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REVIEW ARTICLE

# Modelling particle deposition in human lungs: modelling concepts and comparison with experimental data

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**Abstract**

Deposition of inhaled particles in the human lung is determined by biological factors, such as lung morphology and respiratory physiology, as well as by physical factors, such as fluid dynamics of the inhaled air and physical deposition mechanisms acting upon inhaled particles. Different conceptual particle deposition models vary primarily with respect to lung morphometry and mathematical modelling technique, rather than by using different deposition equations. Current whole lung deposition models permit the prediction of particle deposition in single airway generations or defined regions of the human lung for any combination of particle size and breathing pattern. Although comparisons with experimental data in human subjects indicate that all presently available deposition models correctly predict total and regional deposition, they cannot be validated by comparison with experimental data at the single airway or airway generation level.

**Keywords:** *Inhalation; particle deposition; human lung; modelling*



## Introduction

At present, direct experimental determination of particle deposition in human subjects is limited to total deposition, either inhaling through the mouth or the nose, for a wide range of particle sizes and flow rates (ICRP 1994), while regional deposition, e.g. in the bronchial or alveolar region, can only be obtained indirectly via subsequent retention measurements (ICRP 1994). However, local deposition in human airways, which would be needed for risk assessment of inhaled particles, requires the application of predictive aerosol deposition models. Thus the objectives of the present review are (1) to discuss different concepts of deposition modelling, and (2) to compare the results of theoretical predictions with published experimental data.

## Factors determining inhaled particle deposition

Deposition of inhaled particles in the human lung is determined by biological factors, such as lung morphology and respiratory physiology, as well as by physical factors, such as fluid dynamics of the inhaled air and physical deposition mechanisms acting upon inhaled particles (ICRP 1994).

In whole lung deposition models, the branching airway system in the bronchial and pulmonary region of the human lung is commonly represented by a sequence of cylindrical airways with defined linear dimensions, where parent airways branch into two daughter airways at each airway bifurcation (ICRP 1994, Koblinger & Hofmann 1985, Weibel 1963). The location of individual airways within the lung relative to the trachea is generally characterized by an assigned airway generation number. The main physiological factors determining particle deposition are the breathing frequency and the tidal volume (ICRP 1994). The equivalent physical parameters for particle deposition are the particle velocity or the flow rate.

Since airflow and particle motion are treated separately in whole lung models, particle deposition in individual airways is related to airflow by appropriate

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analytical equations for particle deposition efficiencies under prespecified flow conditions. The major physical forces acting upon inhaled particles are Brownian motion or molecular diffusion due to thermodynamic forces, sedimentation due to gravitational forces and impaction due to inertial forces (ICRP 1994). The main parameters of inhaled particles governing deposition are particle diameter and particle velocity (or flow rate). As the magnitudes of each deposition mechanism vary with airway diameter and particle velocity, they are operating primarily in specific regions of the lung (ICRP 1994).

## Modelling concepts

Different conceptual particle deposition models vary primarily with respect to lung morphometry and mathematical modelling technique, such as (1) semi-empirical models, (2) deterministic, symmetric generation or single-path models, (3) one-dimensional cross section or 'trumpet' models, (4) deterministic, asymmetric multiple-path models, and (5) stochastic, asymmetric generation models.

### *Semi-empirical models*

For radiological protection purposes, the International Commission on Radiological Protection (ICRP 1994) has proposed a semi-empirical model for regional deposition in the human respiratory tract, i.e. for nasal, extrathoracic, bronchial, and alveolar regions. Regional deposition is described by semi-empirical equations as functions of particle size and flow rate, which were derived from mathematical fits through the available experimental data (e.g. Stahlhofen et al. 1989). The major advantages of such semi-empirical models are that they are based on actually measured deposition data in human volunteers and no sophisticated computer programs are necessary. By definition, however, they cannot provide information about particle deposition in single airway generations nor should they be applied to particle sizes and flow rates outside the range of the experimental data they are based on.

