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The Effect of Dead Space on Inhaled Particle Deposition

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ABSTRACT

Mathematical models which have been developed to predict the deposition of particles in the conducting airways of the lung require simplified anatomical models of the dimensions and geometry of the bronchial airways. In order to produce valid deposition predictions, the computed volumes of the conducting airways must be realistic in comparison to anatomical dead space. This requirement must be met even as the developing lung grows to maturity and then undergoes aging. The effect of these age-related changes on predicted particle deposition efficiencies has not been well studied. Numerous authors have suggested that differences in lung volumes (total lung capacity, functional residual capacity, dead space and tidal volume) may account for significant variations between predicted or observed particle deposition but no general age-specific relationship has been proposed. New models are proposed to describe changes in dead space as functions of age and body size, and methods to adjust existing anatomical models to various dead space predictions are given. Also, the effect of these modifications to anatomical models on particle deposition efficiencies are simulated for a variety of breathing patterns for models scaled to represent young children, adults, and aged persons.

INTRODUCTION

Methods for describing the deposition of inhaled particles in the human respiratory tract have received considerable attention in the last twenty years both from theoretical and experimental points of view (Agnew et al., 1984; Bohning et al., 1975; Chan and Lippmann, 1980; Raabe, 1982; Schlesinger et al., 1982; Taulbee and Yu, 1975; Yeh and Schum, 1980; Yu and Taulbee, 1977). Knowledge of the regional deposition patterns of environmental and therapeutic aerosols has wide ranging applications in the areas of risk assessment, medical treatment and inhalation toxicology. Particles that deposit in the upper airways can produce a variety of effects ranging from therapeutic to impaired clearance, immunologic responses, and lung cancer to name a few.

Although considerable advances have been made in understanding inhaled particle deposition, there are still many significant unanswered questions,

Key Words: lung morphology, dead space, particle deposition

including those which relate to the wide variability seen in experimental results. Much of this variability has been attributed to either differences in breathing parameters or to morphological variability of the airways (Bennett, 1988; Heyder et al., 1988). However, the relative importance of these two sources of variation is uncertain.

In addition to normal individual anatomical variability, the variation associated with growth and aging of the respiratory tract must also be considered in modeling aerosol deposition. With respect to the human bronchial tree, it is generally believed that the overall architecture of the lung is established at birth in terms of the numbers of bronchial segments and patterns of branching (Thurlbeck and Angus, 1975), and that postnatal growth of the bronchial tree occurs due to increases in individual bronchial segment lengths and diameters from birth to adulthood. Once this growth phase is complete, additional volumetric changes may occur with age, presumably as muscle tone changes and airway diameters increase. As will be discussed later, the primary evidence for this increase in dead space volume comes from dead space measurements in human subjects and from measurements of airway dimensions on replica casts of bronchial trees.

The morphology of the human bronchial tree has been well studied and numerous models have been developed which describe the overall branching pattern (Weibel, 1963; Horsfield and Cumming, 1968; Horsfield et al., 1971; Phalen et al., 1985; Yeh and Schum, 1980). In contrast to many other mammals, the human bronchial tree is generally dichotomously branched, as opposed to a monopodial branching scheme observed in animals such as dogs and rodents (Raabe et al., 1976; Yeh, 1979). Early studies of the human bronchial tree made from resin casts of the airways (Rahn and Ross, 1957; Weibel, 1963), provided a wealth of information about the tracheobronchial tree and spurred the development of mathematical models which could be used for predicting the deposition of inhaled particles. More sophisticated casting methods using flexible silicone rubber have since been used to expand our knowledge of the morphological variation of the bronchial tree (Kilpper and Stidd, 1973; Phalen et al., 1973; Raabe et al., 1976; Phalen et al., 1985). Measurements of the dimensions of individual bronchial segments and of branching and gravity angles on these casts have been used to develop more realistic mathematical models of the bronchial tree (Yeh and Schum, 1980), and these models continue to be used today for predicting deposition of inhaled particles in humans in a variety of theoretical deposition models (Cuddihy et al., 1988; Egan and Nixon, 1985; Xu and Yu, 1986).

