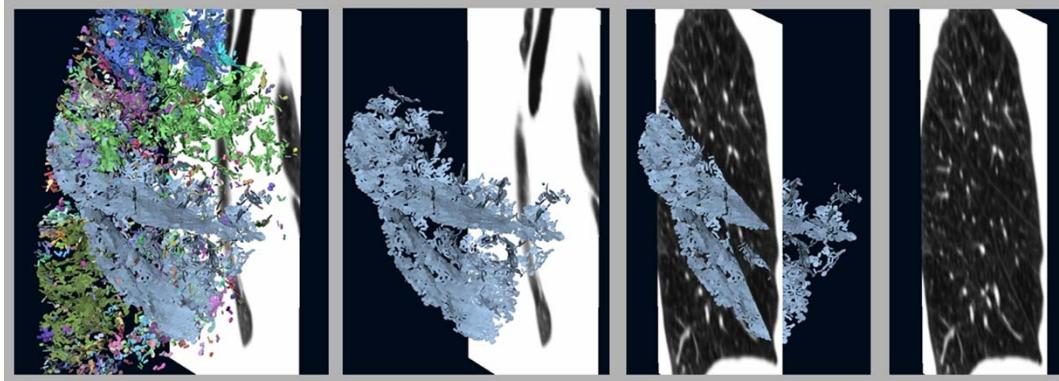


CT Imaging Progress in COPD

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Laboratory of Mathematics in Imaging
Applied Chest Imaging Laboratory

Brigham and Women's Hospital



Status in COPD

Large Multi-Center Cross-Sectional and Longitudinal Studies

COPDGene

Eclipse

Framingham

Emphysema

Airways

Vasculation

Sublet parenchymal changes

Controlling small changes
High Throughput analysis

New targets and opportunities

Controlling variability

Assessing biomarkers

Phantoms

Validation



Toward Methods Qualification

Method Reproducibility

- Remove algorithm biases

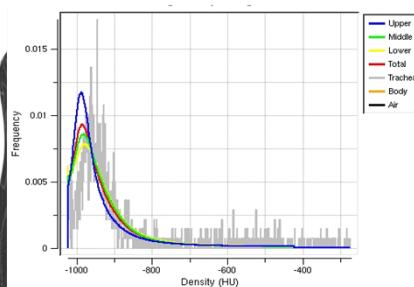
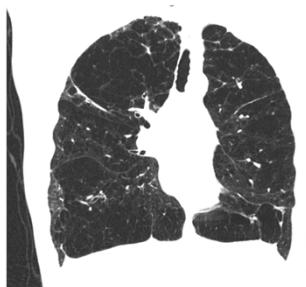
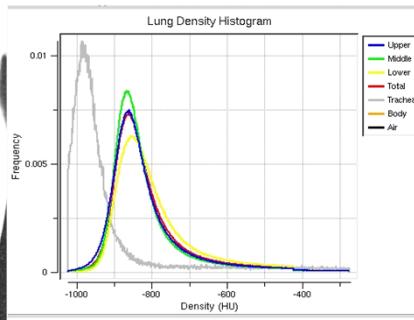
Biomarker Clinical Association

- Increase biomarker/phenotype efficacy in disease description
- Towards therapeutic development

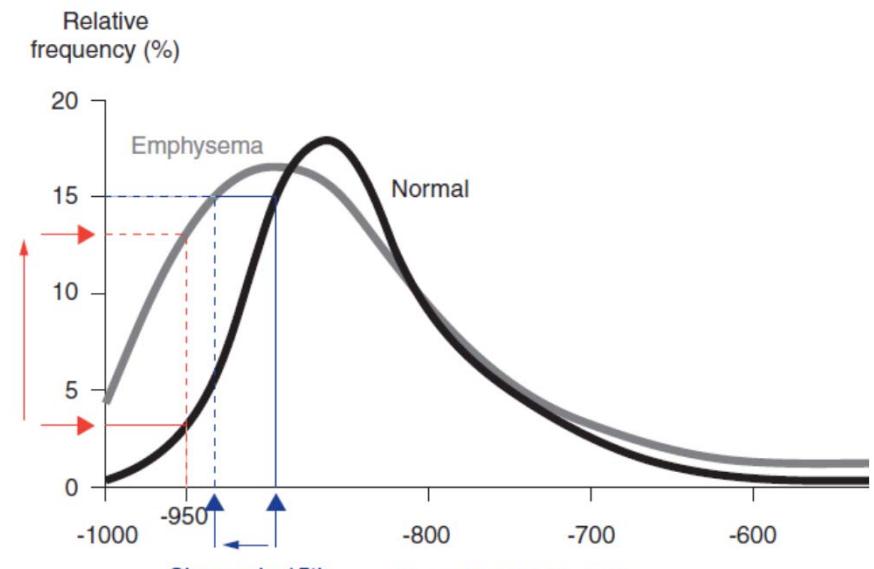


Emphysema based on Global Density

- Low Attenuation Areas % (LAA%)
- Conceptually easier to interpret
- Histopathologic correlates



Change in voxel index (-950HU)
between normal (—) and
emphysematous (- - -) lung



Change in 15th percentile point
between normal (—) and
emphysematous (- - -) lung

