Electrostatic Charge Polarity Effect on Respiratory Deposition in the Glass Bead Tracheobronchial Airways Model

Mohammed Ali  
*University of Arkansas at Little Rock, mxali@ualr.edu*

Malay K. Mazumder  
*University of Arkansas at Little Rock*

Rama N. Reddy  
*University of Arkansas at Little Rock*

Mariofanna Milanova  
*University of Arkansas at Little Rock*

Jing Zhang  
*University of Arkansas at Little Rock*

*See next page for additional authors*

Follow this and additional works at: [http://scholarworks.uark.edu/jaas](http://scholarworks.uark.edu/jaas)

Part of the [Circulatory and Respiratory Physiology Commons](http://scholarworks.uark.edu/jaas/vol61/iss1/5)

**Recommended Citation**
Ali, Mohammed; Mazumder, Malay K.; Reddy, Rama N.; Milanova, Mariofanna; Zhang, Jing; and Biris, Alexandru S. (2007)  
"Electrostatic Charge Polarity Effect on Respiratory Deposition in the Glass Bead Tracheobronchial Airways Model," *Journal of the Arkansas Academy of Science*: Vol. 61 , Article 5.  
Available at: [http://scholarworks.uark.edu/jaas/vol61/iss1/5](http://scholarworks.uark.edu/jaas/vol61/iss1/5)

This article is available for use under the Creative Commons license: Attribution-NoDerivatives 4.0 International (CC BY-ND 4.0). Users are able to read, download, copy, print, distribute, search, link to the full texts of these articles, or use them for any other lawful purpose, without asking prior permission from the publisher or the author.

This Article is brought to you for free and open access by ScholarWorks@UARK. It has been accepted for inclusion in *Journal of the Arkansas Academy of Science* by an authorized editor of ScholarWorks@UARK. For more information, please contact scholar@uark.edu, ccmiddle@uark.edu.
Electrostatic Charge Polarity Effect on Respiratory Deposition in the Glass Bead Tracheobronchial Airways Model

Authors
Mohammed Ali, Malay K. Mazumder, Rama N. Reddy, Mariofanna Milanova, Jing Zhang, and Alexandru S. Biris

This article is available in Journal of the Arkansas Academy of Science: http://scholarworks.uark.edu/jaas/vol61/iss1/5
Electrostatic Charge Polarity Effect on Respiratory Deposition in the Glass Bead Tracheobronchial Airways Model

MOHAMMED ALI, MALAY K. MAZUMDER, RAMA N. REDDY, MARIO FANNA MILANOVA, JING ZHANG, AND ALEXANDRU S. BIRIS

1Donaghey College of Information Science and Systems Engineering, University of Arkansas at Little Rock
ETAS 575, 2801 S. University Ave., Little Rock, AR 72204, USA

Abstract.—The effects of unipolar and bipolar electrostatic charges on the deposition efficiency of therapeutic aerosols in the physical model of human tracheobronchial (TB) airways have been investigated. Respirable size aerosol particles were generated by a commonly prescribed and commercially available nebulizer and charged by a corona charger and then their size and charge distributions were characterized by an Electronic Single Particle Aerodynamic Relaxation Time analyzer to study the drug aerosol particles’ deposition pattern. The experiments were performed with a glass bead tracheobronchial model (GBTBM) (physical model) which was designed and developed based upon widely used and adopted dichotomous lung morphometric data presented in the Ewald R. Weibel model. The model was validated with the respiratory deposition data predicted by the International Commission on Radiological Protection and the United States Pharmacopeia (USP) approved Andersen Cascade Impactor (ACI). Unipolarly and bipolarly charged particles were characterized for two configurations: a) without TB model in place and b) with TB model in place. Findings showed that the deposition of unipolarly charged particles was about 3 times of the bipolarly charged particles. It was also found that bioengineered therapeutic aerosols with good combinations of aerodynamic size and electrostatic charge are good candidates for the administration of respiratory medicinal drugs.