One aspect of these anatomical models is that they provide an estimate of the bronchial dead space volume (volume of the conducting airways from trachea to terminal bronchioles). In reality, this dead space can be quite variable, both from individual to individual, and also for a single individual over the course of a lifetime (Gaultier, 1989; Griscom and Wohl, 1985; Wood et al., 1971). With respect to particle deposition modeling, these differences in dead space as a source of variation have not been well studied, generally because researchers have tacitly assumed that the differences in predicted deposition are minor when only a narrow range of dead space values are considered. However, the variability in dead space, particularly with age, is apparently much greater than would justify such simplification. Thus, there is a clear need for anatomical models which can be scaled to various dead space values, and for mathematical predictions of particle deposition in these scaled models to determine the sensitivity of model predictions to the volume of conducting airways.

The foregoing discussion introduced the major elements of particle deposition modeling and displayed the variety of past approaches. Of necessity, any specific modeling effort involves selecting some approaches and data sets and excluding others. This selection process involves both judgement and preference; there is no single right (or wrong) way to develop a particle deposition model. What follows is a description of our age-related particle deposition model along with discussions concerning the choices made.

APPROACH TO MODEL DEVELOPMENT

For modeling purposes, we postulate a two-stage increase in thoracic anatomic dead space with age: a growth phase followed by an aging phase. For

simplicity, age becomes the scaling variable, but in reality, airway sizes are primarily directly related to body size instead of age. Statistical summaries of age vs. body mass (Altman and Dittmer, 1971; EPA, 1985) show considerable variation of body mass for a given age category. The effect is most pronounced for children. Also, literature values of dead space have been reported as functions of age, height and/or body mass (Wood et al., 1971; Malmberg et al., 1987; Tatsis et al., 1984). For our initial model development, we will assume a single body size for each age (Phalen et al., 1985) recognizing that this relationship is variable. The assumption of a relationship will allow us to use the two units (age and body size) interchangeably.

In order to take advantage of existing morphometric descriptions of the tracheobronchial tree, it is necessary to scale these models to different dead space volumes in order to represent various age groups. Such a scaling procedure can also be used to simulate individual variability within a given age group or even the variability within an individual as a function of tidal volume. For a scaling method to be realistic, its assumptions must be examined. A primary assumption is that lung models developed from replica casts of bronchial airways provide a realistic approximation of the functional anatomical dead space volumes in living subjects. Measurements of this dead space in people will reflect both the volume of the ciliated bronchial airways plus the extrathoracic volume of the oropharyngeal structures. It is further assumed that these volumes, which change with age, can be scaled using body mass as the appropriate scaling variable. In order to examine these assumptions, it is useful to review the clinical measurement methods for determining dead space.

Anatomic dead space is typically measured by examining the concentration profile of a test gas (generally nitrogen or carbon dioxide) in one or more expired boluses of air (Cotes, 1979; Sixt, 1989). A sharp square wave in this profile will ideally exist marking the expired volume at the transition from ciliated, non-respiratory airways to non-ciliated, respiratory airways (alveoli). In reality, this transition is not abrupt, and thus the values reported in the literature are not as precise as is generally believed (Tatsis et al., 1984) so approximations must be made. In the adult this approximate value is accepted to be about 150-160 cm³ (West, 1974). Because of the measurement methodology used, these values represent a complex functional state, and not simply the anatomical volume of the conducting airways. Therefore, these measured values are referred to as physiological or functional dead space volumes. It is generally thought that anatomic dead space and physiological dead space are nearly the same in healthy subjects (West, 1974).

Some studies have shown that functional dead space increases from birth to adulthood (Hart et al., 1963; Wood et al., 1971). These studies show that dead space increases as a function of body mass (and also height), and the values reported are similar. The studies by Hart et al. (1963) yield a somewhat steeper regression slope from that of Wood et al. (1971). Since the Hart equation is based on a larger sample size, spans a greater range of ages, and has a better goodness of fit, it is the relationship which will be used to model the growth phase of increasing dead space with age.

Comparable measurements have not been made for dead space during the aging phase after adulthood. The data reported by Tatsis et al. (1984) show no clear trend of increasing dead space in adults aged 19-65. In their study though, the variation among individuals is large, and the sample size is small, which may conceal a statistically significant increase with age. However, recent studies by Malmberg et al. (1987) have shown a significant positive relationship between physiological dead space and age in normal, non-smoking adults. For our purposes, we assume that the studies by Malmberg et al. can be used to model increasing dead space with age.