Parr, 2010

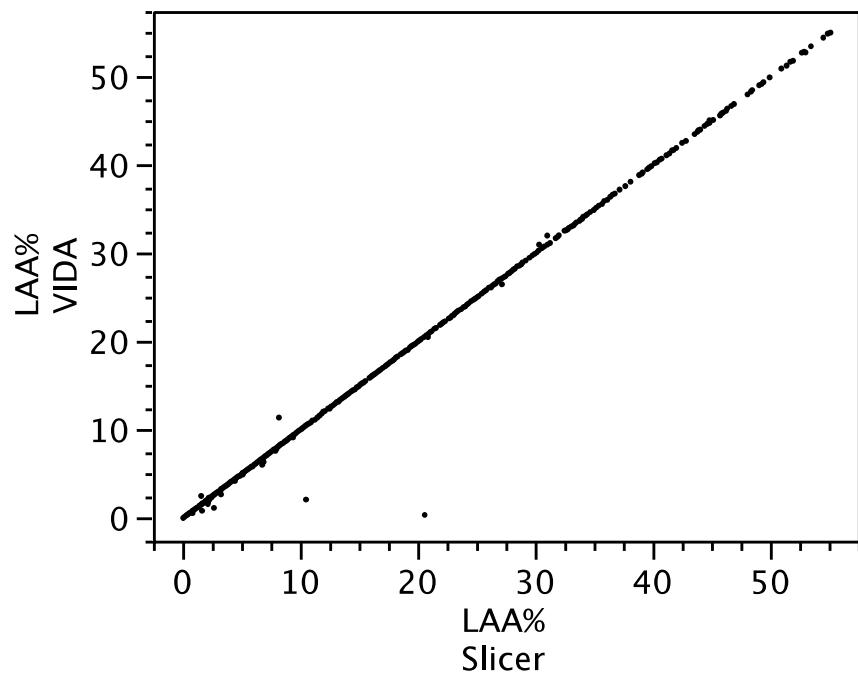
CT Imaging Progress in COPD



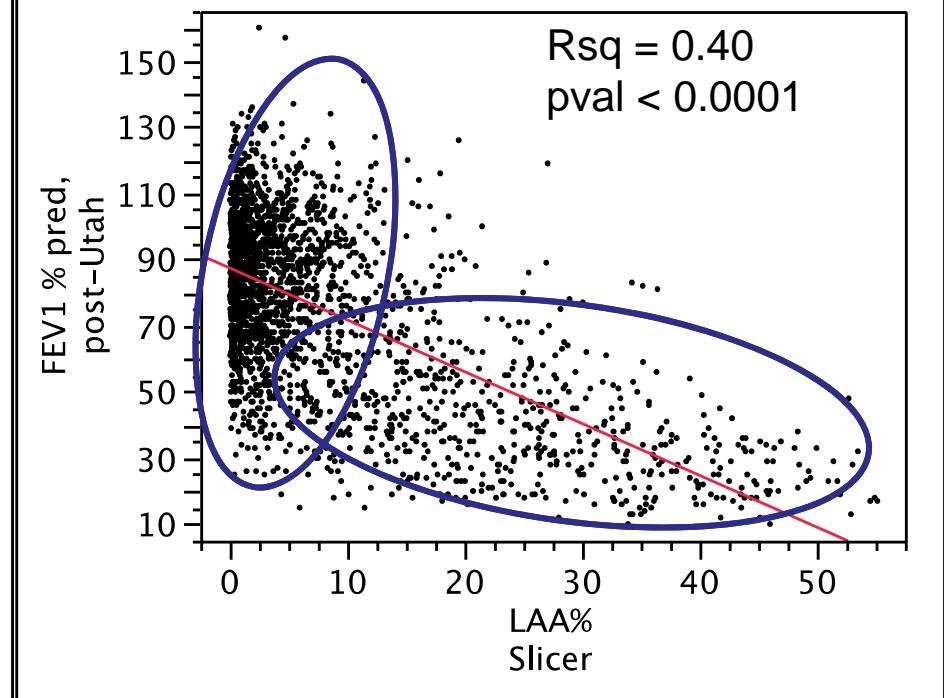
COPDGene: Emphysema Density Analysis

- COPDGene, N=2500

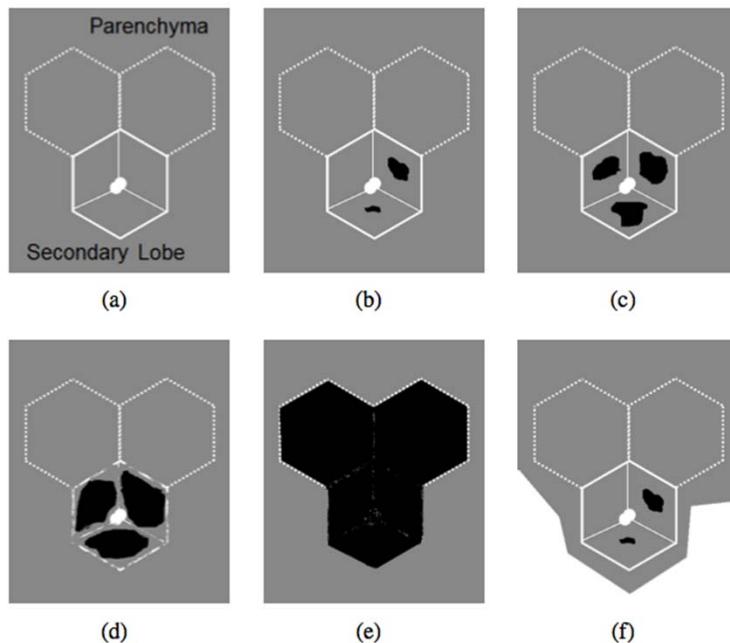
Reproducibility



Clinical Association



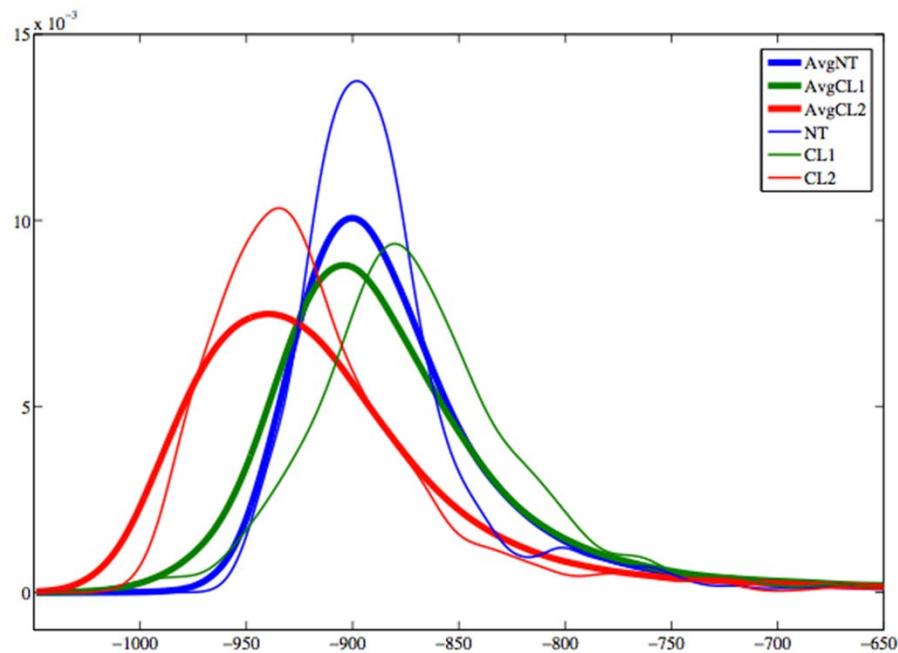
Emphysema Tissue Classification



- Class 1: Normal
- Class 2: Paraseptal
- Class 3: Panlobular
- Class 4: Mild Centrilobular
- Class 5: Moderate Centril.
- Class 6: Severe Centril.

Each Component has a unique local histogram signature

Local Histogram



- Separation between classes based on histogram of local intensities
- kNN classification using L1 norm between the histograms

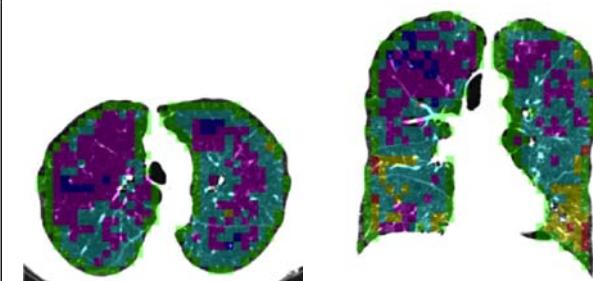
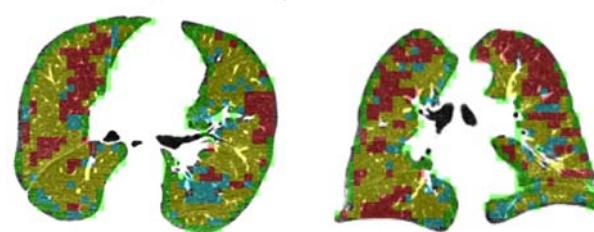
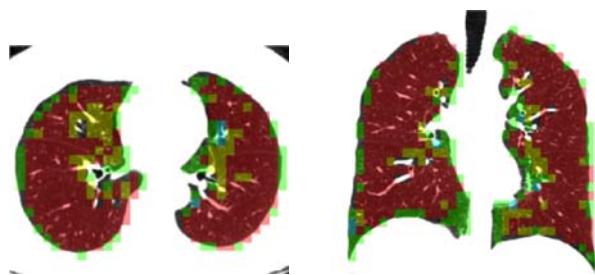
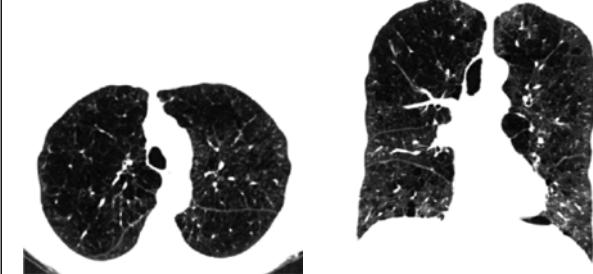
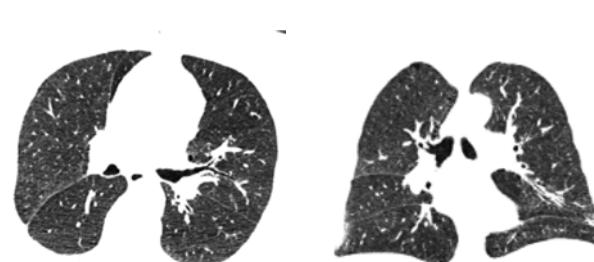
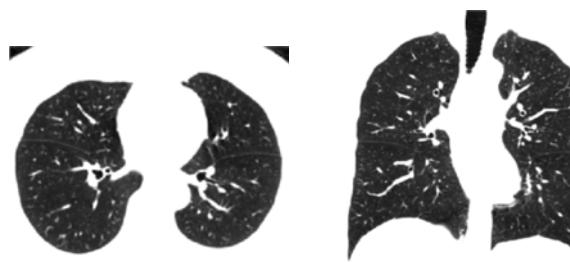