Key words.— unipolar electrostatic charges , bipolar electrostatic charges, therapeutic aerosols, tracheobronchial (TB) airways, human, nebulizer, corona charger, Electronic Single Particle Aerodynamic Relaxation Time, deposition efficiency, dichotomous lung morphometric data, Ewald R. Weibel model, International Commission on Radiological Protection, Andersen Cascade Impactor (ACI),

Introduction

A physical lung model that closely approximates the flow characteristics, surface area, and aerosol deposition patterns of the human lung could serve as a surrogate lung for in-vitro studies during the development of respiratory medicines and inhalation drug-delivery devices. The model will not only be beneficial for studies of regional lung deposition but will also eliminate safety issues and variabilities that are inherent with the use of human subjects. The human respiratory tract is an aerodynamic classifying system for inhaled particles (USEPA 1998). A sampling device can be used as a substitute for the respiratory tract as a particle collector, and it can effectively simulate the mechanisms of electromechanical deposition of the inhaled particles including inertial impaction, gravitational settling, interception, diffusion, and electrostatic force (Fig. 1).

Others have shown that a physical lung model simulated by a multi-layer granular bead filter provides a good approximation of the deposition detected in the in vivo experimental data (Altshuler et al. 1957). Gebhart and Heyder (1985a) developed the first granular bead filter to use as a surrogate for human subjects in their study of aerosol deposition. The filter consisted of a 30-cm long by 15.24-cm diameter acrylic cylinder, sealed by a cone at each end. The cone and cylinder were packed with 2.5-mm glass beads, resulting in airspace of approximately

Fig. 1. Electromechanical deposition mechanisms of drug aerosols in the human lung.

2 L. Their model had several limitations. (A) It possessed a single passageway to simulate all respiratory airways though parameters of successive branching airways differ widely. (B) It was geometrically dissimilar with in vivo anatomy, and (C)
Electrostatic Charge Polarity Effect on Respiratory Deposition in the Glass Bead Tracheobronchial Airways Model

it was unable to test site-specific deposition for corresponding regions of the respiratory tract (Gao 1994).

Numerical analyses show that only 31% of 0.5 μm, 61% of 2 μm, and 63% of 5 μm drug particles deposit due to inertial impaction when the particles contain no elementary charge (Hinds 1998, p. 241). Besides, in-vitro investigation of metered dose inhaler and dry powder inhaler aerosols demonstrated that both respiratory drug delivery devices generate bipolarly charged particles (Glover and Chan 2003). Additionally, several studies have found that the electrostatic charge force influences particle deposition in the human lung along with other deposition mechanisms (Yu 1977, Gebhart and Heyder 1985b, Melandri et al. 1983, Hashish et al. 1994, Balachandran 1997, Bailey et al. 1998, Cohen et al. 1998).

In order to study the regional deposition of aerosol particles, it was necessary to design a multi-Stage models to simulate various regions of the lung anatomy. We designed and developed a physical tracheobronchial model using a USP metal throat, and 2 packed beds (Stages) of glass beads in the shape of a wedding cake (Figure 2), hereafter referred to as the Glass Bead Tracheobronchial Model (GBTBM). Since the GBTBM was constructed to mimic flow parameters and dimensions of the lung airways, it could simulate all 5 mechanisms of deposition of inhaled aerosol particles. The objectives of the current work were to (a) design and develop 2 layers of glass-bead filters to serve as a surrogate for tracheobronchial regions of respiratory airways, (b) investigate the particle deposition of pharmaceutical aerosols generated by a commercially available nebulizer, (c) validate the deposition efficiencies proposed by the International Commission on Radiological Protection (ICRP) deposition model, and (d) study the combined effects of aerosol particle size and charge on deposition in the GBTBM.

