



Quantitative Imaging as a Biomarker

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Why Quantitative Imaging?

Clinical trials often require very large cohorts due to statistical power requirements

Outcome measures dictate clinical trials – events like death or repeat symptoms take time to occur in most situations

Imaging has the potential to be a surrogate outcome measure provided it is sensitive and specific enough.

There is a need to quantify disease in order to:

- a. determine disease severity
- b. determine disease progression or response to treatment

Advantages of Imaging?

Sensitivity will decrease time to determine change in natural course of disease

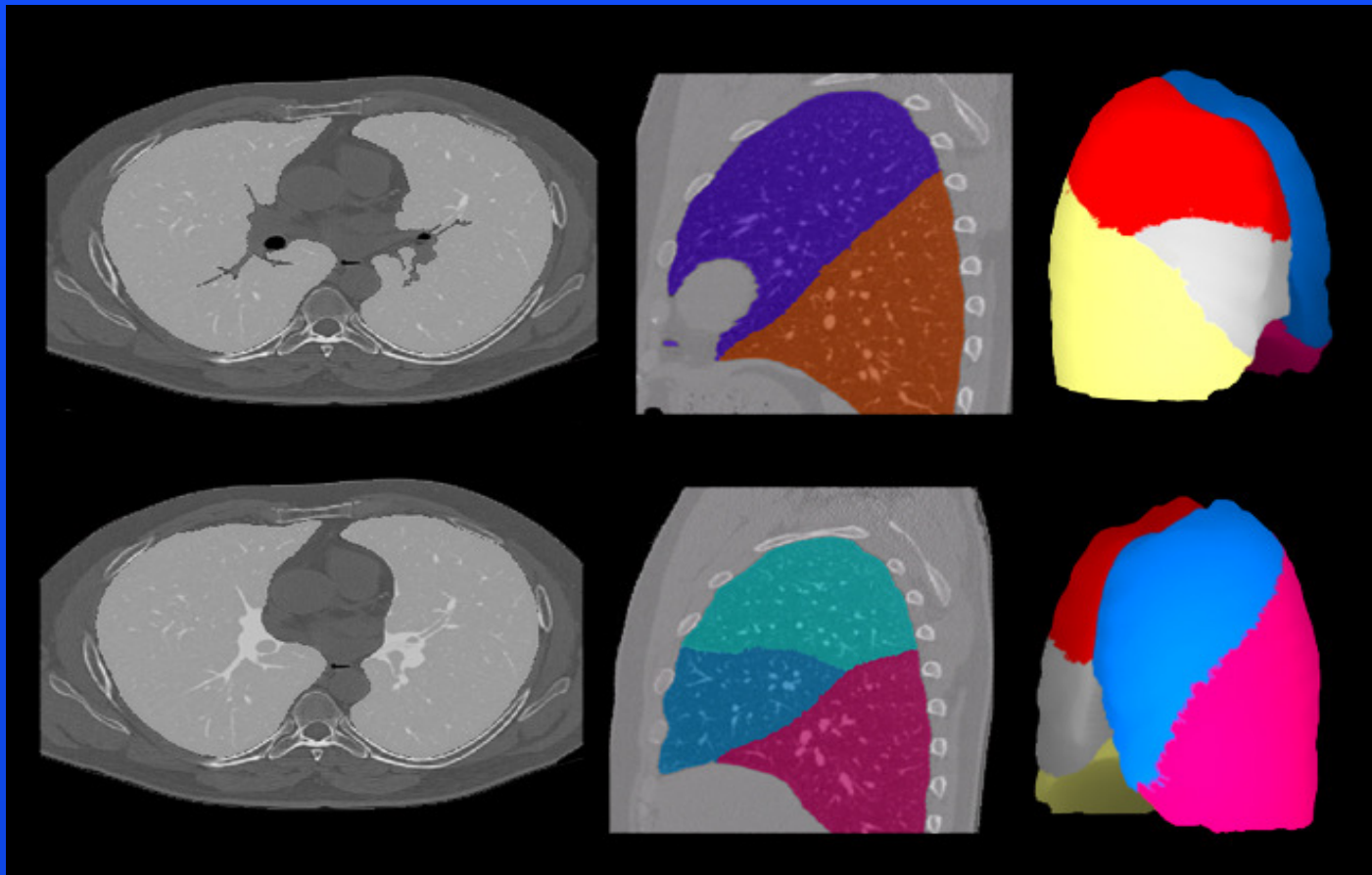
Quantification will help determine treatment effects (either in positive or negative way)

Both the above will decrease the numbers needed to treat

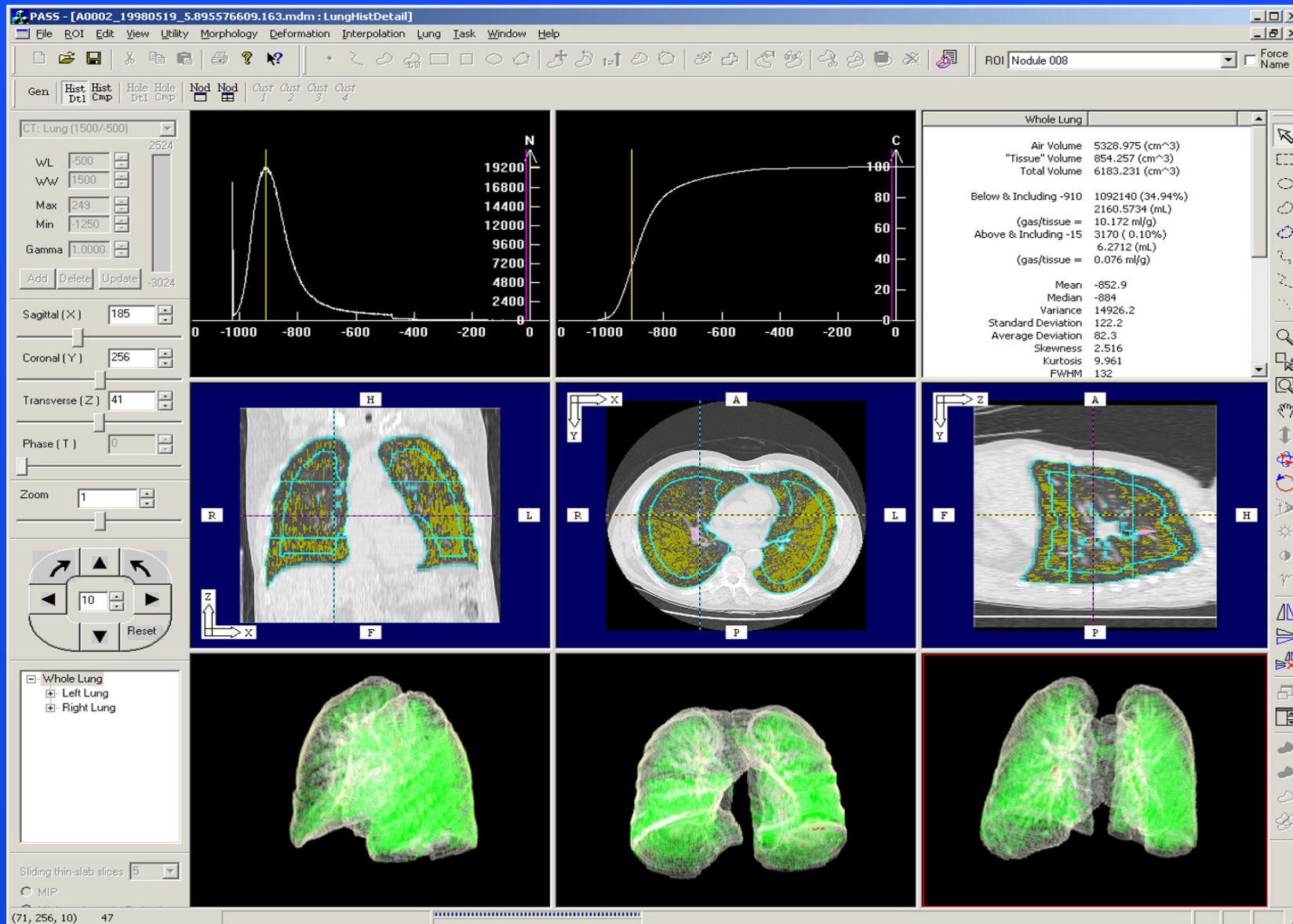
Result is time saved to reach statistical significance