Local Histogram



- █ Normal
- █ Mild CLE
- █ Moderate CLE
- █ Severe CLE
- █ PLE
- █ Paraseptal

Local Histogram

Normal**Moderate****Severe**

■ Normal

■ Mild CLE

■ Moderate CLE

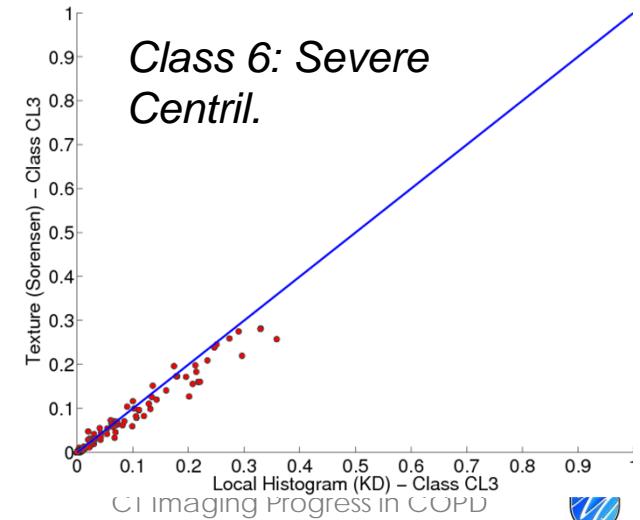
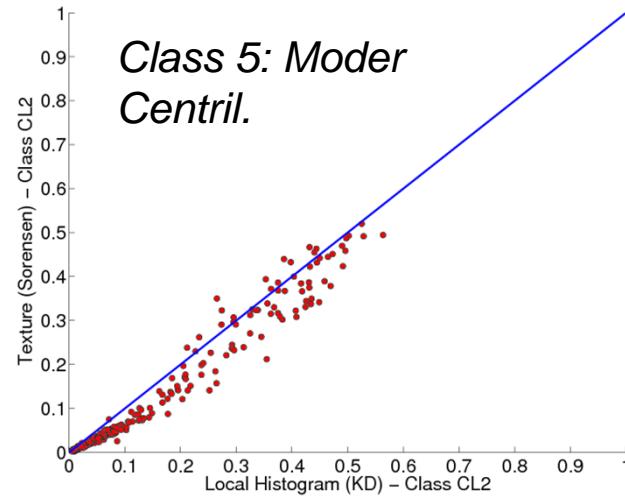
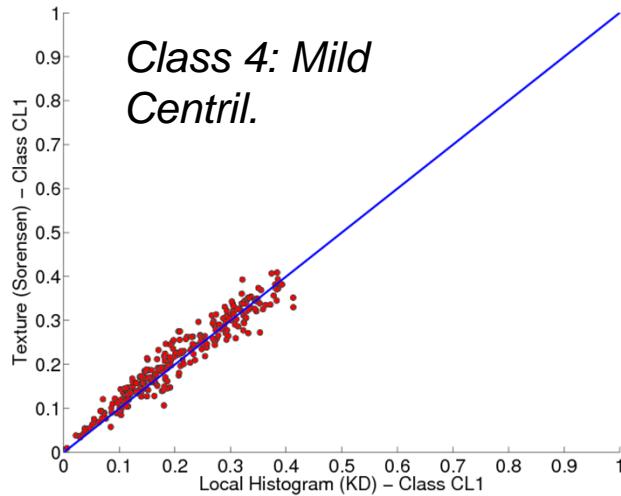
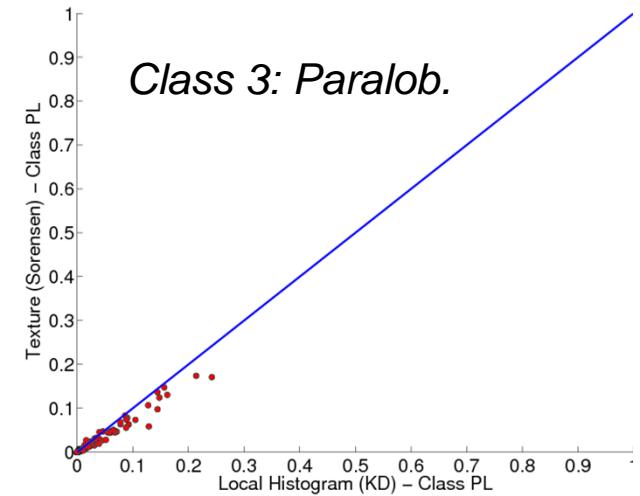
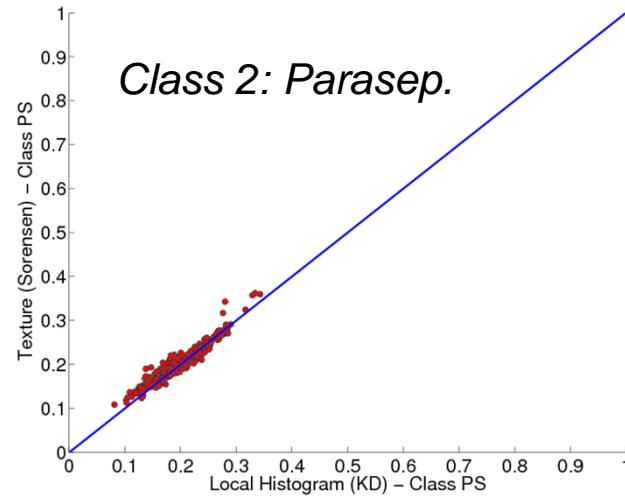
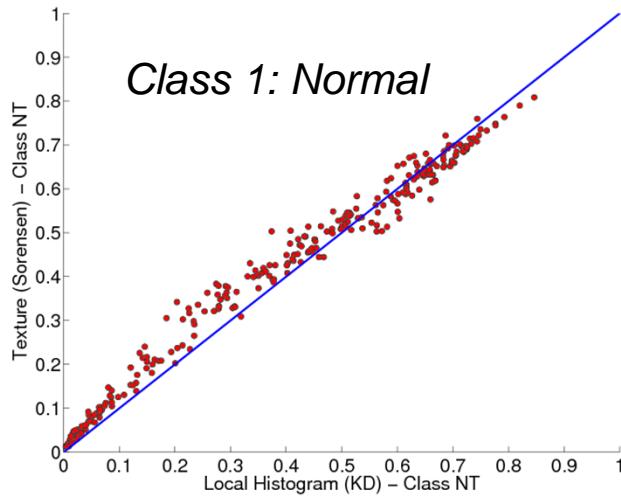
■ Severe CLE

