

**DOSIMETRY/EXPOSURE INDEX OF FIBER AEROSOL
IN HUMAN RESPIRATORY TRACT**

Final report on research carried out under NIOSH Research Grant

RO1 OH003900

Prepared by

Principal Investigator: Yung Sung Cheng, Ph.D.

Research carried out at: Lovelace Respiratory Research Institute

2425 Ridgecrest Dr. SE, Albuquerque, NM 87108

October 2008

TABLE OF CONTENTS

	<u>Page</u>
LIST OF TERMS AND ABBREVIATIONS.....	3
ABSTRACT	5
HIGHLIGHTS/SIGNIFICANT FINDINGS.....	6
TRANSLATION OF FINDINGS.....	7
OUTCOME/RELEVANCE/IMPACT.....	8
BODY OF REPORT	9
BACKGROUND	9
SPECIFIC AIMS	10
SPECIFIC AIM 1.....	11
Materials and Methods	11
1. Human Nasal Airway Cast.....	11
2. Human Respiratory Airway Casts	12
3. Fiber Materials.....	14
4. Experimental Setup	16
5. Sample Preparation, Fiber Counting and Length Measurement.....	18
Results.....	20
1. Fiber Deposition Efficiency in the Human Nasal Airway.....	20
2. Comparison of Nasal Deposition between Fibers and Compact Particles	22
3. Fiber Deposition in the Human Oral Airway	23
4. Fiber Deposition in the Tracheobronchial Airways	27
SPECIFIC AIM 2.....	28
Methods	28
1. Nasal Airway.....	28
2. Tracheobronchial Airways.....	29
Results.....	29
1. Flow Simulation in the Nasal Airway	29
2. Deposition in the Nasal Airway	30
3. Deposition of Particles in the Human Airway Multi-Level Bifurcation Model	31
4. Deposition of Fibers in the Human Airway Multi-Level Bifurcation Model	32
SPECIFIC AIM 3.....	34
1. Comparison of Experimental and Theoretical Models	34
2. Empirical Model for Fiber Deposition in the Nasal Airway	34
3. Empirical Model for Fiber Deposition in the Oral Airway.....	35
4. Empirical Model for Fiber Deposition in the Tracheobronchial Airway.....	36
SPECIFIC AIM 4.....	37
Fiber Exposure Index	37
REFERENCES	38

LIST OF TERMS AND ABBREVIATIONS

ACGIH: American Council for Governmental Hygienists

CFD: computational fluid dynamics

CMD: count median diameter

CML: count median length

d : diameter of the airway

DE : deposition efficiency

d_{ae} : aerodynamic diameter

d_{ev} : volume equivalent diameter

F : a function of bifurcation angle and ratio of parent to daughter radii defined in Equation (13)

g : the gravitational acceleration

IP: impaction parameter ($d_{ae}^2 Q$)

MMVF: man-made vitreous fibers

MRI: magnetic resonance imaging

p : pressure

Q : flow rate

R^2 : coefficient of determination

R : diameter of an airway tube

R_o : diameter of the parent airway tube

SSPD: small-scale powder disperser

Stk : Stokes number

ST: thoracic fraction of inhaled fiber

SVF: synthetic vitreous fibers

U : mean velocity in the airway

u : the fluid velocity

u^* : shear velocity

β : the aspect ratio of a fiber

σ_g : geometric standard deviation

$\kappa_{\perp}$: the dynamic shape factor of a fiber with its long axis parallel to the flow direction

$\kappa_{\parallel}$: the dynamic shape factor of a fiber with its long axis perpendicular to the flow direction

κ_r : the dynamic shape factor of a fiber with random orientation to the flow direction

μ : the viscosity

ρ : fiber density

ρ_0 : density of water

θ : the bifurcation angle

ABSTRACT

Inhalation exposure of fiber aerosol may have serious health consequences including lung cancers. The deposition pattern in the respiratory tract as a function of fiber dimensions is the information critical to understanding respiratory dosimetry and defining the index of exposure for health protection purposes. Controlled studies of fiber deposition in human volunteers are not available because of ethical concerns. However, total and regional depositions of inhaled fibers have been estimated from post-mortem measurement, mathematical modeling, and animal toxicity studies. Increasingly, mathematical deposition models have been used to assess the dosimetry of inhaled man-made vitreous fibers. However, current lung dosimetric models for fibers in the human respiratory tract are based on theoretical equations, which have not been verified with experimental data. This project has three objectives: (1) to develop experimental information on the deposition of fibrous aerosols as a function of fiber diameter and length in realistic human respiratory tract replicas, (2) to verify and improve the prediction of fiber dose estimates in human lungs using both empirical data as well as computational fluid dynamic technique, and (3) to define a size-selective exposure index based on fiber penetration data. In the deposition experiment, a human nasal airway cast and an oral/upper tracheobronchial airway replica were used for the study. Carbon, glass fiber, and TiO_2 fibers were used as the test material. Deposition patterns in the oral airway, nasal airways, and the tracheobronchial region were obtained as a function of fiber dimensions and inspiratory flow rate. For the test fibers, deposition efficiency increased with flow rate and square of aerodynamic diameter, indicating that impaction is the main deposition mechanism of these fibers. The computation fluid technique shows the transport of fiber in the airway and deposition mechanism. Deposition efficiencies of fibers in the nasal, oral, and tracheobronchial airways of fibers were smaller than spherical particles of the same aerodynamic diameter. This appears to be a result of the tendency of fiber to align with flow direction, resulting in lower drag in the axial flow direction. On the other hand, fibers were in the perpendicular direction with respect to the airway wall, resulting in higher drag force in that direction. The end result is that a fiber in alignment with the main flow more easily penetrates the upper respiratory tract. Lower deposition efficiencies in the oral and nasal airways implied higher penetration of fibers into the lower airway regions. Fiber deposition equations in the nasal, oral, and tracheobronchial airways were developed and can be used in the fiber lung deposition model. Because lung diseases caused by inhaled fibers occur in the bronchial, alveolar, and parachymal regions, a thoracic fraction defined as the fraction of particles penetrating the larynx and reaching the lung was defined from the experimental data obtained in this study. The experimental data show that the thoracic fraction of fiber aerosol is different from that of spherical particles obtained in this study. This research also produced essential information on the dosimetry of inhaled fibers in the human lung, data for an improved mathematical lung deposition model, and a definition of the thoracic fraction of fibers for exposure assessment. Sampling devices based on this size-selection definition can be developed in the future for improved assessment of worker exposure.

HIGHLIGHTS/SIGNIFICANT FINDINGS

- (1) Fibers with diameter greater than $0.5\ \mu\text{m}$ deposit in the nasal, oral, and tracheobronchial airways; the deposition efficiency increases with flow rate and square of aerodynamic diameter, indicating that impaction is the main deposition mechanism.
- (2) Deposition efficiency of fiber aerosols in the nasal, oral, and tracheobronchial airways is lower than deposition efficiency of the spherical particles of the same aerodynamic diameter.
- (3) Penetration of fiber aerosol through the nasal, oral, and upper tracheobronchial regions is higher than spherical particles of the same aerodynamic diameter, indicating that even long fibers could penetrate to the lower portion of the lung.
- (4) Empirical deposition equations for nasal, oral airway, upper tracheobronchial impaction mechanism have been developed from the data.
- (5) Comparison of experimental deposition data and theoretical models of fibers showed that only a numerical calculation based on computational fluid dynamics (Zhang et al., 1996) is in general agreement. But that theory was based on fiber deposition in a simple bifurcation and did not agree with experimental data in every case.
- (6) An empirical deposition equation in the tracheobronchial region was developed taking into account the bifurcation angle and diameter ratio of parent and daughter tubes.
- (7) A thoracic fraction is defined based on penetration of fibers through the oral airways. The proposed fiber thoracic fraction is different from that of spherical particles in two aspects. First, the 50% aerodynamic diameter of the curve, $15\ \mu\text{m}$, is larger than $10\ \mu\text{m}$ for spherical particles. Second, the thoracic fraction of fiber is based on fiber count or number, whereas the thoracic fraction for spherical particles is based on mass.

TRANSLATION OF FINDINGS

Our results on the deposition of fiber aerosol in the human nasal, oral and tracheobronchial airways provide new information on the deposition pattern in the human respiratory tract. Together with theoretical investigation, this new information relates deposition efficiency as a function of fiber dimensions, inspiratory flow rate, and airway dimensions. This information has been used to verify various deposition models developed over the years and is also useful in developing new theoretical models in the future. New deposition equations developed from the research can be used in the future in developing lung dosimetric models in predicting deposition doses of inhaled fiber in occupation environments. The new dosimetric information is important in understanding the etiology of inhaled fiber aerosols and can be used as a guide for future research activities.

In terms of realistic application in the working environment, the most important finding is the development of a thoracic fraction of fiber aerosol based on the penetration of fiber through oral airways. Our results indicate that penetration of fiber is higher than that of a spherical particle of the same aerodynamic diameter, therefore the thoracic fraction is different from that of spherical aerosol. The proposed fiber thoracic curve needs additional experimental verification. If the proposed fiber thoracic curve is adopted, then it can affect the sampling of fiber aerosol in the occupational environment. Because the current fiber aerosol sampling methodology is not based on a size-selection principle, research activities are needed to develop size-selective methods for sampling fibers. This research could potentially lead to the new size-selective sampling criteria for fiber aerosol in an occupational environment.

OUTCOME/RELEVANCE/IMPACT

In summary, the scientific findings of this project provide new information on dosimetry of inhaled fibers in the human nasal oral and upper tracheobronchial airways. These findings fill the data gaps that are essential in the investigation of etiology of inhaled fiber aerosols. The results will be useful in the further study of occupational risks of exposure to man-made and asbestos fibers. Second, from the deposition and penetration data of fiber aerosol through the oral/pharynx/larynx airways, we have determined the thoracic fraction curve of fiber aerosol. The proposed thoracic fraction of fiber aerosol is slightly different from that of spherical particles because the fiber has higher penetration in the upper airways as compared to spheres of the same aerodynamic diameter. This provides a technical basis for defining a size-selective sampling criterion. The potential outcome and impact of this finding could influence the regulation of the methodology used to sample fibers in an occupational environment. Unlike sampling of compact aerosol, sampling of airborne fibers in an occupational environment has not involved a size-selective procedure similar to the sampling of compact particles, partly because there are no appropriate criteria.

BODY OF REPORT

BACKGROUND

Inhalation exposure to asbestos causes (1) asbestosis, a diffuse fibrosis in the alveolar and pleural region of the lung, (2) bronchogenic lung cancer, and (3) mesothelioma in pleura and peritoneum (Bogovski et al., 1973; Selikoff and Lee, 1978). Evidence from epidemiological studies and animal experiments is substantial. Other mineral fibers such as erionite may have a similar effect on the exposed human population (Baris et al., 1987). Man-made vitreous fibers (MMVFs), including glass fibers, ceramics, and carbides that replace asbestos in many applications, may have similar biological effects in laboratory animals (Miller et al., 1999; Hesterberg and Hart, 2001; IARC, 2002; Kamstrup et al., 2002). Although the etiology of these diseases has not yet been clearly elucidated, fiber dimensions and durability play an essential role (Stanton and Wrench, 1972; Timbrell, 1973).

Fiber materials contain elongated particles with an aspect ratio (length divided by diameter) over 3. The aerodynamic diameter of a fiber depends primarily on fiber diameter with a secondary dependence on the aspect ratio (Stöber et al., 1970; Cheng et al., 1995). Based on experimental evidence, Lippmann (1988) argued that three diseases are associated with fibers of different dimensions, which may deposit at different locations in the respiratory tract. While occupational exposure to asbestos fibers have decreased because the material was replaced with synthetic vitreous fibers (SVFs) or MMVFs, the main concerns of occupational exposure and health effects are on SVF or MMVF now.

No human data are available from controlled experiments of inhaled fiber aerosols for the obvious reason that most fiber materials are potentially hazardous when inhaled. From the post-mortem examination of lung tissues in miners working in asbestos mines, Pooley and Clark (1980) determined the size distribution of chrysotile, crocidolite, and amosite fibers. Based on post-mortem lung specimens of workers exposed to anthophyllite fibers, Timbrell (1982) showed a bivariate presentation of retention curves for each worker. These results were used to infer the deposition of fibers with respect to fiber length and diameter after the clearance processes were considered.

Glass fiber deposition in the human airway has been observed directly in a single bifurcation tube (Myojo, 1987, 1990) and a more realistic silicon-rubber airway cast, including a simulated larynx, trachea, and bronchiole larger than 3 mm in diameter (Sussman et al., 1991a). Deposition efficiency was higher with increasing flow rates, and deposition densities were much greater at the bifurcation than along the walls of the daughter tubes. An empirical equation that included the impaction and interception parameters was developed to describe the experimental data (Sussman et al., 1991b).

A mathematical deposition model of inhaled fiber aerosols in the human respiratory tract was first developed by Beeckmans (1970) based on Weibel's morphological lung model (1963). This model was an extension of the lung deposition model of spherical particles (Beeckmans, 1965). Harris and Fraser (1976) considered impaction, sedimentation, diffusion, and interception mechanisms and developed a more complete deposition model. A fiber in the airway was considered either in random orientation or parallel to the airflow, depending on flow conditions and the strength of the Brownian motion. The model also considered nasal deposition by interception and impaction mechanisms. These early works were an extension of spherical particle models and did not consider fiber rotation.

Asgharian and Yu (1988, 1989a) recognized the importance of fiber orientation. In a shear flow of an airway tube, the fiber moves in the direction of the air flow, but also undergoes an end-to-end rotation as described by Jeffery (1922). The flow profile and Brownian motion of the particle (Asgharian et al., 1988) determine the particle movement. In lung airways, most fibers move with the long axis parallel to the axial flow in the parent and daughter tubes. Asgharian and Yu (1989b) extended their human deposition model to consider the airway structure and breathing patterns of rats. This model has been improved further (Yu et al., 1994; Asgharian and Anjilivel, 1995, 1998; Ding et al., 1997).

Air sampling of particulate matter in the ambient and occupational environments are based on Size-selective criteria (Phalen et al., 1986). Size-selective criteria have been defined based on the deposition of spherical particles in human volunteers (Phalen et al., 1986). All three size-selective exposure indices have been developed for compact or spherical particles with the aerodynamic diameter as the characteristic parameter. No size equivalent indices for fiber aerosols are specified in the sampling recommendations, although the specified inlet configurations of the sampler will impose some size-selection. A more definitive index based on quantitative information of fiber deposition in the lung is needed.

It is clear that the deposition of fibers in the bronchial and alveolar regions and the subsequent uptake and translocation to the nearby interstitium and other tissues play important roles in the etiology of fiber-associated lung diseases. Mechanisms of fiber deposition in various regions of the human respiratory tract have been proposed and mathematical equations developed. However, few experimental data confirm the model prediction, and there is no fiber deposition equation for the nasal and oral airways. Experimental data are needed on the deposition of fibers in human nasal and oral passages and in the TB trees to ascertain the importance of fiber dimension and flow rate on lung deposition. A consequence of insufficient deposition data is that the current sampling procedure may not be adequate to assess exposure of fibers in occupational settings.

SPECIFIC AIMS

Specific Aim 1: To measure deposition of fibers in realistic replicas of the human respiratory tract. Man-made vitreous fibers (MMVFs) of uniform length will be generated by a new fiber classification technique for the study so the effects of fiber dimensions and flow rate on the deposition efficiency can be determined accurately.

Specific Aim 2: To simulate numerically the motion of the fiber particles and their deposition in the oral, nasal, and TB airways. A computational fluid dynamics (CFD) technique will be used to develop a theoretical flow pattern in the airway and to calculate fiber trajectory and deposition efficiency in different airway regions.

