Using Inhalation Dosimetry Models to Predict Deposition of Ultrafine Particles

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Abstract

The results of several epidemiological studies suggest that exposure to particulate matter (PM) in ambient air may be associated with an increase in respiratory and cardiovascular morbidity and mortality. Due to certain features and their prevalence in ambient air, ultrafine particles (UFPs) may contribute to these adverse health effects. Although ambient concentration is what is measured and regulated, the ultimate biological response is dependent upon the target tissue dose.

Inhalation dosimetry plays a key role in determining the link between environmental exposure to airborne contaminants and observed human health effects. Due to the limited availability of human experimental data and the complex nature of exposure–dose–response scenarios, mathematical modeling is an important tool in studying the mechanisms which dictate the inhaled "dose." Numerous factors affect the inhaled dose, and models include an extensive amount of information regarding physiological and anatomical parameters.

Inhalation Route: Exposure to Airborne Contaminants

- Exposure is the concentration of a chemical at the boundary of the body.
- The anatomy and physiology of the airways determines the concentration in inspired air, which dictates the potential dose.
- Determination of the biologically effective dose is key in risk assessment.

Factors Affecting Inhaled Dose

- Particle geometry & physicochemical properties
  - Size, shape, surface area, hygroscopicity, chemical composition, charge, density, solubility
- Lung morphology
- Respiratory tract (RT) altered by disease, inflammatory state
- Respiratory physiology
- Ventilation rate, activity level, age, gender
- Environmental conditions
- Humidity, temperature, ambient concentration

UFPs are classified according to size or aerodynamic diameter (AD) and many terms are used interchangeably.

- Particle > 100 μm are not generally considered respirable.
- PM<sub>10</sub> (coarse): AD = 10 μm
- PM<sub>2.5</sub>: AD = 2.5 μm
- Fine, Accumulation Mode: AD = 1 μm
- Ultrafine, Nuclei Mode: AD = 0.1 μm
- Nano: AD = 0.01 μm
- UFPs often ignored due to small contribution to overall particle mass
- UFPs often present in high numbers in the atmosphere with measured number concentrations as high as ≥ 1 x 10<sup>6</sup> particles/cm<sup>3</sup>
- Animal studies suggest UFPs induce greater airway inflammation than similar mass concentrations of larger particles.
- Predominant mechanism of deposition is diffusion; the probability of diffusion increases as particle size decreases (smaller particles should be favored in the distal airways and alveoli because reduced airflow increases residence times in these regions).

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Inhalation Dosimetry Models

- MENTOR/SHEDS: Source-to-Dose Exposure Analysis
  - The Modeling Environment for Total Risk (MENTOR)/Somatic Human Exposure and Dose Simulation (SHEDS) framework facilitates the consistent multiscale, source-to-dose, modeling of exposures to contaminants for both individuals and populations.
  - Both respiratory PM deposition and multimedia/multipathway (MMMP) models have been implemented with a flexible design.
  - Modules are interactive with databases of anatomic and physiological parameters
  - Physiological variability due to age, gender, weight, etc.
  - Continuous temporal variability due to physical activity/metabolism
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- Advantages/Disadvantages
  - Empirical and semi-empirical models allow for scaling from individual to population level
  - Determination of cumulative lifetime risk
  - Expansion to "source-to-outcome" framework; flexible applications

- Comparison of Young Adults to Healthy Elderly to Examine the Effects of Aging on Ultrafine Particle Deposition
  - Additional measurements of total lung deposition of UFPs performed by Kim & Jaques (2003) on healthy elderly subjects during controlled breathing:
  - Breathing patterns equivalent to resting and an activity slightly above resting
  - No difference appreciated between healthy elderly and young adults

Experiments conducted by Jaques & Kim (2000) and Daigle, et al. (2003) compare the deposition of UFPs in adults during rest and exercise: the experimental data is then compared to model predictions.

- Experimental deposition of UFPs exceeds that predicted by models.
- Probability of diffusion increases as particle size decreases.
- Diffusional deposition of UFPs (as compared to larger particles) favored in distal airways and alveoli because reduced airflow increases residence time in these regions.
- Total Deposited Particulate Fraction (TDP) varies with breathing pattern
- Increase in TDP expected with increased activity level
- Larger tidal volume (V<sub>T</sub>) should penetrate deeper into the lung where airway diameter is small and wall surface area is large.
- No gender difference in TDP of UFPs appreciated
- Additional experimental work by Kim & Jaques (2005) shows no significant difference between healthy elderly and young adults

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References


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