PHYSICS AND RADIATION BIOLOGY

Radiation Dose Calculations for Inhalation of Tc-99m Sulfur Colloid Radioaerosol

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The radiation dose to the lung from the administration of Tc-99m sulfur colloid aerosol (for ventilation investigations) has been calculated. The dose to the ciliated airway epithelium varies between 0.34 to 2.5 rads, compared with 0.31 rads to the lung parenchyma. The calculation was normalized to a total of 1 mCi of Tc-99m deposited in the lung.

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Pulmonary ventilation imaging using radioaerosols has assumed an increasing role in nuclear medicine (*1–5*), especially for the patient on a respirator, in whom xenon gas studies are awkward and limited to one view (*6*, W. C. Vezina, S. Vinitski, M. J. Chamberlain-unpublished data). Since particle deposition in the lung is nonhomogeneous, detailed dosimetry for electron radiation cannot be made using the MIRD formulation.

Calculations of radiation absorbed dose for the 16 ciliated airway generations (from trachea to terminal bronchioles) and the lung parenchyma (respiratory bronchioles, alveolar ducts, and alveolar sacs), must be based on time-activity curves for each, and these in turn depend upon initial particle deposition and subsequent clearance. Once these curves have been computed, the total cumulated activity for each region can be determined, and the total dose is then calculated with use of the absorbed dose per unit cumulated activity, S. Since the S value for lung, available from MIRD-11 (*7*), assumes a uniform distribution of activity throughout the lung mass, we calculated S values for the ciliated epithelium.

MODEL

Radioaerosol considerations. To determine the optimal deposition and clearance models, one requires knowledge of the particle size distribution and the stability of the aerosol radionuclide tag.

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The aerosol considered here was originally produced by Taplin and his co-workers (*1,2,5*). Measurements of particle size (using an Anderson cascade impactor), for sulfur colloid aerosol as generated in our laboratory by a similar delivery system, indicates that 90% of the aerosol particles are between 1 and 2 μm in diameter.

Stability of the radioaerosol was tested by incubation with artificial extracellular body fluid (*8*) at 37°C for periods up to 52 hr. Results indicated that about 1% of the radioaerosol lost its tag.

Initial particle deposition. Gerrity et al. (*9*) have published a deposition model based on their experimental work and on that of Landahl (*10*) as applied to the morphometric lung model of Weibel (*11*). Weibel's model is a symmetric, dichotomously branching system of airways grouped into 24 generations (0–23) 16 of which are ciliated (0–15), with the last generation (23) being the alveolar sacs. They calculated that 34% of a 1.58 μm aerosol that passes the glottis is deposited in the lungs, the remainder being exhaled. Seventy-two percent of the uptake in the lungs is deposited in parenchyma; the rest is unevenly distributed throughout the 16 generations of ciliated airway. This model (*9*) is in acceptable agreement with the experimental results of others (*12*), and the particle size closely approximates ours. We have therefore used it to estimate the initial deposition of our aerosol for each ciliated airway generation from the trachea (generation 0) to the terminal bronchioles (generation 15) as well as for the lung parenchyma.

Lung clearance. There are two principal types of clearance: tracheobronchial, which is rapid and is effected by the mucociliary escalator, and parenchymal,

which is relatively slow and depends on the macrophages, the solubility of the inhaled material, and other factors.

Tracheobronchial clearance. From the models available (*13–15*), we chose the clearance model of Lee et al. (*14*), because of its agreement with their and our experimental data. This model is based on Weibel's lung model (*11*).

Lee et al. showed that the number of particles $N_{\alpha\beta}(t)$ at any time t in airway generation α, due to the initial deposition of particles in generation β ($\beta \geq \alpha$), can be represented by a set of Bateman equations (*16*). These were originally designed to describe radioactive transformations, and instead the half-lives of radioactive decay, Lee et al. (*14*) incorporated the residence half-times of the particles in each ciliated airway generation. These values were calculated by assuming that the mucus transport rate for any generation α is inversely proportional to the circumference of the generation, with the coefficient of proportionality obtained from the experimentally determined value of the tracheal mucus transport rate (*17*). The calculated residence half-times vary from 2.4 min for the third generation to 303 min for the last ciliated generation (terminal bronchioles). Therefore, the sum of these Bateman equations defines the number of particles present at any time t in generation α as:

$$N_\alpha(t) = \sum_{\beta=\alpha}^{15} N_{\alpha\beta}(t), \qquad (1)$$

where $\alpha = 0,\ldots 15$. This equation was used to calculate separately the cumulated activity for each ciliated airway generation α.

Parenchymal clearance. For relatively insoluble particles the biological half-time of parenchymal clearance ranges from days to months (*18–20*), and depends primarily on particle solubility (*21*). From experiments done in our laboratory, we have found that particles of Tc-99m sulfur colloid have an alveolar residence half-time of approximately five days, which is much longer than the physical half-life of the radiolabel. Consequently, the transfer of some particles from the lung parenchyma to the ciliated airways was neglected in these calculations.

