Aerosol Science and Technology: History and Reviews

Edited by David S. Ensor

RTI Press

RTI INTERNATIONAL

Library of Congress Control Number: 2011936936
ISBN: 978-1-934831-01-4

doi:10.3768/rtipress.2011.bk.0003.1109
www.rti.org/rtipress

About the Cover

The cover depicts an important episode in aerosol history—the Pasadena experiment and ACHEX. It includes a photograph of three of the key organizers and an illustration of a major concept of atmospheric aerosol particle size distribution. The photograph is from Chapter 8, Figure 1. The front row shows Kenneth Whitby, George Hidy, Sheldon Friedlander, and Peter Mueller; the back row shows Dale Lundgren and Josef Pich. The background figure is from Chapter 9, Figure 13, illustrating the trimodal atmospheric aerosol volume size distribution. This concept has been the basis of atmospheric aerosol research and regulation since the late 1970s.

This publication is part of the RTI Press Book series.

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CHAPTER 15

A Brief History of Respiratory Deposition Modeling

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Introduction

Smoke exposure has been a health hazard ever since humans began to use fire for cooking. Although not as ancient as the problem of smoke exposure, aerosol therapy was already in use over 4 millennia ago, according to the description in Ayurvedic medicine. Despite these early experiences in aerosol inhalation, it was not until 1700 that a comprehensive discourse of dust diseases was given in a book on occupational medicine by Ramazzini (1700). It took another 170 years before the first scientific observation of pulmonary deposition was described in a lecture delivered by John Tyndall (1870) at the Royal Institution of Great Britain. Given the complexity of respiratory deposition, remarkable progress has been made in both experimental determination and mathematical modeling of respiratory deposition since the late 1930s.This brief historical account focuses on the progress in mathematical modeling.

The ability to measure and predict respiratory deposition rates is of central importance in environmental health and respiratory drug delivery. The link between inhalation exposure and health response is the particle dose specific to target tissues. It takes a number of steps for particles in ambient air to reach a target tissue in an individual. These steps include entry through the nose or mouth, transport in the respiratory tract, deposition on airway surfaces, translocation of deposited particles to other sites, and dissolution of soluble particles at sites of deposition or during translocation. The rate at which particles go through each of these steps depends on the anatomical and physiological factors of an individual, the airflow characteristics, and particle properties. The factors influencing the fate of deposited particles include deposition site, particle properties, and the health status of an individual. Because of marked intersubject variations in morphometry of the respiratory tract, deposition patterns differ considerably from individual to individual even under identical breathing conditions.

The respiratory tract consists of three distinct regions: the head airways, the tracheobronchial tree, and the alveolar region. These regions have dissimilar anatomical characteristics and clear deposited particles by different pathways. Consequently, the rate at which particles deposit and the length of time deposited particles remain in a region differ from region to region. Furthermore, particles deposit on airway surfaces in nonuniform patterns: the deposition density (number of particles deposited over a unit surface area of the airways) is markedly higher at the carinal ridge where the two daughter tubes intersect in an airway bifurcation. The site of deposition and the deposition density both have great influences on the response to a specific toxicant or therapeutic agent. As a result, assessment of the health effects of inhaled aerosols requires not only data on total deposition (fraction of inhaled particles deposited in the entire respiratory tract) and regional deposition (fraction of inhaled particles deposited in a respiratory region), but also information on local deposition (rate of deposition over a small surface area of the respiratory airways).

Particle deposition in the human lung has been assessed using both experimental methods and theoretical calculations. Since the 1940s, a substantial amount of consistent data has been obtained from experiments with human subjects of markedly different lung morphometry. Although measurements can be made with human subjects to provide data on total and regional deposition, experimental techniques available today are not sufficiently sensitive for quantitative assessment of local deposition in the human lung. However, mathematical modeling is capable of predicting total, regional, and local deposition for any breathing frequency, tidal volume, particle size, and particle density. A deposition model is a computational scheme that contains four elements required for an adequate description of respiratory deposition: morphometry of the respiratory tract, respiratory physiology, aerodynamic characteristics, and particle behavior. It is generally developed using a specified lung structure, but its computational scheme can be applied to any lung morphometry. Validated theoretical models are, therefore, useful for estimating deposition rates for children and patients with damaged lungs, for whom experimental data are difficult to obtain.

Because of anatomical complexity of the respiratory tract, mathematical modeling of particle deposition by necessity makes use of simplifying assumptions on lung morphometry. Two basic types of morphometric models have been used: (1) compartments-in-series models that treat the respiratory tract as a number of compartments connected in series and (2) continuous models that consider the respiratory tract as a continuous conduit of variable cross section (trumpet models) or as a continuous tubular filter bed (Wang, 2005). Both basic types of morphometric models have been used in respiratory deposition modeling. Only compartments-in-series models and trumpet models are discussed in this brief historical account.

