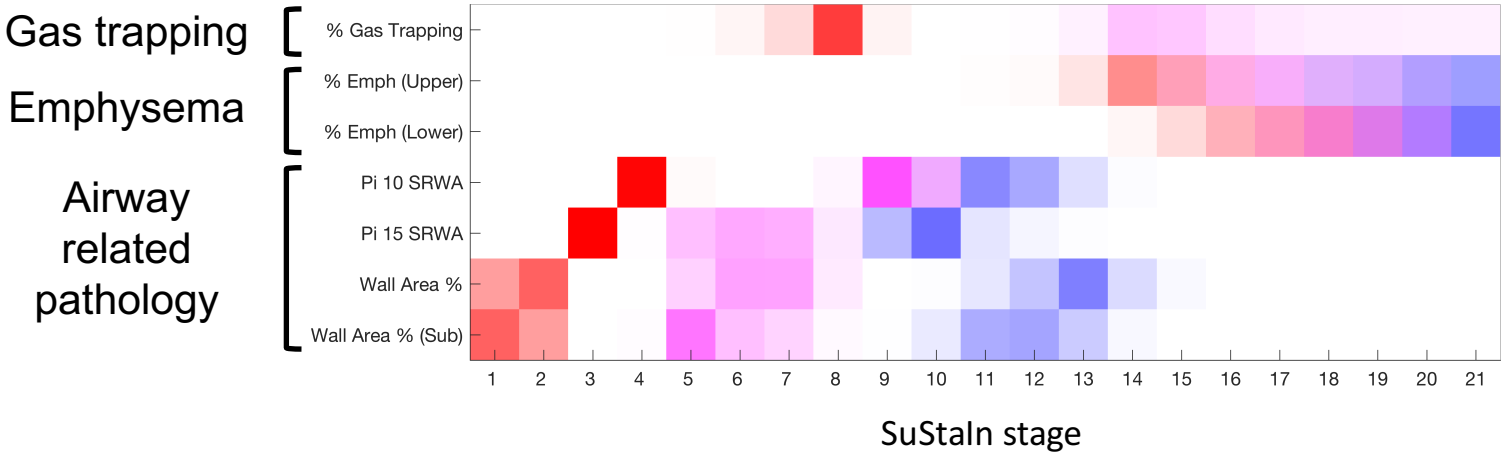
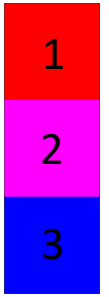


