Journal of Aerosol Science ∎ (∎∎∎∎) ∎∎∎–∎∎∎

Contents lists available at ScienceDirect

Journal of Aerosol Science

journal homepage: www.elsevier.com/locate/jaerosci

Modeling particle deposition in the pig respiratory tract

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ARTICLE INFO

Keywords:
Pig
Lung geometry
Morphometric variables
Particles
Deposition modeling

ABSTRACT

Despite increasing use of pigs as surrogates for humans in inhalation studies, measurements of particle deposition in the lungs of pigs are lacking. No comprehensive models are available for deposition of inhaled particles in the lungs of pigs to bridge the gap between exposure and biological response. In this study, a mathematical model was developed for the deposition of particles in the respiratory tract of pigs. Semi-empirical equations were developed to relate particle deposition efficiency in the pig nasal passages to non-dimensional parameters for diffusion and impaction deposition. The conducting airway tree of pigs was reconstructed from scanned images and other morphometric data in the literature. The pulmonary airway region was reconstructed assuming geometric similarities between humans and pigs due to a lack of information available on the pulmonary airways of pigs. The tracheobronchial and alveolar trees were combined to obtain a limited-monopodial lung geometry for pigs. A lung ventilation model was developed in this geometry based on lung compliance, airway resistance, and airflow inertance using breathing parameters from the literature. The lung deposition model was constructed based on models for lung ventilation, particle transport, and deposition in the asymmetric (monopodial) lung structure to predict particle deposition in the lungs of pigs. Model predictions indicated that the largest airflow and particle deposition occurred in the basal (diaphragmatic) lobes, which possessed the largest airway dimensions and volumes. The predicted site of deposition was related to particle size with larger particles depositing proximally and smaller particles depositing distally. There was limited penetration of coarse particles into the alveolar region because most of these particles were removed from inhaled air in the nasal and tracheobronchial regions. The deposition model developed in this study is a powerful tool to relate exposure environment to biological response and assess the dose of the delivered particles to the lungs.

1. Introduction

Pigs have been exposed to gases and particles by inhalation to study various respiratory responses such as pulmonary inflammation, improvement of impaired lungs in response to nitric oxide delivery, and deleterious effects of inhaled dust and endotoxins (e.g., Goebel et al., 2008; Herpin, Hulin, Dividich, Le, & Fillaut, 2015; Putensen, Räsänen, & López, 1995;

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http://dx.doi.org/10.1016/j.jaerosci.2016.01.016
0021-8502/

Please cite this article as: Asgharian, B., et al. Modeling particle deposition in the pig respiratory tract. *Journal of Aerosol Science* (2016), http://dx.doi.org/10.1016/j.jaerosci.2016.01.016

Urbain et al., 1999). Despite increased interest in using pigs as surrogates for humans in inhalation studies, measurements on particle deposition and gas uptake in the lungs of pigs are scarce. This information is crucial in relating the deposited dose to biological outcomes. The exposure–dose relationship is important for risk assessment from exposure to airborne materials and pharmaceutical drug delivery to elicit the targeted response.

Knowledge of particle deposition in different regions of the pig respiratory tract helps with the design of inhalation studies to target regions for studying biological endpoints of interest. Particle deposition modeling is a valuable asset, in the absence of measurements, to allow predictions of local and regional deposition of particles of various sizes under different exposure and breathing scenarios. However, there is not a complete model of the respiratory tract geometry of pigs, information on nasal and lung airways, nor information on physiological parameters to develop a comprehensive deposition model. Consequently, to date, there exists no model for inhalation of airborne materials into the lungs of pigs. While modeling the deposition of particles in the lungs of pigs is similar to those of other species, there are distinct differences in geometric structure, minute ventilation, and breathing rates, which must be taken into consideration. In particular, the respiratory tract geometry of many large animals such as sheep and pigs exhibit a monopodial branching structure, which cannot be represented accurately by a symmetric lung structure. In addition, calculations of airflow distribution in these lung geometries differ significantly from that in symmetric lung geometries such as humans (e.g., Asgharian, Hofmann, & Bergmann, 2001).

