A model for assessment of alveolar dimensions from recovery of inhaled nanoparticles

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Introduction

A non-invasive technique with the ability to detect morphological changes in the small airways, including changes due to pulmonary emphysema, is aerosol derived airway morphometry (ADAM). ADAM, which has been investigated for almost half a century, provides information on the airway dimensions from comparison of inhaled and exhaled concentrations of monodisperse aerosol particles, often in the range 0.8-1.0 µm. However, ADAM has never been established in clinical practice.

We suggest that measurement of the recovery of inhaled airborne nanoparticles may provide a new and better opportunity for diagnosis: Airspace Dimension Assessment by nanoparticles (AiDA). Here we outline a basic theoretical background on the use of nanoparticles to measure lung morphology.

Theory and results

The fundamental difference between airspace dimension assessment by nanoparticles (AiDA) and micrometre sized particles (ADAM) is the deposition mechanisms. Nanoparticles deposit almost completely by diffusion, while particles around 1 µm (in still air) mainly deposit by gravitational settling.

In ADAM, the dimensions of the peripheral airspaces are approximated based on a mathematical model where the particles are assumed to deposit in a system of identical yet randomly oriented cylindrical tubes. The recovery of inhaled particles is measured after a breath-hold. By measuring recovery with different breath-hold times, the particle half-life time, $t_{½}$, in the lungs is determined. Thereafter, the airway radius, r, is derived from the recovery as:

$$r = \frac{2vt_{½}}{\pi \ln 2} \qquad (1)$$

where v is the terminal settling velocity of the particles. Diffusion is, in contrast to gravitational settling, random in direction and therefore the relationship is not directly transferable. For nanoparticles, airway radius can be estimated as:

$$r = 2.89\sqrt{Dt_{½}} \qquad (2)$$

where D is the diffusion coefficient given by the Stokes-Einstein relation (Goldberg *et al.* 1981). In addition, particle losses at zero breath-hold may provide information on dimensions of the peripheral conducting zone which is often affected in smokers.

Figure 1 illustrates half-life times for different tube radii and particle sizes estimated by Eq. 2. As can be seen $t_{½}$ is 2 to 60 s for particles between 50 and 150 nm. This is roughly setting the boundary for an applicable particle size range.

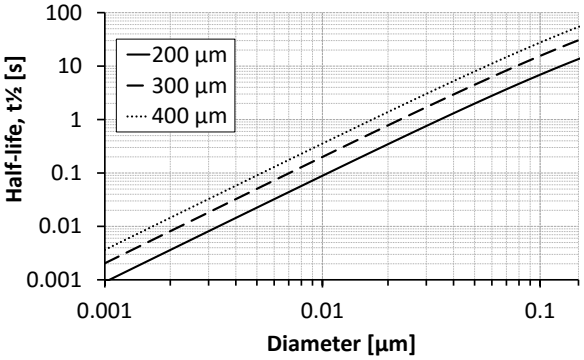

Figure 1. Estimated half-life, $t_{½}$, of inhaled particles during a breath-hold for airways with radius 200, 300 and 400 µm, respectively, which approximately correspond to the range in peripheral dimensions for healthy subjects and patients with early emphysema.

Discussion and conclusion

Using nanoparticles for studying distal airspace dimensions may have several benefits over previous aerosol based methods: (a) Nanoparticles deposit by diffusion, which allows for a simpler breathing manoeuvre without artefacts from inertial impaction. (b) A higher breathing flow rate can be used, which makes it possible to inhale to total lung capacity and thereby eliminates the need to determine lung volumes before measurement. (c) Many recent studies indicate a better penetration of nanoparticles than for micrometer-sized particles into poorly ventilated and diseased regions of the lungs and thus a stronger signal from the abnormal parts could be expected.

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Goldberg IS and Smith RB. Settling and Diffusion of Aerosol-Particles in Small Airways during Breath Holding. *Ann Biomed Eng*. 1981;9:557-575.