IMPROVEMENTS IN DEPOSITION MODELS FOR ESTIMATING DOSE DISTRIBUTION FROM INHALED AEROSOLS

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1. INTRODUCTION

In 1966, the Task Group on Lung Dynamics (ICRP) described improved deposition and clearance models for predicting aerosol dose to the human respiratory system (1). Deposition calculations, based on Findeisen's (2) anatomical model containing only five orders of bifurcation in the tracheobronchial tree, were applied to generalized nasopharyngeal (NP), tracheobronchial (TB) and pulmonary (P) compartments. Predicted total and compartmental deposition for various sized particles were in satisfactory agreement with existing experimental data. Recently, Mercer (3) evaluated the ICRP model in light of new experimental information. The Task Group computations apparently underestimate deposition in the TB compartment due to the paucity of bifurcations in the Findeisen anatomy; as a result, the ICRP model probably overestimates deposition in the critical P compartment. In any event, the ICRP model is limited to compartments and cannot be applied to predict dose distribution within a compartment. The much more realistic tracheobronchial airway anatomy of Weibel (4) was later used by Taulbee and Yu (5) in a refined mathematical model which incorporated some of Beeckman's (6) deposition equations. The use of Weibel's anatomical data allows generation by generation estimates of deposition, though Taulbee and Yu's original paper did not include such information.

The use of dose to a compartment, or even within a given airway, to evaluate hazard underestimates the dose to some tissues while it overestimates that to others. The following sections describe three anatomical factors that presumably produce a more uneven distribution of dose from inhaled aerosols than is predicted by the above models. These factors are: 1) differences in size and airway morphology of various lobes of the lung, 2) systematic changes in the geometrical shapes of airways at various levels within a given lobe, and 3) bronchial bifurcations which produce deposition maxima or "hot spots".

2. NON-UNIFORMITY OF DOSE RELATED TO ANATOMICAL DIFFERENCES AMONG LOBES

Although some still believe that the dose to lung tissue calculated for small radioactive particles must consider the microdose regions around each particle, it has been generally demonstrated that smear-dose calculations for lung tissue are conservative and realistic for estimating the radiological potential for many biological effects. Thus, it is not necessary to consider each particle as an individual radioactive source for hazard assessment even in the case of alpha-emitting particles.

Improved lung models of dose should consider the variations of dose that occur among lung lobes because of consistent differences in relative efficiency of particle deposition. This has been demonstrated by Raabe, et al. (7) in aerosol deposition studies in experimental animals for which anatomical information was available. Hamsters and rats were exposed to radiolabeled monodisperse aerosols of fused silicate spheres. The deposited

activity per unit lung weight was determined for each lobe and compared to the average for the whole lung. In both species the right apical lobe (corresponding to the right upper lobe of the human lung) had an activity concentration varying from 5 to 60% higher than the average for the whole lung. The higher concentration was more pronounced for larger particle sizes (Table 1).

In addition, Raabe, et al. showed that differences in relative lobar deposition were related to the geometric mean number of airway bifurcations between the trachea and terminal bronchioles in each lobe. Those lobes with the highest relative concentration of deposited particles were shown to have the least bifurcations and the shortest average path lengths of airways between the trachea and terminal bronchioles. For rats the ratio of the mean concentration for all particle sizes studied among lobes was roughly equal to the reciprocal of the square root of the mean path lengths from the trachea to the terminal bronchioles for the lobes.

If this same relationship holds for human lungs, the right upper lobe should receive from 50% to 75% higher deposition of radioactive particles than any other lobe. A greater disproportioning of dose would be expected for larger particle sizes. Dose calculations for inhaled radioactive particles deposited in the human lung should therefore give proper consideration to this non-uniformity of dose among the lung lobes.

	Aerodynamic Diameter, Micrometers					
Lobe	3.05	2.09	1.04	0.52	0.2	Mean
R.A.	1.21	1.32	1.12	1.05	1.10	1.15
R.C.	0.93	0.95	1.00	1.02	0.97	0.98
R.D.	0.84	0.99	0.96	0.89	0.93	0.92
R.I.	0.75	0.88	0.95	1.02	1.06	0.94
Left lung	1.21	0.97	1.01	1.06	1.01	1.05
Mean	0.99	1.02	1.01	1.01	1.02	1.01
S.D.	0.11	0.09	0.03	0.03	0.03	0.05

TABLE 1. Relative Lobar Concentration of Inhaled Particles in Rats (Percent of Total Lung Burden/Percent of Total Lung Weight)

3. VARIATIONS IN STRUCTURE WITHIN A LOBE

Deposition models that do not include realistic shapes of bifurcations at various levels (divisions down) in the tracheobronchial tree may not reproduce the dose pattern within a lobe. The noted morphometric data mentioned have shown that the assumptions of constant branching angle, asymmetry ratio (in daughter diameter) or length to diameter ratio throughout a lobe are invalid. The systematic variation in these parameters is shown in Figure 1. Branch angles increase for smaller airways, especially for those with diameters below 4 mm. A maximum asymmetry of about 1.5 in daughter diameter ratios occurs for bronchi of about 2 mm in diameter. The length to diameter ratio has its maximum value of about 3 for airways slightly less than 2 mm in size. Though the net effect of these factors has not been ascertained, it appears that in any model having symmetry in branching angles impactional deposition is likely to be underestimated in the smaller airways within the TB compartment and overestimated in the larger ones. This follows from the observation that branch angles increase rapidly for small airways.