Measurements of functional anatomic dead space are generally made with the subject breathing through a mouth piece. As such, the reported values include the volumes of the mouth, oropharynx, larynx, and the conducting airways from trachea down to and including the terminal bronchioles (Hart et al., 1963). In contrast, the morphometrically-based models of the bronchial tree provide the volumes of the conducting airways exclusive of the extrathoracic volume. In the adult the volume of the mouth, oropharynx and larynx is about 50-60 cm³ (Altman and Dittmer, 1971) and this value has been used in other lung models (Raabe, 1982). Because we wish to scale morphometric model volumes to the predicted values of

Hart et al., the extrathoracic volumes must be subtracted from Hart's measurements to predict the volume of the tracheobronchial tree to which the anatomical models must be scaled. Thus, relationships are needed for extrathoracic volumes as a function of age.

A few researchers have used tracheal diameter (which is known for various age groups) to scale nasopharyngeal volumes as a function of age during the growth phase (Hofmann et al., 1989; Xu and Yu, 1986). Others have used a body size parameter as a scaling variable (James and Roy, in press). Since airflows in the lung are often assumed to be approximately proportional to cross-sectional areas at airway bifurcations, we selected tracheal cross-sectional area during growth as a scaling variable for extrathoracic dead space. Using computed tomography, Griscom and Wohl (1985) have studied tracheal growth in subjects to age 20 and report various tracheal measurements including diameters and cross-sectional areas. These measurements support the assumption that the ratio of tracheal cross-sectional area in subadults to the adult value can be used to predict the volume of extrathoracic airways for various subadult age groups.

To examine the effect of scaled dead space on particle deposition, it is necessary to select the anatomical model data. Thus, we will review some of the common models. Anatomical models of the bronchial airways of the human have been developed using several methods. Even though more recent data are available, the classic model of Weibel (1963) continues to be frequently cited. This model, based on an airway cast and on serial section reconstruction of airway dimensions of a 40 year old male, depicts the lung airways as a series of regular, dichotomously branching parallel tubes consisting of sixteen generations (counting the trachea as generation zero). The volume of the tracheobronchial airways in this model is estimated to be 174.8 cm³. The primary limitation of this model in particle deposition calculations is the omission of branching angles and angles of inclination to gravity in daughter segments. The dimensions of the airways in the Weibel model are those which are presumed to exist in a lung inflated to 3/4 of the functional residual capacity because of artifacts associated with the use of excised lungs and fixation techniques.

Accurate and comprehensive data have been collected by measurements of individual bronchial segments in a replica cast of an adult lung (age 60 years) made in situ (Raabe et al., 1976; Phalen et al., 1973). The measurements of bronchial segments included generation-specific branching angles and angles of inclination to gravity. Yeh and Schum (1980) developed a model using these data, based on the concept of a "typical path" from trachea to terminal bronchiole to represent the whole lung as well as separate models for the individual lobes of the lung. The total volume of the tracheobronchial airways in this model is 221 cm³. As a result of the casting procedure, these dimensions are thought to be representative of the lung volume at total lung capacity. These dimensions were adjusted downwards prior to particle deposition calculations as described in Schum and Yeh (1980).

An alternative model based on less extensive measurements of twenty replica casts made in situ was presented by Phalen et al. (1985, 1988). This model is also similar to the Weibel and Yeh and Schum models (regular, dichotomously branching parallel tubes) but is based on average values per generation made on several individuals. Data include branch angles but not gravity angles. Since casts were available for a number of age groups from infants to young adults, regression methods were used to develop age-specific anatomical models. The published adult model (age 18) has a total volume of the tracheobronchial airways of 85 cm³. For a two year old child the volume is estimated to be 41.8 cm³.

Other published anatomical models include those of Horsfield et al. (1971), Hofmann et al. (1989), Raabe (1982), and others, including numerous variations of the Weibel model. However for the purposes of this report we have selected the models of Weibel, Yeh and Schum, and Phalen et al. for comparison in the particle deposition simulation calculations.

Mathematical calculations of particle deposition in bronchial models require an algorithm relating particle movement in the airways to the probability of deposition, an anatomical model, the airway airflow regime, and the physico-chemical characteristics of the particles. Reviews of these mechanisms, processes and models are provided by Yeh et al. (1976), Raabe (1982), and others.

Two distinct types of algorithms are used in the literature to estimate particle deposition. One method treats the bronchial airways as a continuous expanding "trumpet" to reflect the increasing cross-sectional area with depth in the lung. Time-varying differential equations model the dynamic changes in cross-sectional area accompanying each breathing cycle, and the resulting velocity profile. Particle deposition efficiencies are then calculated by using various equations describing the main deposition mechanisms (Taulbee and Yu, 1975; Egan and Nixon, 1985).