Specific Aim 3: To compare and verify fiber deposition data obtained in experimental data and numerical simulation from the CFD technique. With the verified theoretical results, improved deposition equations can be developed. These equations include appropriate airway dimensions of the head airways as determined in Specific Aim 2 to explain the intersubject variability. We will then compare regional deposition prediction from the existing fiber deposition lung model with experimental data. Deposition equations with experimental verifications may be used to improve the lung deposition model.

Specific Aim 4: To define a thoracic fiber fraction as an index of exposure to fiber aerosols, because fiber-related lung diseases are associated with deposition and biological activities in the bronchial, pulmonary and parenchyma region, but not in the head airway. Fiber aerosols

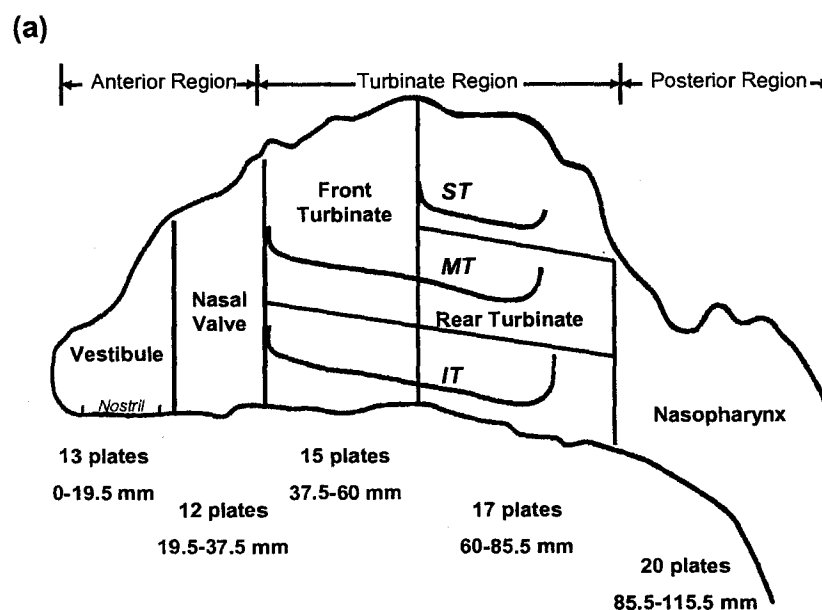
reaching the human thoracic region will be determined from data of aerosols that penetrated the oral airway, as determined in Specific Aims 1 and 2. Based on the experimental data and numerical simulation, the thoracic fraction of fiber aerosols as a function of particle length and diameter will be estimated.

SPECIFIC AIM 1

Materials and Methods

1. Human Nasal Airway Cast

The nasal airway is the major entry to the human respiratory tract, and acts as a first line of defense and a filtration system in preventing hazardous aerosols from entering the lung. The fraction of the inhaled fiber acquired from the nasal airway due to deposition could directly indicate the remaining fraction of the inhaled fiber entering the lower respiratory airway. A replicate human nasal cast was used in this research for the fiber deposition study. This nasal airway cast was made based on the *in vivo* magnetic resonance imaging (MRI) of a nonsmoking Caucasian male (53 years of age, 73 kg in body mass, and 173-cm tall). The MRI images were taken every 3 mm in the nasal airway (Guilmette and Gagliano, 1994). The original images obtained from these MRIs were digitized with a GRAF/PEN sonic digitizer (SAC, Southport, CT), then three-dimensional surfaces were constructed for adjacent perimeter traces using a computer-assisted design software (SmartCAM, Point Control Co., Eugene, OR). The physical nasal airway cast was made by using 1.5-mm-thick acrylic plates and milling with a computer-controlled micro-milling machine (CAMM 3, Roland DG, Los Angeles, CA). The entire nasal airway cast contains 77 acrylic plates (115.5 mm total length) and consists of complete nasal airway structures including an anterior region (first 25 plates: 0–37.5 mm, with vestibule and nasal valve subregions), turbinate region (middle 32 plates: 37.5–85.5 mm, with front and rear turbinate subregions), and posterior region (last 20 plates: 85.5–115.5 mm, with entire nasopharynx region). The turbinate region was further divided into superior turbinate (also known as the olfactory area), middle turbinate (MT), and inferior turbinate (IT) sections. Figure 1 shows the structure and sections of the nasal airway cast used in this research.



(b)

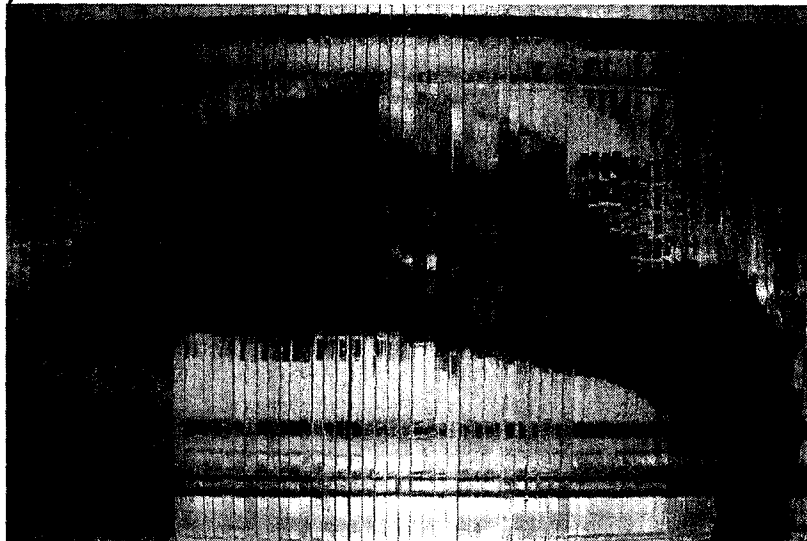
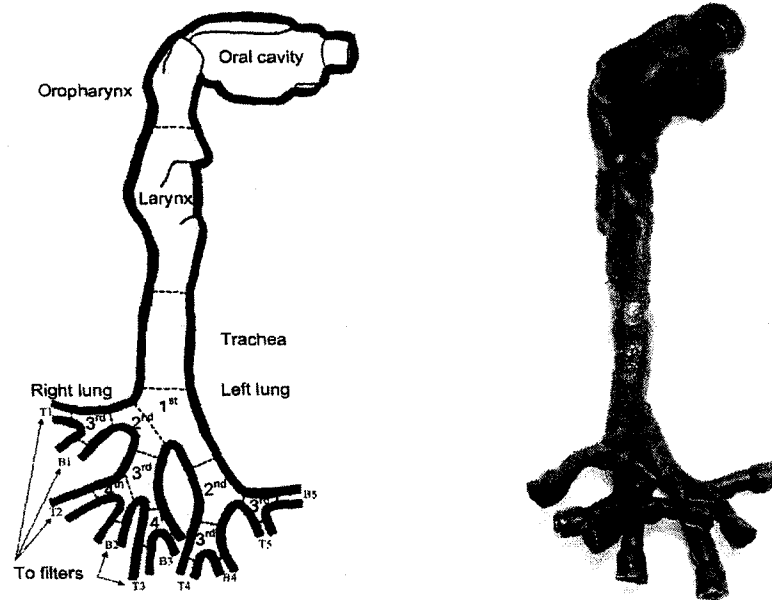


Figure 1. Structure and regions of the human nasal airway replica
(a) schematic diagram and (b) physical model.

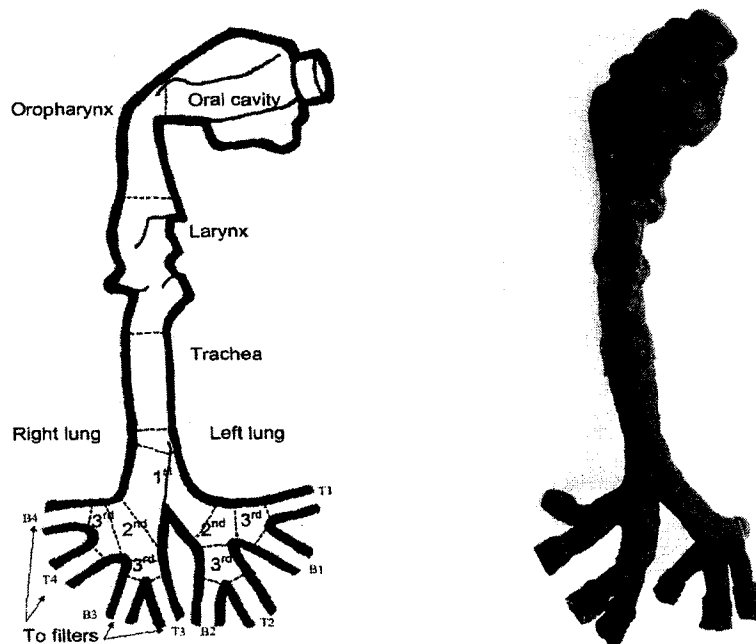
2. Human Respiratory Airway Casts

Production models of human respiratory airways have been developed (Cheng et al., 1997) from *in vivo* measurements (oral cavity) and cadavers (tracheobronchial airways). These production molds can reproduce human respiratory airway casts for deposition study with defined geometric dimension, which has been shown to provide reliable data in experiments of particle deposition in the human respiratory airway (Cheng et al., 1997, 1999, 2001a, 2003; Zhou and Cheng, 2005). Therefore, these airway casts are ideal to be used in this research for the advanced fiber deposition studies.

Two different airway casts (LA and LB) were made from selected production modes. The only information available for these two casts are that the LA cast was made based on a 16-year-old male, and the LB cast was made based on a 21-year-old male. The airway casts were made from conductive silicone rubber (KE-4576, Shin-Etsu Chemical Co., Ltd., Tokyo, Japan). Using conductive material has an advantage for fiber deposition experiments since it can eliminate the unexpected fiber deposition in the airway caused by possible electrostatic effects. Figure 2 shows the structure and physical model for the two airway casts used in this research. Each airway cast consists of an oral cavity, oropharynx, larynx, trachea, and the tracheobronchial airways to the 4th (LA) or 3rd (LB) bifurcation.



Lung cast A (LA)



Lung cast B (LB)

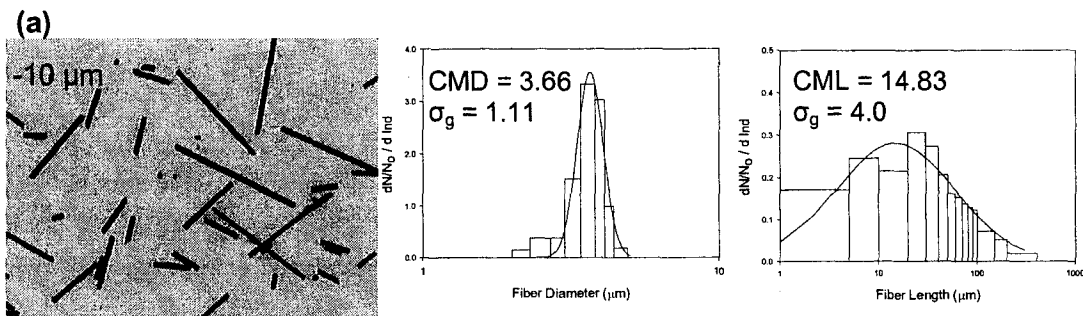
Figure 2. Structure and regions of the human respiratory airway casts.

3. Fiber Materials

Fiber is defined as elongated particles with an aspect ratio, β (the ratio of the length to the diameter), over 3 (NIOSH, 1994). The fiber dimension is the key factor affecting the fiber deposition in the human airway. It has been reported that the aerodynamic diameter of a fiber in the air depends primarily on its diameter and only slightly on its length (Stöber et al., 1970; Cheng et al., 1995). The toxicity of a fiber is strongly related to the fiber length. For instance, it has been reported that long and thin fibers have greater toxicity than short and thick fibers (Timbrell, 1982; Lippmann, 1990; Hill et al., 1995; Bernstein et al., 2001). Therefore, a variety of fiber material is needed for the fiber deposition study in order to determine the relationship between the fiber dimension and the associated deposition pattern in the human respiratory airway.

In this research, three man-made fiber materials were employed in the deposition experiments: carbon, titanium dioxide (TiO_2) and glass. These fiber materials were all uniform in diameter and diverse in length. Using fibers with uniform diameter is a new approach for fiber deposition studies since it provides a simple way to obtain the fiber dimension for the deposited fiber (length measurement only) and a sure way to determine the effect of fiber length or fiber diameter on the deposition pattern. The test carbon fibers were relatively large fibers which were provided by Hercules, Inc. (Wilmington, DE). These carbon fibers are black in color, conductive, monodisperse in diameter (CMD = $3.66 \mu\text{m}$, $\sigma_g = 1.11$), polydisperse in length (CML = $14.83 \mu\text{m}$), and with a density measured at 1.83 g/cm^3 . The test carbon fiber material contains cylindrical fibers and fiber debris. In this research, only fibers with lengths larger than $10 \mu\text{m}$ were counted as contributing to the final deposition data.

The TiO_2 and glass fibers were short fibers compared to the carbon fibers. The TiO_2 fiber used in this research was made in the University of Florida with electro-spinning technology. The TiO_2 fiber is monodisperse in diameter (CMD = $0.59 \mu\text{m}$, $\sigma_g = 1.18$) and polydisperse in length (CML = $3.20 \mu\text{m}$) with a density of 4.23 g/cm^3 . The glass fiber (JM475/100, Johns Manville Co., Littleton, CO) is nearly monodisperse in diameter (CMD = $0.62 \mu\text{m}$, $\sigma_g = 1.30$) and polydisperse in length (CML = $7.67 \mu\text{m}$) with a density of 2.56 g/cm^3 . Similar criteria for fiber measurement were also applied to these two fiber materials: only TiO_2 fibers longer than $2.5 \mu\text{m}$ and glass fibers longer than $3.5 \mu\text{m}$ were counted in the deposition data due to the limitation of the visual measurement. Figure 3 shows images and statistics of these three man-made fibers. Table 1 lists the physical properties of the test fibers.



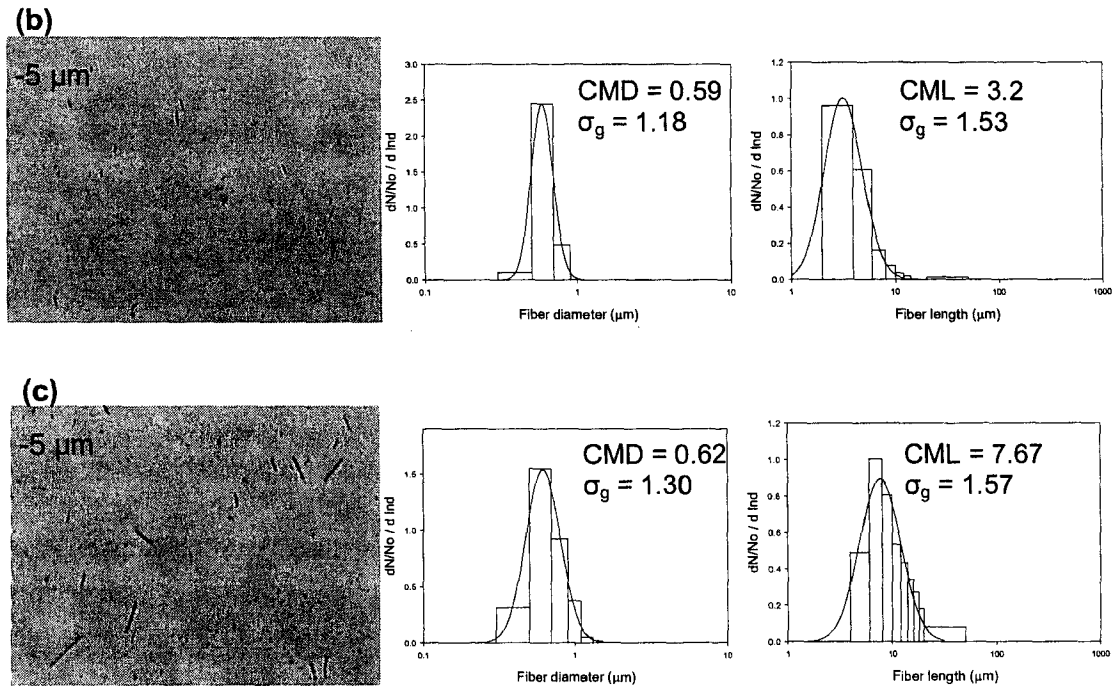


Figure 3. The test man-made fiber materials (a) carbon fiber, (b) TiO_2 fiber, and (c) glass fiber.