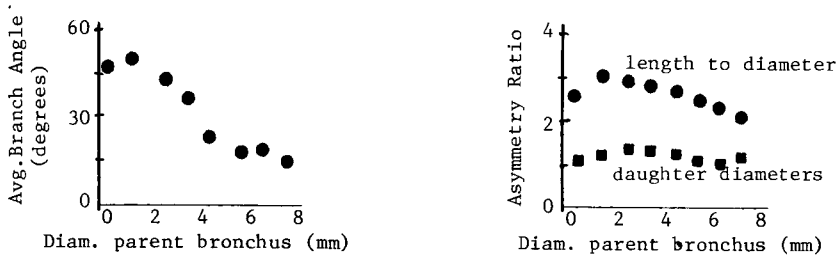

FIGURE 1. Human airway morphology as a function of parent bronchus diameter

4. INFLUENCE OF BIFURCATIONS ON LOCAL DEPOSITION

A major factor leading to uneven deposition in the respiratory tract is the complex geometry, air flow and particle transport behavior at bifurcations. Local deposition maxima or "hot spots" have been observed at lung bifurcations by Nadel, et al. (8). Bell, and Bell and Friedlander (9,10) have quantitated "hot spots" in theoretical and experimental studies using spherical particles in models of a single human airway bifurcation.

Figure 2 shows the deposition pattern for 0.365 um particles measured by Bell (9) in the daughter branch of his bifurcation model. The peak "hot spot" occurs at the carina of the bifurcation within contour A. It has a transfer coefficient 3.4 times larger than the average value over the branch and its surface area is only 0.6% of the total or 11 mm^2. The approximately 150,000 epithelial lining cells in this area at the first bifurcation in a human lung should receive at least 3.4 times more particles than predicted from uniform deposition.

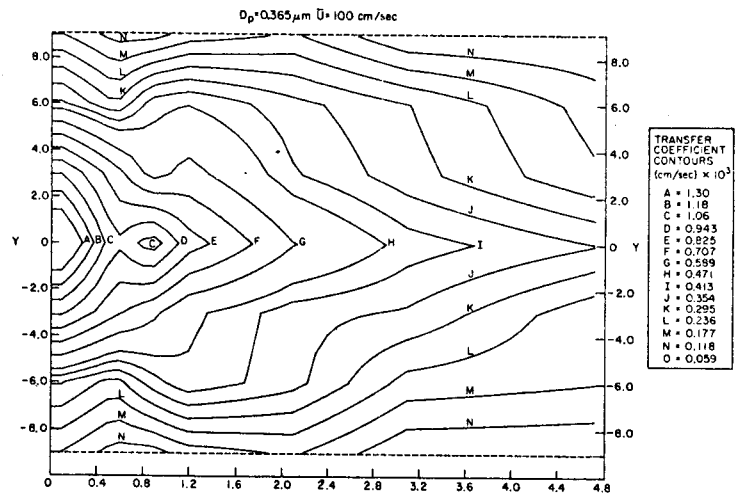

FIGURE 2. Deposition pattern for 0.365 um particles where $k_{av} = 3.83 \times 10^{-4}$ (9)

By normalizing the transfer coefficient in this small carinal area by the average transfer coefficient over the entire branch surface, a "hot spot" intensity or degree of nonuniformity of deposition is obtained. It varied from a high of 25.4 for d_p = 5.7 um and $\bar{U}$ = 200 cm/sec to a low of 3.75 for d_p = 1.1 um and $\bar{U}$ = 100 cm/sec where d_p is particle aerodynamic diameter and $\bar{U}$ is the average flow velocity in the parent branch.

5. SUMMARY

The effects mentioned above all tend to increase the non-uniformity of dose in the respiratory tract. The estimation of hazard based on average dose to the respiratory tract, or a compartment within it, may be seriously over-simplified by the use of even the best existing deposition models. Whether a more uneven dose results in a greater or lesser hazard is a matter of recent controversy and may be strongly dependent on the properties of the specific inhaled aerosol. Solution of this issue will require parallel efforts in theoretical modelling and laboratory studies in living animals.

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