■ PLE

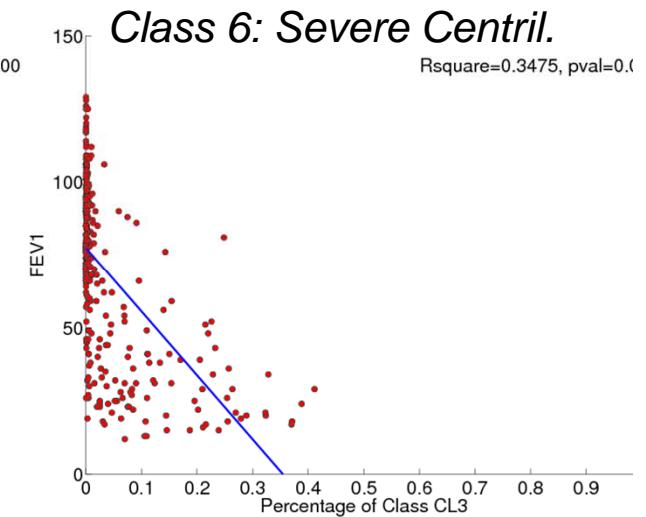
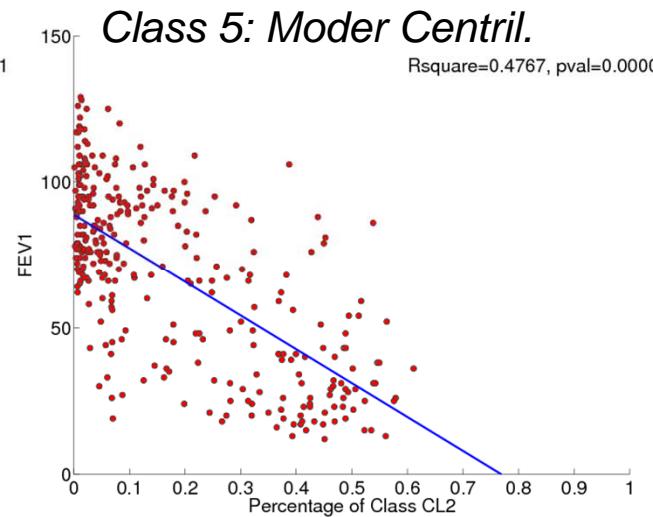
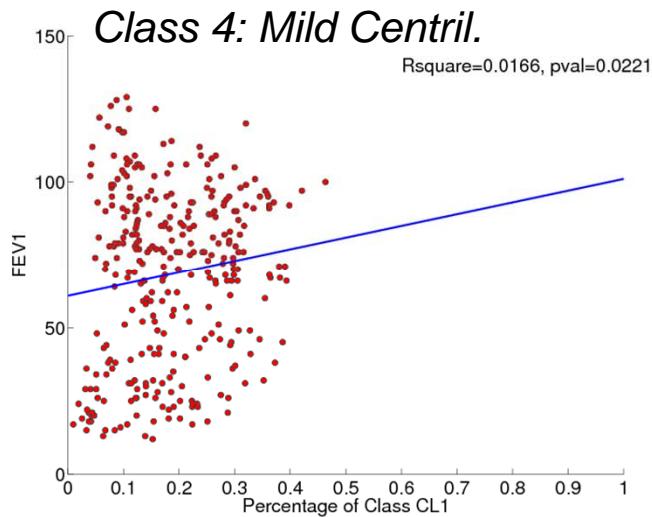
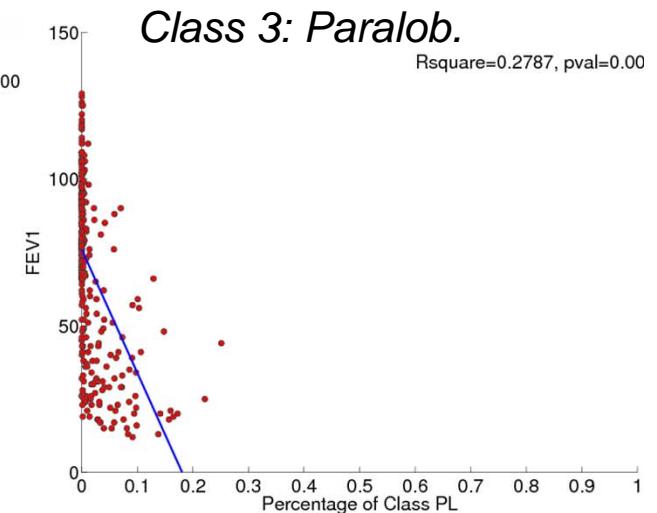
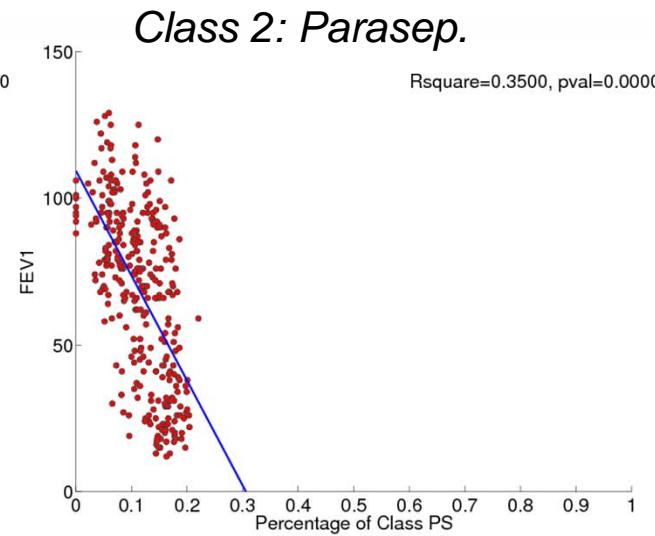
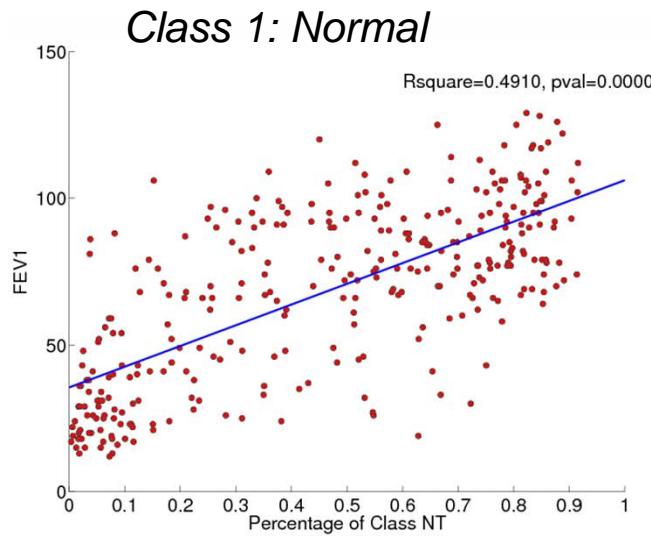
■ Paraseptal



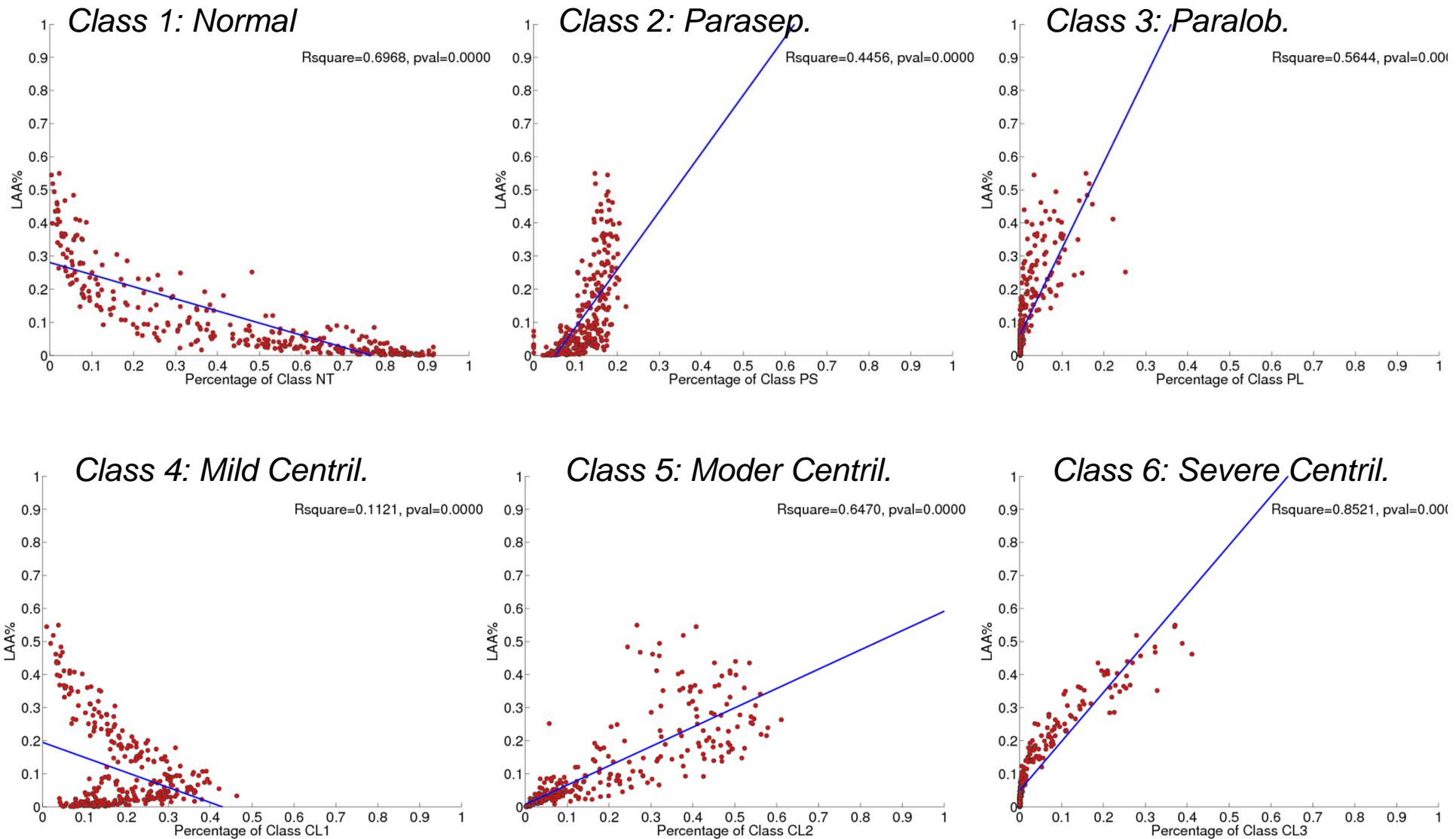
Reproducibility: Local Histogram vs Texture-based approach



