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PARTICLE DEPOSITION IN HUMAN AND CANINE TRACHEOBRONCHIAL CASTS

Annual Progress Report

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November 15, 1991

Prepared for

The U.S. DEPARTMENT OF ENERGY
AGREEMENT NO. DE-FG02-87ER60592

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ABSTRACT

The aim of this work is to measure deposition patterns and efficiencies of aerosol particles within realistic, single-pathway physical models of the tracheobronchial airways of humans and experimental animals over a range of particle sizes for a variety of respiratory modes and rates. This will provide data needed to assess the dose to the bronchial epithelium from inhaled radon progeny.

In prior grant years an empirical expression for diffusional deposition efficiency of particles in the upper airways was obtained based on experimental data collected in central airway casts. The work also provided new quantitative data of airflow distribution in a realistic central airway cast for two species for both steady and pulsatile inspiratory flow and for expiratory flow. Theoretical studies were then extended based on a developing flow model. We concluded that although the developing flow model is a better predictor of the data than assumption of parabolic flow, the predicted deposition is significantly lower than that predicted by our best fit equation. In the current year the experimental results were evaluated in terms of the parametric solution of the convective diffusion equation.

There are no data on the effect of particle charge on airway deposition efficiency for particles with diameters less than 0.3 μm. Theoretical predictions suggest that deposition by image charge forces will be approximately equal to deposition by diffusion for singly charged particles with diameters ranging from about 0.1 to 1.0 μm. We have been developing an experimental system that will enable us to measure and compare the deposition of charged and neutral ultrafine particles in simple tracheal and bronchial models. An aerosol electrometer was designed and constructed, and the performance characteristics have been evaluated.

CONTENTS

I. SCOPE

The research program addresses Goal #2 of the DOE/ER Plan for Radon Exposure and Dose to the Critical Cells of the Respiratory Tract. It responds to the indicated need for data on the effect of particle size and charge, breathing pattern and respiratory tract morphology on the dose to the critical cells of the bronchial epithelium.

The aim of this work is to measure deposition patterns and efficiencies of aerosols within realistic, single-pathway, physical models of the tracheobronchial airways of humans and experimental animals over a range of particle sizes from 0.01 to 1.0 μm, for a variety of respiratory modes and rates. The pathways are a major branch path, a minor branch path and one which consists of alternating major and minor branches. The particle size range has been extended to include aerosols with $d < 0.02$ μm to represent the unattached fraction of Po-218. Substantial deposition is expected for these particles. Additional studies will compare the deposition of singly charged with neutral ultrafine particles. The measurements will permit the development and critical evaluation of quantitative predictive models for the deposition efficiency of the inhaled radioactive particles.

II. SIGNIFICANT RESULTS

Full morphometric and inhalation flow distribution measurements on the human and canine airway casts were completed in the prior grant periods. The work provided new quantitative data of airflow distribution in a realistic central airway cast for two species and for two different airflow patterns; steady inspiratory flow and pulsatile inspiratory flow. Inertance (inertia of the airflow) was demonstrated to carry more of the flow to lower lobes at higher inspiratory flowrate. The effect was substantially greater in the canine cast. The inertial effects seen for constant flow appear to be enhanced by pulsatile flow. The difference is more apparent for the dog cast which is consistent with morphometric differences between the species. We further demonstrated that inertial effects are not nearly as pronounced during exhalation as for inhalation. Air flow resistance in these casts is considerably greater during exhalation than inhalation.

As part of our ongoing efforts to improve the quality of our measurements we investigated the mass size dispersion of particles classified according to their electrical mobilities. This is of primary concern in our experiments in which the radioactivity is a concentration dependent property of the classified particles. For the conditions tested, the multiply charged particles constituted 9-13% of the total particle number concentration and 24-48% of the total mass concentration. When an impactor was inserted directly after the nebulizers the multiply charged particles were effectively removed and the particles were nearly monodisperse. (Asgharian, B., C.P. Fang, and B.S. Cohen, Generation of submicron mass/volume-monodisperse aerosols with a nebulizer-impactor-electrostatic classifier system, Aerosol Sci. Technol., In press.)

An empirical expression for the diffusional deposition efficiency of particles in the upper airways was obtained based on experimental data collected in central airway casts (Cohen, B.S. and Asgharian, B., J. Aerosol Sci., 1990). In the uppermost airways of the lung the deposition predicted using our empirical equation is about twice the value obtained using Ingham's equation for particle deposition by diffusion from parabolic flow. Further theoretical investigation was carried out to more completely evaluate the effect of skin friction and Schmidt number on deposition efficiency. We concluded that although the developing flow model is a better predictor of the data than assumption of parabolic flow, the predicted deposition is significantly lower than that predicted by our best fit equation. In collaboration with Dr. C.P. Yu of SUNY Buffalo, we have, in the current grant year, evaluated the results in terms of the parametric solution of the convective diffusion equation (Appendix A).