Materials and Methods

Mathematical Model.—A mathematical model was first developed to establish the basis for the design and construction of the GBTBM. Motion of a spherical particle in a given geometry is affected by the Stokes number $St_k$, particle size, flow Reynolds number $Re_{flow}$, and non-dimensional settling velocity (Zhang and Finlay 2005, Kim et al. 1994, Schlesinger et al. 1977, Chan & Schreck 1980). It is notable that Stokes number was originated from Stokes's law by solving the unsolvable Navier-Stokes equation based upon several assumptions (Hinds 1998). One of them was that the fluid should be incompressible, which is unlikely in case of drug aerosols. Additionally, in practice, Stokes law is restricted to situations in which flow Reynolds number is less than 1.0 (Hinds 1998). For an inhalation rate of 28.3 L/min, the flow Reynolds number in the tracheobronchial region is very high ($Re_{flow} >> 1.0$). Therefore, the simulation of Stokes number in this study was not considered. Besides, like an asthmatic patient the similar kind of drug aerosols and inhalation rate were used in the GBTBM experiments, which conform that both particle size and non-dimensional settling velocity were also simulated as well. Since the flow Reynolds number determines the nature of the flow, it can simulate the characteristics of 2 fluid flows and the flow profiles irrespective of the actual dimensions of the aerosol flows. Therefore, various regions of the lung can be classified according to the Reynolds numbers of the air flows in the respiratory airways for a given inhalation flow rate. Our calculations, beginning from the Reynolds numbers can be used to calculate the diameter and the number of glass beads for each Stage. Mathematically, the Reynolds number of a fluid flow can be determined from Equation 1.

$$Re = \frac{2D_b v_s} {3\ell (1 - \hat{a})}$$

(1)

where $Re =$ Reynolds number, $D_b =$ packed bed diameter, $v_s =$ superficial velocity through the pipe, $\rho =$ aerosol particle density, $\mu =$ aerosol viscosity, and $\hat{a} =$ bed porosity. The other parameters of the GBTBM were calculated from Equations 2–6.

(2) Superficial velocity due to the packed bed, $v_s = v_m \hat{a}$

(3) Volumetric flow rate through the Stage, $q_v = (\pi/4)D^2 v_m$

(4) Volume of glass beads, $V_g = (\pi/4)D_l^2 L (1 - \hat{a})$

(5) Number of beads, $n = V_g / (\pi/6)d_s^3$

(6) Total surface area of the beads = $n\pi d_s^2$

Where $v_m$ is the average velocity of aerosol flow through the packed bed an approximation based on the range of air velocity from Weibel’s model, $d_s =$ glass bead diameter, $D =$ bed (Stage) diameter, and $L =$ Stage length. Table 1 shows the design parameters of the GBTBM Stages 1 and 2.

<table>
<thead>
<tr>
<th>Design parameter</th>
<th>Stage 1: Trachea</th>
<th>Stage 2: Main and Lobar Bronchi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flow rate through Stage, Q, l/min</td>
<td>28.3</td>
<td>28.3</td>
</tr>
<tr>
<td>Bed Porosity, $\hat{a}$</td>
<td>0.38</td>
<td>0.36</td>
</tr>
<tr>
<td>Mean velocity on packed bed, $v_m$, cm/s</td>
<td>381.5</td>
<td>234.53</td>
</tr>
<tr>
<td>Superficial velocity through Stage, vs, cm/s</td>
<td>145.73</td>
<td>84.43</td>
</tr>
<tr>
<td>Stage diameter, D, cm</td>
<td>2.03</td>
<td>2.67</td>
</tr>
<tr>
<td>Stage Length, L, cm</td>
<td>18.875</td>
<td>18.733</td>
</tr>
<tr>
<td>Volume of the inside Stage, Vp, cm$^3$</td>
<td>61.09</td>
<td>104.65</td>
</tr>
<tr>
<td>Total volume of beads needed, $V_g$, cm$^3$</td>
<td>37.88</td>
<td>66.98</td>
</tr>
<tr>
<td>Bead diameter, dg, cm</td>
<td>1.37</td>
<td>1.1</td>
</tr>
<tr>
<td>Number of glass beads, n</td>
<td>28</td>
<td>50</td>
</tr>
<tr>
<td>Surface area of packed bed, cm$^2$</td>
<td>165.88</td>
<td>293.33</td>
</tr>
<tr>
<td>Reynolds number of packed bed, Re</td>
<td>2135</td>
<td>1198</td>
</tr>
<tr>
<td>Reynolds number in Weibel’s model, Re</td>
<td>2213</td>
<td>1241</td>
</tr>
</tbody>
</table>