Table 1. Comparison of the physical characteristics and aerodynamic diameter for three different man-made fiber materials.

Fiber Type	Density	Diameter	Length	d_{ae}
Carbon	1.83 g/cm ³	CMD = 3.66 μm $\sigma_g = 1.11^c$	CML = 14.83 μm $\sigma_g = 4.00$	7.6–12.8 μm^a , 8.1–14.9 μm^b (L = 10–300 μm)
TiO_2	4.23 g/cm ³	CMD = 0.59 μm $\sigma_g = 0.17$	CML = 3.20 μm $\sigma_g = 0.42$	2.1–2.7 μm , 2.2–3.0 μm (L = 2.5–12.0 μm)
Glass	2.56 g/cm ³	CMD = 0.62 μm $\sigma_g = 0.27$	CML = 7.67 μm $\sigma_g = 0.45$	1.8–2.3 μm , 2.0–2.7 μm (L = 3.5–20.0 μm)

^aFiber aerodynamic diameter with random orientation.

^bFiber aerodynamic diameter with parallel orientation.

^cGeometric standard deviation.

The aerodynamic diameter (d_{ae}) of the test fiber could be approximately calculated by the equations below (Stöber, 1972):

$$d_{ae} = d_{ve} \sqrt{\rho / \rho_o} \kappa \quad (1)$$

where d_{ve} is the fiber volume equivalent diameter, ρ is the density of fiber, ρ_o is the density of water, and κ is the dynamic shape factor for a prolate spheroid. For a prolate spheroid flying in the air with its long axis orientating perpendicular to the flow direction, the dynamic shape factor is $\kappa_{\perp}$

$$\kappa_{\perp} = \frac{\frac{8}{3}(\beta^2 - 1)\beta^{-1/3}}{\frac{2\beta^2 - 3}{\sqrt{\beta^2 - 1}} \ln(\beta + \sqrt{\beta^2 - 1}) + \beta} \quad (2)$$

where β is the aspect ratio. The dynamic shape factor is $\kappa_{\parallel}$, if the long axis of a prolate spheroid orientates parallel to the flow direction.

$$\kappa_{\parallel} = \frac{\frac{4}{3}(\beta^2 - 1)\beta^{-1/3}}{\frac{2\beta^2 - 1}{\sqrt{\beta^2 - 1}} \ln(\beta + \sqrt{\beta^2 - 1}) - \beta} \quad (3)$$

If the orientation of a prolate spheroid is random in the air, the dynamic shape factor is κ_r and can be written as (Happel and Brenner, 1973)

$$\frac{1}{\kappa_r} = \frac{1}{3\kappa_{\parallel}} + \frac{2}{3\kappa_{\perp}} \quad (4)$$

Based on the equations shown above, for a 20- μm -long carbon fiber in the airflow (diameter = 3.66 μm) with its long axis orientating perpendicular to the flow direction (dynamic shape factor = $\kappa_{\perp}$), the aerodynamic diameter of the carbon fiber, $d_{ae(\perp)}$, is 8.4 μm . On the other hand, if the carbon fiber's long axis is parallel to the flow direction (dynamic shape factor = $\kappa_{\parallel}$), the aerodynamic diameter, $d_{ae(\parallel)}$, is 9.7 μm . However, if the carbon fiber orientates randomly in the air (dynamic shape factor = κ_r), the aerodynamic diameter, $d_{ae(r)}$, is 8.8 μm . In contrast, for a 100- μm -long carbon fiber in the air, its $d_{ae(\perp)}$, $d_{ae(\parallel)}$, and $d_{ae(r)}$ are 10.4 μm , 13.0 μm , and 11.3 μm , respectively. Based on the calculation above, Table 1 summarizes the physical characteristics as well as the estimated d_{ae} for these three man-made fibers (all the measured data were obtained after the fiber materials passed through the aerosol generation devices).

4. Experimental Setup

Two different setups were used in this research for the fiber deposition experiments due to the characteristics of the fiber material. The carbon and glass fiber material were dry-powder-like. Therefore they could be aerosolized by a small-scale powder disperser (SSPD, Model 3433, TSI Inc., St. Paul, MN). The related experimental apparatus includes an SSPD, a charge neutralizer, the human airway cast, and the backup filter holder. Figure 4 shows the experimental setup for the fiber deposition study using SSPD. For this experimental setup, the dispersed fibers were first delivered to the Kr⁸⁵ charge neutralizer. Fibers passing through the

neutralizer were at Boltzmann equilibrium and then delivered to the airway cast. A filter holder was attached to the nasopharynx of the nasal airway cast (ten filter holders were connected to the ends of the bronchial airways for lung airway cast) for collecting fibers that passed through the entire cast. A typical experiment lasted from 5 to 20 minutes depending on the inspiratory flow rate selected, and the SSPD rotation plate was set to a speed of 2. All of these operation parameters have proved to provide a sufficient number of fibers for the deposition study.

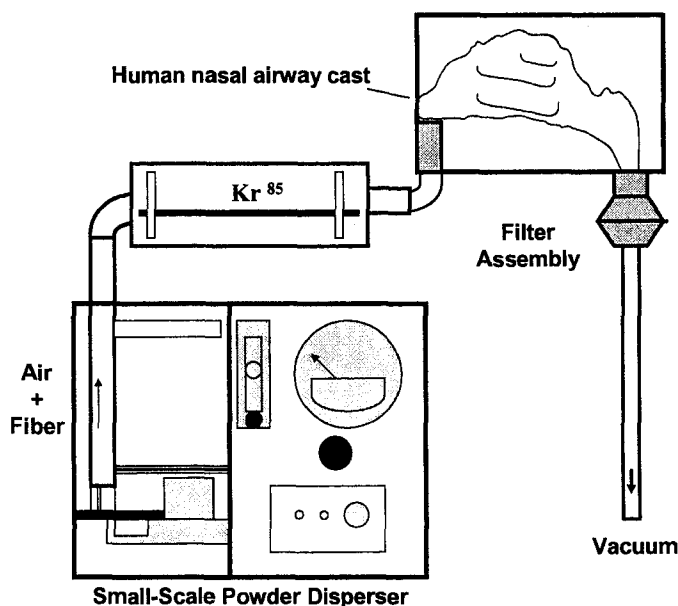


Figure 4. Schematic diagram of the experimental setup for the fiber deposition study with a small-scale powder disperser.

The TiO₂ fiber aerosol was generated by a medication nebulizer (Up-Mist, Hospitak Inc., Farmingdale, NY) due to its material characteristic (plate like). The experimental apparatus included a nebulizer, several alumina drying columns, a charge neutralizer, and the filter holder. Figure 5 shows the experimental setup for the TiO₂ fiber deposition study. Before generating the TiO₂ fiber aerosol, the TiO₂ fiber plates were placed in alcohol and ultrasonicated for 30 s before the aerosol generation process. When generating TiO₂ fiber aerosol, the nebulizer generates TiO₂ fiber aerosol along with the alcohol aerosol (droplets). These aerosols were first transferred to several drying columns and a Kr⁸⁵ charge neutralizer. In this way, sufficient time was provided to ensure that the alcohol mist evaporated and only TiO₂ fiber aerosol remained prior to entering the airway cast.

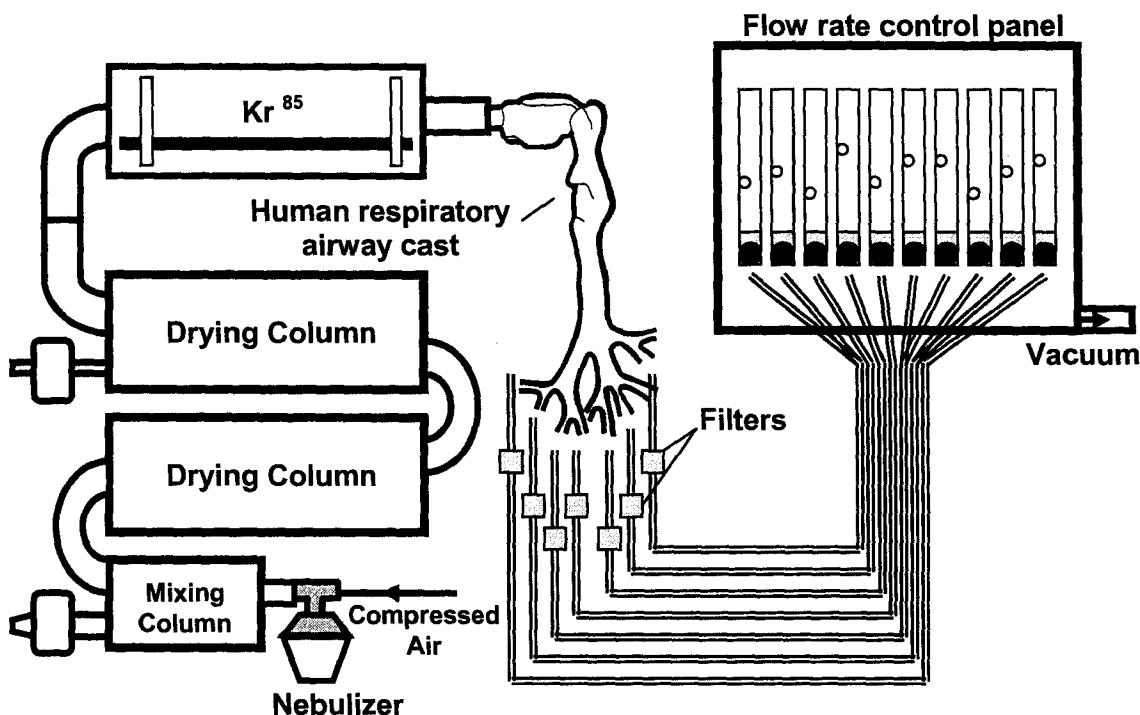


Figure 5. Schematic diagram of the experimental setup for the fiber deposition study with a medication nebulizer.

Before the deposition experiment, silicon oil (550 Fluid, Dow Corning Co., Midland, MI) was applied to the inside surface of the airway casts to simulate the adhesive nature in a real human airway. The oil coating has another advantage that it can force fibers to remain on the place where they originally deposited. The deposition experiments were conducted with constant inspiratory flow rates. Four flow rates (7.5, 15, 30, and 43.5 L/min) were used in the nasal airway studies, and three flow rates (15, 43.5, and 60 L/min) were used in the lung airway studies. These inspiratory flow rates ideally cover an adult breathing rate in different activities from at-rest to moderate work. Three experiments were carried out for each combination of inspiratory flow rate, fiber materials, and airway casts to obtain average deposition values. It is worth noting that in this research, the dimensions of the glottis openings in the respiratory airway casts (LA and LB) were modified based on the inspiratory flow rate conducting to virtually simulate the variation in the laryngeal airways under different respiratory flow rates. The modification of the glottis opening refers to the information reported in Martonen and Lowe (1983).

5. Sample Preparation, Fiber Counting and Length Measurement

After each run of the deposition experiments, the nasal airway cast or the lung airway cast was divided into regions/subregions based on the structure of the human nasal or lung airway. Care was taken when the airway cast was separated apart (nasal airway) or cut into segments (lung airway). Each divided section was flushed by alcohol jet or brushed several times with an artist's brush dipped in alcohol. The fiber-alcohol solution from individual airway sections was vacuum-filtered by a 25-mm filtration assembly to allow fibers to uniformly deposit on a 25-mm mixed cellulose ester membrane filter (GSWP, Millipore Co., Bedford, MA). The filters were then dried at room temperature in a dust-free environment and prepared as sample slides for

later microscopic counting and measurement. In general, nine sample slides were acquired from each run of the nasal airway deposition experiment, and 22 to 26 sample slides were acquired from each run of the lung airway deposition experiment. Each sample slide represents the situation of fiber deposition in a specific region of the human airway.

The sample slides were then examined by an optical microscope (BH-2, Olympus Optical Co., Tokyo, Japan) with a G22 Walton-Beckett graticule (Pyser-SGI Ltd., Kent, UK). Figure 6 shows an example of deposited fibers in a microscopic viewing area (under 40x magnification). The number of fibers and the length of individual fibers in a viewing area were determined based on National Institute of Occupational Safety and Health (NIOSH) method 7400 (the fiber diameter was not measured in each sample slide due to the fact that the fiber materials used are assumed to be uniform). Each sample slide was counted/measured for 200 fibers or 200 viewing areas, depending on whichever came first. In this way, the averaged number of fiber in certain length categories in a specific human airway region could be obtained. When these deposited data are available for all regions of the airway cast, the deposition pattern for the entire airway cast as well as the deposition efficiency for a specific airway region could then be determined.

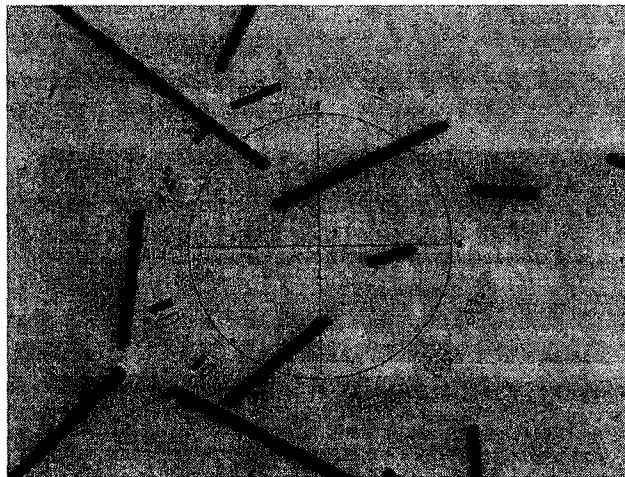


Figure 6. Fiber counting and measurement with G22 Walton-Beckett graticule (under 40x magnification).

Results

1. Fiber Deposition Efficiency in the Human Nasal Airway

Figure 7 shows the fiber deposition patterns as a function of fiber length. The subregions of the nasal airway are shown in Figure 7. The deposition fraction for each subregion is an average value of three experiments. As shown in Figure 7, the deposition pattern for an inspiratory flow rate of 7.5 L/min indicates that most of the fibers passed through the nasal airway and were collected on the backup filter. The fiber deposition fraction in each nasal airway subregion was typically below 10% for every length category. Only one subregion, the inferior turbinate of the front turbinate, was slightly larger than 10% in the long fiber ($> 100 \mu\text{m}$) category (Figure 7d). In addition, the number of fibers collected on the filter decreases as the fiber length increases, which implies that the longer the fiber, the harder it is for it to pass through the nasal airway.

