

University of Medicine and Pharmacy, Târgu Mureş
School of Doctoral Studies

**THE MORPHOMETRY OF THE LOWER AIRWAYS,
UTILITY IN MODELLING STUDIES**

PhD Thesis Abstract

PhD Candidate: Sárkány Zoltán

Scientific Advisor: Prof. Dr. Marius Sabău

Târgu Mureş, 2013

Introduction

The human respiratory tract can be described as a complex system of cylindrical tubes, optimized for the transport of respiratory gases. From a geometrical point of view, the airways assume a tree-like structure, with branches that try to fill efficiently the space they are in, i.e. the thoracic cavity. The way the respiratory tract is optimized for gas transport, while respecting a set of biological, physiological and physical rules, represents a careful balance of design and function. One of the most interesting characteristic of this tree-like structure is its asymmetry: each branch gives birth to two (or sometimes more) daughter branches with different lengths, diameters and branching angles. The deposition of inhaled particles in the human airways has great implications in the assessment of risks associated with the exposure to infectious agents, toxic, radioactive or allergenic substances from the ambient air, but also in the refinement of therapeutic aerosols used in the treatment of chronic respiratory diseases, such as asthma bronchiale. Due to the fact that because of ethical considerations and technical limitations experimental data is limited, currently the most widespread method to study the airway deposition of inhaled particles is to use computerized lung models, which can simulate the transport and deposition characteristics of a wide range of particles in a large number of respiratory conditions. The objective of this study is to use a computerized lung model to study the effect of lung morphometry on the airway deposition of inhaled particles.

Material and methods

The deposition of inhaled particles was modelled with the help of a stochastic lung model, which uses a stochastic asymmetric lung structure, based on the statistical analysis of measured data. In the model the airways are modelled as a sequence of Y-shaped bifurcation units, consisting of a parent tube and two asymmetrically dividing daughter airways. The geometric properties of the daughter branches (diameter, length, branching angle, gravity angle) and particle trajectories are selected randomly for each airway segment, thus all paths of the inhaled particles are different from each other. The stochastic model calculates the deposition probability of each inhaled particle for each bifurcation unit. Simulation results are presented as deposited fractions (the ratio of deposited particles and the total number of inhaled particles) for total, regional, generational and lobar deposition. In order to investigate the effect of lung morphometry, we carried out two series of simulations: in the first series we created a symmetrical, one-path model by modifying the algorithm selecting the morphometric parameters of the airways in which the simulations are carried out. In this symmetrical model, each airway in one airway generation had identical linear dimensions and branches symmetrically into two identical daughter airways. In the second series of simulations we aimed to investigate the effect of an obstructive respiratory disease, such as asthma bronchiale, on the deposition of the inhaled particles. We changed the morphometric parameters of the airways and respiratory parameters to reflect the obstruction caused by an asthma attack. Special attention was given to particles in the 1–6 μm size range, used in the treatment of asthma bronchiale, and to their deposition in the bronchial region of the airways. We modelled the deposition of unit density (1 g/cm^3) particles with diameters between 0.01

and 10 μm . The simulations were carried out for one complete breathing cycle using 100,000 particles, and we assumed the particles are inhaled uniformly during inhalation. The deposition of inhaled particles was investigated in both series of simulations at different breathing conditions, using a wide range of respiratory parameters.

Results

Particle deposition in the human airways is the result of a delicate balance between particle size, lung morphometry, respiratory parameters and deposition mechanisms. Using a symmetrical lung model did not yield significant differences in the deposition fractions of the inhaled particles. The obstruction that occurs in the bronchial region during an asthma attack on the other hand seems to favour the deposition of particles in the 1–6 μm size range in this region, especially in the case of 3–6 μm , which corresponds to the size of particles currently used in most of the inhalation devices used in the treatment of asthma bronchiale. The differences between the bronchial deposition fractions obtained by a healthy subject and an asthmatic subject are especially significant when using the same breathing parameters, deposition fractions being 200% higher during an asthma attack. As far as the effect of respiratory parameters on particle deposition in the bronchial region is concerned, low tidal volumes combined with long inhalation periods, followed by a long breath hold seems to increase the deposition fractions in the bronchial region, these deposition fraction being higher in the case of large particles compared to smaller particles.

Conclusions

Our study shows that the deposition of inhaled particles is highly dependent on particle size, but also on the underlying lung geometry. The difference between deposition fractions obtained with an asymmetrical and a symmetrical lung model are not statistically significant, however these differences become significant once the lung morphometry is modified by obstruction, as in the case of asthma bronchiale. The complexity of the stochastic lung model and the flexibility of its parameters provide the means to carry out further studies regarding the effect of different parameters on particle deposition, with possible implications on the optimization of aerosol therapy.