http://scholarworks.uark.edu/jaas/vol61/iss1/5
Glass Bead Tracheobronchial Physical Model.—Figure 2 shows the GBTBM and the corresponding simulated regions of the human respiratory tract. The dimensions of the lung airway regions were based upon widely used and adopted symmetric and dichotomous lung morphological data in Ewald R. Weibel lung model with some modification due to the more recently published data of Horsfield et al. (Weibel 1963, Horsfield et al. 1971).

Weibel's model portrays the common and standard understanding of human lung anatomy. It divides the human respiratory tract into 24 generations (from G0 to G23). Since inception, it has been regarded as a detailed anatomical approach to lung morphology, the model was tested and validated with experimental results. Weibel's morphometric data provide specific length, diameter, area, and volume for each generation. In our model, Stage 1 simulated the trachea, the first generation (G0) of the respiratory tract (Figure 2). Stage 2 simulated the main and lobar bronchi, the second, third, and fourth generations (G1–G3) of the respiratory tract. Each of these Stages was stacked one on top of the other with wire-mesh supports to maintain the flow of aerosol for uniform distribution over each Stage. Each lung region was represented by a glass-bead-packed bed with a diameter that simulated the surface area of the region and the flow Reynolds number at an inspiratory flow rate of 28.3 l/min.

Ideally, each generation of the respiratory system should be simulated by a single bed of glass beads of relevant size and thickness. However, for expediency in constructing the physical model, three generations of bronchi were represented by Stage 2 in such a way that particle deposition should not have changed significantly. In order to obtain a Reynolds number as close as possible to that of the tracheal region (2235), we made the surface area of packed bed in Stage 1 166 cm². The surface area of packed bed in Stage 2 was made 293 cm² to achieve a Reynolds number (1241) as close as possible to that of the bronchial region. The circular cylinders of the Stages 1 and 2 were made from 2.03-cm and 2.67-cm PVC pipes, respectively (American Valve™, 3/4" and 1" Fix-It Coupling PVC, Model: P232, Lowe's Companies, Inc. North Wilkesboro, NC). The sizes of the glass beads were based upon the required bed porosity in order to achieve the closest possible Reynolds numbers for a fixed inhalation flow rate (Glen Mills Inc., Clifton, NJ). The copper wire mesh supported the glass beads and maintained a uniform flow (TWP Inc., Berkeley, CA).

**Experimental Setup.**—Figure 3 depicts the experimental system, which consisted of several components addressed below.

1. In order to generate therapeutic grade aerosols, we used a nebulizer (PARI LC Plus®, Midlothian, VA) and sodium chloride solution (7 g/ml) aerosols with mass median aerodynamic diameters (MMAD) ranging between 4.0 μm and 5.5 μm.
2. A corona charger was used to charge aerosols before inhalation through the GBTBM. The charger also acted as an aerosol holding chamber (AHC) with dimensions of 21 cm x 18 cm x 21 cm (LxWxH).
3. The USP induction port was used for introducing aerosols into the GBTBM. Manufacturers also specify the use of such a USP port for introducing aerosols into the Andersen Cascade Impactor (e.g., 8 Stage Non-Viable Cascade Impactor of New Star Environmental LLC, Roswell, GA).
4. The Glass Bead Tracheobronchial Model was placed between the USP port and the aerosol isokinetic sampling chamber (ISC). The Stages 1 and 2 could be separated or connected (together or individually) with the USP port and the ISC.
5. The Electronic Single Particle Aerodynamic Relaxation Time (ESPART) analyzer was used to measure aerodynamic sizes and electrostatic charges in real time (Mazumder and Ware 1987). Its working principle was by Mazumder et al. (1989).
6. An aerosol isokinetic sampling chamber (ISC) was used to facilitate the characterization of aerosols isokinetically (Figure 3). The suction mouth of the ESPART analyzer was placed at the center of the chamber and always pointed in the direction opposite of the aerosol flow.