Compartments-in-Series Models

Findeisen's Deposition Model

Findeisen (1935) was the first to develop a mathematical model for deposition of inhaled particles. He worked on this problem during his appointment as a physicist at the Institute for Aviation Medicine and Climate Research in Hamburg (Eppendorfer Hospital). The morphometric model he used consists of nine compartments connected in series, starting with the trachea and ending with alveolar sacs (Figure 1). Each compartment contains a number of parallel airway segments, which have identical diameter and length. A respiratory cycle comprises an inspiratory phase, an expiratory phase, and a short pause following each phase. The inspiratory and expiratory flows are constant. The flow has a uniform velocity profile in each airway segment; therefore, no convective mixing occurs in the airways. Deposition mechanisms considered in the model include inertial impaction, gravitational settling, Brownian diffusion, and interception (deposition due to the finite size of a particle). The efficiency of deposition by each mechanism in an airway segment is calculated using an approximate equation derived with simplifying assumptions. The deposition efficiencies calculated for various mechanisms are then summed to give the combined deposition efficiency. In calculations for the fractional deposition in each compartment, the progressive loss

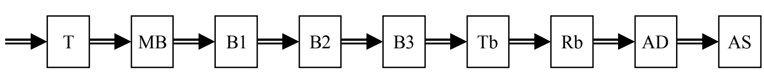


Figure 1. A compartments-in-series model of the respiratory tract used by Findeisen for deposition calculations. T: trachea, MB: main bronchi, B1: bronchi of order 1, B2: bronchi of order 2, B3: bronchi of order 3, Tb: terminal bronchioles, Rb: respiratory bronchioles, AD: alveolar ducts, AS: alveolar sacs.

of particles in the inhaled aerosol as it passes from compartment to compartment is taken into consideration.

A particle can deposit in an airway via several mechanisms (Figure 2). Findeisen's model takes into account the three most important mechanisms: inertial impaction, gravitational settling, and Brownian diffusion. Deposition by interception, which is also considered in the model, is generally negligible except for elongated particles. Electrostatic forces are important only for highly charged particles, and turbulent deposition occurs mainly in upper airways. Thermophoretic and diffusiophoretic forces (not shown in Figure 2) can retard deposition of nanoparticles in upper airways when the temperature and relative humidity of inspired air are lower than those in the respiratory tract (Wang & Friedlander, 2006).

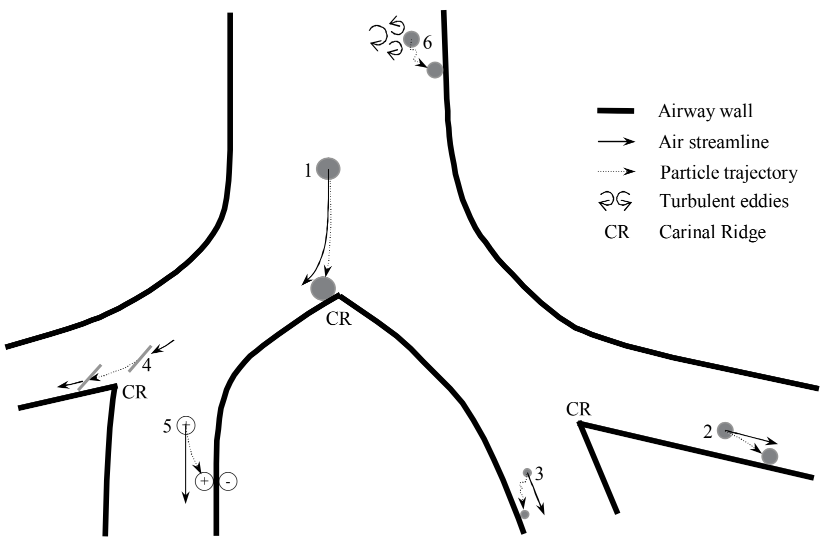


Figure 2. Mechanisms of particle deposition in the respiratory tract: (1) inertial impaction, (2) gravitational settling, (3) Brownian motion, (4) interception, (5) electrostatic forces, (6) turbulent deposition.

Findeisen's model represents a computational scheme containing all four important elements required for an adequate description of respiratory deposition: morphometry of the respiratory tract, respiratory physiology, aerodynamic characteristics, and particle behavior. However, two of the assumptions Findeisen made are inconsistent with the transport processes of air and airborne particles in the lungs: (1) the entire volume of inhaled aerosol reaches every compartment of the lung model and (2) there is no deposition during exhalation. The first assumption tends to overestimate total deposition, while the second leads to a lower estimate. The errors resulting from these two assumptions cancel each other to some extent. Consequently, the model predictions are in fair agreement with the total deposition curves (the curve displaying total deposition as a function of particle size) obtained by experiments for normal breathing.

Modifications of Findeisen's Deposition Model

Following the pioneering work of Findeisen, several modifications were made to the model (Beeckmans, 1965; Landahl, 1950) that incorporate various degrees of refinements in morphology of the respiratory tract, aerodynamic characteristics in the lungs, and equations used in calculations for deposition efficiency.

In Landahl's analysis (1950), the mouth, the larynx, and one extra order of alveolar ducts were added to the morphometric model proposed by Findeisen, and the equations for deposition efficiencies were simplified. An equation was derived for the combined deposition efficiency to account for the simultaneous action of various mechanisms. In addition, the improved model takes into consideration the deposition during exhalation and the progressively smaller volume of inhaled aerosol that passes from compartment to compartment. With these modifications, the predictions of total deposition for various breathing frequencies and tidal volumes are in general agreement with the experimental data of Landahl and Herrmann (1948).