In the second method, the bronchial tree is modeled as a series of parallel, cylindrical tubes occurring in discrete generations or divisions down from the trachea. The velocity in daughter segments is generated by assuming that the airflow is proportioned equally to daughter segments and is inversely proportional to cross-sectional area. Mechanistic equations describing deposition in individual bronchial segments by the main processes of diffusion, impaction and sedimentation are used to calculate deposition efficiencies and total efficiency in each generation is computed and summed for all generations. Complete details of the computational method are given in Schum and Yeh (1980). We selected this second method for calculating particle deposition, and the deposition equations used are given in Phalen et al. (1990).

For the particle deposition calculations, anatomical models with different dead space volumes were generated using a scaling approach similar to that used by Schum and Yeh (1980). In this method, bronchial airway diameters are assumed to vary as the square root of lung volumes. For the Yeh and Schum anatomical model (at or near total lung capacity), the diameters were scaled down to a lung volume near functional residual capacity plus 1/2 of the tidal volume used in the computation. By an analogous procedure, it is possible to scale any of the three anatomical models described above to any assumed dead space, both larger and smaller than the values reported in literature by dividing each bronchial segment diameter by the following scaling equation:

$$(\text{Scaling factor})^2 = \frac{\text{Original dead space volume}}{\text{Adjusted dead space volume}}$$

This adjustment is appropriate for adult lung models in which bronchial lengths are assumed to have reached their final values. For the children's lung, models for each age group are generated from the regression equations given in Phalen et al. (1985). Within a given age group, e.g. a two year old child, variation in dead space can then be modeled by scaling diameters according to the above equation.

An assumption in our scaling method is that the entire tracheobronchial tree is uniformly elastic, although this is probably not appropriate for all cases. There is insufficient data in the literature to determine separate scaling relationships for larger vs. smaller bronchial airway segments. Thus, in our modeling of dead space variation, all tracheobronchial segments are scaled by the same factor.

RESULTS

For our purposes, we assumed a cumulative volume of 50 cm³ for the adult mouth, oropharynx and larynx, and scaled this volume down for ages below 18-20 in linear proportion to the ratio of tracheal cross-sectional areas from the data in Griscom and Wohl (1985). These results are shown in Table 1. Since growth of the extrathoracic airways has not been quantified, we have no experimental data for comparison. Additionally, volumes of the extrathoracic airways, particularly for the mouth, will vary substantially during talking, mouth breathing, etc.

Figure 1 shows the predicted anatomic dead space using the regression equation from Hart et al., the predicted extrathoracic volume from Table 1, and the resulting predicted dead space of the conducting airways. In the adult, no growth of the extrathoracic airways is assumed. Thus, the functional dead space volumes reported in the literature should be reduced by 50 cm³ to predict the thoracic dead space volume to which adult anatomical models should be scaled.

Figure 2 summarizes the predicted anatomic dead space and thoracic dead

TABLE 1. Predicted volume of extrathoracic dead space assuming volume is proportional to tracheal cross-sectional area as a function of age (see text for details).

AGE (yr)	HEIGHT (cm)	MASS (kg)	TRACHEAL CROSS-SECTIONAL AREA (cm ²)	RATIO TO ADULT CROSS-SECTIONAL AREA	EXTRATHORACIC VOLUME (cm ³)
	(1)		(2)		(3)
2	88	10.0	0.317	0.17	8.5
4	104	16.4	0.488	0.26	13.0
6	115	22.0	0.633	0.34	17.0
8	127	27.0	0.817	0.44	22.0
10	138	34.0	1.012	0.54	27.0
12	150	43.0	1.255	0.67	33.5
14	162	54.0	1.531	0.82	41.0
16	170	63.0	1.734	0.93	46.5
18	175	70.0	1.869	1.00	50.0

- (1) Height and body mass predicted from Phalen et al., 1985
 (2) Height vs. area from Griscom and Wohl, 1985
 (3) Includes mouth, pharynx and larynx

space for both the growth and aging phase. The computed dead space values from the Weibel, Yeh and Schum and Phalen et al. models are shown for comparison as reported in the original articles, i.e. bronchial dimensions were not scaled to "equivalent" lung volumes. Based on these results, we have chosen to scale the adult models to tracheobronchial dead space volumes of 100 cm³ and 200 cm³ and a

FIGURE 2. Comparison of computed tracheobronchial model dead space values in three widely used anatomical lung models to predicted dead space values as a function of age. Anatomic dead space predicted from Hart et al. (1963); physiological dead space predicted from Malmberg et al. (1987). Predicted tracheobronchial dead space (---) is total dead space less estimated oropharyngeal dead space.

two year old child to volumes of 20 cm³ and 40 cm³ for our particle deposition calculations. We feel that these values represent the range of morphological variability seen at a given age, and for the adults, may also represent a range seen within a given individual during the aging phase to senescence.