External clean and dry air (18.3 l/min) and nebulized aerosol (10 l/min) were delivered to the AHC to simulate a light physical activity inhalation flow rate of 28.3 l/min through the GBTBM. The flow rate was measured using an Extech Heavy Duty Hot Wire Thermo-Anemometer™ (Extech Instruments, Waltham, Massachusetts, USA). The constant inhalation rate of 28.3 l/min served two purposes. (1) The manufacturer-specified flow rate for a Mark II Andersen Cascade Impactor (ACI) is 28.3 L/min, which enabled GBTBM comparability with the ACI. (2) The vacuum pump and the ESPART could have drawn 27.3 l/min and 1 l/min, respectively. The environmental conditions such as lab temperature (20°C) and humidity (51.2%) were recorded using Testo625™ (Testo GmbH & Co., Lenzkirch, Germany) thermo-anemometer.

In order to find the aerosol particle aerodynamic size, the electrostatic charge distributions and the charging effects upon...
Electrostatic Charge Polarity Effect on Respiratory Deposition in the Glass Bead Tracheobronchial Airways Model

Results

We assumed that the both Stages of the glass bead tracheobronchial model would operate on 1 basic principle. Particles whose inertia exceeds a certain value (cutoff size) would be unable to follow the streamlines and will impact upon the packed bed. In addition, particles would deposit on the bead surfaces due to diffusion, sedimentation, interception, and electrostatic force. Thus, each Stage of the GBTBM would separate aerosol particles into 2 size ranges; particles larger than the cutoff size will be removed from the aerosol stream, and particles smaller than that size will remain airborne and pass through the Stage. As a result, each Stage of the GBTBM will be characterized by a cutoff diameter. Figure 4 shows the cutoff curves, or collection-efficiency curves, of the glass bead tracheobronchial model Stages 1 and 2.

The deposition fraction will be defined as the ratio of the number of particles removed from the aerosol (i.e., deposited) while traveling through the GBTBM to the number of particles originally entering it. Table 2 shows the normalized data from

![Fig. 3. Schematic of the experimental arrangement designed to measure aerodynamic diameters and electrostatic charges of the aerosol particles with and without passing through the glass bead tracheobronchial model.](image)

![Fig. 4. Comparison of the aerosol particle collection efficiency curves of the glass bead tracheobronchial model Stages 1, 2 and without the GBTBM.](image)
10 runs for uncharged particles for experimental scenarios 1.a, 2.a, and 3.a. Table 2 also summarizes the coefficient of variation (COV), count median aerodynamic diameter (CMAD), mass median aerodynamic diameter (MMAD), and the deposition fraction of uncharged particles in the GBTBM Stages 1 and 2.

Table 2. Summary of the normalized data of uncharged particle and deposition efficiency in the glass bead tracheobronchial model (GBTBM).

<table>
<thead>
<tr>
<th>Experimental Scenario</th>
<th>Uncharged Particle</th>
<th>Charged Particle</th>
<th>CMAD</th>
<th>MMAD</th>
<th>DF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>COV</td>
<td>+ ve</td>
<td>(µm)</td>
<td>- ve</td>
<td>SD</td>
</tr>
<tr>
<td>(1.a) By-passed GBTBM Stages</td>
<td>6470</td>
<td>21</td>
<td>3.21</td>
<td>8</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>0.01</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(2.a) Inhaled through GBTBM Stage 1</td>
<td>5085</td>
<td>27</td>
<td>3.18</td>
<td>14</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>0.002</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(3.a) Inhaled through GBTBM Stage 1 &amp; 2</td>
<td>4466</td>
<td>47</td>
<td>3.08</td>
<td>22</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>0.004</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- COV = coefficient of variation
- CMAD = count median aerodynamic diameter
- MMAD = mass median aerodynamic diameter
- SD = standard deviation
- DF = deposition fraction.