In the current grant period we have initiated a study of the effect of particle charge on airway deposition efficiency for particles with diameters less than 0.3 μm. Theoretical predictions suggest that deposition by image charge forces will be approximately equal to deposition by diffusion for singly charged particles with diameters ranging from about 0.1 to 1.0 μm. An aerosol electrometer was designed and constructed, and the performance characteristics have been evaluated (Appendix B).

III. CURRENT TECHNICAL STATUS OF THE PROJECT

A. MATHEMATICAL MODELS FOR PREDICTING AIRWAY DEPOSITION

In prior work carried out in the central airway casts we found that for particles of 0.04 μm, 0.15 μm, and 0.2 μm mean diameter, and inspiratory flow rates of 300 to 600 cm^3/sec, the deposition efficiency was on the average about twice as high as that calculated based on the assumption of diffusion deposition from fully developed laminar flow. The disagreement between the measurements and the predictions were attributed to the deviation of flow in these airways from the parabolic profile. Subsequently, we showed that the discrepancy could not be attributed to the size dispersion of the experimental particles, or to deposition by impaction. In addition, we developed a semi-empirical expression, based on those, data for predicting the fraction of inhaled submicrometer particles that deposit onto airways by diffusion (η_D) at these physiological flow rates.

In the absence of an analytical expression for η_D in the upper airways, we formulated an expression by curve fit of the experimental data with Δ, where Δ is the ratio of the residence time in an airway to the average diffusion time. For an expression of the form $\eta_D = a_0 \Delta a_1$ for $10^{-9} < \Delta < 10^{-4}$, we calculated $a_0 = 2.965$ and $a_1 = 0.568$ by fitting the experimental data obtained previously. The correlation coefficient for the fit, was 0.57. For small Δ, the value for η_D is about twice that of results for parabolic flow, but as Δ increases the logarithmic values converge and for a sufficiently large Δ, predicted values for deposition fractions should agree. This would correspond to a location in the respiratory system where the velocity profile becomes parabolic and deposition by diffusion can be predicted from the parabolic flow expression. This point should occur for $\Delta \approx 10^{-4}$.

In an effort to further define the fluid dynamic determinants of the measured deposition, we subsequently formulated an expression for the collection efficiency of particles by diffusion in developing flows. In developing flows the velocity gradient near the wall is larger than that in parabolic flows. Consequently, more particles are carried near the walls and there is a higher probability of particle deposition.

When the flow enters a tube, it requires distance to become fully developed. The transitional region is defined by a non dimensional entrance length, ξ, as $\xi=\frac{z}{RRe}$, where z is the entrance length, R is the tube radius, and $Re=2Q/\pi R\nu$, with ν being the air kinematic viscosity, Re is the flow Reynolds number. The developing flow becomes fully developed when ξ=0.15. Thus, in the upper region of the lung the flow profile departs considerably from parabolic flow due in part to high flow velocity.

When the Schmidt number, $Sc=\nu/D$, approaches zero, deposition in developing flows can be approximated by the expression derived for uniform (slug) flow, and when Sc approaches infinity, deposition can be calculated from the expression commonly used for parabolic flow. In these limiting cases deposition efficiency is only a function of Δ. For intermediate values of Sc, however, one can not assume such a relationship and a more detailed study becomes necessary. This was discussed in our January annual report.

In accordance with the developing flow analogy, we formulated η_D as

$$\eta_D=a_2\xi^{a_3}Sc^{a_4}.$$

By fitting with the experimental data, coefficients a_2, a_3, and a_4 were found to be 1.73, 0.541, and -0.565 respectively. The results demonstrated that this fit is very similar to that of our simplified initial equation, with a dependence on Δ alone.

Although the developing flow model is a better predictor of the data than the parabolic flow results (lower limit), it is significantly lower than the best fit. Therefore, developing flow will explain the difference only partially.

In collaboration with Dr. C.P. Yu of SUNY Buffalo, we have recently evaluated the experimental results in terms of the parametric solution of the convective diffusion equation.

The deposition of ultrafine particles in the airways is governed by the process of convective diffusion. The basic equation for steady diffusion is:

$$\vec{V}\cdot\nabla C=D\nabla^2 C$$

where $\vec{V}$ is the air velocity, D is the particle diffusion coefficient, and C is the particle concentration. In dimensionless form, this equation can be written as

$$\vec{\upsilon} \cdot \nabla_1 c = \frac{2(L/R)}{Re \cdot Sc} \nabla_2^2 c,$$

where $\vec{\upsilon} = \vec{V}/V_o$, $c = C/C_o$, $\nabla_1 = L\nabla$, $\nabla_2 = R\nabla$, Re = Reynolds number = $2V_oR/\upsilon$, and $Sc = \upsilon/D$, in which V_o is the average velocity in the airway, C_o is the average particle concentration at the entrance of the airway, υ is the kinetic viscosity of the air, and L and R are, respectively, the airway length and radius. Since the velocity $\vec{\upsilon}$ in the airway depends also upon Reynolds number, the solution of c is, therefore, a function of Re, Sc, and L/R.