Flow patterns in the repeatedly bifurcating respiratory tract are complex. During inhalation, the flow velocity distribution in a daughter tube of an airway bifurcation takes the shape of a skewed parabola with the peak shifted toward the inner edge of the tube. As a result of these nonuniform flow profiles and the intrinsic motion of particles, inhaled aerosol has a tendency to mix with residual air in the lungs (Wang, 2005). Landahl (1950) noted the mixing between inhaled aerosol and residual air but did not take it into account in his calculations. Employing an aerosol wash-in and wash-out technique, Altshuler and colleagues (1959) demonstrated that a portion of inhaled aerosol is exchanged with residual air in each respiratory cycle as a result of convective mixing. The data for three healthy subjects indicated that the degree of convective mixing can differ considerably from individual to individual. Subsequently, Altshuler (1959) proposed an expression for convective mixing in the lungs and used it in a filter-bed model for calculating regional deposition.

In an extension of the analyses of Findeisen and Landahl, Beeckmans (1965) modified Altshuler's expression for convective mixing and made some changes in the equations for deposition efficiency. He used the solution derived by Gormley and Kennedy (1949), instead of the empirical equation given by Landahl, to calculate the rate of deposition by convective Brownian diffusion in each airway segment. Using a computer, which became more available in the early 1960s, Beeckmans was able to calculate many points for each deposition curve to study the effects of convective mixing and recycling of particles that remain airborne at the end of exhalation. The calculations for total deposition under various breathing frequencies and tidal volumes are in fair agreement with published experimental data (Landahl et al., 1951; 1952). The calculated total deposition curve shows a minimum in the particle diameter range between 0.3 and 0.4 μm, confirming the results of experimental studies. The minimum occurs because the rates of inertial deposition and gravitational settling increase with increasing particle size, whereas the rate of diffusional deposition increases with decreasing particle size. As a result, none of these mechanisms makes a notable contribution to deposition for particles between 0.3 and 0.4 μm. The deposition model based on the analyses of Findeisen, Landahl, and Beeckmans is known as the Findeisen-Landahl-Beeckmans model.

The ICRP and NCRP Deposition Models

Since 1960, the International Commission on Radiological Protection (ICRP) has published three models for deposition and retention of inhaled radioactive particles. The first model appeared in ICRP Publication 2 (ICRP, 1960), the second in Publication 30 (ICRP, 1979), and the third in Publication 66 (ICRP, 1994). In the second model, developed and published by the Task Group on Lung Dynamics of the International Commission on Radiological Protection (TGLD, 1966), the deposition calculations are essentially identical to the theoretical analyses of Findeisen and Landahl. Minor modifications made by TGLD include use of an empirical equation for nasopharyngeal deposition and the solution of Gormley and Kennedy for convective Brownian diffusion in tracheobronchial and pulmonary regions.

In the latest ICRP model (ICRP, 1994), the respiratory tract used for calculations consists of five regions: (1) the anterior nasal passages; (2) the posterior nasal passages, pharynx, and larynx; (3) the trachea and bronchi; (4) the bronchioles; and (5) the alveolar region. The morphometric model is adopted from several published lung models and, therefore, can be considered as a composite model. By the early 1990s, a substantial amount of deposition data obtained with human subjects and lung casts had been published. Several equations of deposition efficiency used in the ICRP model are empirical expressions derived by curve-fitting procedures using these experimental data, whereas some other empirical equations are based on the theoretical calculations of Egan and colleagues (1989), which have been validated with experimental data. In the theoretical analysis of Egan and colleagues, the respiratory tract is assumed to be a trumpet-shaped continuous conduit, and either empirical or analytical expressions are used for the deposition term in the time-dependent transport equation for particles. The continuous deposition models are discussed in a later section.

Computer programs and simplified equations have been developed to make calculations with the ICRP model easier. A new version of the computer program for the model is now available (Jarvis et al., 2010). By curve fitting the model calculations, Hinds (1999) obtained simplified equations for total and regional deposition of standard density particles during nose breathing. Following is the equation for total deposition fitted to averaged values for men and women at three levels of physical activity (resting, light exercise, and heavy exercise):

$$DF = 0.0587 + \frac{0.911}{1 + \exp(4.77 + 1.485 \, 1\text{n} \, d_p)} + \frac{0.943}{1 + \exp(0.508 - 2.58 \, 1\text{n} \, d_p)} \quad (1)$$

Here dp is particle diameter in micrometers. The equation does not take into account the loss of particles during entry into the nose and, therefore, can be directly compared with the experimental data for nasal breathing. Figure 3 shows that the calculations from Equation 1 agree well with the data reported by Heyder and colleagues (1986).