Figure 8 shows the deposition pattern for a 15-L/min inspiratory flow rate. A considerable percentage of fibers was deposited in the nasal airway. Most of the fibers were in the anterior region (vestibule and nasal valve) and some in the middle turbinate of the front turbinate. However, there were still a considerable percentage of short fibers found passing through the entire nasal airway (33%; Figure 8a). Similarly, as shown in Figure 7, the percentage of fibers passing through the nasal airway in Figure 8 decreases as the fiber length increases. In the long fiber category ($> 100 \mu\text{m}$; Figure 8), only 11% of long fibers passed through the nasal airway and collected on the filter. In the turbinate region, very few fibers were found in the rear turbinate subregion and only a few fibers deposited in the front turbinate subregion, especially in the middle turbinate region. Almost no fibers were deposited in the posterior region (nasopharynx).

The deposition pattern for a 43.5-L/min inspiratory flow rate is similar to that for an inspiratory flow rate of 30 L/min, but relatively more long fibers (fibers $> 70 \mu\text{m}$) were found in the nasal valve and front turbinate subregions. Fibers were mainly deposited in the vestibule, nasal valve, and the front turbinate subregions. More than 99% of the fibers were deposited in these places for each fiber length category. Extremely few fibers ($< 0.5\%$) passed the nasal airway and collected on the filter.

Figure 9 shows the deposition efficiency as a function of the impaction parameter (fiber momentum) for man-made fibers in the nasal airway replica. The fiber deposition efficiency is determined by the fraction of the fiber entering the nasal airway that deposited within it. The d_{ae} used for calculating the impaction parameter

$d_{ae}^2 Q$ is the fiber aerodynamic diameter in random orientation. As

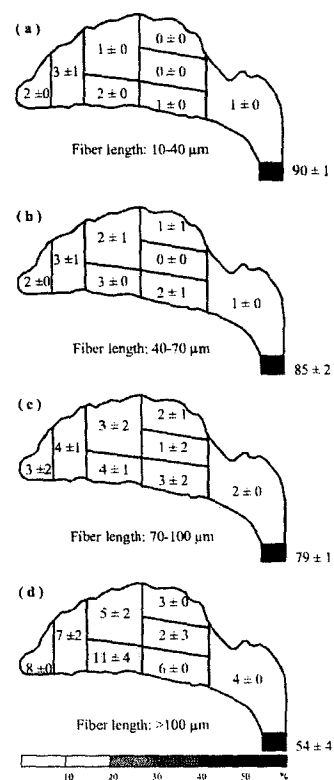


Figure 7. Deposition in the nasal airway for 7.5 LPM.

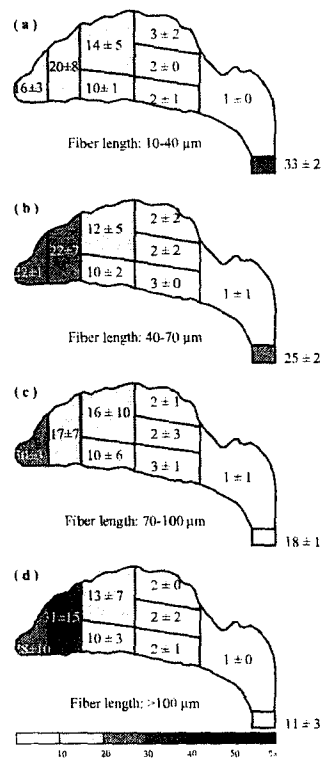


Figure 8. Deposition in the nasal airway for 15 LPM.

can be seen in Figure 9, the trend of the fiber deposition efficiency in the nasal airway is a smooth S-like shape. The lower end of the carbon fiber deposition efficiency is ideally connected to the higher end of the TiO_2 fiber deposition efficiency, which plainly shows the overall continuity between the data sets acquired. Figure 9 shows that the deposition efficiency of the carbon fiber increased proportionally with the impactation parameter. This result indicates that impactation is the main deposition mechanism for the carbon fiber used. The deposition efficiency of the carbon fiber can reach 1.0 when the impactation parameter is greater than $50,000 \mu\text{m}^2 \text{cm}^3/\text{s}$. To the contrary, there was no significant relationship found between the impactation parameter and the deposition efficiency for the TiO_2 and the glass fibers. The deposition efficiencies increased only slightly with an increase in the impactation parameter. In general, the impactation parameters of TiO_2 and glass fibers were both smaller than $6,000 \mu\text{m}^2 \text{cm}^3/\text{s}$, and partially overlapped. The deposition efficiencies of TiO_2 and glass fibers were shown to be similar, and were both less than 0.2.

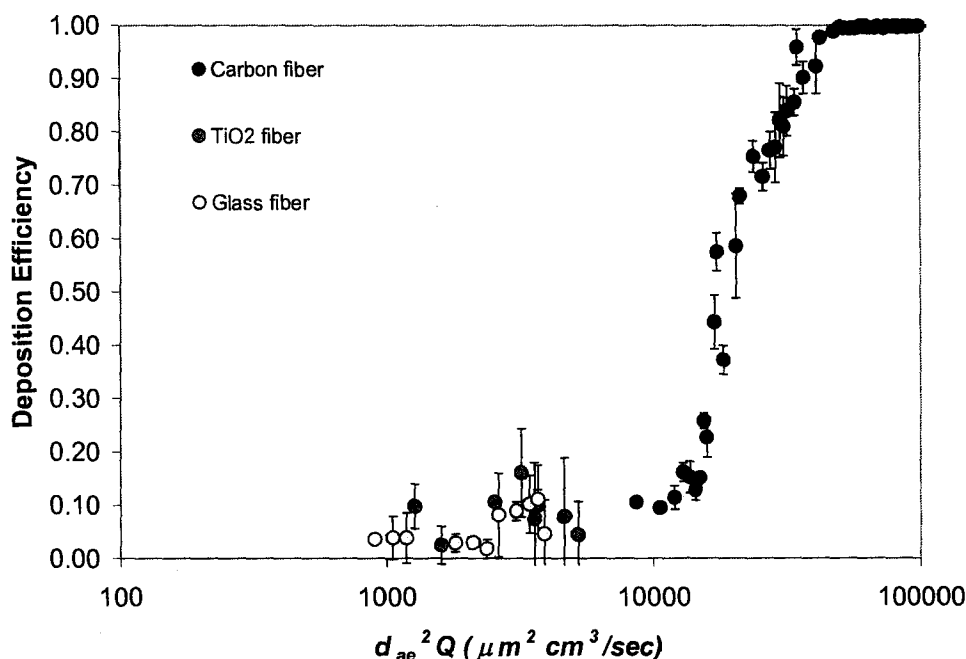


Figure 9. Deposition efficiency as a function of the impactation parameter for different man-made fiber materials in the human nasal airway.

The discrepancy of the deposition efficiencies between the three fiber materials shown in the Figure 9 might be due to the fact that the diameter and length of the carbon fiber are considerably large compared with those of TiO_2 and glass fibers. This large physical dimension gives carbon fibers a significant d_{ae} value and inertia. As a result, the impactation parameter (fiber momentum) as well as the associated deposition efficiency increases substantially when the fiber d_{ae} increased. As shown in Figure 9, most of the high-momentum fibers have a deposition efficiency of 1.0, which implies that high-momentum fibers do not pass through the nasal airway. Thus, the human nose appears to function well for filtering out large fibers such as carbon fibers and preventing them from entering the lower respiratory tract.

On the other hand, the dimensions of the TiO_2 and the glass fibers are relatively small compared with the carbon fiber. Therefore, the fiber d_{ae} , the impaction parameter, and the associated fiber deposition efficiency are all consequently small. It is interesting to note that the diameters of the TiO_2 and the glass fibers are comparable, and the length distribution of the TiO_2 fiber is shorter than that of the glass fiber. However, the calculated d_{ae} and the related impaction parameters of the TiO_2 fibers are, in general, larger than those of the glass fibers. This result is due to the fact that the density of the TiO_2 fiber is greater than that of the glass fiber. Moreover, as mention before, the d_{ae} of a fiber depends primarily on its diameter and only slightly on its length (Stöber et al., 1970; Timbrell, 1982; Cheng, 1995). Therefore, the TiO_2 fiber shows a relatively higher momentum in the nasal airway compared with the glass fiber, and the deposition efficiencies of the TiO_2 fiber agree well with those of the glass fiber where the values of the impaction parameters for these two fibers overlap. As shown in Figure 9, the deposition efficiencies of the TiO_2 and glass fibers all ranged from 0.02–0.2, which implies that small fibers have a high penetration rate (≥ 0.8) through the nasal airway. Therefore, small fibers may present a hazard to the human lower respiratory tract.

2. Comparison of Nasal Deposition between Fibers and Compact Particles

Aerosol deposition experiments in the nasal airway have been conducted intensively with compact particles in the inertia regime (Swift, 1991; Cheng et al., 1999, 2001a, b; Zwartz and Guilmette, 2001; Kelly et al., 2004). It has been shown that most of the experimental data acquired from those studies agree well with each other and the data are all located within a narrow band when the deposition efficiency is plotted against the impaction parameter. In this research, deposition experiments were also carried out with compact particles. The compact particles used had comparable aerodynamic diameters to carbon, TiO_2 and glass fibers in order to compare the coincident deposition efficiencies obtained from fibers. The test particles were fluorescent polymer microspheres (Duke Scientific Co., Palo Alto, CA) with sizes ranging from 2.1 to 10.0 μm ($d_{ae} = 2.2$ to 10.2 μm). Deposition experiments were conducted using a similar experimental method as for the fiber study, and the deposition result was acquired by measuring the florescence intensity in the washed-out solution for each nasal airway region. The deposition pattern and deposition efficiency of the compact particle were obtained with the same method as employed in the fiber study. Figure 10 shows the deposition efficiency and corresponding deposition patterns for fibers and compact particles in the nasal airway. As can be seen, for fibers and compact particles with a large impaction parameter ($\geq 15,000 \mu\text{m}^2 \text{cm}^3/\text{s}$), the deposition efficiencies are at least 0.5 and above, and the fiber deposition efficiencies are smaller than the compact particle deposition efficiencies. In this impaction parameter regime, the anterior region is the site of common deposition.

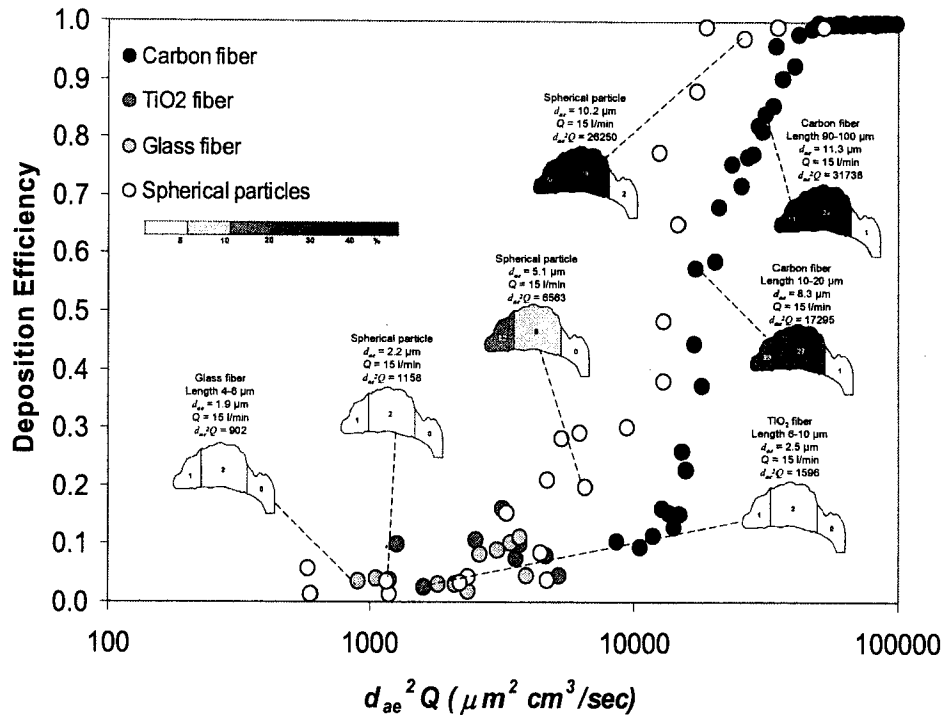


Figure 10. Comparison of the deposition efficiencies and related deposition patterns between fibers and spherical particles.

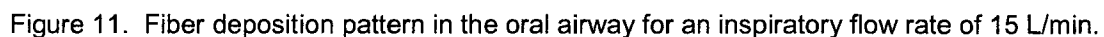
On the other hand, for those TiO_2 fibers, glass fibers, and compact particles with a small impact parameter ($\leq 5,000 \mu\text{m}^2 \text{cm}^3/\text{s}$), the deposition efficiencies are generally small in the nasal airway (less than 0.2), and relatively higher deposition was found in the turbinate region. However, in this small impact parameter regime, no significant difference was found regarding the deposition efficiency between the fiber aerosol and the compact particles. The fiber deposition efficiencies were shown to be fairly close to those of compact particles. These results shown above imply that, in the inertia regime, fibers with low momentum would have similar deposition behavior as compact particles having comparable aerodynamic diameters in the human nasal airway, while fibers with high momentum would behave differently from compact particles having an equal aerodynamic diameter. The main cause that could account for this difference could be the fiber orientation in the inhaled air flow. As has been reported in some theoretical calculations (Asgharian, 1988; Chen and Yu, 1991; Asgharian et al., 1997) and experimental observation (Myojo, 1987), fibers tend to align themselves to the flow direction when they fly through the air. With fibers oriented parallel to the air streamline, it could reduce the deposition of fiber in the human airway to a certain extent. The deposition efficiency of fiber is therefore less than that of compact particles in the nasal airway. This might provide an explanation for the difference of the deposition efficiencies found between fibers and compact particles.

