A Preliminary Approach to Age-Dependent Deposition Modeling for Human Respiratory Tract

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I INTRODUCTION
About 20 years ago, the ICRP Task Group on Lung Dynamics presented their respiratory tract model to use for determination of internal radiation exposures from inhaled radionuclides.1) The ICRP model has been used to set the radiation protection standards for adult workers.2) Since the model is intended to be applied to the occupational exposures, some problems are induced at that time when the radiation doses to the general public from environmental radioactive materials are estimated with this model. The general public includes not only adult ages but also children, infants and neonates who are considered more sensitive to radiation exposures,3) so that the age-dependent dosimetry model should be developed for more practical estimation.

In this article, the author summarized some information to develop the age-dependent respiratory tract model and a computer program to estimate the deposition fraction in the respiratory airways.

II AGE-DEPENDENT RESPIRATORY TRACT MODEL
The respiratory tract includes passages of the nose (mouth), nasal pharynx, oral pharynx, epiglottis, larynx, trachea, bronchi, bronchioles, and small ducts and alveoli of the pulmonary.4) The ICRP divided these airways into three functional regions: (1) nasopharynx (NP) region, (2) tracheobronchial (TB) region, and (3) pulmonary (P) region.

A number of adult models have been proposed, the most familiar of which are those of WEIBEL,5) LANDAHL,6) and HORSFIELD and CUMMING.7) Except for HORSFIELD and CUMMING's asymmetry model of the airway branching scheme, other models assumed symmetry within the lung, with each generation consisting of airways of identical size.

The age-dependent values for respiratory parameters may be desired by noting that relative regional volumes should remain invariant during growth, so that regional volumes at a given age may be defined as a fixed fraction of the total lung volume.8) In addition, the number of airways in a given region may be assumed to be constant with age for regions located proximally to the respiratory passages, with the number increasing for the distal sections as one age.

HOFFMAN, STEINHAUSLER and POHL,9) and CRAWFORD8) have defined the age-dependent regional volume for the space above the respiratory bronchioles as

\[ V_n(\alpha) = V_n(A) \times V_{DB}(\alpha) / V_{DB}(A) \quad (1) \]

where

\( V_n(\alpha) \): age-dependent regional volume in the \( n \)-th region (cm³),
$V_n(A)$ : adult regional volume (cm³),
$V_{DS}(A)$ : adult volume of "dead-space" (cm³).

The regional volumes in distal airways are also calculated from Eq. (1) after replacing the values for "dead-space" by those determined for the total alveolar volume.

Since the regional volume is dependent on both diameter and length of the airways in a region, the regional radius and the length are calculated after assuming that the ratio of the airway diameter to length remains invariant with age.

\[ R_n(\alpha) = \left[ \alpha_n(A) \cdot (V_n(\alpha) / \pi) \cdot N_n(\alpha) \right]^{1/3} \]
\[ L_n(\alpha) = R_n(\alpha) / \alpha_n(A) \]

where
- $R_n(\alpha)$ : age-dependent regional radius in the $n$-th region (cm),
- $L_n(\alpha)$ : age-dependent regional length in the $n$-th region (cm),
- $\alpha_n(A)$ : ratio of airway diameter to length for adult,
- $N_n(\alpha)$ : age-dependent number of airways.

### III DEPOSITION IN AGE-DEPENDENT RESPIRATORY TRACT

Several processes contribute to the deposition of atoms, molecules and aerosol particles in a cylindrical tube. The most important mechanisms of deposition are impaction, sedimentation and diffusion.

Impaction dominates deposition of larger particles in the NP and TB regions. In this process, changes in direction or magnitude of air velocity streamlines or eddy components are not duplicated by airborne particles because of their inertia.

The probability of deposition in the $n$-th region by impaction is given by

\[ P_I(n) = \frac{150 \cdot p \cdot d_P^2 \cdot U_{n-1}(\alpha)}{[R_n(\alpha) + 150 \cdot p \cdot d_P^2 U_{n-1}(\alpha)]} \]

where
- $P_I(n)$ : probability of deposition in the $n$-th region by impaction,
- $p$ : particle density (g/cm³),
- $d_P$ : particle diameter (cm),
- $U_{n-1}(\alpha)$ : linear velocity in the $n-1$ region (cm/sec).

