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Improvements and additions to the multiple path particle dosimetry model

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ABSTRACT

A little over a decade ago, the first UC Irvine dosimetry conference was held entitled "Frontiers in Aerosol Dosimetry Research". At that time, mechanistic dosimetry models, such as the multiple path particle dosimetry (MPPD) model, primarily focused on humans, with a model for the Long Evans rat also being available. In the intervening years, advances have occurred on a number of fronts that have led to improvements and additions to the user-friendly MPPD software program that is available free to the public. Here, we review a number of the expanded capabilities of the MPPD model. These include:

- Calculating deposition and clearance simultaneously for up to 4 lognormal distributions having different mass median aerodynamic diameters and geometric standard deviations. This feature is useful whenever the exposure atmosphere is multimodal as is often the case with workplace exposure atmospheres and can occur in inhalation toxicology studies if the particulate aerosol is difficult to generate stably.
- The ability to adjust the total aerosol deposition for the amount of particle "X" when "X" is a subset of the total aerosol. This is particularly important for workplace exposures where the particles of interest (e.g., copper containing particles) are part of the total dust aerosol that was measured.
- The ability to specify clearance rates and mucous velocities for both animals and humans so any type of particle can be modeled as well as various lung disease states.
- The addition of dose metrics for the upper respiratory tract and enhancements to dose metrics for the lower respiratory tract.
- Addition of a lung geometry/morphometry model and physiologic input variables for mice (Balb/c and B6C3F1), Sprague-Dawley rats, male rhesus monkeys, sheep, and pigs. The deposition and clearance of particles in these species can now be examined.

1. Introduction

Regulatory bodies make use of interspecies dosimetric adjustments and high to low dose extrapolation in using animal toxicological data to determine reasonable exposure limits for humans. In addition, therapeutic aerosols are examined using dosimetry models for finding effecting treatment regimens. The multiple path particle dosimetry (MPPD) model is a

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mechanistic dosimetry model that facilitates the calculation of regional and site-specific deposition and clearance of particles. The MPPD model software is available to the public free of charge (http://www.ara.com/products/mppd.htm) and is popular with users because of the user-friendly menu-driven selections that can be made for the various input variables.

Since the first publication by Anjivel and Asgharian (1995) using the multiple path modeling approach, the MPPD model has been applied to the human lung (Asgharian et al., 2001), the rat lung (Asgharian et al., 2003), particle deposition (Asgharian & Price, 2007; Asgharian et al., 2014; Jarabek, Asgharian, & Miller, 2005), as well as fiber deposition in humans (Asgharian & Anjivel, 1998). At the time of the first UC Irvine dosimetry conference held in October of 2005, the MPPD model treated Long Evans rats and humans and poorly soluble particles. Since then a number of improvements and additions have been made to the MPPD model software in the treatment of aerosol distributions, clearance parameters, dose metrics, species geometry models, and report output files. Here, we briefly discuss these improvements and additions and give examples of them to make the reader aware of the currently greatly expanded capabilities of the MPPD model for use in studying the deposition and clearance of particles.

2. Aerosol distributions

Workplace dust exposures typically involve a mixture of particles arising from the various manufacturing or industrial processes that are being used in a given facility. Regulatory bodies for worker health protection establish short- and long-term exposure limits for total dust and for some of its components. The short-term exposure limits typically are intended to protect against irritation or acute injury of the nasal passages or the conducting airways of the lower respiratory tract while the long-term limits are intended to protect against the development of chronic effects.

Thus, total particle deposition in the respiratory tract relates to total dust exposure standards. However, to protect workers from health effects that can be caused by particles that are a subset of the total dust, such as copper, nickel, or iron containing particles, the amount of such particles depositing in the lungs also needs to be determined. Given the different processes and workplace locations, workplace air is typically a multimodal log normal distribution.

Recently, the MPPD software was modified to be able to handle up to 4 overlapping log normal distributions, enabling more complex aerosol distributions to be modeled for deposition and clearance calculations. Each of the individual mode size distributions had to be combined into a single size distribution for use in MPPD. Based on the input parameters provided by the user for each mode, a single multimodal size distribution is constructed computationally to reflect the overall distribution of particle sizes. The size range of this multimodal particle distribution is then subdivided into logarithmically spaced intervals, and the total number of particles in each size interval is calculated in order to assist MPPD calculations of deposition and clearance.

Table 1 gives cascade impactor data for total dust on various stages as well as data for the analysis of the amount of insoluble and soluble copper on these stages in workplace air at a brass recycling and extrusion facility. The facility specializes in extruded brass rod, bars, and wire and is a leading manufacturer of extruded brass shapes. The sampling at this facility involved the casting area for melting scrap brass and casting it into ingots. For additional details on the count distribution data and the procedure for estimating the overall particle density of the total workplace dust aerosol, see Miller et al. (2013). The analyses in Table 2 show that the cascade impactor sample required 3 overlapping lognormal distributions to fit a continuous function to histograms based on particle mass per size interval. Two fine mode lognormal distributions

Table 1
Brass recycling facility: total dust and copper content in cascade impactor sample.[a]

Dekati stage	D_A (μm)	Total dust (mg/m^3)	Copper (μg/m^3)			Copper as % of Dust	
			Soluble	Insoluble	Total	On stages	In total sample
–	100	ND	ND	ND	ND	–	–
Inlet	30	ND	ND	ND	ND	–	–
1	10	0.063	–	4.90	4.90	7.778	0.825
2	7	0.055	0.26	3.80	4.06	7.382	0.684
3	4.3	–	–	2.60	2.60	**7.382**	0.438
4	2.7	0.077	–	2.10	2.10	2.727	0.354
5	1.8	0.098	–	1.50	1.50	1.531	0.253
6	1.1	0.093	–	0.54	0.54	0.581	0.091
7	0.7	0.088	–	0.59	0.59	0.670	0.099
8	0.4	0.120	0.46	0.63	1.09	0.908	0.184
9	0.3	–	–	0.25	0.25	**0.908**	0.042
10	0.2	–	–	–	–	–	–
11	0.1	–	–	–	–	–	–
12	0.06	–	–	0.34	0.34	**0.908**	0.057
13	0.03	–	–	–	–	–	–
TOTAL		0.594	0.72	17.25	17.97		3.027

[a] Data taken from Miller et al. (2013). Bolded numbers are worst-case estimates where no mass was detected on a stage but chemical analyses revealed some copper. D_A is aerodynamic diameter and ND stands for not detected.

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