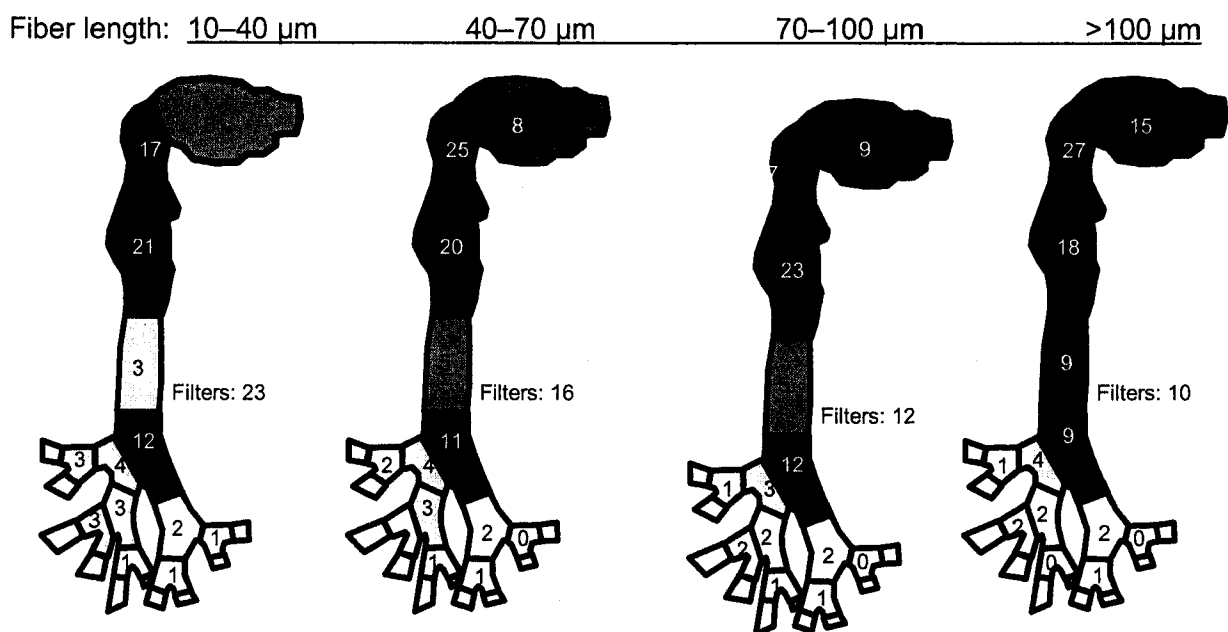
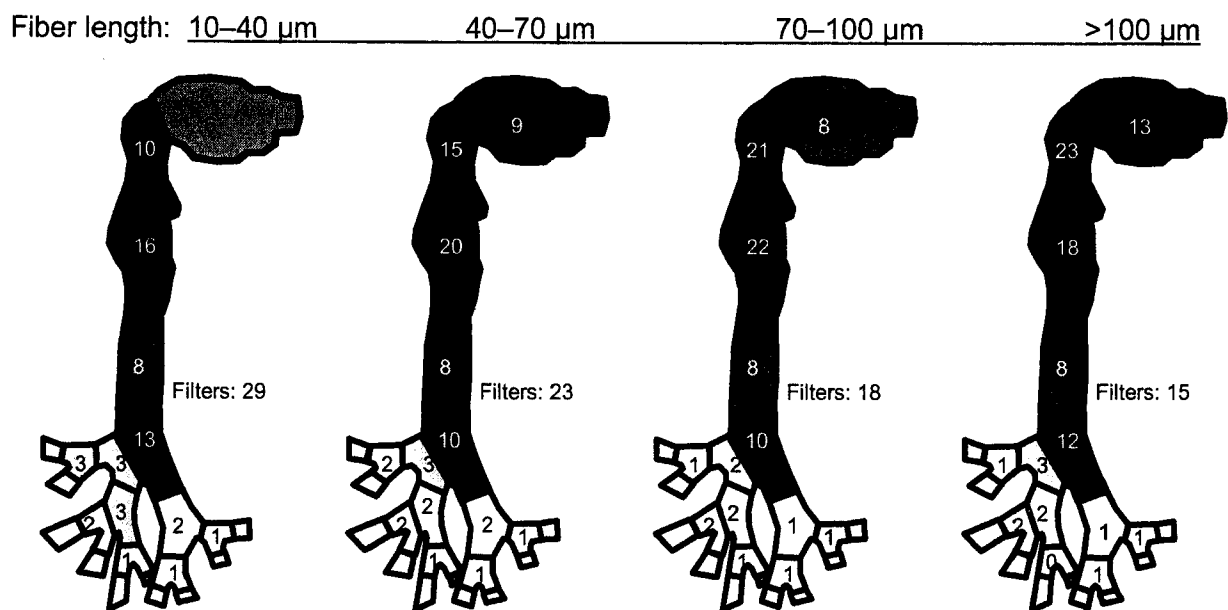
3. Fiber Deposition in the Human Oral Airway

Figures 11–13 show the fiber deposition patterns for three inspiratory flow rates as a function of fiber length. The deposition fraction for each region is an average value of three experiments. For a low inspiratory flow rate of 15 L/min (Figure 11), the deposition pattern indicates that most of the fibers (at least 63%) passed through the entire human airway replica.

Figure 12 shows the deposition pattern for a 43.5-L/min inspiratory flow rate. A considerable percentage of fibers was deposited in the human airway at this inspiratory flow rate. Most of the deposition were at the oropharynx to larynx area and some were at the first bifurcation. Approximately 30% of the short fibers still passed through the replica, but only 15% of the long fibers were able to penetrate through the replica. The deposition fraction for a specific region basically increased as the fiber length increased, which is similar to Figure 11. It is worth noting that the deposition fraction in the oropharynx gradually became significant.

Fiber length: 10–40 μm 40–70 μm 70–100 μm >100 μm





The oral airway is the major air entry for some workers because of the need for a large respiratory flow rate while performing moderate-to-heavy work. However, aerosol collection in the human oral airway is less efficient compared with that in the nasal airway due to the smaller inhalation air velocity caused by the larger dimension of the oral airway. Therefore, when breathing by mouth, a considerable portion of the inhaled fibers are able to penetrate the oral airway and then enter the tracheobronchial airways. The fiber deposition efficiency found in the

oral airway can be used as an index of the oral penetration rate of interest which can then indicate the amount of fibers that enters the lower respiratory airway. Figure 14 shows the fiber deposition efficiency as a function of the impaction parameter $d_{ae}^2 Q$ (d_{ae} is the fiber aerodynamic diameter calculated by parallel orientation, and Q is the inspiratory flow rate) in the oral airways for the two casts.

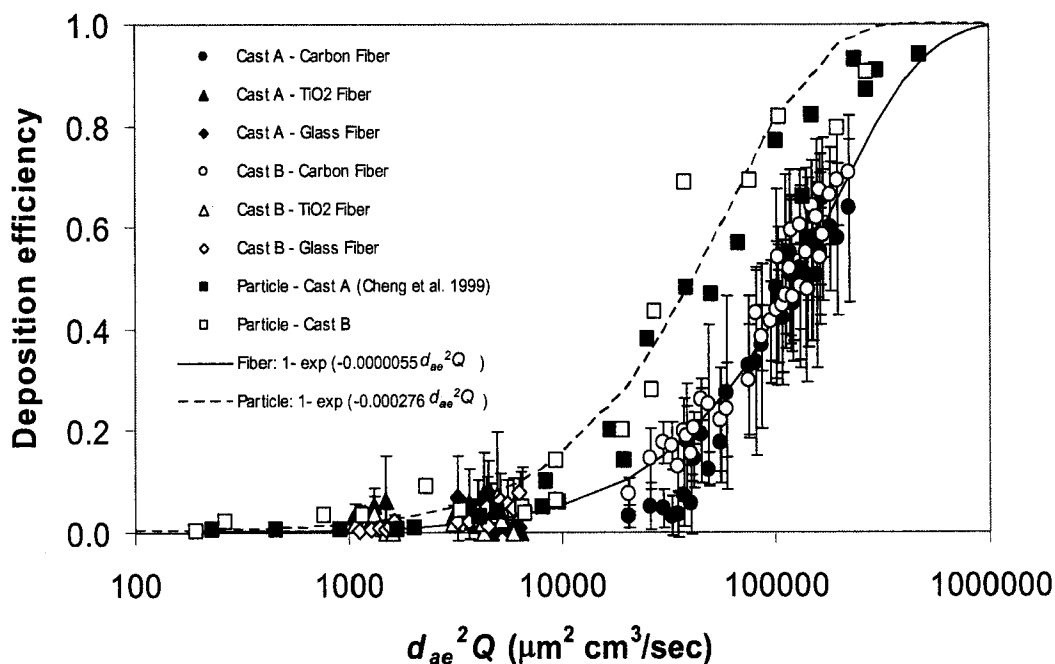


Figure 14. Deposition efficiency as a function of the impaction parameter for fibers and compact particles in the human oral airway.

The oral airway here was defined as the regions from the oral cavity to the larynx in the airway casts. The fiber deposition efficiency in the oral airway was determined by the fraction of the fiber entering the oral airway that deposited within it. Also shown in Figure 14 are the deposition data of compact particles from our previous work for cast A (Cheng et al., 1999) together with the new results from this study for cast B. Fluorescent polymer microspheres (Duke Scientific Co., Palo Alto, CA) with an aerodynamic diameter from 0.5 to 16.4 μm were used as the test particles. The deposition studies of the compact particles were carried out using the same experimental method as described in the nasal airway deposition study. The particle deposition in the airway was acquired by measuring the fluorescence intensity in the washed-out solution of the oral airway.

As can be seen in Figure 14, the magnitudes and the configurations of the fiber deposition efficiencies in the oral airways were comparable in both casts, which indicates that the intersubject variability was insignificant in this study. For TiO₂ and glass fibers, there was no significant relationship shown between the impaction parameter and the deposition efficiency. The deposition efficiencies increased very slightly as the impaction parameter increased. The magnitudes of the deposition efficiencies were all similar and less than 0.1. This result indicates that thin man-made fibers could have a high penetration rate (≥ 0.9) in the human oral airway. In contrast, the deposition efficiency for carbon fiber increased proportionally with the impaction parameter and reached 0.6. This result implies that impaction is the major deposition

mechanism in the oral airway for thick man-made fibers, and fibers with large momentum would have difficulty penetrating the oral airway. In general, Figure 14 reveals an overall continuous match between data obtained from different fiber materials in both airway casts, and a relationship between the deposition efficiency and the impaction parameter is clearly shown.

Figure 14 also shows that the deposition efficiencies of compact particles are comparable in the two casts in terms of magnitude and configuration, which is similar to the results found in the fiber deposition studies for insignificant intersubject variability. Cheng et al. (1999) suggested an empirical model for the deposition of compact particles in the oral airway based on the available *in vivo* data. The predicted values using the suggested model are also shown in Figure 14. It was interesting to note that the empirical model suggested by Cheng et al. (1999) agreed quite well with the experimental data acquired in this study for both airway casts. This result validated the practicability of this empirical model. When comparing the deposition efficiency of compact particles with that of fibers in both airway casts, the data showed that the deposition efficiencies of compact particles were generally higher than those of fibers. As was discussed above, this result is presumed to be attributed to the fiber alignment in the inhaled airflow. Here, this deposition phenomenon was shown again, which supported the fact that fibers tend to fly parallel to the air stream in the human respiratory airway. With prevailing parallel orientation for fibers flying in the human airway, it could be assumed that "interception" therefore, is not a critical deposition mechanism for fiber deposition in the oral airway (oral cavity, pharynx and larynx). The major deposition mechanism in the oral airway is still thought to be impaction solely. The interception would be an important deposition mechanism when the dimension of the airway has a similar scale as the fiber length (e.g., in the lower tracheobronchial airways).

4. Fiber Deposition in the Tracheobronchial Airways

Figure 15 shows deposition efficiency of spheres and fibers in the third generation of airway in the upper TB region, plotted as a function of Stokes number, which is a dimensionless

impaction parameter, ($Stk = \frac{\rho d_{ev}^2 U}{18 \mu d}$),

where d_{ev} is the volume equivalent diameter of the fiber, U and d are the mean velocity and diameter of the parent airway, respectively, as defined by Zhang et al. (1996). Similar to deposition in the human nasal/oral airways, we also show that deposition efficiencies of spherical particles are higher than those of fibers for the same impaction parameter. This can be explained by the orientation of fibers, which tend to align with the flow direction as shown in Figure 16 (Zhang et al., 1996).

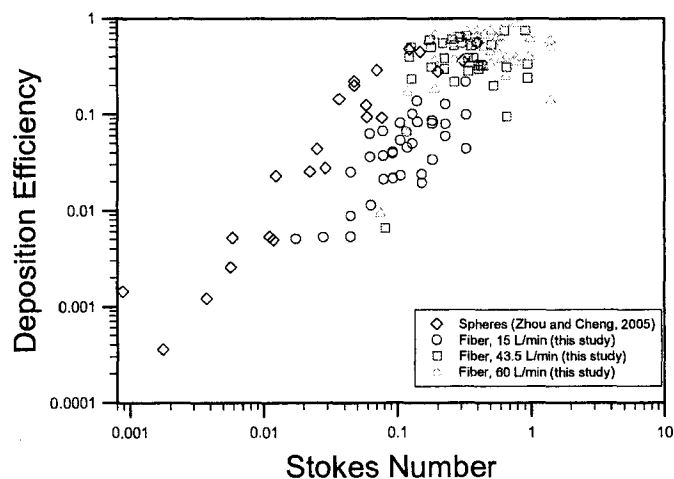


Figure 15. Deposition of spheres and fibers in the third generation of the TB airway.

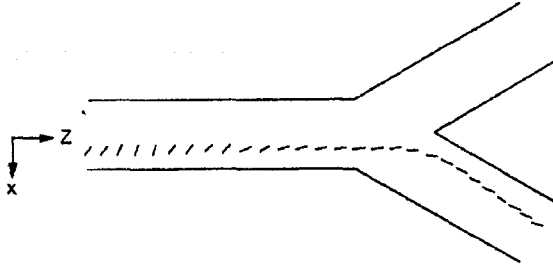


Figure 16. Movement of a fiber in an airway bifurcation, showing rotation of the fiber resulting in alignment of the fiber with the flow (Zhang et al., 1996).

Figure 17 shows comparisons with our experimental data and numerical simulation (Zhang et al., 1996), which can be expressed as:

$$\begin{aligned} DE &= 0.0007 \exp(-47.58 Stk^{1.325}) \cdot Re^{1/3} \cdot \sin\theta \quad \text{for } Stk < 0.08 \\ DE &= 0.1265 - 0.1287 \exp(-3.656 Stk^{1.726}) \cdot Re^{1/3} \cdot \sin\theta \quad \text{for } Stk < 0.08 \end{aligned} \quad (5)$$

where θ is the bifurcation angle. Our experimental data show large variability but generally agree with the numerical simulation results. One of the contributing factors of this large variability of deposition efficiency in the TB airway is that the airway geometry is not symmetrical, which leads to uneven flow and aerosol distribution in the daughter airway as shown.

SPECIFIC AIM 2

Methods

1. Nasal Airway

MRI scans of a healthy, adult male human subject were used to form the flow volume representing the right nasal passage.

The slice data with separation distance of 3 mm were loaded into the preprocessing software GAMBIT™ and key perimeter points were identified. These points were then used to construct surfaces in the stream-wise direction, adjoining the slices into a 3D volume (Zamankhan et al., 2006). The final computational domain stretched from the tip of the nose to the entrance to the nasopharynx. The volume was filled with tetrahedral elements totaling 965,000 and corresponded to 250,000 computational nodes.

Airflow simulations were carried out by numerically solving the conservation of momentum and mass equations. The steady-state version of the conservation equations for incompressible flow is,

$$\rho \mathbf{u} \cdot \nabla \mathbf{u} = -\nabla p + \mu \nabla^2 \mathbf{u} + \rho \mathbf{g} \quad (6)$$

$$\nabla \cdot \mathbf{u} = 0 \quad (7)$$

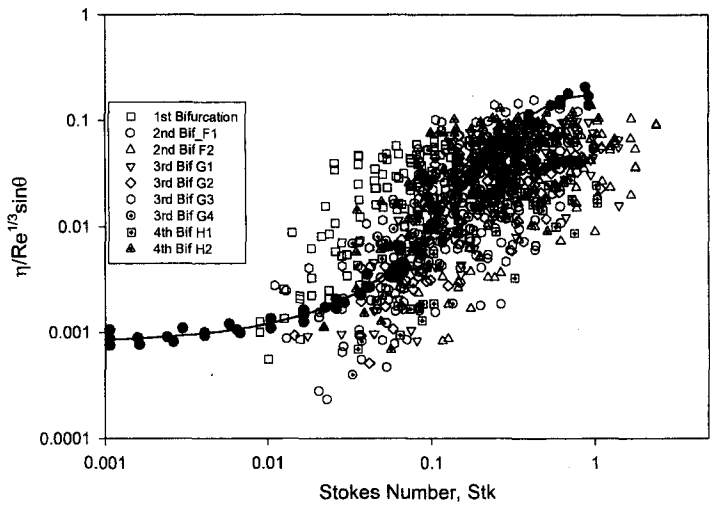


Figure 17. Comparison of fiber deposition data in the upper TB region with the theoretical prediction of Zhang et al. (1996) in blue points.

