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Particle deposition in tracheobronchial airways of an infant, child and adult

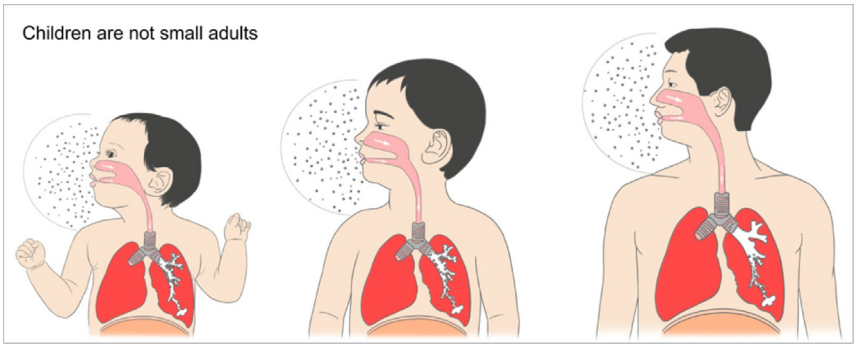
Qihong Deng [a,b,*], Cuiyun Ou [a], Jiao Chen [a], Yuguang Xiang [a]

[a] School of Energy Science and Engineering, Central South University, Changsha, China
[b] XiangYa School of Public Health, Central South University, Changsha, China

HIGHLIGHTS

- Particle deposition in the tracheobronchial (TB) airways was examined using computational fluid dynamics.
- Particle deposition in the TB airways of an infant or child is higher than that for an adult.
- Particles are deposited in the upper airways to a greater extent than in the lower for an infant.
- Particles are deposited in the lower airways more than in the upper airways for an adult.
- Particle deposition in TB airways is related to the airway structure and deposition mechanism.

GRAPHICAL ABSTRACT



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ABSTRACT

Background: Particle deposition in human airways is important for assessing both health effects of inhaled particles and therapeutic efficacy of inhaled drug aerosols, but is not well understood for infants and children.
Objective: We investigate particle deposition in infants and children by using computational fluid dynamics (CFD), and compare this with particle deposition in adults.
Methods: We chose three population age groups: 7-month infant, 4-year old child, and 20-year old adult. Both airway structures and breathing conditions are considered to vary as a human grows from infancy to adulthood. We investigated deposition of micron-size particles (1–10 μm) in both the upper (G3–G6) and lower (G9–G12) tracheobronchial (TB) airways under sedentary conditions.
Results: We found that particle deposition in both upper and lower airways is the highest in an infant, next in a child, and lowest in an adult. As age increases, particle deposition decreases in the upper airways but increases in the lower. For infants, inertial impaction is the dominant deposition mechanism, thus particles are deposited more in the upper airways than in the lower. However, particles are deposited more in the lower airways than in the upper in adults, as gravitational sedimentation is the dominant deposition mechanism.
Conclusion: Given the differences in the airway structure and particle deposition mechanisms, particle deposition in infants and children differs from that in adults, not only in the efficiency of deposition but also in the site. Our findings provide evidence that "children are not small adults".

* Corresponding author at: School of Energy Science and Engineering, Central South University, Changsha, China.
E-mail address: qhdeng@csu.edu.cn (Q. Deng).

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1. Introduction

Particulate air pollution or particulate matter (PM) can be inhaled deep into human lungs subsequently entering the blood circulatory system and finally affecting other organs and tissues. PM has been associated with increases in mortality and morbidity all over the world (Brunekreef and Holgate, 2002; Pope and Dockery, 2006). According to an estimate of the global burden of disease in 2010, 3.2 million premature deaths and 3.1% of global disability-adjusted life years (DALY) were attributed to ambient PM (Lim et al., 2013). On the other hand, aerosol inhalation is widely used for direct administration of drugs to the respiratory tract for the treatment of pulmonary diseases (Kleinstreuer et al., 2008a; Patton and Byron, 2007). Thus, the details of particle deposition in the human respiratory tract are important to human health for assessing both the health effects of inhaled air pollutants and the efficacy of inhaled drug therapy.

Infants and children are the most susceptible population to air pollution exposure, because of their immature and developing systems, higher levels of physical activity, higher inhalation rates, and lower body weight with respect to adults (Kumar et al., 2017; Peled, 2011). PM exposure has been associated with deficits in lung function, lung function growth, increased respiratory problems, and increased number of hospitalizations for respiratory diseases in children (Heinrich and Slama, 2007). Mounting evidence further suggests that early life PM exposure can be associated with an increased risk of infant mortality (Glinianaia et al., 2004; Scheers and Nawrot, 2011) and the later development of childhood diseases (Clark et al., 2010; Deng et al., 2015).

Infants and children are also a unique population group with regard to aerosol inhalation therapy (Tenenbaum et al., 2016). Pediatric patients are different from adult patients with respect to airway anatomy and breathing patterns (Amirav and Newhouse, 2012). However, the vast majority of drugs and devices that are prescribed for these populations have been designed and approved based on studies in adults. Very limited information is available on the acceptability of dosage forms in relation to the age of a child, and this warrants further study.