More men
Older
Lower BMI

Airway-Tissue 23.7%

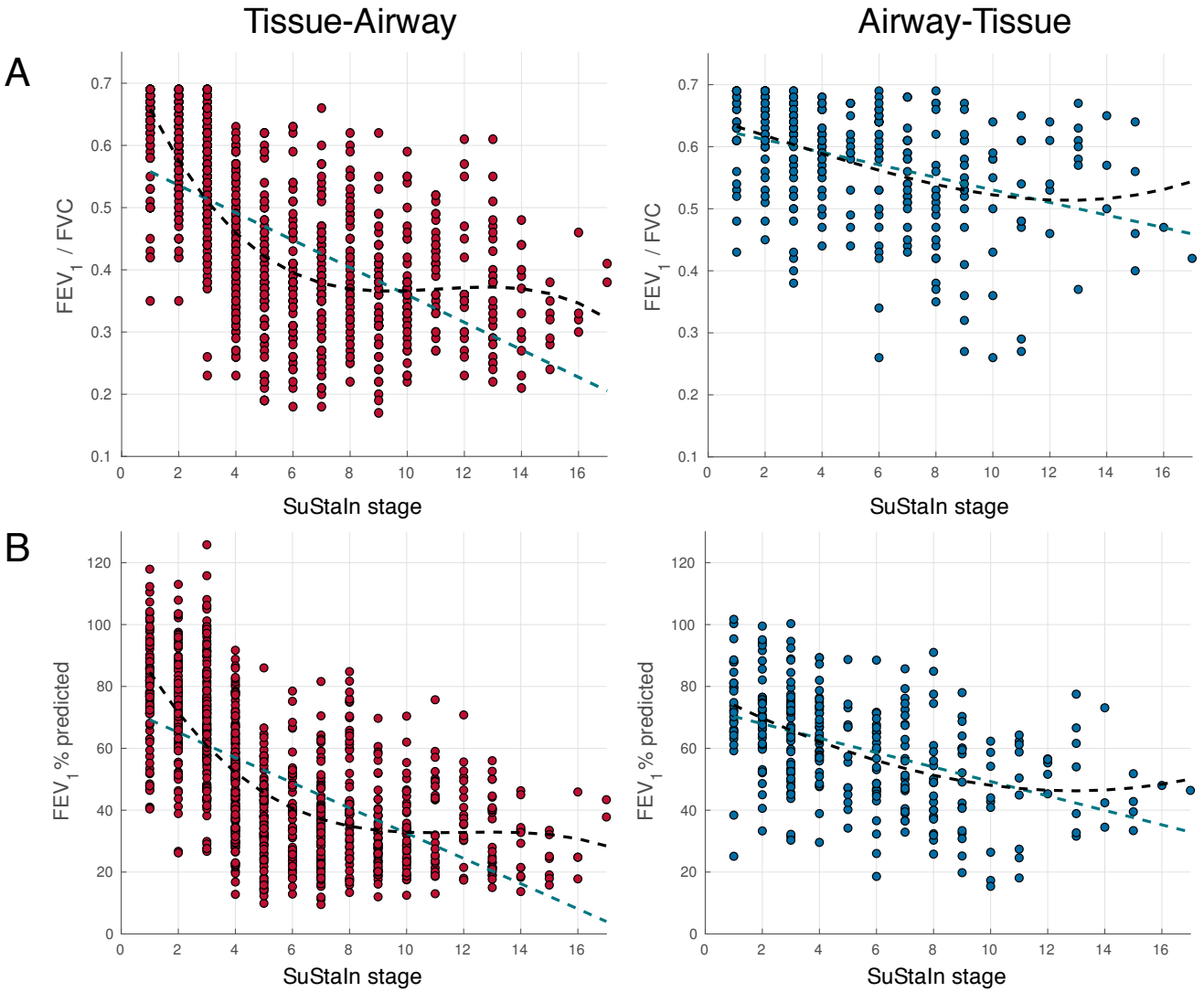
Airway related pathology → Emphysema





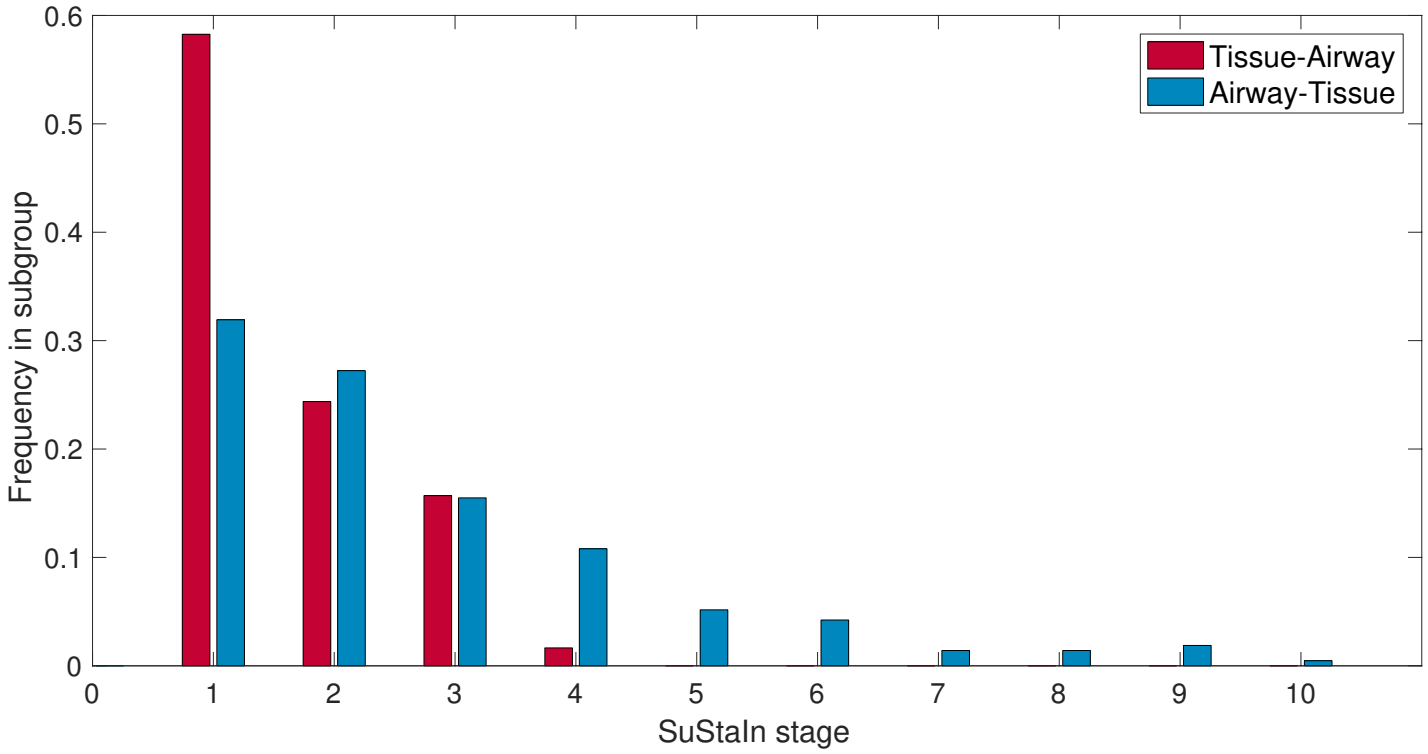
More women
Younger
Higher BMI

Subtypes correlate with decline in lung function



Early stages of COPD may be identifiable in a group of smoking controls

61% Stage 0 (no abnormalities)
39% Stage 1+
11% Stage 3+



Summary

- Identify two COPD subgroups that mirror classical descriptions of COPD phenotypes
- **Tissue-airway**: emphysema and low BMI
- **Airway-tissue**: chronic bronchitis and high BMI

- In each subgroup, SuStaIn stage is significantly correlated with lung function decline

- Early stages may be identifiable in a fraction of smoking controls

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