Association: Correlation with FEV1



Association: Correlation with LAA%

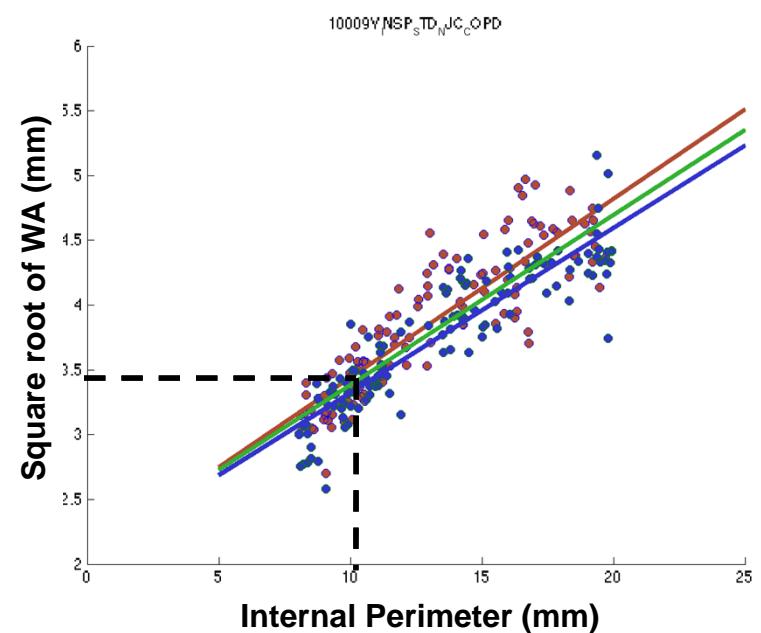
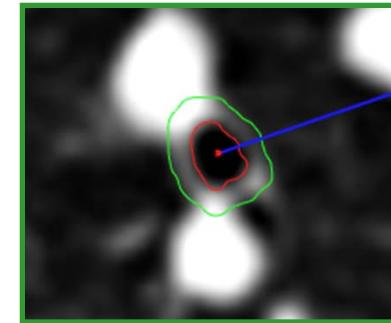


Airway Size

- Airway size phenotypes
 - Wall Thickness
 - Wall Area % (WA%)
 - Pi10: Extrapolated square root of wall area of an ideal airway of 10 mm internal Perimeter.