Time is money! (fewer patients needed, shorter duration of clinical trial, shorter time from trial to market, greater period to use patents increases income to company)

Lung and Lobe Segmentation

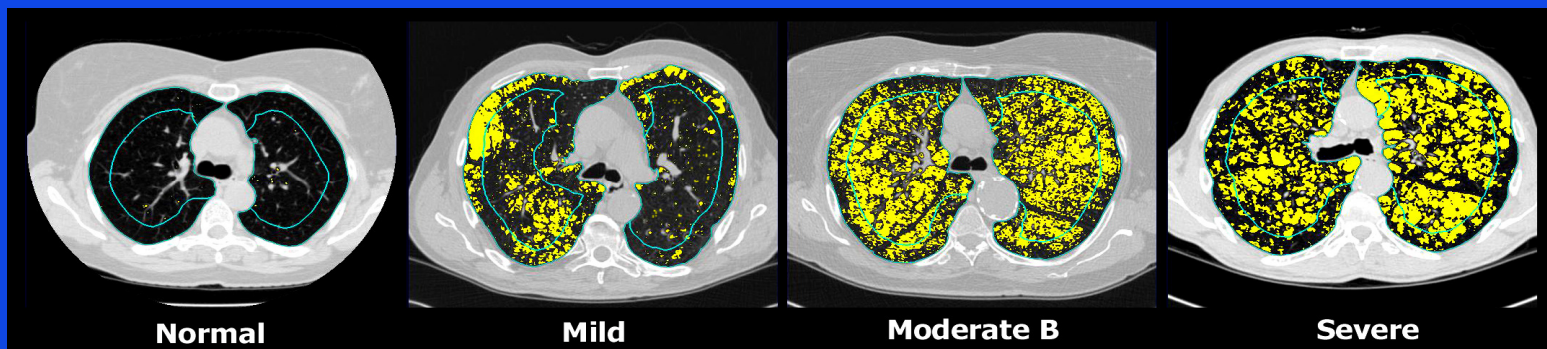
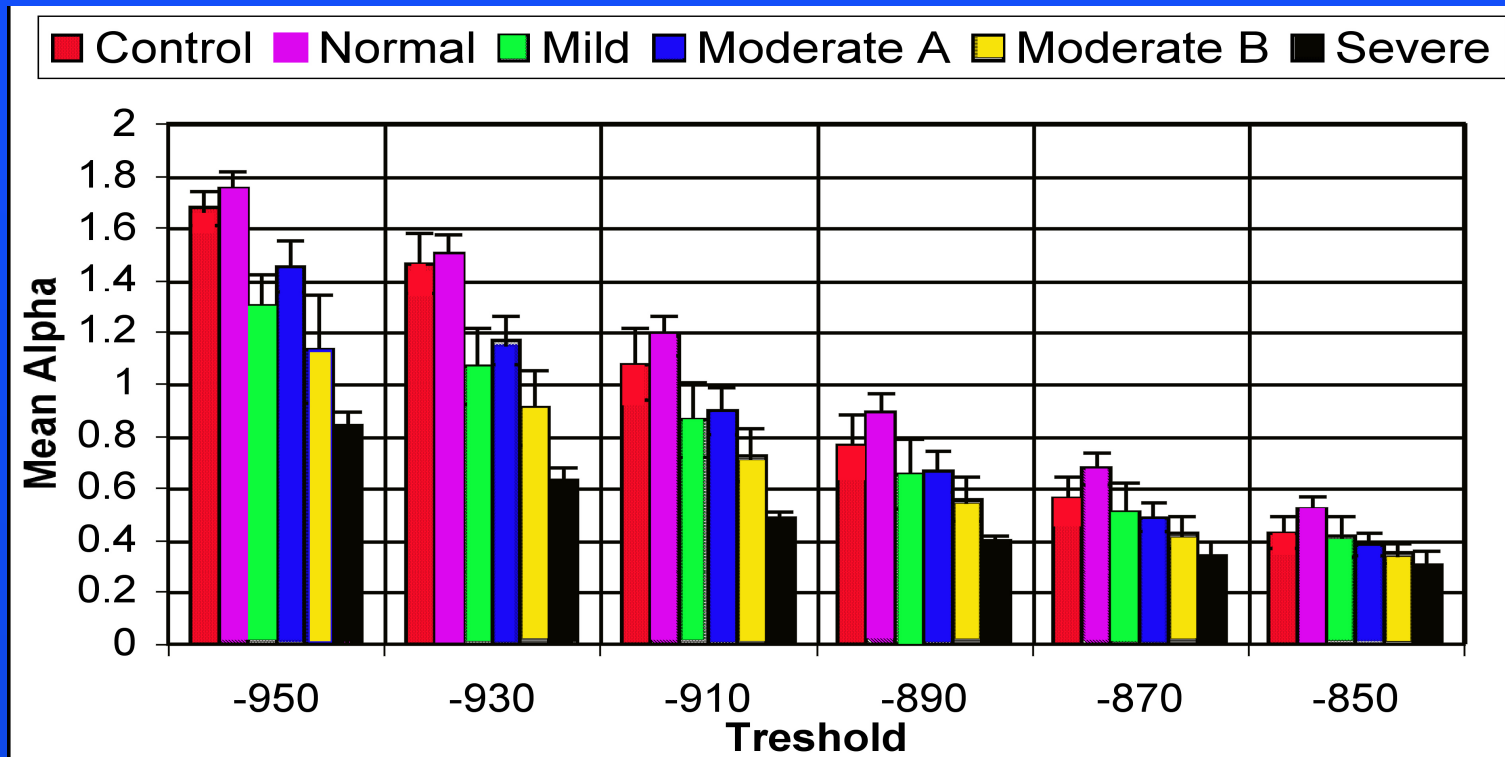