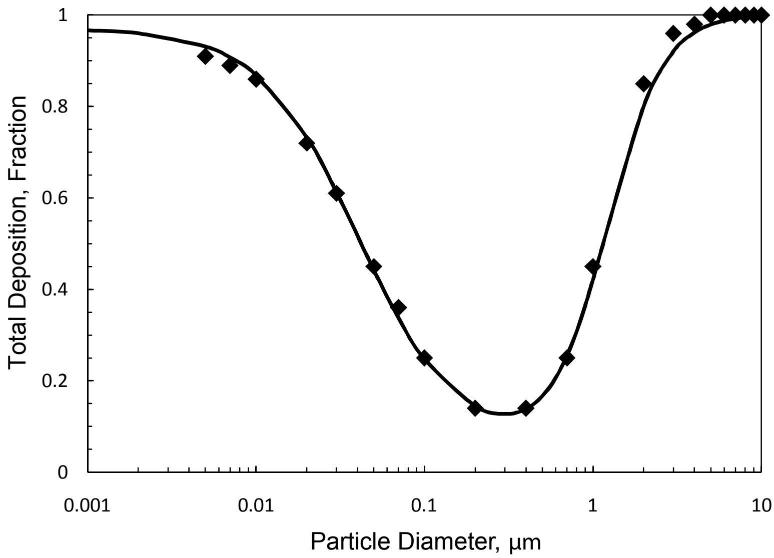


Figure 3. Comparison of measured and calculated total deposition of standard density spheres during nasal breathing. Experimental data are from Heyder et al. (1986) for the breathing pattern: 750 cm^{3}s^{-1} mean flow rate, 4 s breathing cycle period, and 1,500 cm^3 tidal volume.

Three years after publication of the latest ICRP model, the National Council on Radiation Protection and Measurements (NCRP) presented its own model for deposition and retention of inhaled radioactive substances (NCRP, 1997). To avoid confusion in the radiation protection community, the NCRP recommended adopting the ICRP model for exposure calculations and indicated that publication of its own model was only intended to be NCRP's contribution to the field of radiation protection.

The NCRP deposition model is mainly based on the work of Yeh and Schum (1980). The respiratory tract used for calculations consists of three regions: (1) the naso-oro-pharyngo-laryngeal region, (2) the tracheobronchial region, and (3) the pulmonary region. The tracheobronchial region contains 16 generations of airways extending from the trachea to terminal bronchioles, and the pulmonary region consists of eight generations of airways and the alveoli. These airway generations are connected in series. Each airway generation comprises a number of parallel airway segments that have identical diameter and length. Empirical equations are used to calculate deposition in head airways, whereas either analytical or empirical expressions are used for deposition in each generation of airways in the tracheobronchial and alveolar regions. Convective mixing is not considered in the model.

To compare the ICRP and NCRP models, Yeh and colleagues (1996) used both models to calculate regional deposition for the same particle size distribution, lung volume, and breathing pattern. The results indicate that the deposition fractions in head airways calculated by the two models are very similar for the range of particle diameter between 0.001 and 10 μm, but for particles smaller than 0.1 μm the NCRP model gives somewhat higher deposition in the tracheobronchial tree and consequently lower deposition in the alveolar region. The difference arises probably because convective mixing is not considered in the NCRP model, and different expressions are used in the two models to calculate enhanced deposition that occurs near the carinal ridge of an airway bifurcation. Enhanced deposition is discussed in a later section.

Multiple-Path Deposition Models

The deposition models described in the preceding subsections are known as single typical path models, because the respiratory tract is represented by a single series of compartments in which the same values of diameter and length are assumed for all airways in the same generation. In fact, the human respiratory tract does not bifurcate regularly, and airway bifurcations are not symmetric. To account for variations in deposition rate among the five lobes in the lungs, Yeh and Schum (1980) used one typical pathway for each lobe to calculate the deposition fraction. The morphometric models for the five lobes, each of which has a symmetric structure, were developed from detailed measurements of a silicone rubber cast of the human tracheobronchial tree (Raabe et al., 1976) and an idealized model of the alveolar region. Calculations for each lobe are based on the computational scheme of Landahl (1950) with some modifications. The analytical solution given by Ingham (1975) is used to compute the rate of deposition by Brownian diffusion from laminar flow in each airway segment, whereas deposition efficiencies by other mechanisms are evaluated using empirical expressions. The fraction of air flow distributed to a lobe, a parameter required for lobar deposition calculations, is assumed to be proportional to the number of terminal bronchioles associated with the lobe. Results for a normal breath show that, for standard-density particles between 0.01 and 10 μm, the deposition fractions in the right lower lobe and the left lower lobe are notably higher than in other lobes.

Extending Yeh and Schum's analysis, Asgharian and colleagues (2001) used 10 asymmetric, structurally different human respiratory tract models to calculate deposition fractions in the tracheobronchial tree, the alveolar region, each of the five lobes, and each generation of airways. The tracheobronchial trees of the 10 respiratory tract models are also based on the morphometric measurements of Raabe and colleagues (1976). Each of the 10 structurally different models is constructed with the values of airway parameters chosen randomly in accordance with their statistical distributions, instead of the mean or median values. Calculations are carried out with the computational scheme developed earlier for a multiple-path model of particle deposition in the rat lung (Anjilvel & Asgharian, 1995). The equations given by Cai and Yu (1988), Ingham (1975), and Wang (1975) are used to calculate deposition due to inertial impaction, convective diffusion, and gravitational settling, respectively. Results for regional deposition are similar to those calculated from a single typical path model and the five-lobe lung model of Yeh and Schum, but lobar deposition is found to be strongly dependent on the lung morphometry used in calculations. A software program based on a refined version of the multiple-path deposition model has been developed (Price et al., 2002).