The linear velocity is calculated as

\[ U_{n-1}(\alpha) = (V_T/t) / [N_{n-1}(\alpha) \cdot \pi \cdot R_{n-1}(\alpha)^2] \]

where
- $V_T$ : tidal air volume (cm³),
- $t$ : inspiration period (sec).

Sedimentation occurs because of the influence of the gravity on small particles. Deposition by sedimentation of particles can occur in all airways.

The probability of deposition by sedimentation is given by

\[ P_S(n) = 1 - \exp\left[ -0.8 \cdot U_t \cdot t_n \cdot \cos \phi_n / R_n(\alpha) \right] \]

where
- $P_S(n)$ : probability of deposition by sedimentation in the $n$-th region,
- $U_t$ : terminal settling velocity (cm/sec),
- $t_n$ : period during which air is present within the $n$-th region (sec),
- $\phi_n$ : average angle of inclination of the airway with respect to the horizontal (degree).

The terminal settling velocity is given by STOKE's equation.

\[ U_t = C \cdot g \cdot \rho \cdot d_P^2 / 18 \cdot \eta \]

where
- $C$ : CUNNINGHAM's slip correction factor,
- $g$ : gravity acceleration (cm/sec²),
- $\eta$ : viscosity of air (poise).

The CUNNINGHAM's slip correction factor is given by

\[ C = 1 + \frac{\lambda}{d_P} \left[ 2.514 + 0.800 \cdot \exp\left( -0.55 \cdot \frac{d_P}{\lambda} \right) \right] \]

where
- $\lambda$ : air mean free path (cm).

Deposition by diffusion results from the random (Brownian) motion of very small particles caused by bombardment of the gas molecules in air. The magnitude of this property can be described by the diffusion coefficient for a given physical diameter.

The probability of deposition by diffusion in an airway tube of length $L_n(\alpha)$ is given by

\[ P_D(n) = 5.50 \cdot \mu^{1.2} - 3.77 \mu, \quad \text{for } \mu < 0.007 \]
\[ P_D(n) = 1 - 0.819 \cdot \exp(-11.5 \cdot \mu) - 0.0975 \cdot \exp(-70.1 \cdot \mu) - 0.0325 \cdot \exp(-179 \cdot \mu), \quad \text{for } \mu \geq 0.007 \]
where 
\[ P_D(n) \text{: probability of deposition by diffusion in the } n\text{-th region}, \]
and 
\[ \mu \text{: deposition parameter for diffusion given as follows}^{(10)} \]
\[ \mu = 4 \cdot \Delta \cdot (L_n(a)/\pi) \cdot d_t^2 \cdot U_n(a) \]
\[ \Delta = k \cdot T \cdot (C/3) \cdot \pi^2 \cdot \eta \cdot d_t \]
where 
\[ \Delta \text{: particle diffusion coefficient}, \]
\[ d_t \text{: airway diameter (cm)}, \]
\[ k \text{: BOLTZMANN's constant (dyn-cm/°K)}, \]
and 
\[ T \text{: absolute temperature (°K)}. \]

The probability of deposition is calculated as the difference between unity and the product of the probabilities of transmission through a given duct or series of ducts.\(^8\) Hence, the probability of deposition for the combination of impaction, sedimentation and diffusion for a single region is given by
\[ F(n) = 1 - [1 - P_I(n)] \cdot [1 - P_S(n)] \cdot [1 - P_D(n)] \]  
(8)

Pattle published the empirical function of the deposition in the NP region from the experiment with methylene blue particles with the diameter of 1.0 to 9.0 pm.\(^{11}\) The ICRP utilized the empirical function in the respiratory tract model.\(^1\) The function is given by
\[ F(NP) = -0.62 + 0.475 \cdot \log(dp^2 \cdot Q) \]  
(9)
where 
\[ F(NP) \text{: deposition probability in the NP region}, \]
\[ dp \text{: particle diameter (μm)}, \]
and 
\[ Q \text{: volumetric flow rate (l/min)}. \]

The author has also utilized the following relation, which was introduced from HEYDER and RUDOLF's experiment,\(^{12}\) for \( F(NP) < 0.01 \).
\[ F(NP) = -0.03065 + 0.03065 \cdot \log(dp^2 \cdot Q) \]  
(10)

Since these equations are only a function of the particle diameter and volumetric flow rate, they cannot be extrapolated directly to predict deposition in the respiratory tract of younger individuals.