Density Histogram-based Evaluation

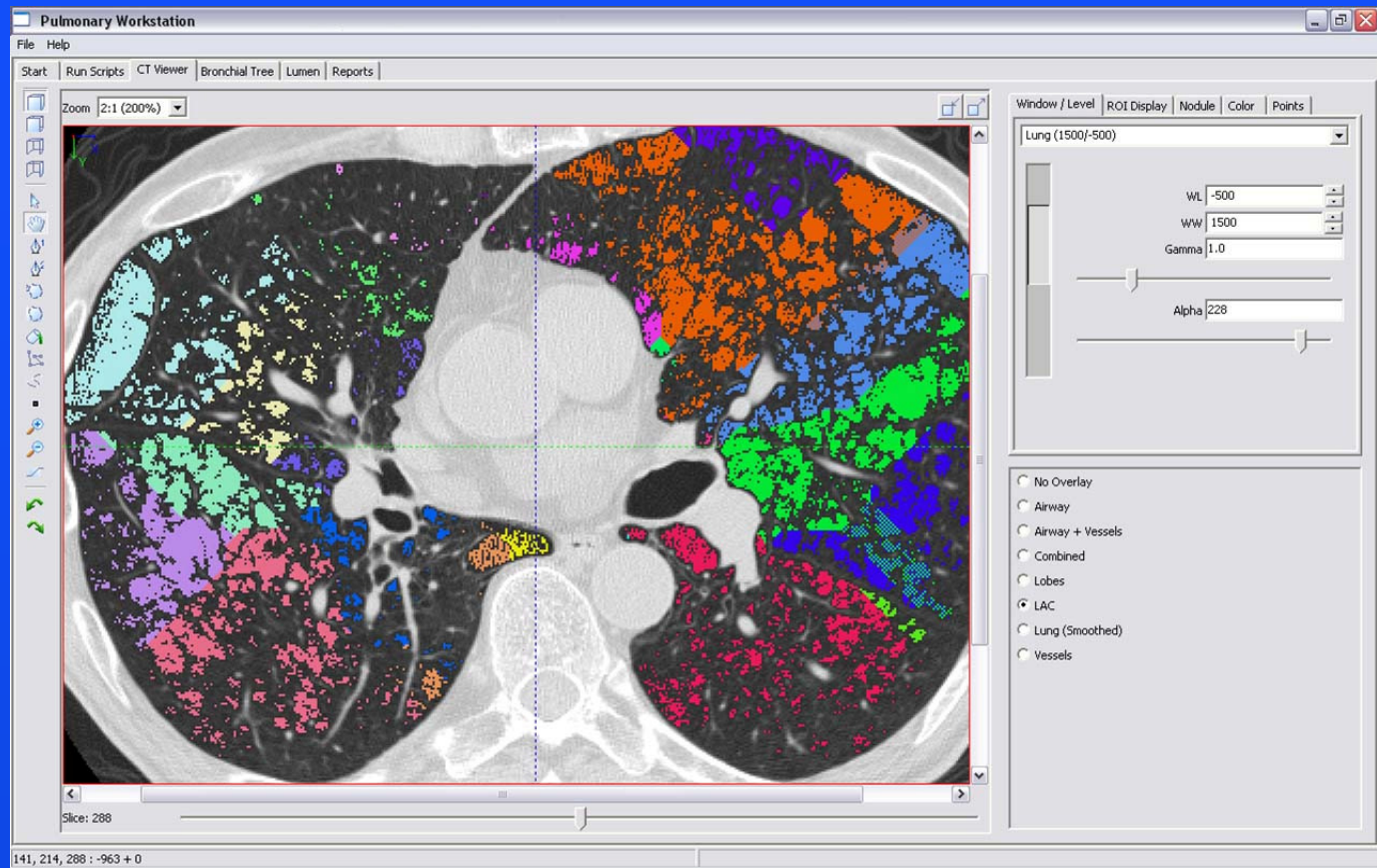
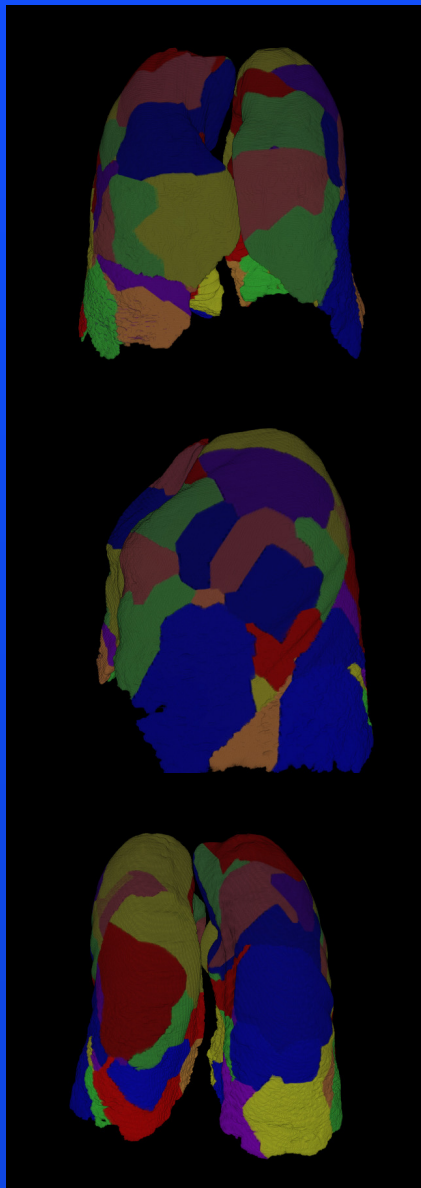


- ✓ **Lung Volumes**
- ✓ *Right, Left*
- ✓ *U, M, L*
- ✓ *Core, Rind*
- ✓ *Tissue, Air*
- ✓ **Histogram-Based Metrics**
- ✓ *Emphysema*
- ✓ *Normal*
- ✓ *Distribution*
- ✓ **Hole Size Distribution**
- ✓ *("Fractal")*