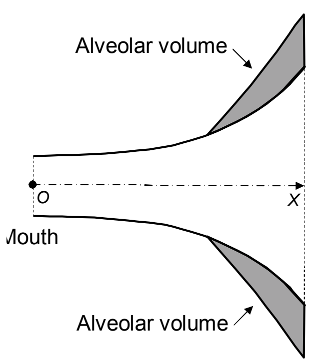
As a variation from typical path models, Koblinger and Hofmann (1988) introduced a stochastic approach to account for the effect of asymmetry in lung structure. In this multiple-path model, each inspired particle moves through a single pathway selected randomly by a Monte Carlo code from a lung model with statistically distributed airway dimensions. Each pathway comprises a number of airway bifurcation units connected in series. The model retains the concept of airway generations but takes into consideration the variations in diameter, length, and branching angle of airways in each generation. Deposition probabilities are calculated using the equations previously employed by Yeh and Schum (1980) in the five-lobe lung model. For each airway bifurcation unit, the model is used to simulate the transport of about 10,000 particles and the results are then used to obtain a statistical mean value of deposition fraction. Results for lobar deposition are in reasonable agreement with those of Yeh and Schum (1980). Because the coordinates of each airway are specified in the simulation, the model is capable of providing detailed three-dimensional deposition patterns in the entire respiratory tract.

Using the same stochastic approach but different assumptions on selection of parameter values for the airways, Goo and Kim (2003) developed another computational scheme for tracking the movement of inspired particles. The equations employed by Yeh and Schum (1980) in the five-lobe lung model are used to calculate deposition probabilities for each airway segment. For submicron size particles, results of the stochastic model and the single typical path model are in good agreement, but for deposition of micron size particles in large conducting airways, the stochastic model gives higher deposition. The discrepancy indicates that the stochastic model is more sensitive to the parameters governing inertial impaction.

Continuous Models

As a notable departure from the compartments-in-series model, Taulbee and Yu (1975) proposed a continuous model for particle deposition. A trumpet-shaped conduit with a continuously increasing cross section along its axis (Figure 4) is used to represent the respiratory tract; therefore, the model is known as a trumpet model. As a result of deposition, the concentration of airborne particles in the conduit varies with position and time. An apparent diffusion coefficient is used to account for the effect of aerosol mixing along the axial direction. The axial flow velocity and particle concentration are assumed to be uniform at each cross section of the conduit. Under these assumptions, a mass balance for airborne particles over a short section of the conduit gives the following time-dependent transport equation:

Figure 4. A trumpet model of the respiratory tract.



$$A_T \frac{\partial n}{\partial t} = -A_A U \frac{\partial n}{\partial x} + \frac{\partial}{\partial x}\left(A_A D_e \frac{\partial n}{\partial x}\right) - L_d \tag{2}$$

Here $n(x, t)$ is the mean particle concentration at the axial coordinate x and time t, $A_A(x)$ the cross-sectional area of the conduit obtained by summing over all airways at x, $A_T(x, t)$ the time-dependent total cross-sectional area of the conduit (in the alveolar region the additional cross-sectional area contributed by the alveolar volume is included; the area is time dependent because of the change in alveolar volume during a breath), $U(x)$ the average axial flow velocity, $D_e(x)$ the apparent diffusion coefficient in the axial direction, and $L_d(x, t)$ a function representing the particle deposition rate per unit length of the conduit. The functions for deposition due to diffusion and gravitational settling in nonalveolated airways are derived from the expressions used by Beeckmans (1965), whereas an empirical expression is used for inertial deposition. For alveolated airways, approximate expressions are derived for deposition due to gravitational settling and Brownian diffusion.

According to Taulbee and Yu (1975), the apparent axial diffusion of aerosol particles arises from the distribution of flow velocities in various airways of the same generation, which in turn is caused by the distributions of airway length and diameter in each generation of the respiratory tract. If the flow velocities are assumed to be normally distributed with a standard deviation of 0.6, the apparent diffusion coefficient is shown to be $0.3Ul_t$, where l_t is the length of an airway segment.

Taulbee and Yu solved Equation 2 with the values of airway diameter and length given in Weibel's lung model A (Weibel, 1963). For particles in the diameter range between 0.05 and 5 μm, calculated total deposition fractions for normal breathing are in fair agreement with the experimental data of Heyder and colleagues (1973). Equation 2 can be used to calculate the concentration of airborne particles at the mouth during a sequence of breaths. The calculated fractional recovery of half-micron particles in each breath during aerosol wash-in and wash-out is in good agreement with the experimental results of Davies and colleagues (1972).

