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Penetration of inhaled aerosols in the bronchial tree

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ABSTRACT

It has long been recognized that the pattern of particle deposition in the respiratory tree affects how far aerosols penetrate into the deeper zones of the arterial tree, and hence contribute to either their pathogenic potential or therapeutic benefit. In this paper, we introduce an anatomically-inspired model of the human respiratory tree featuring the generations 0–7 in the Weibel model of respiratory tree (i.e., the conducting zone). This model is used to study experimentally the dynamics of inhaled aerosol particles (0.5–20 µm aerodynamic diameter), in terms of the penetration fraction of particles (i.e., the fraction of inflowing particles that leave the flow system) during typical breathing patterns. Our study underline important modifications in the penetration patterns for coarse particles compared to fine particles. Our experiments suggest a significant decrease of particle penetration for large-sized particles and higher respiratory frequencies. Dimensionless numbers are also introduced to further understand the particle penetration into the respiratory tree. A decline is seen in the penetration fraction with decreasing Reynolds number and increasing Stokes number. A simple conceptual framework is presented to provide additional insights into the findings obtained.

1. Introduction

Breathing is the way that the respiratory tree interacts with the outside environment. The act of inspiring brings to the respiratory tree not only air, but also aerosol particles [1–3]. The study of the deposition and distribution of inhaled aerosols is essential to the understanding of both the health risks associated with inhaled environmental aerosols and the therapeutic dose delivered by inhaled pharmacological drugs.

Aerosol particles have variable sizes, composition, and shapes [1,4–6]. The sizes of aerosols cover a wide diameter range, and they are classified into two different modes: fine particles (aerodynamic diameter less than 2.5 µm) and coarse particles (aerodynamic diameter equal or larger than 2.5 µm). The respiratory system consists of upper respiratory tract (i.e., it comprises nasal and oral cavities to the larynx) and the lower respiratory tract (i.e., it comprises trachea to the alveolar sacs) [7–9]. The latter can be further divided into a conducting zone and a respiratory zone. Mucus coats the passageways of the conducting zone, which conducts air from the trachea to the gas exchange surfaces found in the respiratory zone.

In the flow of suspensions through the respiratory tree, dispersion and deposition of aerosol particles may occur in the airways. Dispersion is influenced by the rhythmic pattern of inhalation and exhalation flows through the branching site [10,11]. It impacts how far particles penetrates into the airways, and is responsible by a larger flow of suspension of particles into deeper regions of the respiratory tree than would be expected by a steady flow [10,11]. Particles suspended in the air which hit the side wall of the airways are trapped (deposited) in this mucus layer [8,9]. The fraction of the aerosol particles that can penetrate into the respiratory system is classified as: inhalable (i.e., fraction of aerosols that can be breathed into the nose or mouth), thoracic (i.e., fraction of particles that can penetrate the head airways and enter the conducting zone of the respiratory tree), and respirable (i.e., fraction of inhaled aerosols that can penetrate beyond the terminal bronchioles into the respiratory zone) [12,13]. For noncharged particles the major mechanisms by which aerosols deposit are inertial impaction, gravitational sedimentation, diffusion, interception and Brownian diffusion [1,4,14]. The importance of these mechanisms for deposition depends on the characteristics of particles (size and density), the air velocity through the airway, and the geometry of the airways. Particles with a high momentum are unable to adjust direction and often deposit by inertial impaction. Particles less than 0.5 µm in size are likely to experience Brownian diffusion. Gravitational sedimentation is a mechanism of deposition that affects particles in the size range of 2–5 µm at respiratory zone of the air-

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ways [14]. Once deposited in the respiratory tree, inhaled aerosol particles are either cleared from the tree or absorbed into the systemic circulation. It is important to note that blood flow from the trachea to the terminal branches represents 1% of the cardiac output (in bronchiectasis disease it can reach ∼30%), and is via the systemic circulation [15].

The literature dealing with the aerosol dynamics through the respiratory tree includes experimental and numerical studies. Numerical investigations consist in solving equations for the airflow and for the transport and deposition of aerosol particles in a representation of the respiratory tree. Comprehensive reviews of this literature are presented by Asgharian et al. [16], Kleinstreuer and Zhang [17], Hofmann [18], Di et al. [19], and Rostami [20]. Experimental determination of particle deposition in the respiratory tree may be obtained in airway models, in airway casts, and from animal toxicological studies. Since the study reported by Kim and Iglesias [21] in single bifurcation tube models, several works have been published. Kim and Fisher [22] studied deposition in double bifurcation tubes (size similar to the 3rd–5th generation bronchial airways) using monodispersed particles with diameter ranging from 2.9 to 6.7 µm. Zhou and Cheng [23] studied aerosol deposition patterns in the tracheobronchial replica (trachea and four generations of bronchi) made from an adult cadaver. Monodispersed particles in the size range of 0.93–30 µm were generated as test aerosols and were drawn through the lung cast with the airflow rates ranging from 15 to 60 l/min. Comprehensive reviews of this experimental literature can be found, for example, in Islam and Cleary [1], Inthavong et al. [3], Kim [24], Wang et al. [25], and Kleinstreuer and Feng [26]. To our best knowledge, there has not been any study on the deposition of particles from the trachea (generation 0) all the away to the generation 7.