Here u is the fluid velocity, ρ is the constant mass density of the fluid, μ is the dynamic viscosity, p is the pressure, and g is the gravitational acceleration. Particle motion is governed by Newton's second law. For simulation of the airflow and particle transport and deposition in the nose, the FLUENT™ code, which is a finite volume-based code, was used. To discretize the governing equations, the SIMPLE scheme with an upwind formulation was used and the resulting discretized equations were solved by a segregated approach in which the discretized governing equations for each quantity were solved separately and then the values for those quantities were used in a subsequent equation. The particle transport and deposition analysis was performed using the FLUENT™ code.

2. Tracheobronchial Airways

Based on the asymmetric and symmetric bifurcation model elements, a multi-level computational model for simulation of airflow and particle transport in the lung is developed. In this approach, a single lung bifurcation serves as the base element, and the subsequent airway generations are generated by scaling down the base element according to the airway specifications (as suggested by Weibel [1963]). The entire tracheobronchial tree (with the exception of the alveolar region) can be constructed by using a sequence of these base elements with proper scaling. The schematic of the multi-level bifurcation model of human tracheobronchial upper airways is shown in Figure 18.

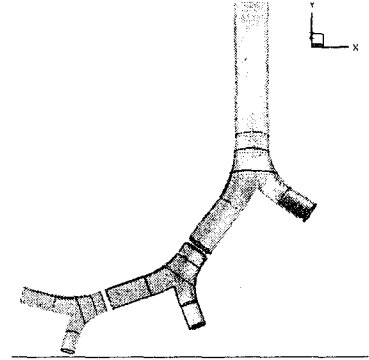


Figure 18. A multi-level TB bifurcation model.

In our study, the flow simulations were performed by using both the laminar and the turbulent flow models. Then comparisons of the particle deposition predictions in the human upper tracheobronchial airways between the simulation data and the experimental measurements were made. The comparison clearly showed that turbulence conditions prevailed in the trachea and the first two generations, while beyond the third generation the airflow is predominantly laminar. The breathing rates used were: 15 L/min, 37 L/min and 60 L/min.

Results

1. Flow Simulation in the Nasal Airway

To study the airflow patterns inside of the nasal passage, a series of simulations for different breathing rates between 4 to 14 L/min were performed. The features of the simulated flow fields are discussed in this section.

Stream-traces in the nasal cavity for breathing rates of 4 L/min and 14 L/min are shown in Figure 19. Comparison between stream-traces in Figure 19a and Figure 19b shows the general pattern of the airflow inside of the nasal cavity did not change when the breathing rate increases from 4 L/min to 14 L/min. Figure 19a and 19b show that most of the stream-traces passes through the middle airway, the inferior airway and the region between the middle and the inferior airways in the septum side of the section.

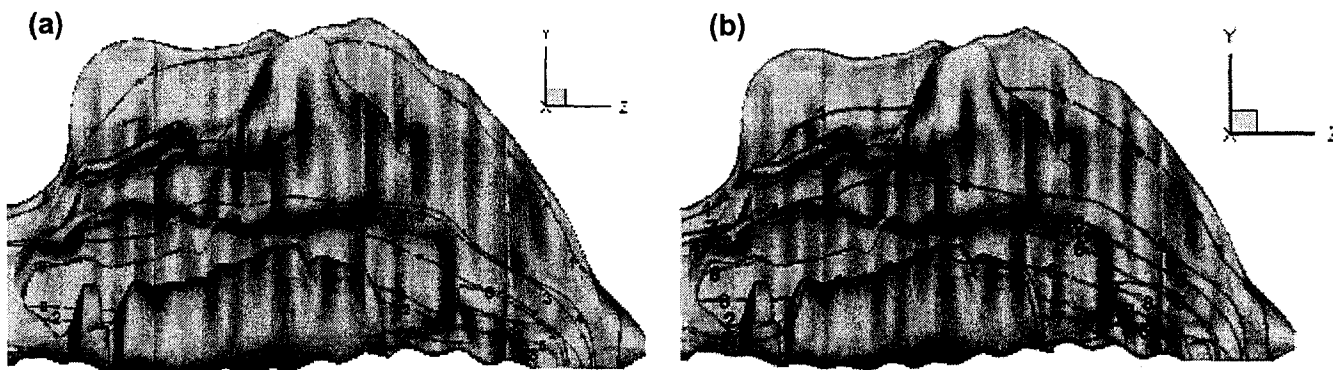


Figure 19. Stream-traces for breathing rates of 4 and 14 L/min, (a): Stream-traces for 4 L/min, (b): Stream-traces for 14 L/min.

2. Deposition in the Nasal Airway

Figure 20 shows nasal cavity deposition efficiency as a function of aerodynamic diameter for different flow rates. As expected, larger particles more readily impact the nasal surfaces, increasing the deposition efficiency of the cavity. Also obvious from Figure 20 is that breathing rate plays an important role on deposition efficiency.

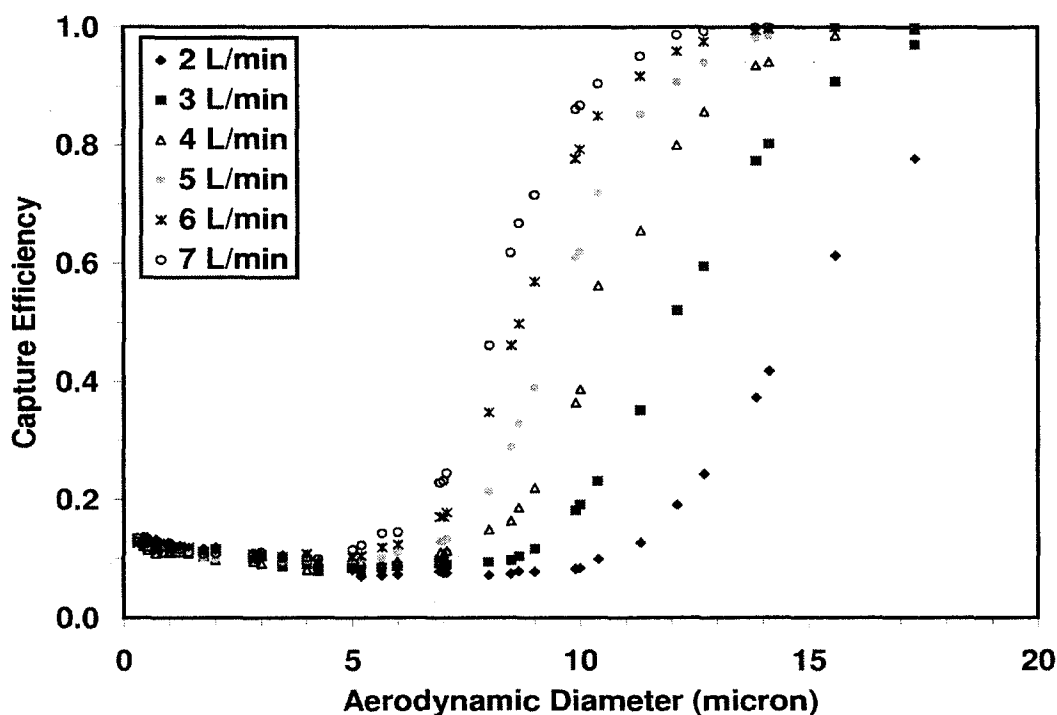


Figure 20. Particle deposition efficiency as a function of inspiratory flow rate and particle diameter.

Figure 21 shows the use of impaction parameter ($IP = d_{ae}^2 Q$) to collapse all data from Figure 20 onto a single curve. Particles with higher IP have a higher deposition rate and

particles with lower IP escape into the nasopharynx. Good agreement is seen between the present simulations and the available experimental data. Some slight deviations can be seen; particularly for low IP our simulations predict 4% to 5% greater deposition than the experimental data, and for mid-range IP the experiments show a more rapid increase in deposition efficiency than the present simulations. These differences most likely can be attributed to the large effects minor differences in anatomy can have on inertial deposition as explained by Kelly et al. (2004).

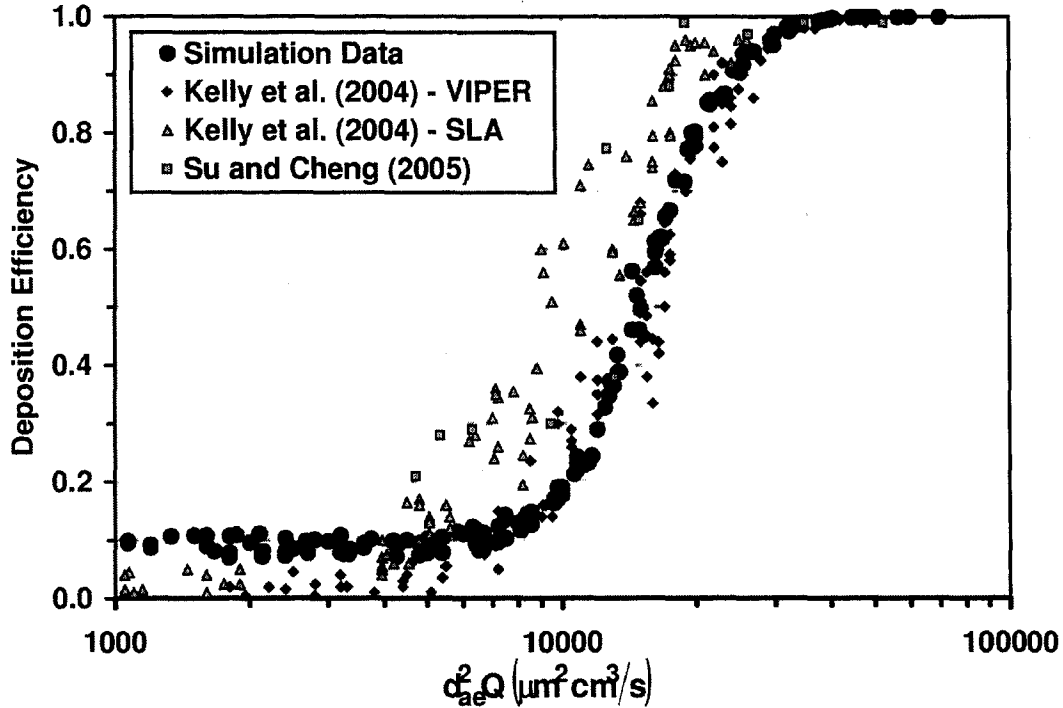


Figure 21. Nasal cavity deposition efficiency as a function of impact parameter.

3. Deposition of Particles in the Human Airway Multi-Level Bifurcation Model

Figure 22 presents the deposition efficiency of the inhaled aerosol particles in the third bifurcation. It is seen from Figure 22 that, among all the simulations, the deposition efficiency from the laminar model is closest to the experimental measurement. At the third bifurcation, the Reynolds number drops to about 700. The simulation indicates that the turbulence originated from the larynx jet penetrates into the first couple of bronchial generations, and gradually dissipated through the airway passages.

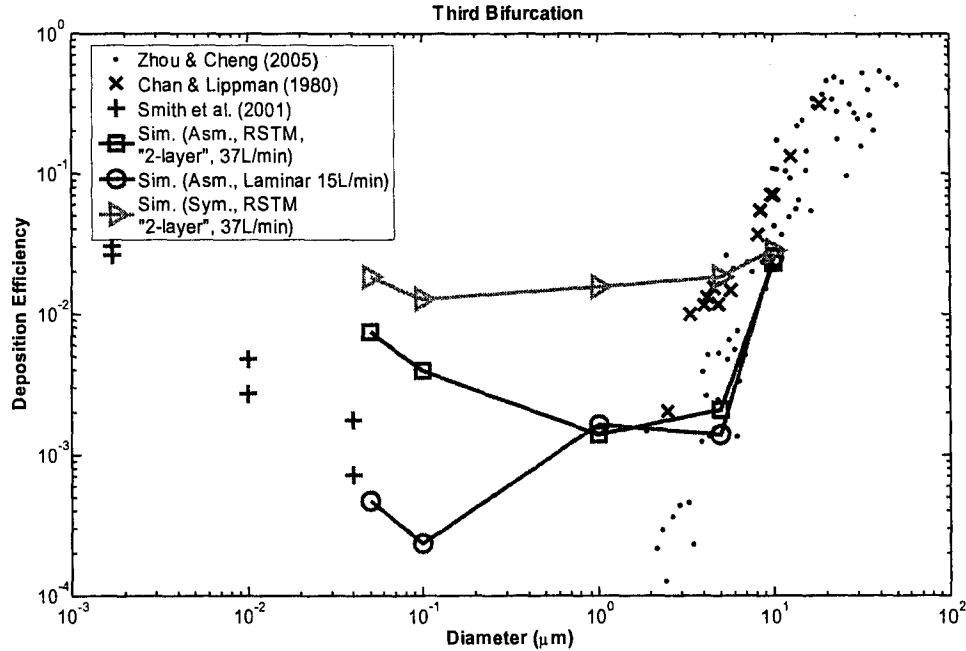


Figure 22. Comparison of the deposition efficiency in the third bifurcation.

4. Deposition of Fibers in the Human Airway Multi-Level Bifurcation Model

Figure 23 shows that the numerical predictions of the fiber deposition efficiency for varying breathing conditions agree well with the experimental data. Due to the rather complex geometry of the 3D-bifurcation model, in the simulations a range of the shear velocity ($0.05 < u^* < 1$ m/s) is used in the numerical simulations. The shear velocity is related to the airflow rate as well as the airway geometries. The simulation results qualitatively as well as quantitatively agree with the experimental measurements of both Zhou et al. (2007), and Wang and Hopke (2008). It is conjectured that the scatter of the fiber deposition efficiency in Figure 23 is due to the effect of random diffusion by turbulence fluctuations in the airway. The complexity of the human airway bifurcation structures in the vicinity of the carina ridge causes significant variations in the wall shear stress and the corresponding shear velocity. Thus, in the simulation a range shear velocity was used.

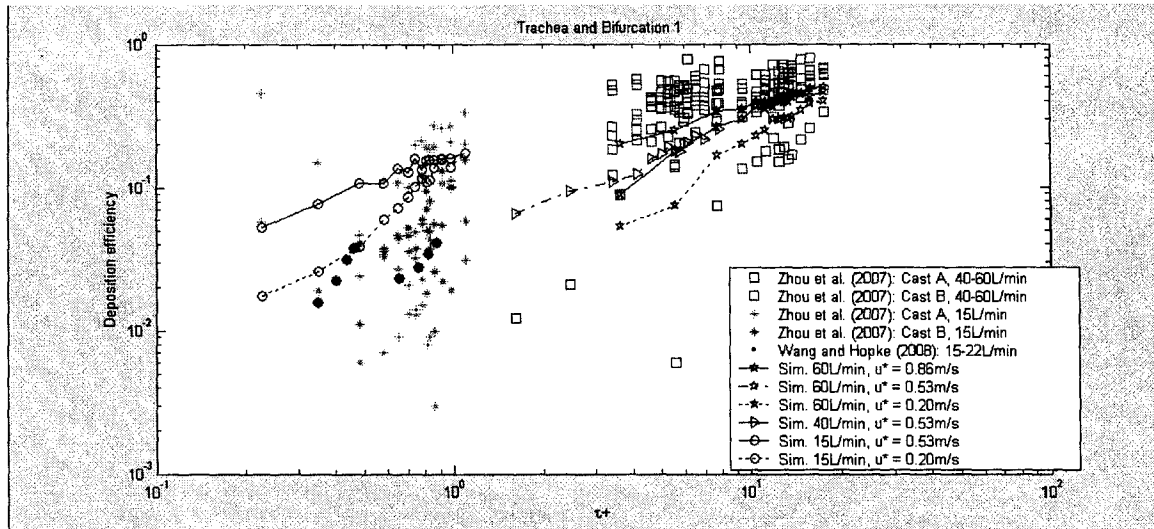


Figure 23. Comparison of fiber deposition efficiency in the trachea and the first bifurcation with the experimental data.