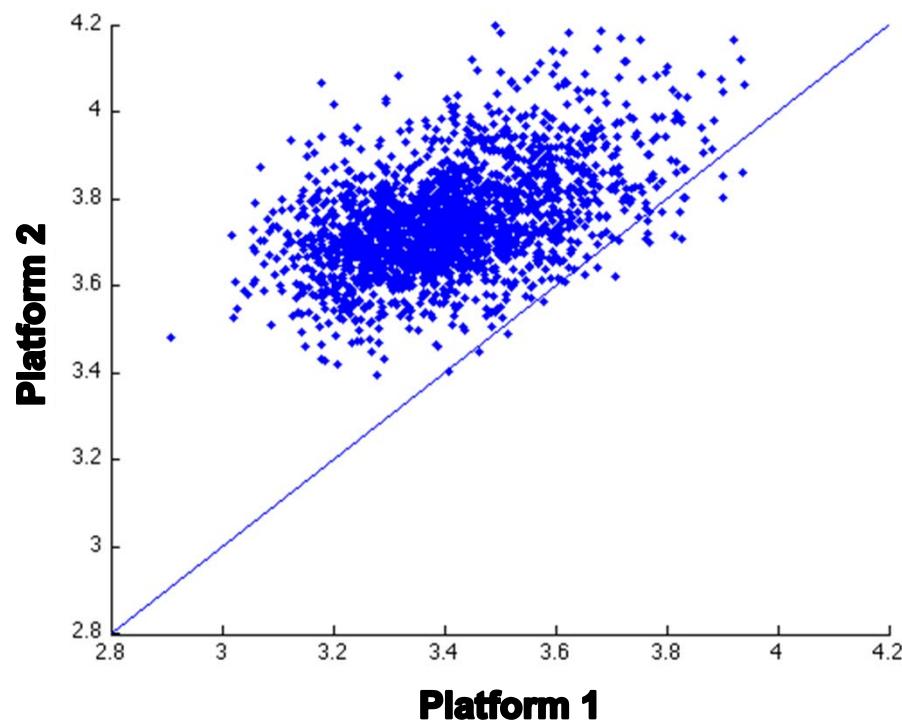
Per segment



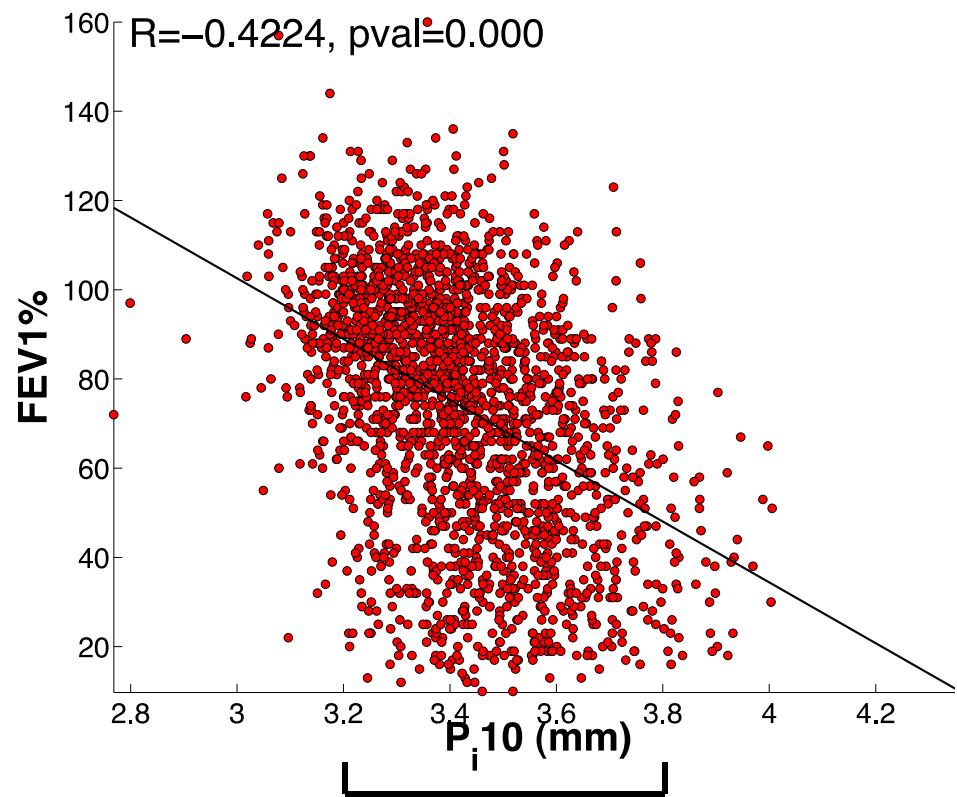
COPDGene: Pi10

- COPDGene, N=2500

Reproducibility



Clinical Association

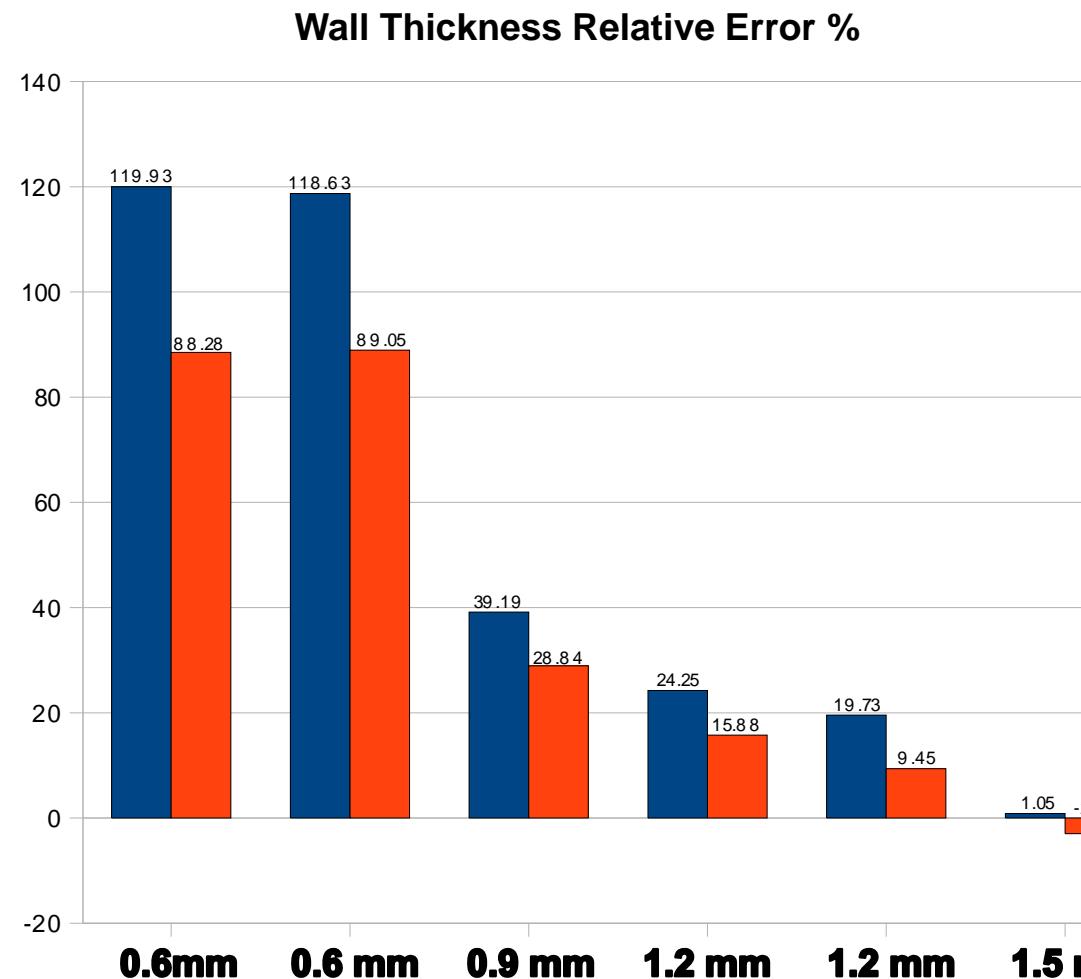


Delta = 0.6 mm

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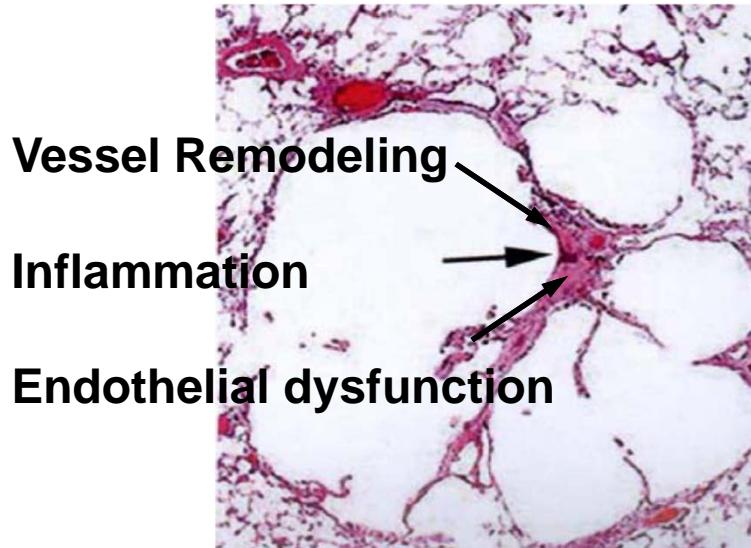


COPDGene Phantom



Pulmonary Vasculature Disease in COPD

- Estimated prevalence of PVD: 26–90%^{1,2}
- Presence associated with
 - Increased health care utilization³
 - Increased mortality⁴
- Pathologic changes seen even in smokers with normal lung function



