Measurement of pulmonary deposition of nanoparticles as a means for morphometry of the distal air spaces and diagnosis of emphysema

Per Wollmer
Dept. of Translational Medicine
Lund University, Sweden
Nanoparticles are deposited by diffusion

The probability of deposition by diffusion depends on 
- time – standardised 
- distance to surface

Normal: short distance, high deposition, low recovery in exhaled air

Emphysema: long distance, low deposition, high recovery in exhaled air
Airspace dimension assessment: AiDA
Recovery falls exponentially with residence time
Modelling of recovery

• Estimation of $r_{\text{AiDA}}$ is obtained by solving the diffusion equation for cylindrical tubes

$$r = 2.89 \sqrt{D t_{1/2}}$$

• $D = \text{diffusion coefficient}$

• $r_{\text{AiDA}}$ is the effective airspace radius at a specific volumetric lung depth

• The calculated radius is weighted towards larger, distal airspaces

By selecting different sample volumes, we can measure dimensions at different volumetric lung depths.
Computed tomography
Magnetic resonance imaging using hyperpolarised gases

- Hyperpolarised $^{129}$Xe inhaled in a single breath
- Measurement of the free diffusion in the alveoli during breath-hold

Healthy subject vs. Patient with emphysema
Pulmonary function tests + AiDA: Malmö

MRI + $^{129}$Xe: Sheffield
Conclusions

- $r_{\text{AiDA}}$ shows consistent values beyond a volumetric lung depth of 1 L in normal subjects.

- $r_{\text{AiDA}}$ correlates well with measures of free diffusion of gas in the distal lung in normal subjects.

- Larger $r_{\text{AiDA}}$ in smokers with COPD and in subjects with $\alpha_1$-antitrypsin deficiency as well as the correlation with emphysema measured by CT support AiDA as a potential biomarker for emphysema.
What good is it?

• Studies of pulmonary pathophysiology

• Diagnosis of COPD
  • Routine: Dynamic spirometry (FEV$_1$, FVC)
  • Approx. 25 % of smokers with normal spirometry have evidence of emphysema at CT
    → missed diagnosis

• Stratification of patients in clinical trials

• Outcome measure in studies of treatment of emphysema
Co-workers:

Dept. of Translational Medicine:
Laura Aaltonen
Sophia Zackrisson
Sandra Diaz

University of Sheffield:
Jim Wild
Ho-Fung Chan

Dept. of Ergonomics and Aerosol Science:
Jakob Löndahl
Jonas Jakobsson
Madeleine Petersson Sjögren