Figure 3 shows respiratory variables scaled to different ages using predicted body mass at given age as a scaling metric. These data are interpolated and extrapolated from a variety of data summarized by Altman and Dittmer (1971). The functional relationships used between age, body mass and body height are shown in Table 3. These patterns are valid only for ages from birth to adulthood and do not reflect changes in ventilatory patterns from a young adult to senescence. As anatomic dead space increases with age after adulthood, it seems likely that there will be some compensatory changes in ventilation to maintain an adequate degree of alveolar ventilation.

Our computational method uses inspiratory flow rate (= twice the minute volume when there is no pause between inhalation and exhalation) to calculate deposition probabilities. Thus, only the values for minute volumes are used directly in the particle deposition results we present. The other curves shown in Fig. 3 though are useful to relate these flow rates to typical breathing patterns associated with these flow rates, recognizing that various combinations of tidal volume and respiratory frequency can lead to equivalent flow rates, but not necessarily equivalent regional aerosol deposition patterns. Since our intent in this paper is to address specifically the effect of dead space on tracheobronchial deposition efficiency, we have not extended our modeling results to cover effects of various breathing patterns.

The results of the tracheobronchial deposition calculations are summarized in Figure 4 and Tables 2-3. For a given airway model and a given flow rate, changing the dead space does not significantly alter deposition of particles that deposit primarily due to the diffusion mechanism: the deposition efficiencies for a specific anatomical model (e.g. Weibel) scaled to different dead space volumes are essentially identical for particle diameters below about 0.2 μ m. The effect of altered dead space on the deposition of particles with diameters larger than about 1 μ m is significant, with greater inhalation deposition efficiencies predicted in anatomical models scaled to smaller dead space volumes. This is an important size range since pulmonary deposition efficiencies (both calculated by various models and observed in experimental conditions) generally show a maximum

FIGURE 3. Typical respiratory parameters as functions of body mass and activity level during somatic growth. Values interpolated and extrapolated from Altman and Dittmer (1971): a) minute ventilation in liters/minute (l/min) ; b) respiratory frequency in breaths/minute (bpm); c) tidal volume in cubic centimeters (cm³) calculated from (minute ventilation) / (respiratory frequency).

for particles in the 2- 3 μ m diameter size range. With the reduced inhalation deposition efficiencies seen in the larger dead space models, more particles will penetrate to the pulmonary region, and pulmonary deposition would be expected to increase.

The three tracheobronchial anatomical models, based on measurements of replica casts are compared in Figure 4. Even when these models are scaled to have equivalent dead space volumes (100 and 200 cm³) there are significant differences in the predicted particle deposition efficiencies. This is not surprising when one considers the anatomical differences among these models. Weibel's model tends to have longer major airways than the others and Yeh and Schum's model has the largest diameter airways (down to generation 14). In Weibel's model we assigned values for branch and gravity angles of 45° after the trachea. The branch and gravity angles in the Yeh and Schum model were based on actual measurements (only down to generation 13 for gravity angles). Gravity angles in the last two generations were assigned a value of 60° (0° being vertical), based on theoretical considerations. The Phalen et al. model used measured branch angles and adopted the gravity angles of Yeh and Schum except for the last three generations, where 45° was used based on extrapolation of the measured values for previous generations.

The differences in deposition among the models are all within the wide range of values of deposition estimated in clinical studies on actual people (Lippmann, 1977). Therefore, except for perhaps the Weibel model adjusted to a

FIGURE 4. Computed inhalation deposition efficiencies vs. particle diameter for three widely used adult tracheobronchial models each scaled to dead spaces (V_d) of 100 and 200 cm^3 . Calculations are for a minute ventilation ($\dot{V}_m$) of 20 l/min (constant inspiratory flow rate = 40 l/min) for spherical particles with a density of 1 gm/cm^3 .

100 cm^3 dead space, any of the anatomical models could be used to estimate adult tracheobronchial deposition.