Such extrapolation has been accomplished by assuming that deposition in the NP region is primarily by impaction.\(^{15}\)

A generalized expression for the deposition fraction by impaction was proposed by LANDAHL as\(^{14}\)
\[ F_{IM} = x/(1 + x) \]  
(11)
\[ x = \rho \cdot d_P^2 \cdot U \cdot \sin \theta / 9 \cdot \eta \cdot \delta \]  
(12)
where 
\[ F_{IM} \text{: deposition probability by impaction}, \]
\[ U \text{: average air velocity in parent airways (cm/s)} \]
\[ \theta \text{: branching angle (degree)}, \]
\[ \delta \text{: diameter of daughter airways (cm)}. \]

JOHNSTON, ISLES, and MUIR rewrote Eq.(11) as Eq.(13), by assuming a flux of homogeneous monodisperse particles to flow through a given generation of airway\(^{14}\).
\[ F_{IM} = B \cdot Q \cdot \sin \theta / (1 + B \cdot Q \cdot \sin \theta) \]  
(13)
\[ B = 0.14 \cdot \rho \cdot d_P^2 \cdot d_t^2 \]  
(14)
where 
\[ d_t \text{: diameter of parent airways (cm)}. \]

If \( \sin \theta \) is equal to one for the NP region and the age-invariant coefficient, \( A \), is introduced then Eq. (13) may be rewritten as
\[ F_{IM}(NP) = A \cdot B \cdot Q / (1 + A \cdot B \cdot Q) \]  
(15)
where 
\[ A \text{: age-invariant coefficient to normalize the deposition against the data of PATTLE, and HEYDER and RUDOLF}. \]

The coefficient, \( A \), is calculated from Eq. (15) with the adult values for \( F_{IM}(NP) \), \( B \) and \( Q \).

The impaction probability for non-adult’s NP region is then computed using this coefficient, \( A \), and known changes in \( B \) and \( Q \).

Deposition of inhaled aerosols in a given region of the respiratory tract or in the entire tract is expressed as deposition fraction of inhaled particles. Deposition fraction is the ratio of the number of mass of particles deposited in the respiratory tract to the number or mass of particles inhaled. The undeposited fraction represents those particles that are exhaled air after inhalation. The deposition in the \( i \)-th region is given by Eq. (16), for particles in the air passed into alveolar sacs.\(^9\)
where

\[ D_1(i) = F(i) \cdot \prod_{j=1}^{m} (1 - F(j)) \cdot (V_T - \sum_{n=1}^{m} V_n) \]  

(16)

and \( m \): total number of regions proximal to the alveolar region.

The remainder of inhaled air, equal in volume to \( \sum_{n=1}^{m} V_n \) or to \( V_T \), whichever is smaller, passed into the "dead space," remains for a time equal to the length of breathholding, and is completely exhaled.

The deposition in the \( i \)-th region during inhalation is given by

\[ D_2(i) = \prod_{j=1}^{i-1} (1 - F(j)) \cdot [F(i) \cdot (\sum_{n=1}^{i-1} V_n - \sum_{n=1}^{i} V_n)]\]

\[ + \frac{1}{2} F(i) \cdot (V_{i,e} - V_{i,L}) \]  

(17)

where

\( V_{i,e} \): volume of air entering the \( i \)-th region (cm), \( V_{i,e} = \sum_{n=1}^{i} V_n - \sum_{n=1}^{i-1} V_n \)

\( V_{i,L} \): volume of air passing through that region and into the next,

\[ V_{i,L} = \sum_{n=1}^{m} V_n - \sum_{n=1}^{i-1} V_n \]

\[ V_{i,e} - V_{i,L} = \begin{cases} V_{i,e} - V_{i,L} & \text{if } V_{i,e} < V_{i,L} \\ V_{n} & \text{if } V_{i,e} > V_{i,L} \end{cases} \]

Following inhalation, there is a period of breathholding of length \( \tau \), usually set equal to 1/8 of the total breathing cycle.8

\[ D_3(i) = \prod_{j=1}^{i-1} (1 - F(j)) \cdot \left[ 1 - \frac{1}{2} F(i) \right] \cdot F_\tau (\tau) \cdot (V_{i,e} - V_{i,L}) \]  

(18)

where

\( D_3(i) \): deposition in the \( i \)-th region during breathholding,

\( F_\tau (\tau) \): probability of deposition in the \( i \)-th region during breathholding.

