

Uncertainty Analysis of Physical Properties of Pharmaceuticals on Pulmonary Drug Delivery

Jun Lu, Jinxiang Xi, Joseph Langenderfer and Tiancheng Yang
Central Michigan University
Mt Pleasant, MI

Abstract

Background: To reliably predict the dose-response relation of inhalation therapies, it is vital to obtain the detailed information of particle deposition from drug delivery. There are lots of investigations about the distribution of the drug particles at different zones in the respiratory system using deterministic approaches, but the uncertainty analysis of the delivered doses has rarely been explored before. Considering the ubiquitous uncertainties in variables related to delivery devices, medications, and patients, it's more realistic to report the delivered doses with calculated uncertainties or reliabilities.

Objectives: This research aims to rank the sensitivity level of different drug properties and quantify both the dosage and uncertainties in pulmonary drug delivery. The drug properties to be considered include particle diameter and particle density.

Method: The mouth-lung model including the nose, throat and lung was developed based MRI images and was used to obtain the inner flow fields in the human's respiratory system with computational fluid dynamics software Fluent. With User Defined Functions (UDF), the exact amount of deposited particles at different positions was achieved by adopting discrete phase models. Uncertainty analysis software Nessus was used to compute the possibility of particle deposition by using different probabilistic analysis methods, including Advanced Mean Value and Monte Carlo method.

Result: The amount of particle deposition varies with different particle diameter and density. The larger the diameter and density are, the more depositions will happen in the respiratory system. However, particle diameter and density have different importance factors to the possibility of particle deposition. With a certain mean value and standard deviation, the amount of the medications delivered to the lungs is more sensitive to the variance of particle diameter than that of particle density.