Hole Size Evaluation: Correlation of Alpha with PFT-based COPD Severity



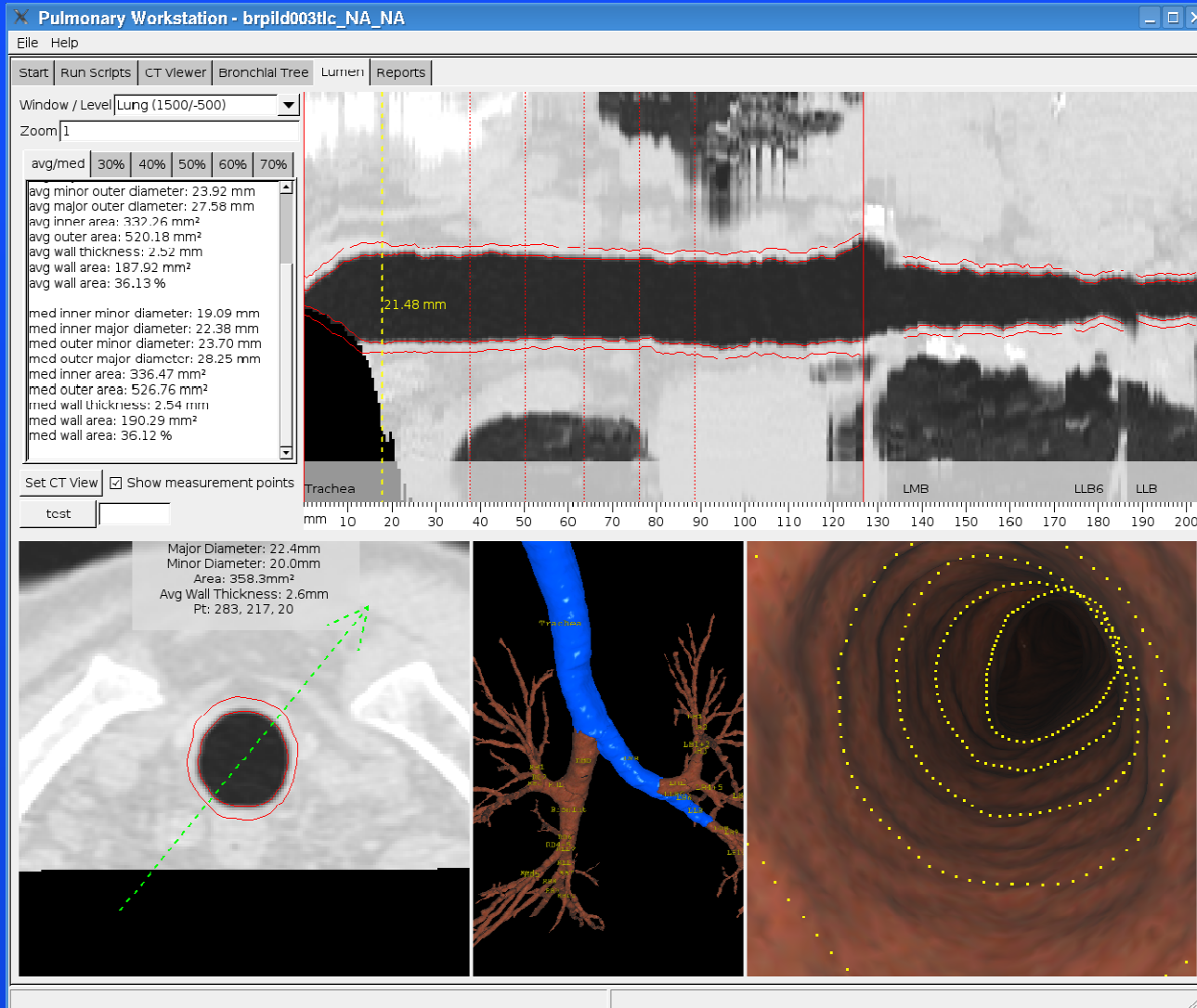
Density map based on quantitative CT



Subsegmental analysis of lung structure based on HU density, color map display. In this case: emphysema.

www.vidadiagnostics.com

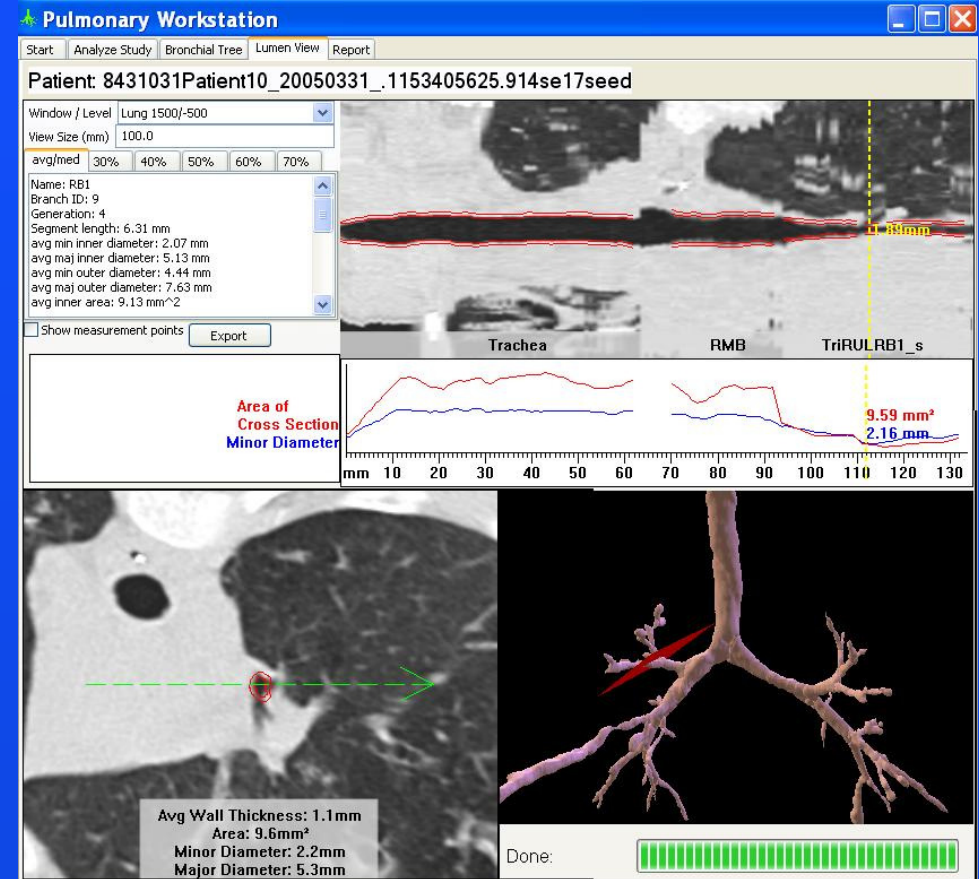
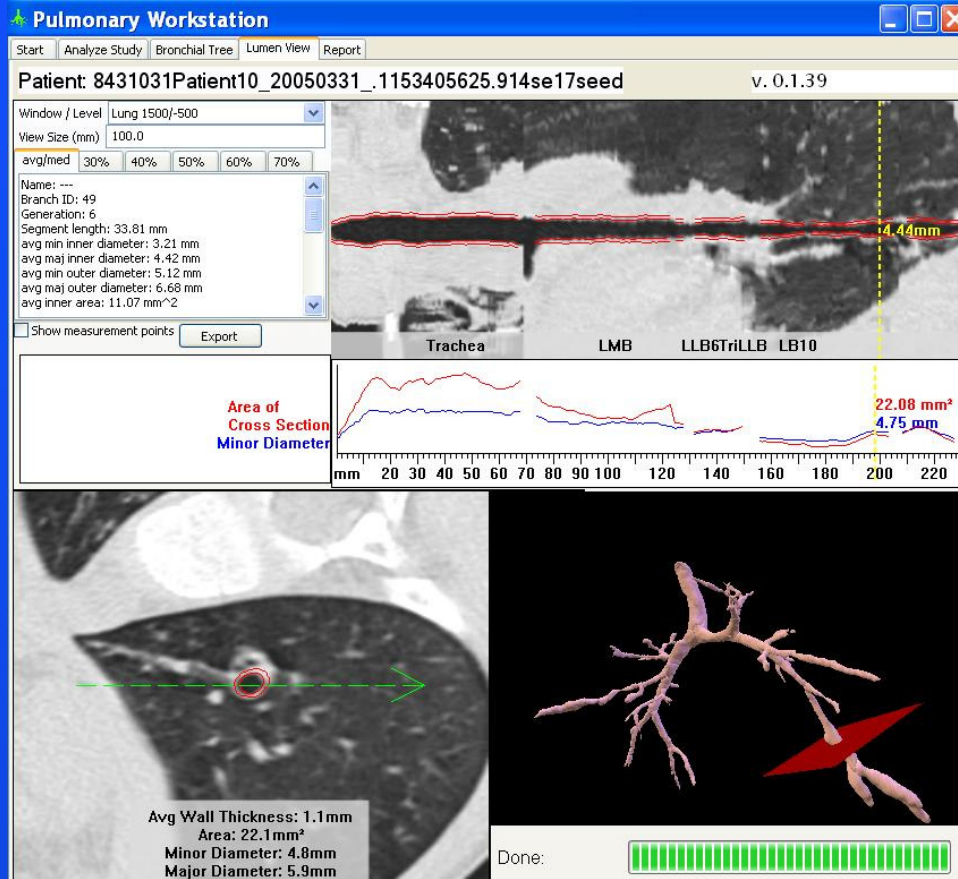
Quantitative airway analysis



Allows for the following:

- Airway segmentation
- Inner and outer diameter
- Wall thickness
- Virtual bronchoscopy
- Segmentation out to approximately 6th-8th order airways