Egan and Nixon (1985) also used Equation 2 to develop a continuous model. Their model differs from that of Taulbee and Yu in the expression for the apparent axial diffusion coefficient and particle deposition functions. In Egan and Nixon's model, two empirical expressions proposed by Scherer and colleagues (1975) for gas mixing in bronchial airways are used: $De(x) = D + 1.08Ud_t$ for inspiration and $De(x) = D + 0.37Ud_t$ for expiration, where D is the particle diffusion coefficient and d_t the diameter of an airway segment. These two expressions are in fact quite similar to the one used by Taulbee and Yu, for the particle diffusion coefficient is negligibly small and d_t is generally about one-quarter to one-half of l_t. The analytical solutions derived by Pich (1972) and Ingham (1975) are used in Egan and Nixon's model for deposition due to gravitational settling and convective diffusion in nonalveolated airways, whereas empirical expressions are used for inertial deposition. For alveolated airways, approximate expressions are derived for deposition due to gravitational settling and Brownian diffusion. For particles in the diameter range between 0.2 and 3 μm, calculated total depositions under various breathing conditions are in good agreement with published experimental results (Heyder et al., 1975). The agreement is fair between model calculations of regional deposition and the experimental data of Stahlhofen and colleagues (1980). As noted earlier, some empirical equations of deposition efficiency used in the ICRP model are based on the calculations with this continuous model.

Local Deposition

Deposition is enhanced near the carinal ridge of an airway bifurcation (see Figure 2), because particles are brought closer to the wall surface that faces the approaching airflow during inhalation. Enhancement in deposition occurs for particles of any size but is considerably greater for larger particles approaching the carinal ridge at higher velocities. Information on local deposition is useful for estimating tissue doses of highly toxic particles.

Detailed studies on local deposition began in the early 1970s. Using a three-dimensional airway model with dimensions approximately equivalent to the first lung bifurcation, Bell (1978) measured deposition velocity (the number of particles deposited on a unit surface area per unit time divided by the main stream concentration, also known as local transfer coefficient) over the entire surface area of an airway segment downstream of the carinal ridge. To describe the degree of nonuniformity in deposition, Bell introduced the term hot spot intensity, defined as the ratio of local deposition velocity to the average deposition velocity over the entire wall surface of an airway segment. If the local deposition velocity is obtained by averaging over 0.6% of the total surface area, the hot spot intensity is 25.4 for 5.7 μm latex particles and 200 cm/s air velocity in the airway preceding the carina. For 1.1 μm latex particles and 100 cm/s air velocity, the hot spot intensity is 3.35. The area chosen to calculate the hot spot deposition velocity, 0.6% of the total surface area of an airway segment in the bifurcation model, corresponds to roughly 150,000 epithelial cells.

Since the early 1990s, advances in computational software have made it possible to solve the three-dimensional particle transport equations numerically to provide information on local deposition in an airway bifurcation (Gradon & Orlicki, 1990). To express the enhancement of deposition at hot spots, Balásházy and colleagues (1999) introduced a local deposition enhancement factor, defined as the ratio of the local deposition density in a given surface element to the average deposition density in the entire surface area of an airway bifurcation. For deposition in the upper bronchial airways during inhalation, the enhancement factor for any particle size in the range between 0.01 and 10 μm has a maximum value of about 100 for a surface element of 100 × 100 μm, which corresponds to about 10 × 10 biological cells, an area needed for development of tumors.

Conclusion

Respiratory deposition modeling is difficult because lung structure and aerodynamic characteristics in lung airways are complicated. Nevertheless, substantial progress has been made during the past 7 decades. Refinements in deposition models mainly came from improved morphometric data of the human lung, better understanding of air flow and particle transport in the bronchial tree, and advances in computational fluid dynamics. With these advances and improvements, deposition models available today are capable of predicting local deposition density in an airway segment of the bronchial tree under any breathing conditions for a variety of particle types, including compact particles, elongated particles, nanoparticle aggregates, charged particles, and hygroscopic particles. Information obtained from improved deposition models has found applications in respiratory drug delivery, environmental health, occupational health, and aerosol diagnosis such as assessment of airway obstruction and mucociliary transport.

Further progress in deposition modeling can be made when the distribution of air flow among various lobes in response to changes in airway resistance and parenchymal compliance of the lungs are better understood. Another area for improvement is incorporation of particle transport by thermophoretic and diffusiophoretic forces into deposition models. If the temperature and relative humidity of ambient air are lower than the conditions in the lungs, inspired air will be gradually heated and humidified as it passes through head airways and the first few generations of the tracheobronchial tree. Consequently, gradients in temperature and water vapor concentration are established in a thin boundary layer near the walls of each airway segment. For nanoparticles, the thermophoretic and diffusiophoretic velocities resulting from these temperature and vapor concentration gradients are comparable in magnitude to Brownian deposition velocities. The combined phoretic motion is directed away from airway walls and, as a result, can lead to considerable suppression of deposition in head airways and the trachea. Reduction of deposition in upper airways will bring additional inhaled particles to lower airways, thereby increasing the deposition fractions in bronchiolar and alveolar regions (Wang & Friedlander, 2006).