### *Deterministic, symmetric generation or single-path models*

In the commonly used symmetric models, all airways in a given airway generation have identical linear dimensions, and each parent airway branches into two identical daughter airways (e.g. Weibel 1963). Thus all pathways of an inhaled particle from the trachea to the alveolar sacs are identical and thus can be represented by a single path. Because of the symmetric branching, the inhaled airflow is equally distributed among all airways in a given generation, leading to identical deposition fractions in each airway. Deposition fractions are computed by applying analytical deposition equations for specified flow conditions in straight and bent tubes for the different physical deposition mechanisms. Deposition in a given airway generation is then obtained by multiplying the deposition fraction in an airway by the number of airways in that generation. The deterministic, symmetric deposition models published in the past differ primarily by applying different morphometric lung models and analytical deposition equations (e.g. Hofmann et al. 1989, Martonen 1982, Yeh & Schum 1980). The advantage such of single-path models are their simplicity and their applicability to an average path without requiring detailed knowledge of the branching structure of the lung.

### *One-dimensional cross section or 'trumpet' models*

In one-dimensional cross-section models, the human airway system is approximated by a one-dimensional, variable cross-section channel, where the cross-sections are functions of the generation number and thus each airway within a given generation is characterized by its axial distance from the origin of the trachea. In the alveolated generations, additional volume for the alveoli encircles the channel. The cross-sectional area increases sharply with distance from the trachea, adopting a trumpet-like shape. The breathing process is pictured as the movement of air into and out of this channel as the airway and the alveolar volume expand and contract uniformly. The transport of inhaled particles by convective and diffusive (axial diffusion) processes, their deposition along the axis of the channel and mixing between tidal air and reserve volume are described mathematically by a mass balance equation with different loss terms for the various deposition mechanisms, using analytical equations for deposition by diffusion, sedimentation and impaction. Initially developed by Taulbee and Yu (1975), the trumpet model was further developed by Nixon and Egan (1987), Darquenne and Paiva (1994) and Mitsakou et al. (2005).

### *Deterministic, asymmetric multiple-path models*

Multiple-path models are more realistic than single-path models because they are based on actual airway measurements rather than on average values, and thus capture the asymmetric branching pattern of the lung. However, a complete deterministic asymmetric description of the human lung is presently not available. Thus, 10 asymmetric, structurally different multiple-path bronchial airway models were constructed on the basis of the stochastic lung model (Asgharian et al. 2001, Hofmann

et al. 2002). These bronchial trees were supplemented by attaching acini to each terminal bronchiole based on the typical-path model of Yeh and Schum (1980).

At an airway bifurcation, the flow in each asymmetrically branching airway is assumed to be proportional to its distal volume, and computed by a procedure known as a tree traversal (Asgharian et al. 2001). For each airway of the lung, particle concentrations as a function of time are determined for the proximal and distal ends. Knowing the concentration of particles at the proximal end of an airway, the concentration at its distal end is calculated by considering the deposition efficiencies for the various deposition mechanisms.

### *Stochastic, asymmetric generation models*

The main advantages of stochastic deposition models over the commonly used deterministic models are: (1) the determination of average deposition fractions is based on a more realistic description of the human airway morphology, considering structural asymmetry and biological variability (Koblinger & Hofmann 1985), and (2) the effect of intra-and intersubject variability in airway dimensions on particle deposition in individual airway generations or lung regions can be quantified in terms of statistical distributions.

A fully stochastic deposition model (IDEAL), simulating the trajectories of single particles was presented by Koblinger and Hofmann (1990) and Hofmann and Koblinger (1990), and further developed by Hofmann et al. (1999, 2002, 2005, 2006). The term 'stochastic particle deposition' refers to the transport of inspired particles through a stochastic asymmetric lung structure by randomly selecting the sequence of airways for each individual particle, and to the application of stochastic modelling techniques, such as the Monte Carlo method. Deposition in individual airways is based, however, on the average behaviour of an ensemble of particles as given by analytical equations for different deposition mechanisms. For the simulation of random paths through the lungs, the geometric properties of the two daughter airways are randomly selected at each bifurcation from their probability density functions, although constrained by correlations among some of the parameters. The actual path of the particle through either the major or the minor daughter branch is then randomly selected from the flow splitting distribution based on distal lung volumes. As a consequence of the variability of the selected sequence of airways, all paths of inspired particles are different from each other, and so are the deposition fractions in the individual airways. By simulating the random paths of many particles, typically of the order of tens of thousands, statistical means can be calculated for total, regional and generation-by-generation deposition, providing also information on the underlying statistical distributions.