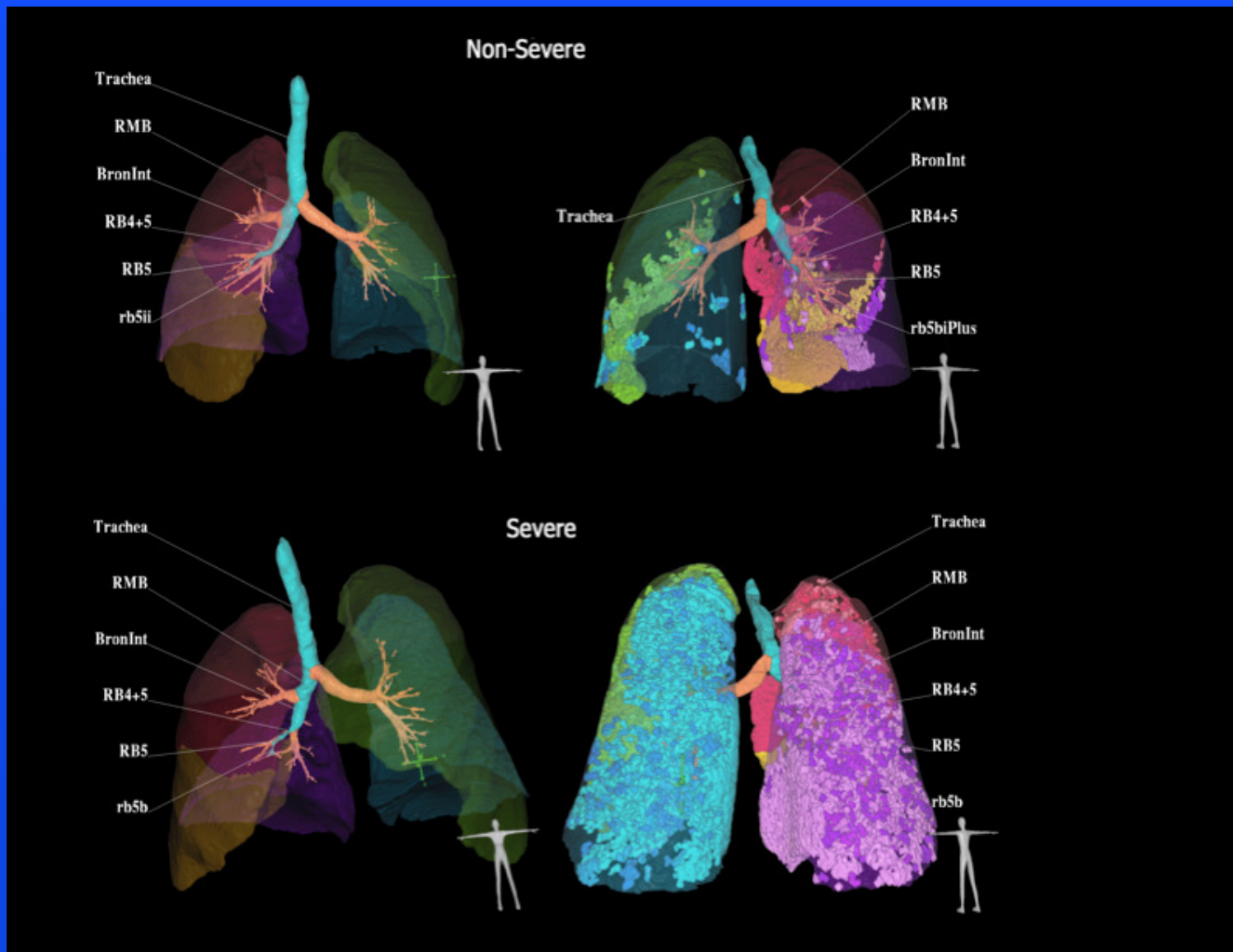
Quantitative airway analysis – E.g. Cystic Fibrosis



We can follow any predetermined pathway of the airway tree, and give size measurements – opens opportunity to assess long-term treatment effects!

Imaging data from Harm Tiddens, Erasmus MC, Rotterdam, NL

Asthma – Expiratory Air trapping



Eric Hoffman

Blue Sky – Under Development

Novel computer software for quantification and parenchymal analysis (Adaptive Multiple Features Method – AMFM)

Perfusion CT

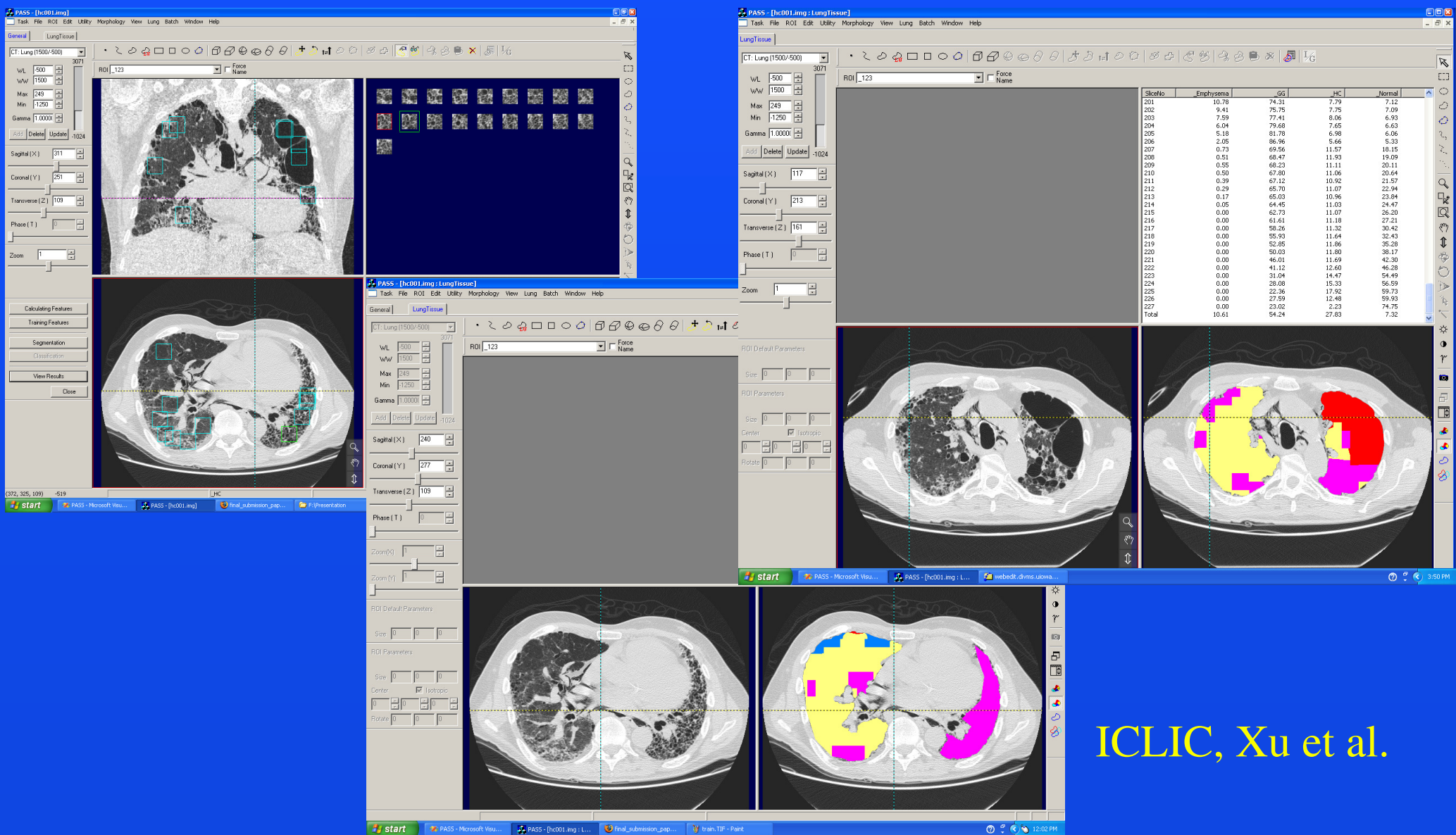
Xenon CT (with Dual Energy Imaging)