The volume of air in each region will then pass through the "dead-space" during exhalation, traveling in the opposite direction to that experienced during inhalation.

The deposition in the \( i \)-th region is given by

\[ D_4(i) = \left\{ \sum_{K=1}^{M} \prod_{j=1}^{K-1} [1 - F(j)] \cdot \left[1 - \frac{1}{2} F(K)\right]^2 \cdot [1 - F_K(\tau)] \cdot \prod_{n=1}^{K-1} [1 - F(n)] \right\} \cdot F(i) \cdot (V_{i,e} - V_{i,L}) \]  

\[ + \frac{1}{2} F(i) \cdot (V_{i,e} - V_{i,L}) \]  

(19)

where

\( D_4(i) \): deposition in the \( i \)-th region during exhalation,

\( M \): total number of regions proximal to the alveolar region.

IV COMPUTER PROGRAM

A computer program written in BASIC language has been made to compute the age-dependent deposition fractions in the NP, TB and P regions.

User must set the following parameters before computation.

\( V_1 \): age-dependent tidal volume (cm³),

\( G_9 \): adult volumetric flow rate in the NP region (l/min),

\( E_9 \): adult volumetric flow rate in the NP region (cm³/s),

\( T_1 \): age-dependent inspiration period (sec),

\( T_2 \): age-dependent breathholding period (sec),

\( V_{X(N)} \): age-dependent regional volumes (cm³),

and

\( N_4(N) \): age-dependent regional number of airways.

Some results computed by the computer program are shown in Figs. 1 and 2, from which the percent deposition in the NP, TB and P regions
for adult and infant ages are given for inhaled monodisperse particles.

The parameter values for Weibel's model are shown in Tables 1 and 2.\textsuperscript{5,15}

\section*{V DISCUSSION}

In this article, the author described the age-dependent respiratory tract model and the computer program to estimate the regional deposition in the respiratory airways. The computer program is applicable for estimating the percent deposition of inhaled monodisperse particles in the NP, TB and P regions.

Most aerosol particles, however, are polydisperse and have particle sizes that range over two or more order of magnitude.

If the particles are log-normally distributed, then the percent depositions for polydisperse particles may be given by using the frequency function.

The calculated results for the adult are similar to the experiments and estimations done by other workers.\textsuperscript{1,15,16,17}

Because the activity conditions are not the same in Figs. 1 and 2, the difference between adult and infant ages could not discuss here. After the other workers, there is a small variation with age in the total respiratory deposition fractions, but there could be a strong age-dependence in the deposition fractions of particles larger than 10 $\mu$m deposited in the TB and P regions.\textsuperscript{9,17,18}

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\textbf{REFERENCES}


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8) D.J. Crawford; A generalized age-dependent lung model with applications to radiation stand-
### Table 1 Age-dependent regional volume and number of airways for Weibel's respiratory model.

<table>
<thead>
<tr>
<th>Region</th>
<th>Infant (1 y)</th>
<th>Adult</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Regional volume (ml)</td>
<td>No. of airways</td>
</tr>
<tr>
<td>NP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1.88</td>
<td>1</td>
</tr>
<tr>
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<td>1.88</td>
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<tr>
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### Table 2 Age-dependent respiratory standards.

<table>
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<tr>
<th>Age</th>
<th>Activity</th>
<th>$TV$ (ml)</th>
<th>$f$ (1/mm)</th>
<th>$MV$ (l/min)</th>
<th>$T_1$ (sec)</th>
<th>$T_2$ (sec)</th>
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<tbody>
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<td>15</td>
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<tr>
<td>Infant</td>
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<td>1.5</td>
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<td>0.25</td>
</tr>
</tbody>
</table>

Remarks

- $TV$: tidal volume (ml),
- $f$: breathing frequency (1/mm),
- $MV$: minute volume (l/min),
- $T_1$: inspiration period (sec),
- $T_2$: breathholding period (sec).


13) D.J. Crawford-Brown; (personal communication).