Acknowledgments

I would like to thank Professor Lutz Mädler for helping me search for information about W. Findeisen and calling to my attention the lecture entitled "On Dust and Disease," delivered by John Tyndall at the weekly evening meeting of the Royal Institution of Great Britain on January 21, 1870.

References

Altshuler, B. (1959). Calculation of regional deposition of aerosol in the respiratory tract. *Bulletin of Mathematical Biophysics, 21, 257*–270.

Altshuler, B., Palmes, E. D., Yarmus, L., & Nelson, N. (1959). Intrapulmonary mixing of gases studied with aerosols. *Journal of Applied Physiology, 14,* 321–327.

Anjilvel, S., & Asgharian, B. (1995). A multiple-path model of particle deposition in the rat lung. *Fundamental & Applied Toxicology, 28*, 41–50.

Asgharian, B., Hofmann, W., & Bergmann, R. (2001). Particle deposition in a multiple-path model of the human lung. *Aerosol Science & Technology, 34*, 332–339.

Balásházy, I., Hofmann, W., & Heistracher, T. (1999). Computation of local enhancement factors for the quantification of particle deposition patterns in airway bifurcations. *Journal of Aerosol Science, 30*, 185–203.

Beeckmans, J. M. (1965). The deposition of aerosols in the respiratory tract-I. Mathematical analysis and comparison with experimental data. Canadian *Journal of Physiology & Pharmacology, 43*, 157–172.

Bell, K. A. (1978). Local particle deposition in respiratory airway models. In D. T. Shaw (Ed.), *Recent developments in aerosol science* (pp. 97–134). New York, NY: Wiley.

Cai, F. S., & Yu, C. P. (1988). Inertial and interceptional deposition of spherical particles and fibers in a bifurcating airway. *Journal of Aerosol Science, 19*, 679–688.

Davies, C. N., Heyder, J., & Subba Ramu, M. C. (1972). Breathing of half-micron aerosols. I. Experimental. *Journal of Applied Physiology, 32*, 591–600.

Egan, M. J., & Nixon, W. (1985). A model of aerosol deposition in the lung for use in inhalation dose assessments. *Radiation Protection Dosimetry*, *11*, 5–17.

Egan, M. J., Nixon, W., Robinson, N. I., James, A. C., & Phalen, R. F. (1989). Inhaled aerosol transport and deposition calculations for the ICRP task group. *Journal of Aerosol Science, 20*, 1301–1304.

Findeisen, W. (1935). Über das Absetzen kleiner, in der Luft suspendierter Teilchen in der menschlichen Lunge bei der Atmung. *Pflügers Archiv für gesamte Physiologie des Menschen und der Tiere, 236*, 367–379.

Goo, J. H., & Kim, C. S. (2003). Theoretical analysis of particle deposition in human lungs considering stochastic variations of airway morphology. *Journal of Aerosol Science, 34*, 585–602.

Gormley, P., & Kennedy, M. (1949). Diffusion from a stream flowing through a cylindrical tube. *Proceedings of the Royal Irish Academy, 52A*, 163–169.

Gradon, L., & Orlicki, D. (1990). Deposition of inhaled aerosol particles in a generation of the tracheobronchial tree. *Journal of Aerosol Science, 21*, 3–19.

Heyder, J., Armbruster, L., Gebhart, J., Grein, E., & Stahlhofen, W. (1975). Total deposition of aerosol particles in the human respiratory tract for nose and mouth breathing. *Journal of Aerosol Science, 6*, 311–328.

Heyder, J., Gebhart, J., Heigwer, G., Roth, C., & Stahlhofen, W. (1973). Experimental studies of the total deposition of aerosol particles in the human respiratory tract. *Journal of Aerosol Science, 4*, 191–208.

Heyder, J., Gebhart, J., Rudolf, G., Schiller, C. F., & Stahlhofen, W. (1986). Deposition of particles in the human respiratory tract in the size range 0.005–15 μm. *Journal of Aerosol Science, 17*: 811–825.

Hinds, W. C. (1999). *Aerosol technology: Properties, behavior, and measurement of airborne particles* (2nd ed.). New York, NY: Wiley.

International Commission on Radiological Protection (ICRP). (1960). Recommendations of the International Commission on Radiological Protection, Report of Committee II on permissible dose for internal radiation (1959). (ICRP Publication 2). Elmsford, NY: Pergamon Press.

International Commission on Radiological Protection (ICRP). (1979). Limits for intakes of radionuclides by workers. (ICRP Publication 30. Part 1). Elmsford, NY: Pergamon Press.

International Commission on Radiological Protection (ICRP). (1994). Human respiratory tract model for radiological protection. A report of a Task Group of the International Commission on Radiological Protection. *Annals of the ICRP, 24*, 1–482.

Ingham, D. B. (1975). Diffusion of aerosols from a stream flowing through a cylindrical tube. *Journal of Aerosol Science, 6*, 125–132.