MR 4D Angiography

MR perfusion

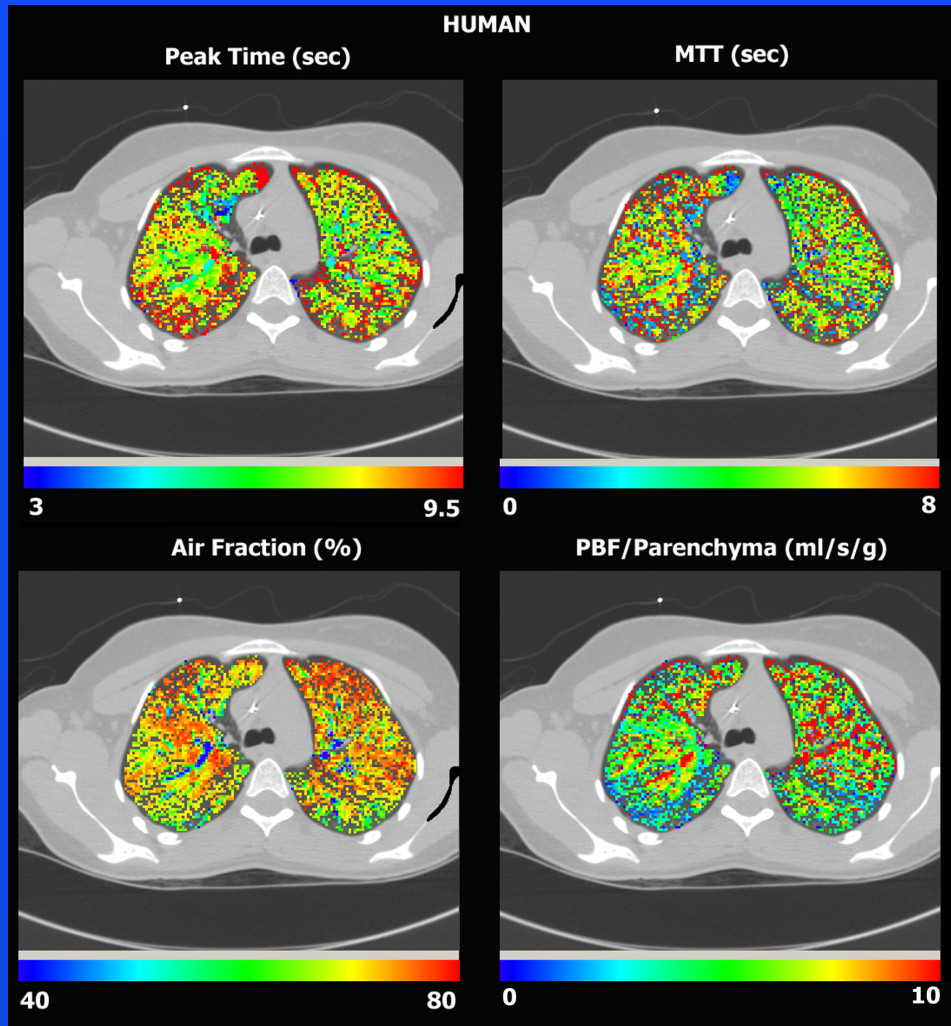
(Hyperpolarized gas imaging)

AMFM-Based Parenchymal Characterization



ICLIC, Xu et al.

CE-CT based texture analysis



Sharp contrast bolus allows peak time (seconds), mean transit time (seconds), air fraction (%) and pulmonary blood flow/parenchyma to be determined.

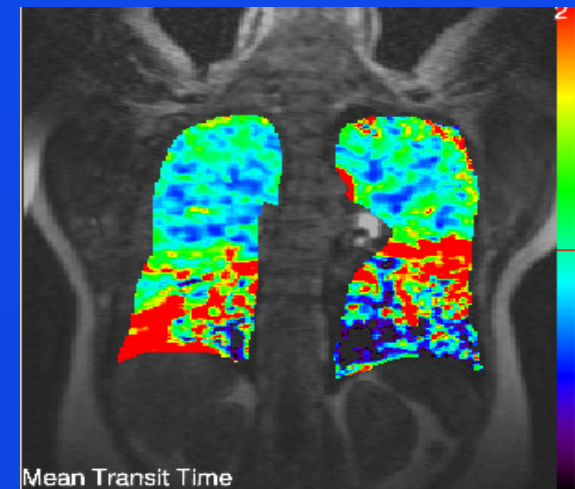
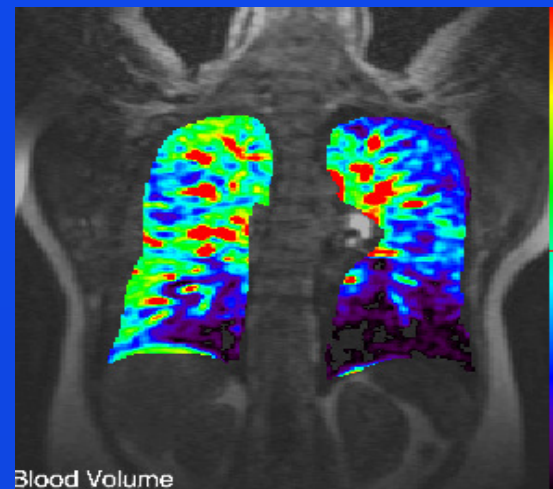
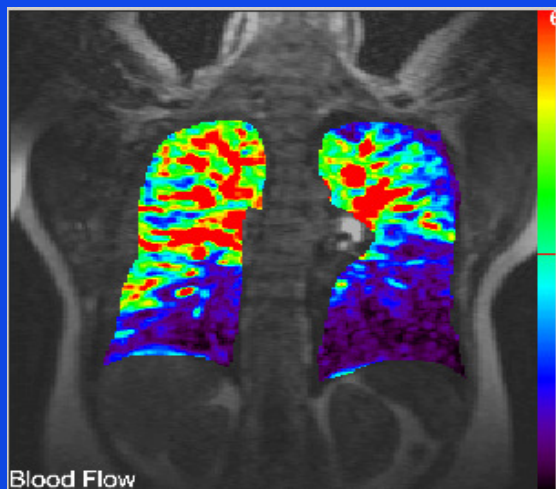
This in turn allows estimation of total parenchyma and the changes seen in lung disease can thus be quantified

Alford et al. PNAS (2010)