Data from animal studies may be also used to assess the deposition to humans. This approach has limitations since, the fate of inhaled aerosols is very like to differ based on anatomical factors [27,28]. Anatomical differences are not only on macroscopic scale but also on microscopic scale, and they influence airflows rates and residence times, and thus the dynamics of aerosol particles.

Here, we study experimentally inhaled particle dynamics within the respiratory tree. Using glass fiber tubing, a true-scale model of the generations 0–7 in the Weibel model of respiratory tree was constructed to study aerosol transport under different respiratory frequencies. The study was performed in conditions of humidity near saturation to account for the conditions occurring in the respiratory tree.

2. Materials and methods

2.1. Tree network of airways

The respiratory tree consists of a network of tubes in which each tube splits into two daughter tubes [8,29,30]. This dichotomous branching follows the relationship known in physiology as the Hess–Murray law [29,30]. The idea behind this law is that the diameters of parent and two equal daughter tubes are related as $2^{1/3}$ [31]. By following this geometric ratio between the diameters of daughter and parent vessels, the entropy generation upward and downward the bifurcation is the same [32]. Bejan et al. [33] also found a similar relationship between the length of parent and the lengths of equal daughter tubes (i.e., the cube of the length of a parent vessel should equal the sum of the cubes of the lengths of the daughter vessels). These third-power rules are justified based on the minimization of the energy required to synthesize, maintain and pump fluid (principle of minimum work) [31], or on the minimization of hydraulic resistance (maximum flow access) in a constrained space [33].

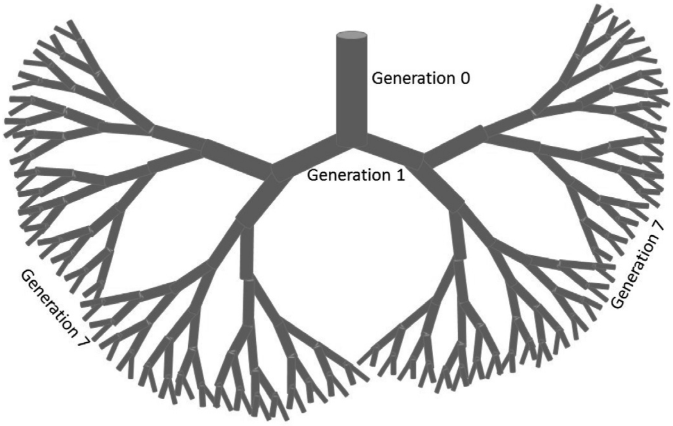

Fig. 1. Schematic representation of a dichotomous tree-shaped flow network corresponding to a 0–7 generation bifurcation of Weibel model [34].

Here we adopt Weibel's model [34], which the human respiratory tree is viewed as repeated bifurcations from the trachea (generation 0, G0) to the alveoli (generation 23, G23). The tree network tested in this study is made of cylindrical tubes made of glass fiber (Fig. 1), and corresponds to the generations 0–7 of respiratory tree. In order to project this network of tubes, we apply the allometric scaling law for diameters and lengths (i.e., diameters or lengths of parent and daughter tubes are related as $2^{1/3}$), to ensure that this tree network represents this part of the respiratory tree as closely as is possible. The first tube (G0) is 12 cm in length, with an internal diameter of 2 cm, and reproduces the size of the trachea (the normal human trachea has a length of 10–12 cm and a diameter of 1.5–2.0 cm [8,9]).

The number of tubes (exits), $N_{\mathrm{tubes(exists)}}$, for the network can be obtained from

$$N_{\mathrm{tubes(exits)}} = 2^n \tag{1}$$

where n is the number of generations beginning at G0 and ending at G7 ($n = 7$).

As mentioned, our G0–G7 tree was constructed based on the relationship that the sizes between parent and daughter tubes is $2^{1/3}$ [29–33]. Therefore, the size of the first tube (G0) and the size of any tube at level n (Gn), are related according to

$$\frac{D_n}{D_0} = 2^{-n/3} \tag{2}$$

$$\frac{L_n}{L_0} = 2^{-n/3} \tag{3}$$

where D_n and L_n are the diameter and length of the tube at level n, respectively. For tubes with cylindrical shape, the volume V of the network can be calculated as follows

$$V = \frac{\pi}{4}\sum_{i=0}^{n} 2^i D_i^2 L_i = \frac{\pi}{4} D_0^2 L_0 (n+1) \tag{4}$$

Table 1 summarizes the geometric characteristics of the tree network of glass fiber tubes used to study the transport of aerosol particles.

2.2. Test aerosol

Alumina particles (Al_2O_3) of 0.5 to 20 µm are selected for this study [35]. Notably, it includes particles in the size range of fine and coarse particles. A fluidized bed aerosol generator (3400A, TSI Inc.) is used to disperse these particles. As recommended by the manufacturer, in this generator, bronze beads are used to break up

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