It is therefore crucial to evaluate particle deposition in different population age groups. Over the past few years, experimental and theoretical models have been developed to predict the total and/or regional particle deposition in human airways for different age groups. These models showed that there was higher deposition in children than in adults (Asgharian et al., 2004; Borojeni et al., 2014; Ginsberg et al., 2008; Musante and Martonen, 2000; Oldham et al., 1997). Computational fluid dynamics (CFD) modeling has recently attracted more attention since it is able to provide detailed information on local particle deposition patterns. It can identify hot spots that are more relevant to health outcomes than information regarding the total or regional deposition (Balashazy et al., 2003; Hofmann, 2011; Kleinstreuer et al., 2008b; Longest and Holbrook, 2012). However, very few CFD studies investigating particle deposition in the respiratory airways of infants and children have so far been reported (Xi et al., 2012).

The objective of our study is to investigate particle deposition in human tracheobronchial (TB) airways for infants, children, and adults using CFD modeling. We considered that both airway structure and breathing conditions vary as a human grows from birth to adulthood. We compared the micron-size particle deposition in both upper and lower TB airways. Results of this study may lead to a better understanding of the effects of developmental respiratory physiology on children's health response to particulate air pollution and the medical outcome from aerosol inhalation therapy.

2. Methods

2.1. Airway models for infant, child, and adult

According to the age classifications used by the United States Food and Drug Administration (Montnemery et al., 2003) and the World Health Organization (WHO) (Kwok and Chan, 2014), we consider an infant at 7 months old, a child at 4 years old, and an adult at 20 years old.

The human respiratory system consists of 24 generations (G0–G23) of airway branches (Martini, 2002), beginning at the trachea (G0) and ending in the alveoli (G23). The respiratory system can be divided into two zones, the TB conducting airways (G0–G16) and the respiratory zone (G17–G23), as shown in Fig. 1 (Martini, 2002). A planar and symmetric model was assumed (Weibel, 1963) and we adopted the detailed mathematical description of the geometry of airway bifurcations suggested by (Hegedus et al., 2004). For our study, we selected two regions, the upper airways G3–G6 and the lower airways G9–G12 (Fig. 1). To consider the age effect, the TB airways were scaled to represent the growing lungs at different ages (Hofmann, 1982; Isaacs and Martonen, 2005). The detailed geometric parameters for the airways of an infant, child, and adult are given in Table 1.

2.2. Governing equations

2.2.1. Airflow

In the conducting airways, the airflow can be assumed to be laminar (Kleinstreuer et al., 2007). The three-dimensional Navier-Stokes equations for airflow are as follows:

$$\nabla \cdot \mathbf{v} = 0 \tag{1}$$

$$\rho(\mathbf{v} \cdot \nabla)\mathbf{v} = -\nabla p + \mu\nabla^2\mathbf{v} \tag{2}$$

where $\mathbf{v}$ is velocity vector and p is static pressure. The density and dynamic viscosity of the air are $\rho = 1.225\ kg/m^3$ and $\mu = 1.789\times10^{-5}$ kg/(m·s), respectively.

2.2.2. Particle transport

In the selected conducting airways (G3–G6 and G9–G12) models, we only consider micron-size particles (d_p = 1–10 μm) meaning that only inertial impaction and gravitational sedimentation deposition mechanisms are considered (Kleinstreuer et al., 2007). The trajectory equation for particle transport can be written as:

$$\rho_P d_p \frac{d^2\mathbf{x}_p}{dt^2} = \frac{3}{4}\rho C_D(\mathbf{v}-\mathbf{v}_p)|\mathbf{v}-\mathbf{v}_p| + \rho_P d_p \mathbf{g} \tag{3}$$

where $\mathbf{x}_p$ is particle displacement, $\mathbf{v}_p$ is particle velocity, $\mathbf{g}$ is gravity vector, C_D is drag coefficient, and ρ_p and d_p are respectively particle density and diameter.

2.3. Inhalation and boundary conditions

2.3.1. Inhalation conditions

We assumed steady inhalation and sedentary conditions. The inhalation airflow rate is defined as:

$$Q_{in} = 2fV_T \tag{4}$$

where f is the breathing frequency (breath/min) and V_T is the tidal volume (ml/breath). Based on reported data (Hofmann, 1982), the inhalation rates were set to be 2.94 L/min for an infant, 6.69 L/min for a child, and 14 L/min for an adult (Table 2).

2.3.2. Boundary conditions

For the airflow field, a no-slip condition is applied on the airway walls, a uniform velocity profile is assumed at the inlet according to above inhalation conditions, and a pressure-outlet boundary condition is assumed at the outlets. For the particle transport calculation, the mono-disperse particle profile is injected at the inlet with the same velocity as the airflow, a trap condition is applied on the airway walls with the assumption that particles are deposited once they touch the wall surfaces, and an escape condition is employed at the outlets.