## Comparison with experimental data

Current whole lung deposition models permit the prediction of particle deposition in single airway generations or lung regions for any combination of particle size and breathing pattern. By integrating generational deposition fractions over all airway generations in a given region, or over all regions in the human respiratory tract, local, regional and total deposition fractions can be obtained.

At present, direct experimental determination of particle deposition in human subjects is limited to total deposition, either inhaling through the mouth or the nose, for a wide range of particle sizes and flow rates (ICRP 1994). Regional deposition, e.g. in the bronchial or alveolar region, can only be obtained indirectly via subsequent retention measurements by assigning specific clearance rates to specific lung regions (ICRP 1994). However, the interpretation of such retention measurements hinges upon the magnitude of the bronchial slow clearance phase (ICRP 1994), which still requires further investigations. Additional experimental deposition data can be supplied by deposition studies in surrogate airway models or lung casts, restricted for practical reasons to large bronchial airways, by the analysis of SPECT measurements, or by inhalation of a narrow aerosol bolus targeted to different lung depths. Indeed, calculations with the stochastic deposition model IDEAL exhibit fair agreement with the various experimental data, suggesting that particle deposition models correctly predict deposition patterns within the various lung regions (Figure 1).

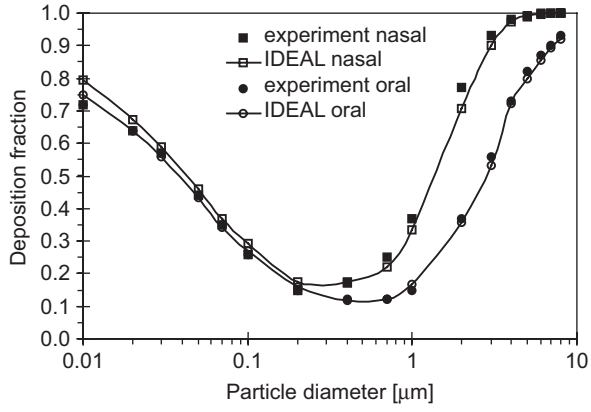


**Figure 1.** Comparison of stochastic modelling predictions with the experimental data of Heyder et al. (1986) for oral and nasal breathing conditions with a breathing frequency of 15 $min^{-1}$ and a tidal volume of 1000 ml (flow rate = 500 ml $s^{-1}$).

## Discussion

Current whole lung deposition models permit the prediction of particle deposition in single airway generations or defined regions of the human lung for any combination of particle size and breathing pattern. Comparisons with experimental data in human subjects indicate that all presently available deposition models correctly predict total and regional deposition.

In contrast to whole lung deposition models, which refer to particle deposition in the whole respiratory tract for a full breathing cycle, local scale models consider deposition in selected components of the branching airway system, such as bronchial bifurcations (e.g. Balashazy et al. 1999, Zhang et al. 2002). This geometric limitation, however, permits the combined solution of airflow and particle transport equations by numerical techniques (computational fluid and particle dynamics (CFPD) models). Such CFPD models allow the calculation of highly non-uniform, localized deposition patterns within defined airway components, such as the carinal ridge in bronchial airway bifurcations.

Although comparisons with experimental data in human subjects indicate that all presently available deposition models correctly predict total, regional and, to some extent, also local deposition, they cannot be validated by comparison with experimental data at the single airway or airway generation level. Moreover, it must be kept in mind that lung morphologies currently used for deposition modelling were derived from specific subjects, which may differ from those of the human test persons participating in the inhalation studies. Thus given the significant intersubject variability of lung morphology and respiratory physiology, the prediction of particle deposition for an individual person presents a major challenge for future research efforts.



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