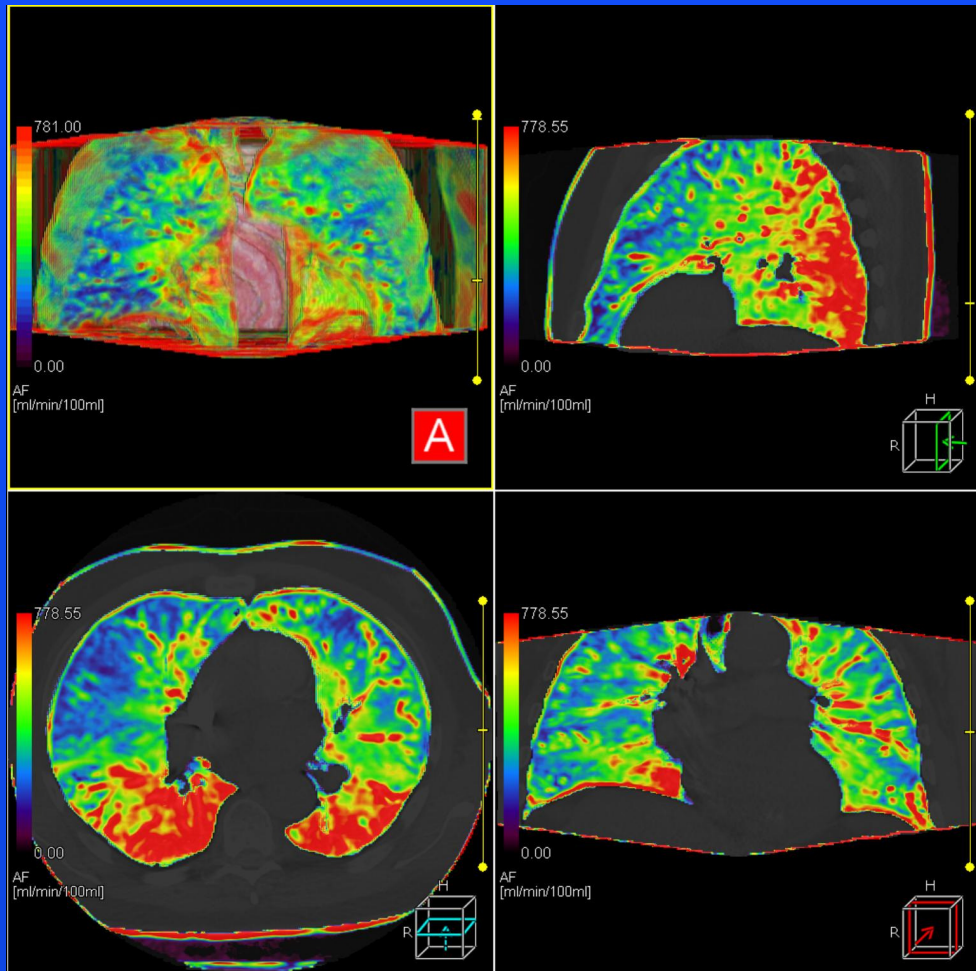
3D Quantitative Perfusion MRI



Kuder et al.
Eur Radiol
2007

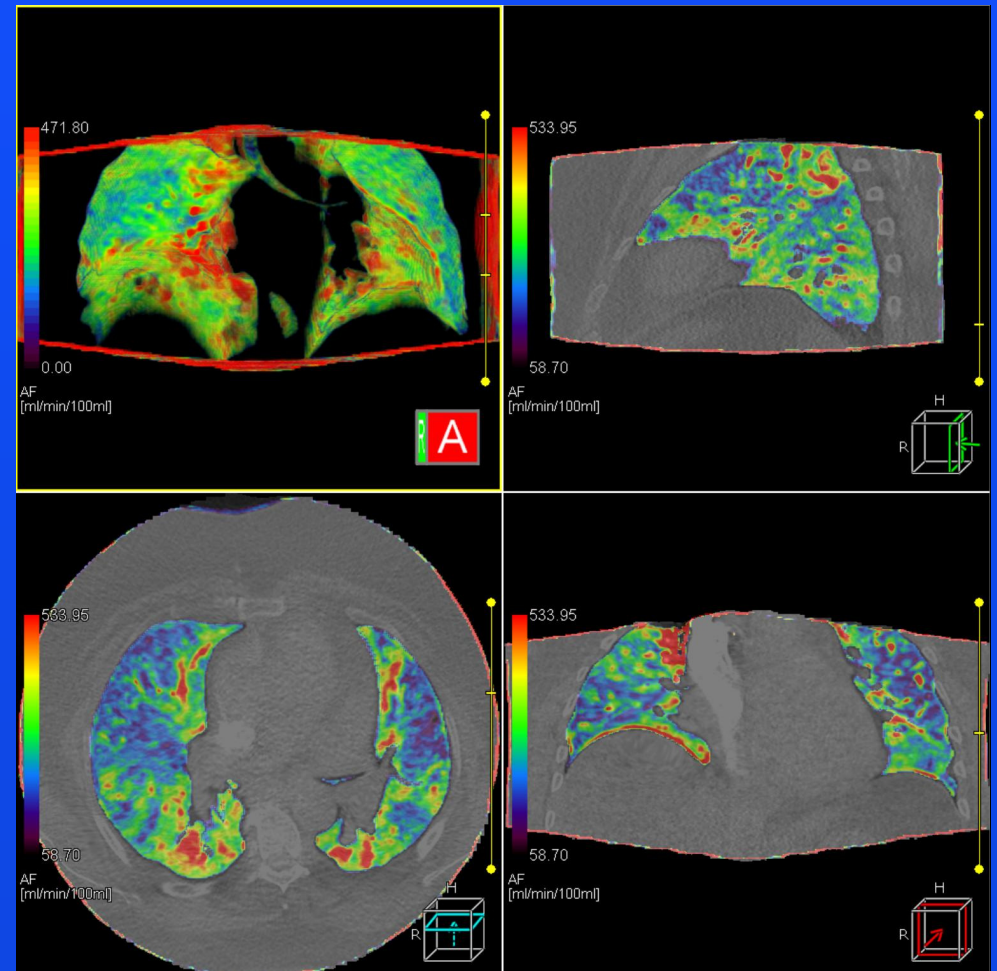


3D Quantitative Perfusion CT



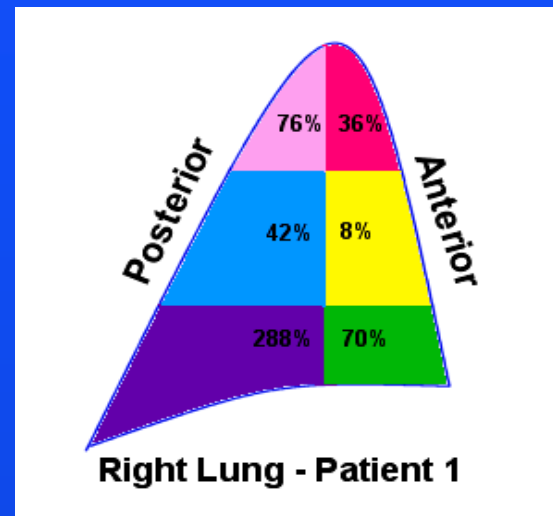
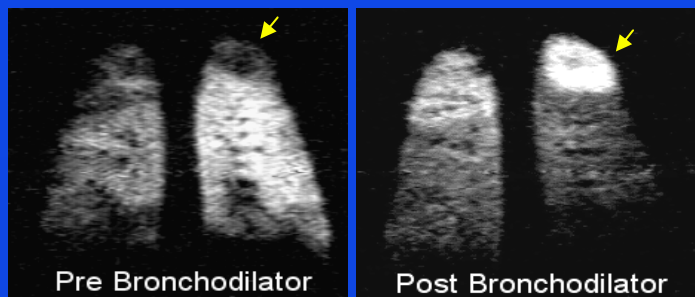
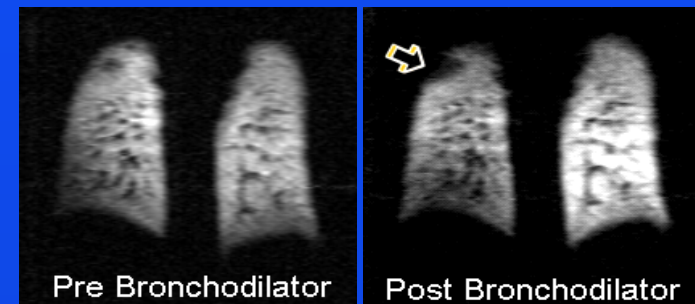
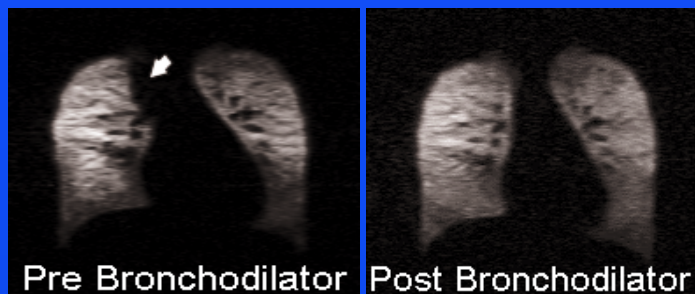
Normal