The predicted deposition efficiencies in Fig. 4 were calculated using a constant inspiratory flow rate and are for the inhalation phase of a breathing cycle. To estimate exhalation deposition efficiencies, the filtering effect of the pulmonary compartment must be known in addition to the aerosol fraction removed on inspiration. However, we do not have anatomical models for the pulmonary compartment in children which contain sufficient information about weight, height, age and lung volumes that allow the models to be easily coupled to our tracheobronchial models scaled to various anatomic dead spaces for particle deposition calculations. In order to determine whether or not our results for inhalation would hold up when exhalation was included in the model, it was necessary to adapt an existing pulmonary deposition model.

Recently, Hofmann et al. (1989) have published deposition calculations which included estimated pulmonary deposition fractions for adults and children, and which we have selected as representative for the range of parameter values used for our deposition calculations. By adding their estimated pulmonary deposition to our calculated inspiratory deposition (both done for mouth breathing), we estimated what the concentration, as a fraction of that entering the trachea, would be at the respiratory bronchiole at the beginning of exhalation (analogous to initializing the concentration at the trachea to 100% on inspiration). This "initial concentration on expiration" was then used to complete the calculations for expiration. Following Yeh and Schum (1980), we assumed that there was no deposition by the impaction mechanism during exhalation.

In Tables 2 and 3 we compare the predicted particle deposition efficiencies as functions of age (adult and two year old child), activity (resting and heavy exertion), and anatomic dead space. Since no significant dead space effects were observed in the smaller particle size range in Fig. 4, calculations are shown only for particles from 0.1 to 10.0 μm . Flow rates for the calculations for inhalation and exhalation were determined from Fig. 3. However, pulmonary deposition fractions estimated from Hofmann et al. (1989) were based on values

TABLE 2. Estimated thoracic deposition efficiencies in the 2-year old child tracheobronchial anatomical model of Phalen et al. (1985) scaled to dead space volumes of 20 cm³ and 40 cm³ for two levels of physical activity.

2-YEAR OLD CHILD		PARTICLE AERODYNAMIC DIAMETER (μm)						
		0.1	0.25	0.50	1.0	2.5	5.0	10.0
<u>High Activity (Minute ventilation 16.4 l/min)</u>								
Pulmonary Deposition Efficiency (1)		0.15	0.08	0.05	0.05	0.05	0.01	0.00
Bronchial Inhalation Efficiency								
20 cm ³ dead space		0.043	0.036	0.063	0.177	0.667	0.993	1.000
40 cm ³ dead space		0.040	0.026	0.033	0.075	0.327	0.796	0.999
Bronchial Exhalation Efficiency								
20 cm ³ dead space		0.031	0.017	0.013	0.011	0.006	0.000	0.000
40 cm ³ dead space		0.031	0.018	0.014	0.013	0.017	0.015	0.000
Total Bronchial Efficiency								
20 cm ³ dead space		0.074	0.053	0.076	0.188	0.673	0.993	1.000
40 cm ³ dead space		0.071	0.044	0.047	0.088	0.344	0.811	0.999
Total Deposition Efficiency								
20 cm ³ dead space		0.224	0.133	0.126	0.238	0.723	1.000*	1.000
40 cm ³ dead space		0.221	0.124	0.097	0.138	0.394	0.821	0.999
<u>Low Activity (Minute ventilation 2.75 l/min)</u>								
Pulmonary Deposition Efficiency (2)		0.18	0.10	0.05	0.06	0.22	0.22	0.02
Bronchial Inhalation Efficiency								
20 cm ³ dead space		0.100	0.047	0.040	0.062	0.232	0.633	0.987
40 cm ³ dead space		0.100	0.048	0.037	0.048	0.168	0.491	0.953
Bronchial Exhalation Efficiency								
20 cm ³ dead space		0.072	0.039	0.029	0.029	0.048	0.040	0.000
40 cm ³ dead space		0.072	0.040	0.031	0.034	0.071	0.102	0.023
Total Bronchial Efficiency								
20 cm ³ dead space		0.172	0.086	0.069	0.091	0.280	0.673	0.987
40 cm ³ dead space		0.172	0.088	0.068	0.082	0.239	0.593	0.976
Total Deposition Efficiency								
20 cm ³ dead space		0.352	0.186	0.119	0.151	0.500	0.893	1.000*
40 cm ³ dead space		0.352	0.188	0.118	0.142	0.459	0.813	0.996

(1) Estimated from Hofmann et al. (1989), Figure 5, "Maximal Activity"

(2) Estimated from Hofmann et al. (1989), Figure 2, "Sedentary Activity"

* Calculated inhalation efficiency + estimated pulmonary efficiency > 1.0; this results from higher bronchial inhalation efficiencies predicted by Phalen et al. (1985) than those predicted by Hofmann et al.

for "sedentary activity" and "maximal activity"; the flow rates used in their computations are generally similar for the resting or sedentary cases, but are based on very extreme flow rates for maximal exertion. In addition, their computational method used different equations for deposition. As such, the predicted deposition efficiencies shown for both exhalation and for total bronchial deposition are composite values that should only be used for illustrative purposes.