Figure 24 displays the predicted fiber deposition efficiency in the trachea and the first bifurcation versus the equivalent-volume Stokes number. Four sets of carbon fibers with diameters of 1, 3, 5, and 10 μm are used in the simulations. For each set of carbon fibers, aspect ratios of 4, 8, 14, 24, and 36 were considered. For the sake of comparison, for the same Stokes numbers, a series of simulations for spherical particles with diameters of 1, 3, 5, and 10 μm were performed. The experimental measurements by Zhou et al. (2007) for the carbon fibers, and Zhou and Cheng (2005) for spherical particles in a human tracheobronchial tree replica were plotted in Figure 24 for comparison. It is seen from this figure that generally the fiber deposition efficiency increases as the equal-volume Stokes number, Stk_v , increases. It is also seen that the fiber deposition efficiency in addition to the equal-volume Stokes number, varies with particle diameter. It is also observed that the rate of increase of the deposition efficiency of the fibers with Stk_v within each class of fibers increases sharply as the fiber diameter increases. This observation implies that the fiber deposition rate becomes more sensitive to the aspect ratios as the fiber diameter increases.

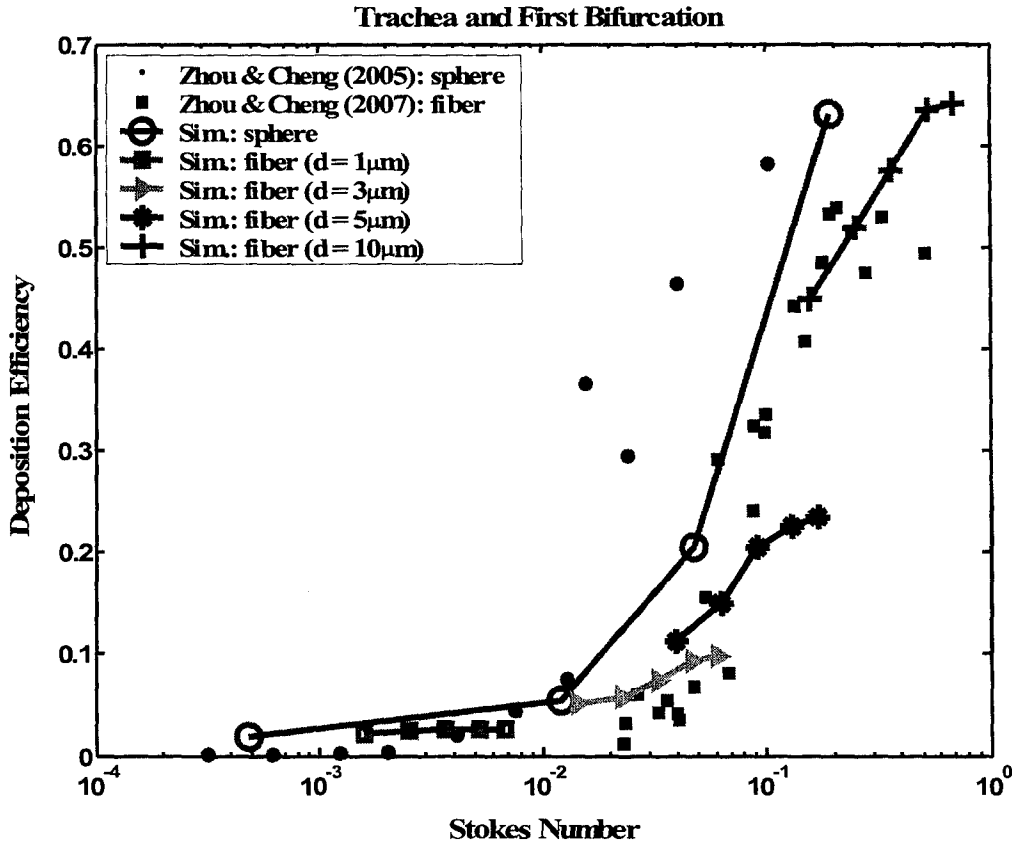


Figure 24. Comparison of the fiber deposition efficiency in the trachea and the first bifurcation.

Figure 24 also shows that the deposition efficiency of the fibers in the trachea and the first bifurcation is generally lower than the corresponding spherical particles with the same equivalent volume Stokes numbers. This figure also shows that the predicted fiber deposition in the trachea and the first bifurcation is in good agreement with the experimental data of Zhou and Cheng (2005) and Zhou et al. (2007).

SPECIFIC AIM 3

1. Comparison of Experimental and Theoretical Models

Figure 21 compares the particle deposition efficiency in the human nasal airways indicating the theoretical and experimental data are in good agreement. It showed that the impaction is the dominant deposition mechanism in the nasal airways.

Figures 23 and 24 compare the deposition efficiencies in the tracheobronchial airways for both spherical and fiber aerosols. It showed agreement of experimental and theoretical approaches. It also shows the fiber deposition efficiency is lower than that of spherical particles.

2. Empirical Model for Fiber Deposition in the Nasal Airway

Based on all the fiber deposition data shown above, an attempt was made to find an empirical model for the practical estimation of the fiber deposition efficiency in the human nasal

airway. As stated in Kelly et al. (2004), nasal deposition can be expressed by the following expression:

$$DE = 1 - \exp [-(a d_{ae}^2 Q)^b] \quad (8)$$

where a and b are constants to be determined from curve fitting process. In this research, Equation (1) was adopted for searching the best-fit equations for fiber and available compact particle data. A nonlinear fitting procedure in SigmaPlot (SPSS Inc., Chicago, IL) was used as the fitting tool. Recent published compact particle data from Kelly et al. (2004), and from the current study were used in the fitting process. It is worth noting that the nasal airway cast used in Kelly et al. (2004) was made from the same MRI scans. The best-fit curve obtained for the fiber deposition efficiency is $a = 4.262 \times 10^{-5}$, $b = 2.46$ with $R^2 = 0.98$. The best-fit curve found for compact particle is $a = 6.426 \times 10^{-5}$, $b = 1.89$, and $R^2 = 0.90$. Figure 25 shows the best-fit curves for the deposition of fiber and compact particles in the nasal airway plotted along with the related experimental data. It is clearly shown that, given the same impaction parameter, fibers deposit less in the human nasal airway compared with the compact particles. Therefore, it implies that compared with general particles in the ambient air, relatively more fibers could penetrate into the human lower respiratory tract, causing adverse health effects.

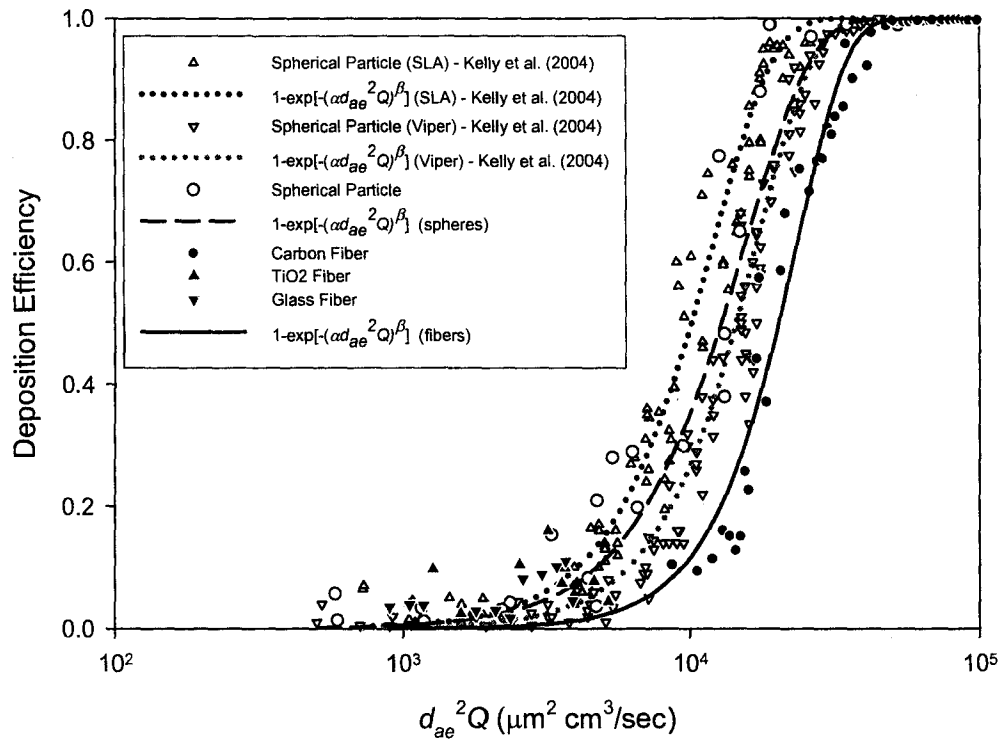


Figure 25. The best-fit equations of the nasal deposition for fibers and spherical particles.

3. Empirical Model for Fiber Deposition in the Oral Airway

An empirical model is proposed for fiber deposition in the oral airway based on the equation format suggested by Cheng et al. (1999).

$$DE_{(oral)} = 1 - \exp(-(a d_{ae}^2 Q)), \quad (9)$$

where $DE_{(oral)}$ is the fiber deposition efficiency in the oral airway, a is a constant needed to be determined, and $d_{ae}^2 Q$ is the fiber impaction parameter. The nonlinear regression program used in finding the nasal airway empirical model was employed again as the fitting tool. All fiber data shown in Figure 14 were used in the fitting process. The best-fitted parameter was $a = 5.47 \times 10^{-6}$ with $R^2 = 0.96$, and the result was plotted beside the experimental data in Figure 14. As can be seen, this proposed empirical model can fairly well predict the fiber deposition efficiency in the oral airway, and is believed to be useful in any given fiber exposure scenario (within similar experimental conditions) for estimating the fiber deposition in the human oral airway.

4. Empirical Model for Fiber Deposition in the Tracheobronchial Airway

In order to be able to predict the fiber deposition in human lungs, an empirical model was developed. This derivation of this empirical equation followed the approach we used for deposition of spherical particles (Zhou and Cheng, 2005). The basic equation was considered as the same as described in Zhou and Cheng (2005),

$$\eta = 1 - \exp(-a \cdot Stk^b), \quad (10)$$

where a and b are constant numbers for each individual bifurcation or trachea, the Stk here is defined based on the volume equivalent diameter (Zhang et al., 1996).

The experimental data in each bifurcation of cast A and B, which were obtained in our previous study (Zhou et al., 2007), were used to obtain the fitted Equation (10). The result for the constant values of a and b is listed in Table 2. We treated b as a constant value as we did for spherical particles (Zhou and Cheng, 2005). We found that the average value of b (1.34 ± 0.19) is exactly the same as we obtained for spherical particles although the standard deviation was relatively large. For value a , we plotted data of F as a function of a as we did for the spherical particle study (Zhou and Cheng, 2005). F is a function of bifurcation angle and ratio of parent to daughter radii (Cai and Yu, 1988):

$$F = \frac{4 \sin \theta}{\pi \left[\frac{R}{R_o} \right]} \quad (11)$$

An equation of $a = 1.70 F$ was obtained even though the linear relation was not as good as spherical particles.

Table 2. Constant values of a and b obtained by Equation (5) for each bifurcation.

	*Bifurcation #	F	a	b
Cast A	1_E	0.75	3.51	1.515
	2_F1	1.33	1.43	1.525
	2_F2	0.51	0.19	1.504
	3_G1	0.97	0.91	1.201
	3_G2	0.49	0.41	1.177
	3_G3	0.69	1.01	1.234
	3_G4	0.93	1.05	1.263
	4_H1	1.03	0.79	1.261
	4_H2	1.09	2.41	1.222
Cast B	1_E	0.72	2.45	1.605
	2_F1	0.93	2.27	1.53
	2_F2	0.80	1.00	1.036
	3_G1	1.30	11.44	1.719
	3_G2	0.79	1.51	1.191
	3_G3	1.03	2.53	1.256
	3_G4	1.43	2.13	1.26

*Details of the bifurcation number were described in Zhou et al., 2007.

Thus, the empirical fiber deposition model for the different bifurcations is expressed as:

$$\eta = 1 - \exp(-1.70 F \cdot Stk^{1.34}) \quad (12)$$

SPECIFIC AIM 4

Fiber Exposure Index

The fiber fraction of particulate matter is defined by the American Council for Governmental Hygienists (ACGIH) as the particulate fraction that by virtue of aerodynamic size and behavioral properties is expected to penetrate the head airway and enter the lung airways during mouth breathing (Phalen et al., 1986). This thoracic fraction represents the worst-case potential exposure of the whole lung to particles. The definition of thoracic fraction is used as an index of exposure for particles that may have adverse effects in large and small airways in the lung (Phalen et al., 1986). Because the known adverse health effects of inhaled fibers are in the TB, alveolar, and parenchymal regions of the lung, a thoracic fraction will be used as the index of exposure. Similar to the thoracic fraction curve for spherical particles, experimental deposition data of fibers in the oral airways obtained at the flow rate of 43.5 L min^{-1} are used to develop the size-selective criteria. Figure 26 shows that fiber penetration through oral airways plotted as a function of aerodynamic diameter. Our data show that penetration of fibers is higher than those of spheres in human oral airways, because large fibers tend to align with air

flow as shown in Figure 16. Following the same procedure for spherical particles, we define a thoracic fraction for fiber (ST) as:

$$ST = [1 - F(x)] \quad (13)$$

$$\text{where } F(x) = \int_{-\infty}^x \frac{dy}{\sqrt{2\pi}} \exp(-y^2/2), \text{ is a}$$

function of fiber aerodynamic diameter d_{ae} ;

$$y = \frac{\ln(d_{ae} / d_{ae}(50\%))}{\ln(\sigma_g)}; d_{ae}(50\%) = 15 \mu\text{m}; \text{ and}$$

$\sigma_g = 1.5$. The thoracic curve is to the right of experimental values to provide a conservative measure, because some individuals will have penetration values greater than the experimental data obtained here due to variability of airway geometry (ACGIH, 1985).

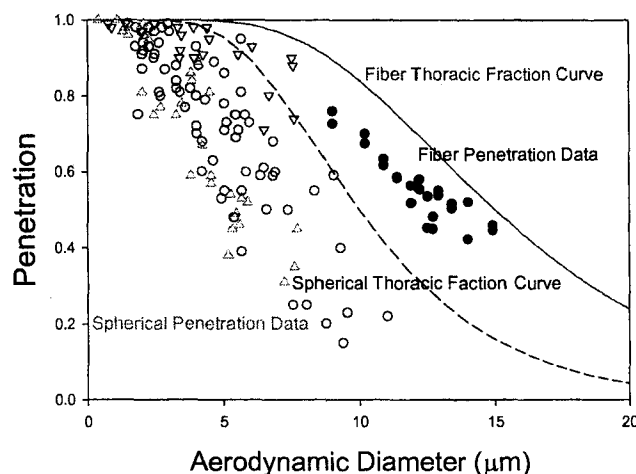


Figure 26. Fiber penetration data for thoracic fraction curve.

