Implementation of morphometric mouse lung data into a stochastic deposition model

P. Madl, R. Winkler-Heil and W. Hofmann

Department of Materials Research and Physics, University of Salzburg, 5020 Salzburg, Austria
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Presenting author email: pierre.madl@sbg.ac.at

The laboratory mouse is often used as a human surrogate in aerosol inhalation studies. The proposed simulation for aerosol inhalation and deposition calculations represents a significant step forward by reducing animal studies and at the same time speeding up predictions in deposition of particles with a given size.

Due to the lobar anatomical structure of mice lungs that nicely reflect observed differences in bronchial anatomy between different lobes of individual lungs along with intrasubject variability of airway dimensions within a given lobe, makes it possible to construct random airway geometries for Monte Carlo deposition calculations that ultimately enables extrapolation modeling of mouse deposition data to man. Here we present preliminary results of the implementation of morphometric lung data obtained from transgenic mice (Balb/c) into the stochastic lung deposition model originally developed for the rat (Koblinger and Hofmann, 1995).

As a consequence of the more monopodial airway branching in the mouse lung compared to the more dichotomous structure of the human lung, Madl et al. (2010) recommended classifying the mouse lung airways by their diameters and not by generation numbers. The distributions of the geometric airway parameters and the correlations among them are used to confirm the predictions made of Monte Carlo deposition calculations.

Implementation of morphometric mouse data is carried out in two steps. Due to the similarity between the rat and mouse bronchial airway structures, the first approach utilizes an existing rat lung model (Koblinger and Hofmann, 1995) in which relevant morphometric and respiratory parameters are downscaled to mouse size. The second approach applies then real bronchial morphometric data of Balb/c mice (Oldham et al., 2007), such as airway dimensions, termination probabilities and branching as well as gravity angles.

For the acinar region of the mouse, hardly any data can be found in the open literature, except for alveolar diameters and their numbers. Thus in the present version of the deposition model, acinar airway dimensions are downscaled to mouse size, assuming again similarity among mouse and rat acinar structures.

Table 1 summarizes total lung deposition fractions of monodisperse unit density aerosols with three different particle diameters at 25 ml minute ventilation, excluding extrathoracic deposition. The table also lists experimentally obtained deposition fractions (Oldham et al., 2009). Given the preliminary status of the deposition calculations, theoretical predictions for the mouse agree favorably with the experimental evidence.

Table 1. Comparison of total deposition fractions between various computer simulations.

	Diameter	0.5 [μm]	1 [μm]	2 [μm]
depos.[%]	Rat	18.2	20.5	53.5
	Scaled Rat	40.2	45.6	57.4
	Mouse	59.0	71.8	80.0
	Mouse (Exp.)	74.6	72.7	68.8

The distribution of total deposition fractions among bronchial and acinar mouse generations of the Balb/c mouse is illustrated in Figure 1 for 1-μm unit density particles. In contrast to the human lung, the majority of particles are deposited in bronchial generations, exhibiting a distinct peak in generations 6-8.

Although current mouse deposition fractions are still of a preliminary nature – as the code will be further refined – deposition calculations represent a promising tool for the extrapolation of beneficial effects of therapeutic aerosols in humans based on experimental data in mice.

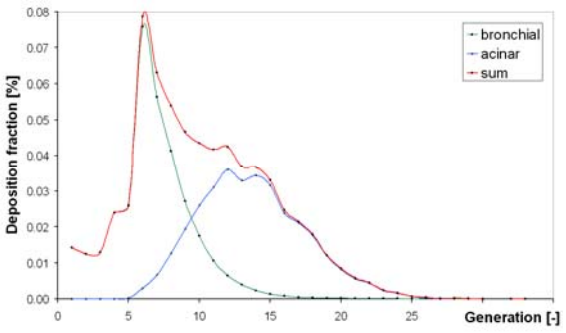

Figure 1. Deposition fractions for a monodisperse aerosol (1 μm) of the Balb/c mouse lung, excluding extrathoracic deposition.

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