In this study, airflow and particle deposition computations were conducted in the nasal passages of a pig reconstructed from scanned images to develop semi-empirical relationships for particle deposition by the mechanisms of Brownian diffusion and inertial impaction. In addition, geometric information was collected on airway lung parameters to construct an anatomically accurate lung geometry for pigs. Furthermore, physiologically realistic ventilation models of inhalation were developed based on lung compliance, airway resistance, and airflow inertance. Finally, a deposition model was developed for pigs based on asymmetric lung structure and ventilation. The deposition model was then used to predict local and regional deposition of particles in the pig respiratory tract.

2. Materials and methods

The mathematical model to predict particle deposition in the pig respiratory tract after aerosol exposure follows that of other species. Infeasibility of a full 3D, fluid dynamics approach due to complexity of airway structure, multi-dimensionality of airways, large numbers of airways, and uncertainty regarding the initial and boundary conditions for airflow provides justification to apply simplifying yet realistic assumptions based on physical grounds for lung geometry and airflow and particle transport to reduce the governing transport equations to 0D and 1D. Lower resolution modeling allows predictions of particle deposition for the entire respiratory tract. Basic assumptions include cylindrical airway geometry, symmetric lung structure when detailed morphometric information was missing, fully developed airflow in all airways when the flow Reynolds number dropped below unity, and replacement of the boundary conditions at airway walls by a sink term in the transport equations to account for particle removal from the inhaled air. These assumptions enabled separate calculations of airflow distribution in the upper respiratory tract (URT), which extended from the tip of the nose to the beginning of the trachea, and lower respiratory tract (LRT). In addition, because particle–airflow interaction was negligible, modeling of lung ventilation and particle transport in the LRT could be pursued independently. Predictive modeling of particle deposition involved performing four serial steps: calculation of particle deposition in the URT, reconstruction of LRT structure and

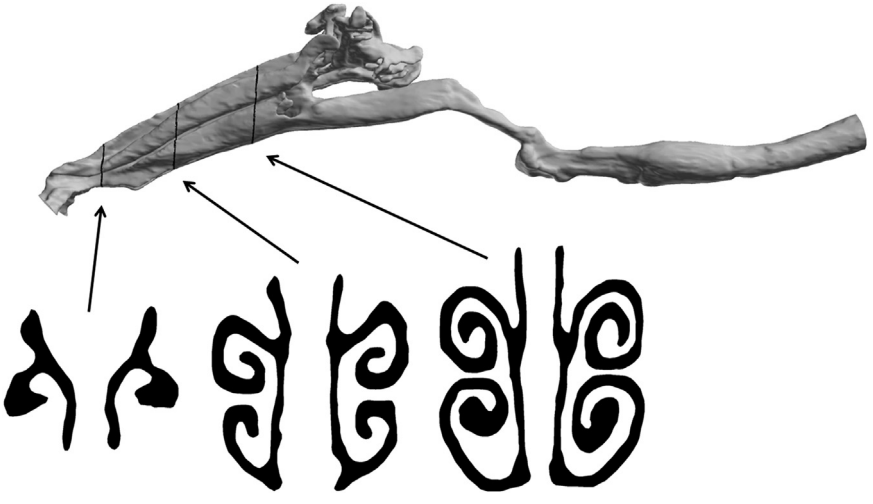

Fig. 1. Lateral view of the pig URT CFD model. Three coronal cross-sections are shown in the main nasal cavity to demonstrate the airway structure.

Please cite this article as: Asgharian, B., et al. Modeling particle deposition in the pig respiratory tract. *Journal of Aerosol Science* (2016), http://dx.doi.org/10.1016/j.jaerosci.2016.01.016