The results shown in Tables 2 and 3 are generally consistent with the pattern seen in Fig. 4. Inhalation deposition efficiency and total bronchial deposition (sum of inspiration and expiration efficiencies) are greater in lung models scaled to smaller dead space volumes. However, exhalation efficiencies show the opposite pattern - greater deposition efficiencies are observed in the

TABLE 3. Estimated thoracic deposition efficiencies in the adult tracheobronchial anatomical model of Phalen et al. (1985) scaled to dead space volumes of 100 cm³ and 200 cm³ for two levels of physical activity.

20-YEAR OLD ADULT	PARTICLE AERODYNAMIC DIAMETER (μm)						
	0.1	0.25	0.50	1.0	2.5	5.0	10.0
<u>High Activity (Minute ventilation 40 l/min)</u>							
Pulmonary Deposition Efficiency (1)	0.15	0.08	0.05	0.05	0.02	0.02	0.00
Bronchial Inhalation Efficiency							
100 cm ³ dead space	0.030	0.019	0.021	0.043	0.182	0.540	0.962
200 cm ³ dead space	0.030	0.017	0.016	0.024	0.085	0.277	0.722
Bronchial Exhalation Efficiency							
100 cm ³ dead space	0.024	0.014	0.012	0.011	0.016	0.023	0.007
200 cm ³ dead space	0.024	0.015	0.016	0.012	0.023	0.049	0.065
Total Bronchial Efficiency							
100 cm ³ dead space	0.054	0.033	0.033	0.054	0.198	0.563	0.969
200 cm ³ dead space	0.054	0.032	0.032	0.036	0.108	0.326	0.787
Total Deposition Efficiency							
100 cm ³ dead space	0.204	0.113	0.083	0.104	0.218	0.583	0.969
200 cm ³ dead space	0.204	0.112	0.082	0.086	0.128	0.346	0.787
<u>Low Activity (Minute ventilation 10.0 l/min)</u>							
Pulmonary Deposition Efficiency (2)	0.22	0.13	0.08	0.10	0.35	0.40	0.08
Bronchial Inhalation Efficiency							
100 cm ³ dead space	0.059	0.031	0.024	0.031	0.098	0.310	0.771
200 cm ³ dead space	0.059	0.030	0.024	0.029	0.090	0.284	0.740
Bronchial Exhalation Efficiency							
100 cm ³ dead space	0.043	0.024	0.020	0.020	0.032	0.051	0.080
200 cm ³ dead space	0.042	0.025	0.020	0.023	0.042	0.075	0.120
Total Bronchial Efficiency							
100 cm ³ dead space	0.102	0.055	0.044	0.051	0.130	0.361	0.851
200 cm ³ dead space	0.101	0.055	0.044	0.052	0.132	0.359	0.860
Total Deposition Efficiency							
100 cm ³ dead space	0.322	0.185	0.124	0.151	0.480	0.761	0.931
200 cm ³ dead space	0.321	0.185	0.125	0.152	0.482	0.759	0.940

(1) Estimated from Hofmann et al. (1989), Figure 5, "Maximal Activity"

(2) Estimated from Hofmann et al. (1989), Figure 2, "Sedentary Activity"

larger dead space models. Overall though, total tracheobronchial deposition still exhibits the same pattern as for inhalation alone, with some reduction due to the reversed pattern seen for exhalation.

These results clearly show that inertial impaction is the dominant mechanism underlying the increased deposition efficiencies predicted for lungs scaled to smaller dead space volumes. At the higher flow rates, the effects are magnified. On exhalation, where no impaction deposition is included in the deposition equations, greater deposition is observed in the larger dead space models due to an increased particle residence time mainly increasing the sedimentation efficiency. In the range of particle sizes where the effects are the greatest (1-5 μm), diffusion is small compared to sedimentation.