1. NEJM 1972; 286: 912-8
2. AJRCCM 2002; 166: 314-22
3. AJRCCM 1999; 159: 158-64
4. Am Rev Resp Dis 1979; 119: 895-902



PVD Radiographic Manifestation

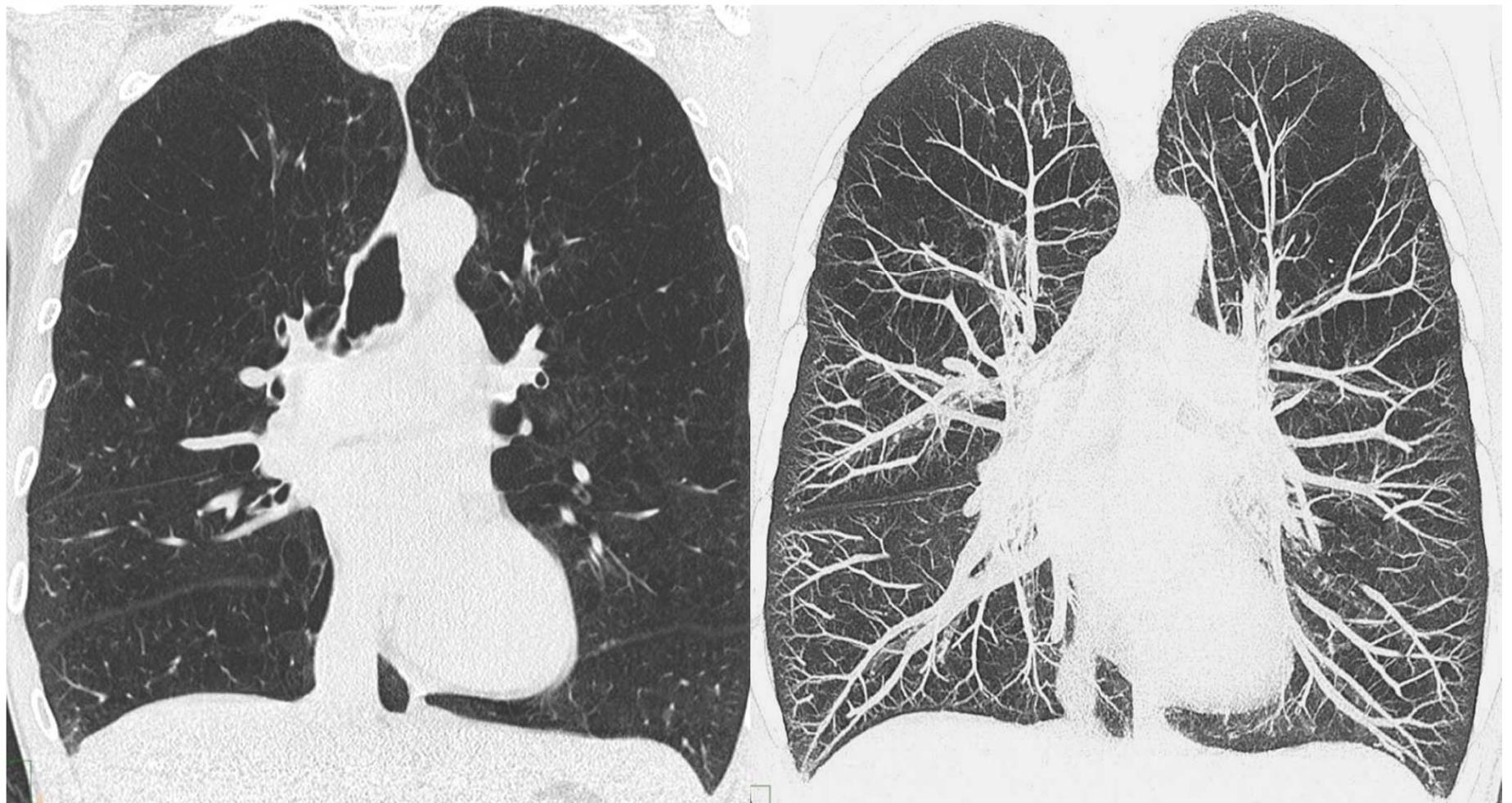


Slide provided by Philippe Grenier

CT Imaging Progress in COPD



PVD Radiographic Manifestation



Slide provided by Philippe Grenier

CT Imaging Progress in COPD



CT Quantification of PVD

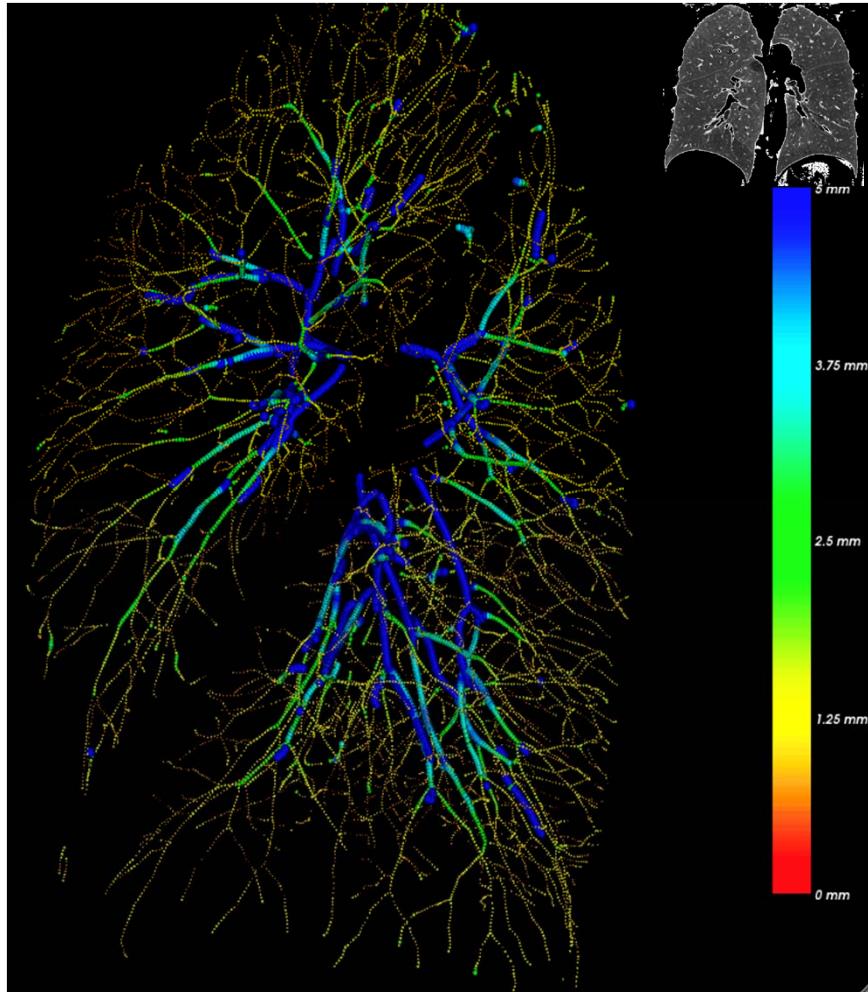


Smoker moderate disease

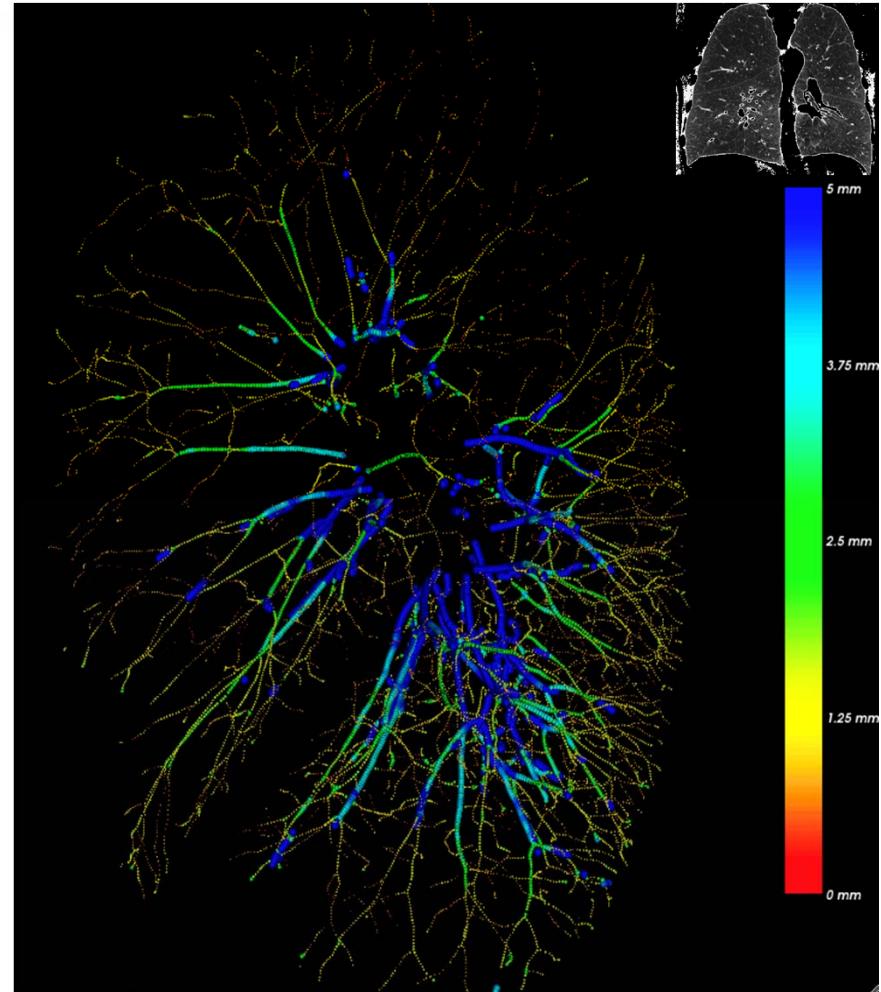
Smoker severe disease



CT Quantification of PVD



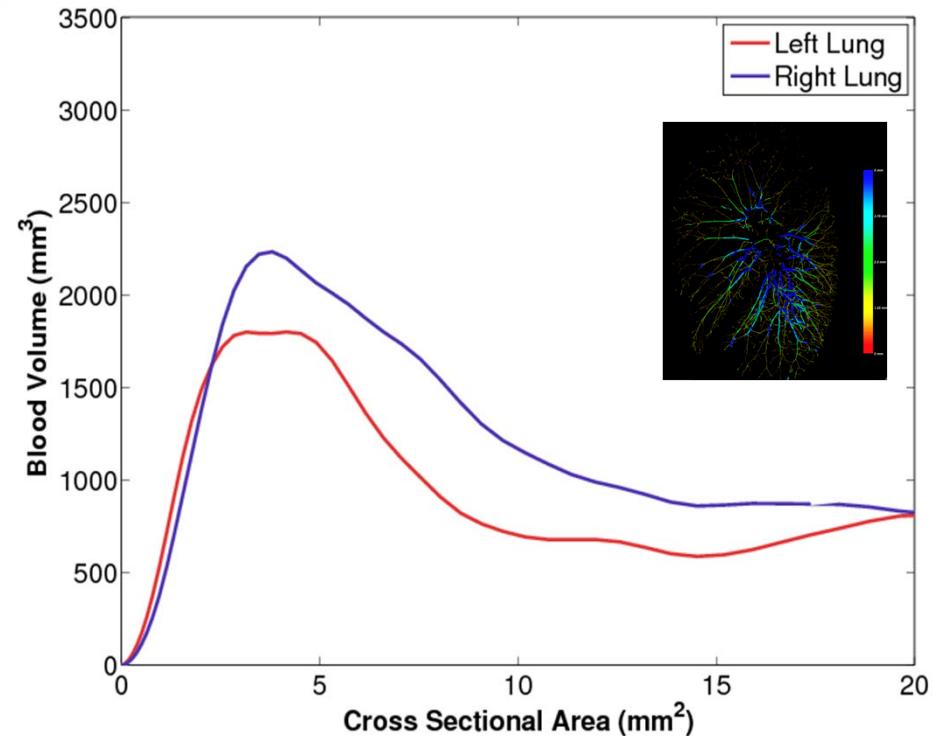
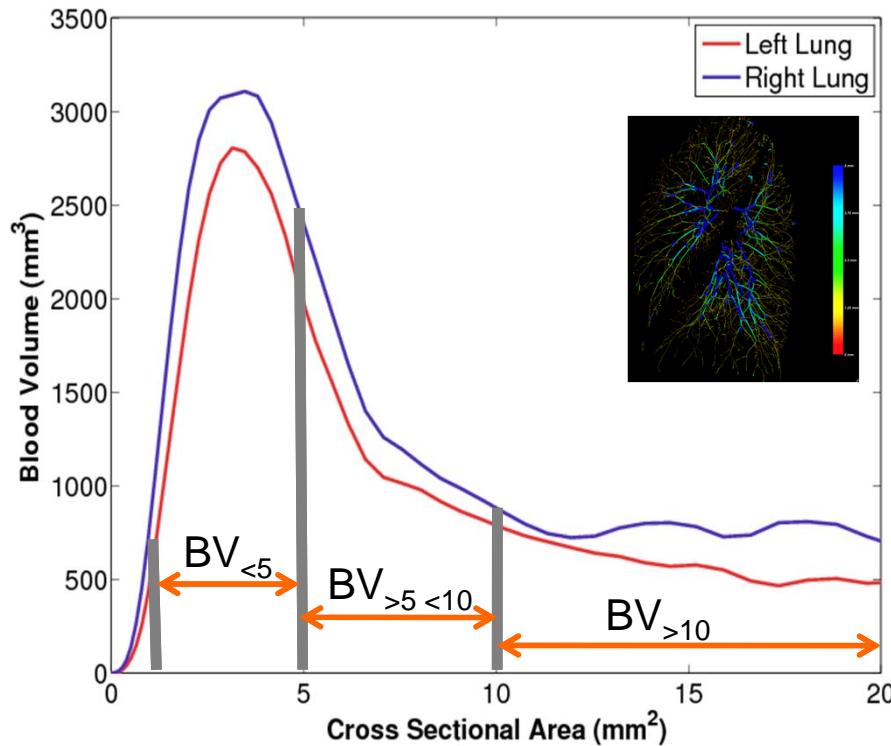
Smoker moderate disease



Smoker severe disease



PVD Phenotypes



- PVD phenotypes: Blood volume ratios
 - $\text{BV}_{<5} / \text{TBV}$
 - $\text{BV}_{>5 <10} / \text{TBV}$
 - $\text{BV}_{>10} / \text{TBV}$



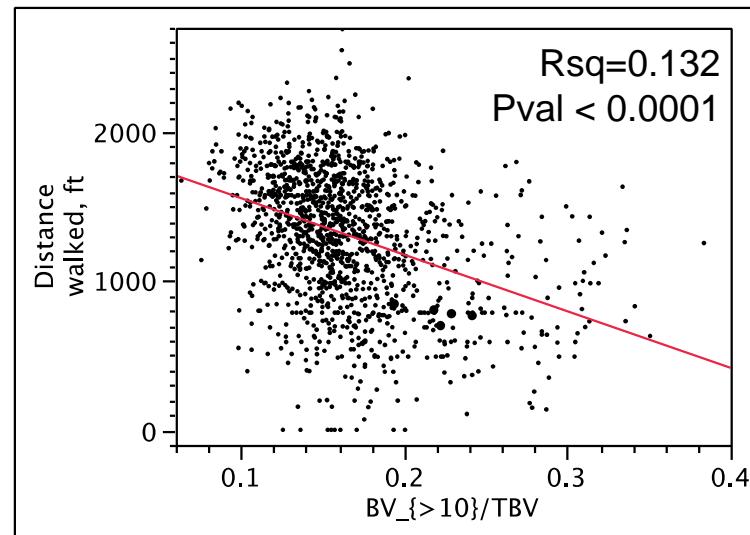
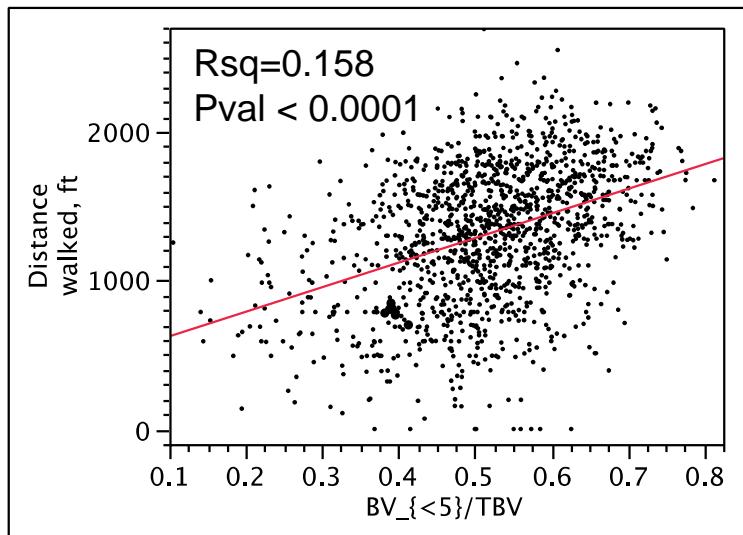
Preliminary Results

- COPDGene Subjects: N=1380
 - Homogenous distribution across GOLD stage
- Multivariate model to predict 6 Minute Walk Test
- Multivariate model to predict BODE
 - Multidimensional predictor of mortality in COPD



Preliminary Results

- Multivariate model to predict 6 Minute Walk Test



- Adjusted for FEV1%, BMI, %LAA, WA%
- BV_{<5} / TBV regression coeff: **796.67** (pval<0.0001)
- BV_{>10} / TBV regression coeff: **-1735.64** (pval<0.0001)



Preliminary Results

- Multivariate model to predict BODE
 - Adjusted for %LAA, WA%
 - $BV_{<5}$ / TBV regression coeff: **-1.76** ($pval<0.0001$)
 - $BV_{>10}$ / TBV regression coeff: **3.12** ($pval=0.03$)



Conclusions

- Large studies are showing the capabilities and weaknesses of current methods
- Basic emphysema characterization is there
 - Good method reproducibility
 - Still a global/heterogeneous measure
- Airways quantification is still limited
 - Extreme of linear/volume changes

Data, Data, Data

Opportunities, Opportunities, Opportunities...