Jarvis, N. S., Birchall, A., James, A. C., Bailey, M. R., & Dorrian, M. D. (2010). LUDEP 2.07: Personal computer program for calculating internal doses using the ICRP publication 66 respiratory tract model. Retrieved from http://www.hpa.org.uk/Publications/Radiation/Software/softwareLUDEP.

Koblinger, L., & Hofmann, W. (1988). Monte Carlo model for aerosol deposition in human lungs. In J. Dodgson, R. I. McCallum, M. R. Bailey, & D. R. Fisher (Eds.), *Inhaled particles VI, Proceedings of the Sixth International Symposium on Inhaled Particles*, Organized by the British Occupational Hygiene Society, Cambridge, England, September 2–6, 1985. *Annals of Occupational Hygiene, 32*, Suppl. 1, 65–70.

Landahl, H. D. (1950). On the removal of airborne droplets by the human respiratory tract: I. The lung. *Bulletin of Mathematical Biophysics, 12*, 43–56.

Landahl, H. D., & Herrmann, R. (1948). On the retention of air-borne particles in the human lung. *Journal of Industrial Hygiene & Toxicology, 30*, 181–188.

Landahl, H. D., Tracewell, T. N., & Lassen, W. H. (1951). On the retention of air-borne particulates in the human lung: II. *A.M.A. Archives of Industrial Hygiene & Occupational Medicine, 3*, 359–366.

Landahl, H. D., Tracewell, T. N., & Lassen, W. H. (1952). Retention of air-borne particulates in the human lung: III. *A.M.A. Archives of Industrial Hygiene & Occupational Medicine, 6*, 508–511.

National Council on Radiation Protection (NCRP). (1997). *Deposition, retention and dosimetry of inhaled radioactive substances.* (NCRP Report 125). Bethesda, MD: National Council on Radiation Protection and Measurements.

Pich, J. (1972). Theory of gravitational deposition of particles from laminar flows in channels. *Journal of Aerosol Science, 3*, 351–361.

Price, O. T., Asgharian, B., Miller, F. J., Cassee, F. R., & De Winter-Sorkina, R. (2002). Multiple Path Particle Dosimetry model (MPPD v1.0): A model for human and rat airway particle dosimetry (Report No. 650010030). [CD-ROM]. Bilthoven, The Netherlands: National Institute of Public Health and the Environment (RIVM).

Raabe, O. G., Yeh, H. C., Schum, G. M., & Phalen, R. F. (1976). Tracheobronchial geometry: Human, dog, rat, hamster—A compilation of selected data from the project Respiratory Tract Deposition Models (Report LF-53). Albuquerque, NM: Lovelace Foundation.

Ramazzini, B. (1700). *De Morbis Artificum Diatriba*. Mutinae: Typis Antonii Capponi. Translated by W. C. Wright as *Diseases of workers* (Chicago, IL: The University of Chicago Press, 1940). (Reprinted in 1964, New York, NY: Hafner).

Scherer, P. W., Shendalman, L. H., Greene, N. M., & Bouhuys, A. (1975). Measurement of axial diffusivities in a model of the bronchial airways. *Journal of Applied Physiology*, *38*, 719–723.

Stahlhofen, W., Gebhart, J., & Heyder, J. (1980). Experimental determination of the regional deposition of aerosol particles in the human respiratory tract. *American Industrial Hygiene Association Journal*, *41*, 385–398.

Taulbee, D. B., & Yu, C. P. (1975). A theory of aerosol deposition in the human respiratory tract. *Journal of Applied Physiology*, *38*, 77–85.

Task Group on Lung Dynamics (TGLD). (1966). Deposition and retention models for internal dosimetry of the human respiratory tract. A report prepared by the Task Group on Lung Dynamics for Committee II of the International Commission on Radiological Protection. *Health Physics*, *12*, 173–207.

Tyndall, J. (1870). On dust and disease. *Proceedings of the Royal Institution of Great Britain*, *6*, 1–14.

Wang, C. S. (1975). Gravitational deposition of particles from laminar flows in inclined channels. *Journal of Aerosol Science*, *6*, 191–204.

Wang, C. S. (2005). Inhaled particles. Amsterdam, The Netherlands: Elsevier.

Wang, C. S., & Friedlander, S. K. (2006). Effects of thermophoresis and diffusiophoresis on regional deposition of inhaled nanoparticles. In R. F. Phalen, M. J. Oldham, S. W. Akhavan, M. D. Hoover, & K. Asotra (Eds.), *Proceedings of the Conference on Frontiers in Aerosol Dosimetry Research* (pp. 5-85–5-96). (APHEL Report No. 06-01). Irvine, CA: University of California, Air Pollution Health Effects Laboratory.

Weibel, E. R. (1963). *Morphometry of the human lung*. New York, NY: Academic Press.

Yeh, H. C., Cuddihy, R. G., Phalen, R. F., & Chang, I. Y. (1996). Comparisons of calculated respiratory tract deposition of particles based on the proposed NCRP model and the new ICRP66 model. *Aerosol Science & Technology*, *25*, 134–140.

Yeh, H. C., & Schum, G. M. (1980). Models of human lung airways and their application to inhaled particle deposition. *Bulletin of Mathematical Biology*, *42*, 461–480.