Table 3 shows the normalized data from 10 runs of charged particles for experimental treatments 1b and 3b. It also summarizes the coefficient of variation (COV), count median aerodynamic diameter (CMAD), mass median aerodynamic diameter (MMAD), electrostatic net charge-to-mass ratio, and the deposition fraction in the GBTBM Stages 1 and 2 combined.

Figure 5 shows a comparison of the respiratory deposition fraction in the GBTBM airways to the International Commission on Radiological Protection tracheobronchial (ICRP TB) airways for the respirable range aerosol particles. Although the basic ICRP deposition curve was developed for particles in the size range of 0.001 µm – 100 µm, we have compared our GBTBM with the ICRP’s respirable (therapeutic) size range (0.5 µm - 10 µm) portion only.

Figure 6 shows the comparison of the cumulative respiratory deposition fraction of bipolar-charged versus unipolar-charged aerosols in the GBTBM airways.
**Discussion**

In this study, we are reporting physical simulations of the tracheobronchial airways of the human lung were reported. We have demonstrated the model's design and development validity. Secondly, our model showed a consistency with the ICRP66 Model in particle deposition for particles in the therapeutic aerosol particle size range. Finally, it showed the deposition pattern of bipolar versus unipolar-charged aerosol particles in the GBTBM.

*Validation of the Design and Development of the GBTBM.* A 2-Stage GBTBM was designed and developed to simulate the human respiratory tract Generation 0 (trachea, G0) and Generations 1, 2, and 3 (main and lobar bronchi, G1-G3), respectively. The first Stage simulated Reynolds number was 2135, which was in close approximation with the flow Reynolds number in the trachea of 2213 (ideal case) for an inhalation flow rate. The second Stage simulated Reynolds number was 1198, which was also in close approximation with the average Reynolds number of 1241 for the first, second, and third bronchi for the given inhalation flow rate. However, for convenience in constructing the physical model and to achieve the closest possible flow parameters, the surface areas of the packed bead Stages were 5 and 17 times the *in vivo* surface areas, respectively. In spite of these differences in surface areas between the actual tracheobronchial morphology and the GBTBM, simulated depositions are in accordance with previous studies conducted by the ICRP (ICRP66 1994). The collection efficiency or cutoff points of the GBTBM Stages are in the range of 1 μm - 3 μm, which showed the lowest deposition in the tracheobronchial regions. We observed that the most efficient bipolar charged particles were in the size range of 1 μm - 3 μm, which showed the lowest deposition in the tracheobronchial region (Figure 6). This finding suggests that bioengineered therapeutic aerosols with good combinations of aerodynamic size and electrostatic charge are good candidates for the administration of pulmonary medicinal drugs.

Compared to the commonly used ACI aerodynamic classifying system, which provides a quick estimation for aerosol depositions, the GBTBM described in this paper offers a more detailed description of aerodynamic size and electrostatic charge distribution of the deposited particles (Figures 4, 5, and 6). Whereas the ACI Stages are made of electrically conductive materials, the GBTBM Stages are not. This is a limitation that can be overcome in the production of future GBTBMs by constructing Stage cylinders of similarly conductive materials.

**Conclusions**

A two-Stage GBTBM of the upper airways of the human lung has been designed, developed, and realized. It is comparable to the Mark II ACI. In addition, the GBTBM simulated by packed bed media is simple, inexpensive, and a prospective model for the *in-vitro* investigation of aerosolized drug delivery. The respirable size range for therapeutic aerosols deposition in the GBTBM is comparable with the mathematical and theoretical results reported in the ICRP66 model. Bipolar aerosol particles, or particles balanced with positive and negative polarity, pass through the tracheobronchial regions more successfully than the unipolar charged aerosol particles and provide better delivery to the bronchiolar and alveolar regions of the human lung. Our study is an important step in finding an alternative to the ACI, which is unable to simulate the interactive behaviors of deposition mechanisms in respiratory airways.
Mohammed Ali, Malay K. Mazumder, Rama N. Reddy, Mariofanna Milanova, Jing Zhang, and Alexandru S. Biris

**Literature Cited**