The results for the adult models shown in Table 3 are less pronounced than those seen in the children's models in Table 2, although the same overall patterns are observed. The larger dead space adult model may represent an elderly male. In this case we may conclude that older people may have substantially lower

tracheobronchial deposition efficiencies for particles in the 2-10 μm size range than do young adults for a given minute ventilation.

DISCUSSION

Several general patterns emerge from the different simulation results (Figure 4, Tables 2-3). The most significant result is that inhalation deposition efficiency is always less in anatomical models with larger anatomic dead space volumes for particle sizes larger than about 1 μm at a fixed inspiratory flow rate. Because of the scaling methods used, this implies that smaller airway diameters will have greater particle deposition than larger airways at a fixed minute ventilation. This conclusion is consistent with the results reported by Heyder et al. (1988), although our results are applicable only to the tracheobronchial airways. In the computational model used for our simulation results, we used a constant inspiratory flow rate. Since different combinations of tidal volumes and respiratory frequencies can produce the same flow rate, it is not possible to address directly the significance of breathing pattern vs. lung morphology on the variability seen in human deposition studies (Bennett, 1988). However, given the wide range of dead space volumes seen between individuals, it seems likely that lung morphology accounts for a substantial portion of the variability seen in experimental studies.

The greater deposition efficiencies seen in anatomical models with smaller dead space volumes is particle size dependent with the maximum differences observed in the 2-5 μm aerodynamic size range. In this size range, deposition is generally dominated by impaction (Bohning et al., 1975; Raabe, 1982). The results that show the biggest differences between deposition efficiencies in large and small dead space scaled models occur at the highest minute ventilation rates, which is expected for impaction dominated deposition. Thus, in individuals with small anatomic dead spaces breathing at moderate to heavy workloads, there will be much greater deposition of mid-sized particles in the bronchial airways than in individuals with either a larger dead space or who breathe at lower ventilation rates. This effectively acts as a filter for particles which might otherwise penetrate to the pulmonary airways. Since there is generally a maximum in pulmonary deposition of particles in the 2-3 μm size range, variations in dead space can significantly affect the deposition of particles in the pulmonary region.

No significant differences in deposition efficiencies can be detected for any given model scaled to various dead space volumes for particle sizes below 0.5 μm for a fixed inspiratory flow rate. This result is also expected since diffusion dominates deposition efficiency in this size range. The effect of dead space in this size range is mixed though. When an airway diameter is increased, but the volumetric air flow remains constant, two compensating phenomena occur. Particles diffusing towards the walls will have a greater residence time in the airway, but they will also have greater average distances to travel to a wall for deposition. The net result, then, of increasing an airway diameter is that diffusional deposition efficiency is essentially unchanged.

Using functional dead space volumes obtained from the literature provides a practical way to scale existing anatomic models of the tracheobronchial airways to reflect morphological variation seen between individuals and to simulate aging of the bronchial tree for single individuals. However, care must be taken in deciding which reported values are suitable and how to appropriately scale the various anatomic models available. Functional dead space measurements are typically made in sitting subjects breathing at rest with inspirations beginning at or near functional residual capacity (Martin et al., 1979), so anatomic models scaled to these values, and computational particle deposition models must further adjust the scaled airway dimensions depending on tidal volumes used (e.g. Schum and Yeh, 1980). Functional dead space volumes are strongly correlated with height and body mass of the subjects, with a wide range of values reported, and "mean" values for anatomic dead space generally obscure these relationships. Our results underscore the variability in particle deposition predictions which can result from variation in dead space alone.

Our results have a number of restrictions stemming from the many assumptions which must be made, the most fundamental of which is the concordance of anatomic models such as the "typical path" of Yeh and Schum (1980). However, particle deposition calculations using this model are in good agreement with experimental observations in living subjects. Our results suggest that some of the differences between predicted and observed deposition may result from differences in dead space which cannot be controlled in experimental studies. Our results are primarily applicable for the inspiratory phase of a single breath. Additional deposition will also occur on expiration, but this will be strongly influenced by the amount of particle size-dependent pulmonary deposition. Also, we have made no corrections for extrathoracic deposition which will tend to reduce the degree of differences seen in our results for larger particle sizes particularly for nose breathing.

Other restrictions affecting the interpretation and use of the results include particle characteristics (assumed to be spherical, 1 gm/cm³ density, nonhygroscopic and uncharged), respiratory characteristics (constant inspiratory flow rate, no pause, well mixed bulk flow), and the suitability of the computational model and deposition equations to accurately predict upper airway particle deposition.

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