ml/min/100ml tissue



Abnormal

Bronchodilator response assessment using hyperpolarized 3He MRI

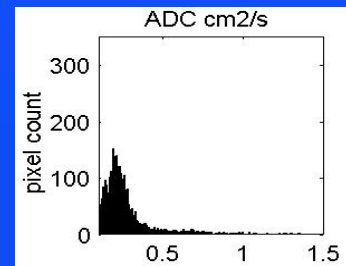
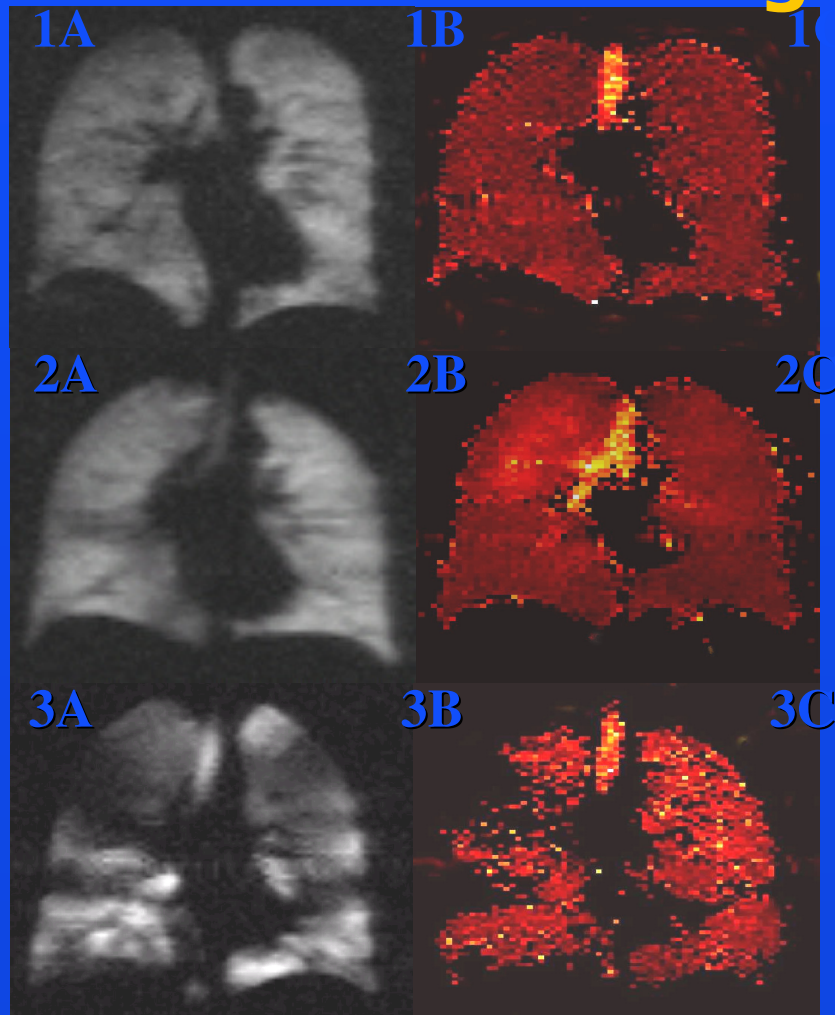


quantify
ventilation
change
with scoring

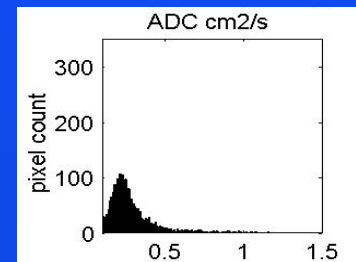
Longitudinal studies feasible

Woodhouse N et al ISMRM 2005
Prys-Picard et al Thorax, 2004. 59(1): p. 51

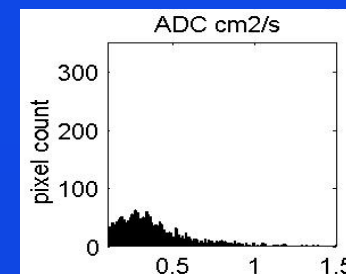
Coronal ventilation (A) and ADC (B) ^3He MR images and the corresponding ADC histogram (C)



Healthy non-smoker

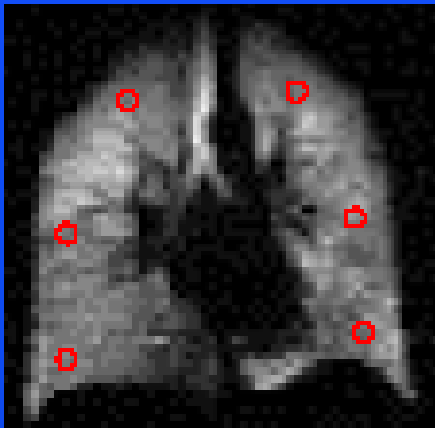


Healthy smoker

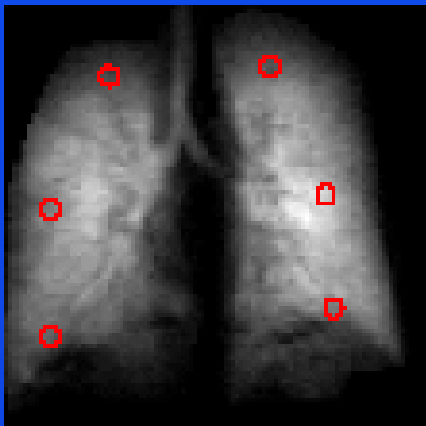
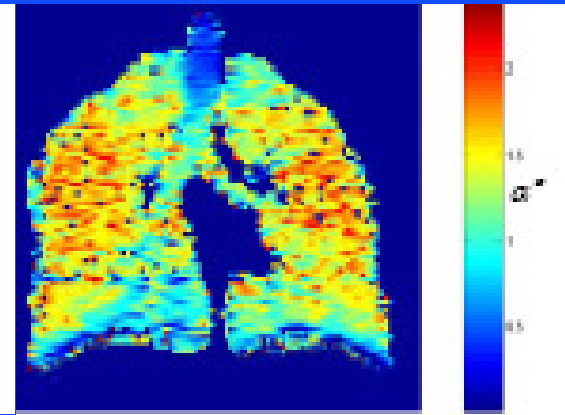
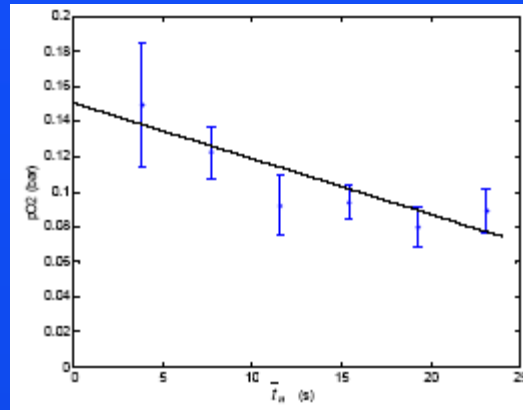


COPD patient

3D oxygen tension map now feasible



2D



3D

Slope of the curve is the signal decay as a function of partial oxygen tension. This represents oxygen uptake from ventilated lung into perfused state

Wild et al. MRM 2005

Conclusions

Imaging has the potential to alter clinical trials provided it is quantitative

In the lung this is being achieved using both MRI and CT methods in combination with software developments

It is imperative that companies consult early with imaging experts to devise appropriate measurement tools to help answer the questions of a clinical trial

Both positive effects and adverse effects of new treatments can be studied using imaging methodologies