The proposed thoracic fraction is different from that of spherical particles in two aspects. First, the 50% aerodynamic diameter of the curve, 15 μm , is larger than 10 μm for spherical particles. Second, the thoracic fraction of fiber is based on fiber count or number, whereas the thoracic fraction for spherical particles is based on mass. These differences will be reflected in air samplers designed to collect thoracic fraction of fibers and methods to analyze samples.

REFERENCES

- Asgharian, B. (1988). *Theoretical Deposition of Fibrous Particles in the Respiratory System of Human and Rats*. Doctoral dissertation, University of New York at Buffalo, Buffalo.
- Asgharian, B. and Ahmadi, G. (1998). Effect of fiber geometry on deposition in small airways of the lung. *Aerosol Sci. Technol.*, 29:459-474.
- Asgharian, B. and Anjilivel, S. (1995). Movement and deposition of fibers in an airway with steady viscous flow. *Aerosol Sci. Technol.*, 22:261-270.
- Asgharian, B. and Anjilivel, S. (1998). A multiple-path model of fiber deposition in the rat lung. *Toxicol. Sci.*, 44:80-86.
- Asgharian, B. and Yu, C.P. (1988). Deposition of inhaled fibers in the human lung. *J. Aerosol Med.*, 1:37-50.
- Asgharian, B. and Yu, C.P. (1989a). A simplified model of interceptional deposition of fibers at airway bifurcations. *Aerosol Sci. Technol.*, 11:80-88.
- Asgharian, B. and Yu, C.P. (1989b). Deposition of fibers in the rat lung. *J. Aerosol Sci.*, 20:355-366.
- Asgharian, B., Yu, C.P., and Gradon, L. (1988). Diffusion of fibers in a tubular flow. *Aerosol Sci. Technol.*, 9:213-219.
- Asgharian, B., Zhang, L., and Fang, C.P. (1997). Theoretical calculations of the collection efficiency of spherical particle and fibers in an impactor. *J. Aerosol Sci.*, 2:277-287.
- Baris, I., Simonato, L., Artvinli, M., Pooley, F., Saracci, R., Skidmore, J., and Wagner, C. (1987). Epidemiological and environmental evidence of the health effects of exposure to erionite fibres: A four-year study in the Cappadocian region of Turkey. *Int. J. Cancer*, 39:10-17.

- Beeckmans, J.M. (1965). The deposition of aerosols in the respiratory tract. 1: Material analysis and comparison with experimental data. *Can. J. Physiol. Pharmacol.*, 43:157-172.
- Beeckmans, J.M. (1970). The deposition of asbestos particles in the human respiratory tract. *Int. J. Environ. Study*, 1:31-34.
- Bernstein, D. M., Riego Sintes, J. M., Ersboell, B. K., and Kunert, J. (2001). Biopersistence of synthetic mineral fibers as a predictor of chronic intraperitoneal injection tumor response in rats. *Inhal. Toxicol.*, 13:851-875.
- Bogovski, P., Gilson, J.C., Timbrell, V., Wagner, J.C., and Davis, W. (1973). *Biological Effects of Asbestos*. IARC Scientific Publication No. 8, Lyon.
- Cai, F.S. and Yu, C.P. (1988). Inertial and interceptional deposition of spherical particles and fibers in a bifurcating airway. *J. Aerosol Sci.*, 19:679-688.
- Chen, Y.K. and Yu, C.P. (1991). Sedimentation of fibers from laminar flows in a horizontal circular duct. *Aerosol Sci. Technol.*, 14:343-347.
- Cheng, Y.S., Powell, Q.H., Smith, S.M., and Johnson, N.F. (1995). Silicon carbide whiskers: Characterization and aerodynamic behavior. *Am. Ind. Hyg. Assoc. J.*, 56:970-978.
- Cheng, Y.S., Smith, S.M., and Yeh, H.C. (1997). Deposition of ultrafine particles in human tracheobronchial airways. *Ann. Occup. Hyg.*, 41(Suppl. 1):714-718.
- Cheng, Y.S., Zhou, Y., and Chen, B.T. (1999). Particle deposition in a cast of human oral airways. *Aerosol Sci. Technol.*, 31:286-300.
- Cheng, Y.S., Fu, C.S., Yazzie, D., and Zhou, Y. (2001a). Respiratory deposition patterns of salbutamol pMDI with CFC and HFA-134a formulations in a human airway replica. *J. Aerosol Med.*, 14:255-266.
- Cheng, Y.S., Holmes, T.D., Gao, J., Guilmette, R.A., Li, S., Surakitbanharn, Y., and Rowlings, C. (2001b). Characterization of nasal spray pumps and deposition pattern in a replica of human nasal airway. *J. Aerosol Med.*, 14:267-280.
- Ding, J.Y., Yu, C.P., Zhang, L., and Chen, Y.K. (1997). Deposition modeling of fibrous particles in rats: Comparison with available experimental data. *Aerosol Sci. Technol.*, 26:403-414.
- Guilmette, R.A. and Gagliano, T.J. (1994). Construction of a model of human nasal airways using in vivo orphological data. *Ann. Occup. Hyg.*, 38:69-75.
- Happel, J. and Brenner, H. (1973). *Low Reynolds Number Hydrodynamics*. Noordhoff, Leyden, p. 207.
- Harris, R.L. and Fraser, D.A. (1976). A model for deposition of fibers in the human respiratory system. *Am. Ind. Hyg. Assoc. J.*, 37:73-89.
- Hesterberg, T. W. and Hart, G.A. (2001). Synthetic vitreous fibers: A review of toxicology research and its impact on hazard classification. *Crit. Rev. Toxicol.*, 31:1-53.
- Hill, I.M., Beswick, P.H., and Donaldson, K. (1995). Differential release of superoxide anions by macrophages treated with long and short fibre amosite asbestos is a consequence of differential affinity for opsonin. *Occup. Environ. Med.*, 52:92-95.
- IARC (2002). *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol. 81, Man-made Vitreous Fibers*. IARC Press, Lyon, France.
- Jeffery, G.B. (1922). The motion of ellipsoidal particles immersed in a viscous fluid. *Proc. Roy. Soc. Lond.*, A102:161-179.
- Kamstrup, O., Ellehauge, A., Collier, C.G., and Davis, J.M.G. (2002). Carcinogenicity studies after intraperitoneal injection of two types of stone wool fibres in rats. *Ann. Occup. Hyg.*, 46(2):135-142.
- Kelly, J.T., Asgharian, B., Kimbell, J., and Wong, B.A. (2004). Particle deposition in human nasal airway replicas manufactured by different methods. Part I: Inertial regime particles. *Aerosol Sci. Technol.*, 38:1036-1071.
- Lippmann, M. (1988). Asbestos exposure indices. *Environ. Res.*, 46:86-106.
- Lippman, M. (1990). Effects of fiber characteristics on lung deposition, retention, and disease. *Environ. Health Perspect.*, 88:311-317.

- Martonen, T.B. and Lowe, J. (1983). Assessment of aerosol deposition patterns in human respiratory tract casts. In *Aerosols in the Mining and Industrial Work Environments*. Vol. 1. pp.151-164, Ann Arbor Science, Ann Arbor, MI.
- Miller, B.G., Searl, A., Davis, M.G., Donaldson, K., Cullen, R.T., Bolton, R.E., Buchanan, D., and Soutar, C.A. (1999). Influence of fibre length, dissolution and biopersistence on the production of mesothelioma in the rat peritoneal cavity. *Ann. Occup. Hyg.*, 43(3):155-166.
- Myojo, T. (1987). Deposition of fibrous aerosol in model bifurcating tubes. *J. Aerosol Sci.*, 18:337-347.
- Myojo, T. (1990). The effect of length and diameter on the deposition of fibrous aerosol in a model lung bifurcation. *J. Aerosol Sci.*, 21:651-659.
- NIOSH (1994). Asbestos and other fibers by PCM. In *NIOSH Manual of Analytical Methods*.
- Phalen, R.F., Hindo, W., John, W., Liou, P.J., Lippmann, M., McCawley, M.A., Raabe, O.G., Soderholm, S.C., and Stuart, B.O. (1986). Rationale and recommendations for particle size-selective sampling in the workplace. *Appl. Ind. Hyg.*, 1:3-12.
- Pooley, F.D. and Clark, N.J. (1980). A comparison of fibre dimensions in chrysotile, crocidolite and amosite particles from samples of airborne dust and from post-mortem lung tissue specimens. In *Biological Effects of Mineral Fibres*, J.C. Wagner (ed.), IARC Scientific Publication No. 30, Vol. 1, pp. 79-86.
- Selikoff, I.J. and Lee, D.H. (1978). *Asbestos and Disease*. Academic Press, New York.
- Stanton, M.F. and Wrench, C. (1972). Mechanisms of mesothelioma induction with asbestos and fibrous glass. *J. Nat. Cancer Inst.*, 48:797-821.
- Stöber, W. (1972). Dynamic Shape Factors of Nonspherical Aerosol Particles, In *Assessment of Airborne Particles*, T. Mercer et al. (eds.), pp. 249-289, Charles C. Thomas Publisher, Springfield, IL.
- Stöber, W., Flachsbarth, H., and Hochrainer, D. (1970). The aerodynamic diameter of latex aggregates and asbestos fibres. *Staub-Reinhalt Luft*, 30:1-12.
- Sussman, R.G., Cohen, B.S., and Lippmann, M. (1991a). Asbestos fiber deposition in human tracheobronchial cast. I. Experimental. *Inhal. Toxicol.*, 3:145-160.
- Sussman, R.G., Cohen, B.S., and Lippmann, M. (1991b). Asbestos fiber deposition in human tracheobronchial cast. II. Empirical model. *Inhal. Toxicol.*, 3:161-179.
- Swift, D. L. (1991). Inspiratory inertial deposition of aerosols in human nasal airway replicate casts: Implication for the proposed NCRP lung model. *Radiat. Prot. Dosimetry*, 38(1/3):29-34.
- Timbrell, V. (1973). Physical factors as etiological mechanisms. In *Biological Effects of Asbestos*, IARC, Lyon, France.
- Timbrell, V. (1982). Deposition and retention of fibres in the human lung. *Ann. Occup. Hyg.*, 26:347-369.
- Wang, Z., Hopke, P.K., Ahmadi, G., and Cheng, Y.S. Fibrous particle deposition in human nasal passage: The Influence of particle length, flow rate and geometry of nasal airway. *J. Aerosol Sci.* (in press).
- Weibel, E.R. (1963). *Morphometry of the Human Lung*. Academic Press, New York, NY.
- Yu, C.P., Zhang, L., Oberdorster, G., Mast, R.W., Glass, L.R., and Utell, M.J. (1994). Deposition modeling of refractory ceramic fibers (RCF) in the rat lung. *J. Aerosol Sci.*, 25:407-417.
- Zamankhan, P., Ahmadi, G., Hopke, P. H., Wang, Z., Cheng, Y. S., Su, W. C., and Leonard, D. (2006). Airflow and deposition of nano-particles in a human nasal cavity. *Aerosol Sci. Technol.*, 40:463-476.
- Zhang, L., Asgharian, B., and Anjilvel, S. (1996). Inertial and interceptional deposition of fibers in a bifurcating airway. *J. Aerosol Med.*, 3:419-430.
- Zhang, L., Asgharian, B., and Anjilvel, S. (1997). Inertial deposition of particles in a human upper airway bifurcations. *Aerosol Sci. Technol.*, 26:97-110.

- Zhou, Y. and Cheng, Y.S. (2005). Particle deposition in a cast of human tracheobronchial airways. *Aerosol Sci. Technol.*, 39:492-500.
- Zhou, Y., Su, W.C., and Cheng, Y.S.(2007). Fiber deposition in the tracheobronchial region: Experimental measurements. *Inhal. Toxicol.*, 19:1071-1078.
- Zwartz, G.J. and Guilmette, R.A. (2001). Effect of flow rate on particle deposition in a replica of a human nasal airway. *Inhal. Toxicol.*, 13:109-127.

Publications Generated from the Present NIOSH-funded Study

Note: this list contains three applicable journal articles that will be submitted to PubMed Central within 12 months of publication.

1. Ahmadi G: [2003] Computational Modeling Multiphase Flows - Environmental Applications. In AFI-2003, Fluid-Informatics for Biomedical and Environmental Quality Applications, Ed. H. Higuchi and T. Hayase, pp. 15-20.
2. Cheng YS: [2003] Aerosol Deposition in the Extrathoracic Region, *Aerosol Sci. Technol.* 37:659-671.
3. Zhou Y, Cheng YS: [2005] Particle deposition in a cast of human tracheobronchial airways, *Aerosol Sci. Technol.* 39:492-500.
4. Gilbertson K, Finlay WH, Lange CF, Brett M, Vick D, Cheng YS: [2005] Generation of Fibrous Aerosols from Thin Films, *J. Aerosol Sci.* 36:933-937.
5. Wang Z, Hopke PK, Baron PH, Ahmadi G, Cheng YS, Deye G, Su WC: [2005] Fiber Classification and the Influence of Average Air Humidity, *Aerosol Sci. Technol.* 39:1056-1063.
6. Su WC, Cheng YS: [2005] Deposition of Fiber in the Human Nasal Airway, *Aerosol Sci. Technol.* 39:888-901.
7. Cheng YS, Holmes TD, Fan B: [2006] Evaluation of Respirator Filters for Asbestos Fibers, *J. Occup. Environ. Hyg.* 3:26-35.
8. Zamankhan P, Ahmadi G, Hopke PK, Wang Z, Cheng YS, Su WC, Leonard, D: [2006] Airflow and Deposition of Nano-particles in a Human Nasal Cavity, *Aerosol Sci. Technol.* 40:463-476.
9. Su WC, Cheng YS: [2006] Fiber Deposition Pattern in Two Human Respiratory Tract Replicas, *Inhal. Toxicol.* 18:749-760.
10. Su WC, Cheng YS: [2006] Deposition of Fiber in the Human Respiratory Tract, *J. Aerosol Sci.* 37:1429-1441.
11. Zhou Y, Su WC, Cheng YS: [2007] Fiber Deposition in the Tracheobronchial Region: Experimental Measurements, *Inhal. Toxicol.* 19:1071-1078.
12. Zhang H, Ahmadi G, Asgharian B: [2007] Transport and Deposition of Angular Fibers in Turbulent Channel Flows, *J. Aerosol Sci.* 41: 529-548.
13. Tian L, Ahmadi GA: [2007] Particle Deposition in Turbulent Duct Flows – Comparisons of Different Model Predications, *J. Aerosol Sci.* 38: 377-397.
14. Su WC, Cheng YS: [2008] Deposition of Man-made Fiber in the Human Nasal Airway, *Aerosol Sci. Technol.* 42: 173-181.

15. Zhou Y, Su WC, Cheng YS: [2008] Fiber Deposition in the Tracheobronchial Region: Deposition Equations, Inhal. Toxicol. (in press).
16. Wang Z, Hopke PK, Ahmadi G, Cheng YS: [2008] Fibrous Particle Deposition in Human Nasal Passage: The Influence of Particle Length, Flow Rate and Geometry of Nasal Airway, J. Aerosol Sci. (in press).
17. Tian L, Ahmadi GA, Wang Z, Hopke KH: [2008] Transport and Deposition of Ellipsoidal Fibers in Low Reynolds Number Flows, J. Aerosol Sci. (in press).
18. Shanley KT, Zamankhan P, Ahmadi G, Hopke PK, Cheng YS: [2008]. Numerical Simulations Investigating the Regional and Overall Deposition Efficiency of the Human Nasal Cavity, J. Inhal. Toxicol. (in press).
19. Su, WC, Cheng, YS: Deposition of Man-Made Fibers in Human Respiratory Airway Casts, J. Aerosol Sci. (in press).