Airspace Dimension Test (ADT) – A novel technique for diagnosis of chronic obstructive pulmonary disease with nanoparticles

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Introduction

Chronic Obstructive Pulmonary Disease (COPD) is one of the most common causes of death worldwide and is projected to increase to the third leading cause of death by 2030, depending on smoking habits, air pollution and demographic changes in many countries (Murray et al, 1997).

An early diagnosis is crucial to the outcome for the patient but current methods lack in precision.

It has been theoretically and experimentally shown that lung deposition of nanoparticles differ between healthy human subjects and COPD patients. This makes it plausible that lung deposition could be used as a diagnostic technique for COPD and emphysema (Löndahl et al., 2012).

The objective of this study was to develop and characterize a novel technique, named airspace dimension test (ADT), for lung diagnosis with inhaled nanoparticles.

Methods

An instrument was constructed to perform measurements of lung deposition of nanoparticles in human subjects over a single breath.

A well-controlled aerosol of polystyrene nanosphere particles with a narrow size distribution is generated. The aerosol is diluted with clean air to a concentration around 2000 particles/cm^3.

The subject inhales the aerosol with a vital capacity manoeuvre, holds breath for a determined period of time and then exhales into a sample collector. The particle concentration of the inhaled and exhaled aerosol is measured by a condensation particle counter (CPC). The exhaled aerosol is compared to the inhaled aerosol and the deposition fraction (DF) is calculated.

The sensitivity, precision and resolution of the technique was characterized by measurements with varying particle sizes and breath hold times in a small group of healthy subjects.

Results

DF increased with increasing particle size and decreasing breath hold time as could be expected for particles in the diffusion dominated size regime. The observed data agrees with adjusted simulations using a semi empirical lung deposition model. (Figure 1). Figure 1 shows how the DF depends on the inhaled particle size and the dwelling time in the lungs of a human subject.

The standard deviation for three consecutive measurements with 50 nm particles on the same volunteer was found to be 0.35%, while the intersubject variability was 3.3%. Thus, the instrument has sufficient precision to differentiate between individuals.

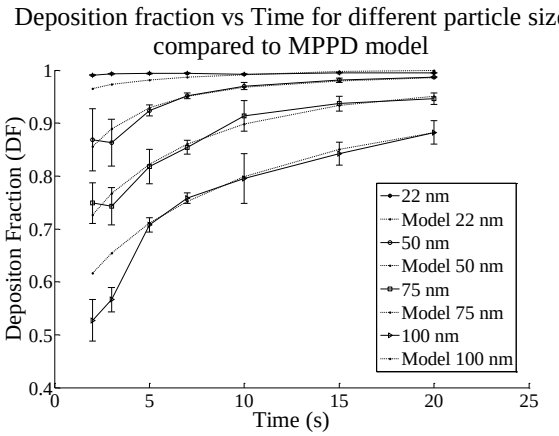

Figure 1. Lung deposition fraction depends on the inhaled particle size and breathing pattern.

Conclusions

The instrument shows both sensitivity and precision. Because lung deposition of nanoparticles (<100 nm) is controlled mainly by diffusion, a process depending on particle size, time and distances, it seems likely that the measurements reflect the geometrical airway dimensions of the lung. The observed data supports this.

ADT measurements are expected to yield information similar to that of a MRI examination of the lungs, using hyperpolarized ^{3}He, but at a fraction of the cost and with minimal discomfort for the subject.

Hopefully this technology can provide a valuable contribution to the diagnosis of COPD and emphysema in a near future.

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Murray, C. J. L. & Lopez, A. D. (1997), *Alternative projections of mortality and disability by cause 1990-2020: Global burden of disease study. Lancet*, 349**,** 1498-1504.

Löndahl J, Swietlicki W, Rissler J, Bengtsson A, Boman C, Blomberg A, Sandström T. (2012), *Experimental Determination of Diesel Combustion Particles in Patients with Chronic Obstructive Pulmonary Disease.* Particle and Fibre Toxicology 2012, 9:30