The deposition efficiency is defined as: $\eta = 1 - \bar{c}_L$, where $\bar{c}_L$ is the average particle concentration at the airway exit, which is a function of Re, Sc and L/R. We therefore can write $\eta = \eta(Re, Sc, L/R)$. This has an appropriate form for deposition efficiency in a straight tube. For the real airway geometry, the branch angle θ of the airway or the airway curvature should be also included as another independent parameter. Thus the more general form is: $\eta = \eta(Re, Sc, L/R, \theta)$.

The governing equation of convective diffusion for ultrafine particles is identical to that of convective heat transfer. Several solutions of η for a straight short tube have been obtained in the literature for heat convective problems. The equivalent solutions for diffusion are: $\eta \sim Re^{-1/2}\ Sc^{-1/2}$ for slug flow; $\eta \sim Re^{-2/3}\ Sc^{-2/3}$ for parabolic flow; and $\eta \sim Re^{-1/5}\ Sc^{-1/2}$ for turbulent flow.

For a given branch angle θ, we may therefore assume that deposition efficiency in the airway has the form: $\eta = aRe^bSc^c(L/R)^d$. Where a, b, c and d are constants to be determined from experimental data. In general, a is a function of θ. Because θ does not vary appreciably in the airways, we neglect such a dependence in the present analysis.

Using the method of linear regression on the log-log scale, the constants a, b, c and d were found from the experimental data of the bronchi to be a = 1.2027, b = -0.6067, c = -0.5108, d = 0.5081. In the trachea, the deposition data measured were substantially higher than the bronchial data due to the effect of the laryngeal jet. We therefore treated the tracheal data separately and found a = 20630, b = -2.2004, c = -0.2339, d = 1.0. The correlations obtained for experimental deposition efficiency as compared with that calculated from these equations for the trachea and bronchi appear to be satisfactory.

B. DEPOSITION OF CHARGED PARTICLES

Our efforts to date have been to develop an experimental system that will enable us to measure and compare the deposition of charged and neutral ultrafine particles in simple tracheal and bronchial models. Subsequent measurements will be performed in the hollow airway cast system.

An aerosol electrometer was designed and constructed, and the performance characteristics have been evaluated. The design of the NYU Faraday Cup together with performance test data are shown in Appendix B. The mean background level was 5.9×10^{-14} amperes with a standard deviation of 7×10^{-15} amperes. Performance was tested against a commercially available aerosol electrometer. When challenged with monodisperse aerosols of number concentration greater than 10,000/ml at a flow rate of 50 ml/s (to produce a signal-to-background ratio greater than 2.5), the two electrometers responses agreed within 10%. The coefficient of variation of the measurements, for a range of particle sizes, was less than 3%. The accuracy and precision of measurement are not satisfactory when the signal to background ratio is less than 2.5. Thus we can begin our studies in airway models for those particle diameters for which we can produce sufficiently high aerosol concentrations.

Experiments conducted in hollow airway casts and *in vivo* in humans have all shown an increase in deposition due to the particle charge. *In vivo* experimental results showed that there exists a threshold value of charge on the particle, q_c, above which deposition is enhanced. The value of q_c depends on the particle size as well as the airway size. These experiments were performed for particles for which deposition by diffusion is small ($d \geq 0.3$ μm). Theoretical predictions suggest that deposition by image charge forces will be approximately equal to deposition by diffusion for singly charged particles with diameters ranging from about 0.1 to 1.0 μm.

We have initiated studies in a simple conducting cylindrical tracheal model. The dielectric properties of the hollow airway cast system will be modified as needed, for subsequent studies. Efforts continue to improve the detection sensitivity because we cannot, at present, generate sufficiently high concentrations of charged particles with diameters < 40 nm.

C. PARTICLE DEPOSITION IN THE HUMAN TEST CAST

We are continuing to collect deposition data in the full airway cast and have extended the size range over which measurements are made to include monodisperse particles up to 0.4 μm in diameter.

IV. PUBLICATIONS

Cohen, B.S., Deposition of Ultrafine Particles in the Human Tracheobronchial Tree: A Determinant of the Dose from Radon Daughters, In: Radon and Its Decay Products: Occurrence, Properties and Health Effects (Ed., P. Hopke), American Chemical Society, Washington, DC 20036, pp. 475-486, 1987.

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Cohen, B.S., Radon and its short-lived decay product aerosols, In: Aerosol Measurement: Principles, Techniques and Applications (Eds., K. Willeke and P. Baron), Van Nostrand Reinhold, In press.

Yu, C.P. and B.S. Cohen, Tracheobronchial deposition of ultrafine particles, Ann. Occup. Hyg., In press.

V. REPORT OF EFFORT - P.I.

The PI has devoted 3.25 person months to the project in the curent calender period (5/1/91-11/15/91). She will devote 2.75 more person month to the project prior to the end of the current grant year (4/30/92).

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7/2/92