Calculations. *Cumulated activity of each ciliated airway ($\tilde{A}_\alpha$) and parenchymal region ($\tilde{A}_{pl}$).* To calculate the cumulated activity for each ciliated airway, we assumed that the activity deposited is proportional to the number of particles deposited, whence the cumulated activity for airway generation α can be calculated from Eq. (1) as:

$$\tilde{A}_\alpha = \int_0^\infty A_0 \cdot \frac{N_\alpha(t)}{N_T(0)} \cdot \exp\left(-\frac{\ln 2}{T_p} \cdot t\right) \cdot dt \qquad (2)$$

Here A_0 is the initial activity deposited in the whole lung, $N_T(0)$ is the total number of particles initially deposited, and T_p is the physical half-life of the radionuclide. Since the ratio of $N_\alpha(t)$ to $N_T(0)$ is available (*9,14*), Eq. (2) can be evaluated for all 16 ciliated regions.

The cumulated activity for the parenchymal region ($\tilde{A}_{pl}$) is taken as:

$$\tilde{A}_{pl} = 1.44 \left(\frac{N_T(0) - \sum_{\alpha=0}^{15} N_\alpha(0)}{N_T(0)} \right) \cdot A_0 \cdot T_{eff}, \qquad (3)$$

where in the calculation of T_{eff} we have taken the biological half-time to be five days.

Equations (2) and (3) were used separately for calculations regarding electron radiation. For gamma radiation, we assumed that the photon flux was homogeneous throughout the lung; that is, the cumulated activity is simply the sum of the 17 equations.

Cumulated activity for stomach and intestine. We have assumed that the particles that are cleared by the mucociliary elevator are inevitably swallowed and passed through the gastrointestinal tract. The cumulated activity due to the particles outside the lung contributes not only to the gastrointestinal dose, but also to the whole-body dose and lung dose due to photon radiation. Cumulated activity for the stomach and the small and large intestines was calculated assuming biological half-times of 0.2 hr, 2 hr, and 24 hr, respectively. The stomach half-time value is obtained from Chaudhuri (*22*) and the intestine values from observations in our laboratory. The input of particles to the stomach was assumed to be the output of particles from the trachea.

Calculation of absorbed dose per unit cumulated activity (S). It has been assumed that the radioactive particles lie on the surface of the mucus, and calculations were applied to a bronchial epithelium of 100 μm thickness.

To calculate the electron dose to the ciliated epithelium, an infinite planar source distribution was assumed, since the approximate range of the electrons in tissue is significantly smaller than the radius of all ciliated airways (*11,23*).

For each converted and Auger electron (i), the energy dissipation function [$F_i(z)$] of a planar isotropic source was obtained by integrating data for a point isotropic source in water. The point source data for carbon were taken from Spencer (*24*), scaled to water as suggested by the MIRD formulation (*25*), and the required electron ranges were taken from Berger and Seltzer (*26*).

The absorption fraction ϕ_i of electrons with initial energy E_i was obtained by:

$$\phi_i = \frac{\int_5^{100} F_i(z)\, dz}{\int_0^\infty F_i(z)\, dz} \qquad (4)$$

TABLE 1. RADIATION DOSE IN RADS PER MILLICURIE OF Tc-99m DEPOSITED IN LUNGS

Region	Generation	Electron	Photon
Trachea	0	2.3	0.091
Main bronchi	1	2.3	0.091
Lobar bronchi	2	2.3	0.091
	3	2.3	0.091
Segmental bronchi	4	2.1	0.091
	5	1.9	0.091
	6	1.7	0.091
Bronchi with cartilage in wall	7	1.6	0.091
	8	1.3	0.091
	9	1.1	0.091
	10	0.93	0.091
Terminal bronchi	11	0.76	0.091
	12	0.63	0.091
Bronchioles with muscle in wall	13	0.48	0.091
	14	0.36	0.091
Terminal bronchioles	15	0.25	0.091
Parenchymal region		0.22	0.091

TABLE 2. RADIATION DOSE (RADS) FOR VENTILATION PROCEDURES IN NUCLEAR MEDICINE

Organ	Radioaerosol Tc-99m*	Inert gas Xe-133†
Trachea	2.4	1.1
Lung	0.37‡	0.065
Total body	0.016	0.009
Testes	0.001	0.007
Ovaries	0.017	0.008
Stomach wall	0.022	—
Small intestine	0.039	—
Large intestine	0.14	—

* For a total of 1 mCi deposited in the lung

† For a rebreathing period of 5 min and subsequent washout, where an initial spirometer of 10-l capacity with a concentration of 1 mCi/l is assumed. Tracheal values were taken from Goddard and Ackery (*30*), and the remainder from Atkins et al. (*31*).

‡ For the radioaerosol this value represents an average for the entire lung (airways, blood vessels, etc.).

The upper integration starts at 5 μm since it is reasonably assumed that a 5-μm layer of mucus lines the mucosal surface (*27*).

The S_α value for generation α is equal to:

$$S_\alpha = \frac{\sum_i \phi_i \Delta_i}{m_\alpha}, \qquad (5)$$

where m_α is the mass of an airway epithelium 95 μm thick, calculated from Weibel's model (*11*), and Δ_i is the equilibrium dose constant. We have assumed that the value $\Sigma_i \phi_i \Delta_i$ is the same for all airways, and calculated it to be 0.024 g-rad/μCi-hr for electron radiation.

S values for photon radiation for the lung were calculated using tables in MIRD pamphlets 5 (*28*) and 10 (*29*), while for the rest of the body the S values for both photon and electron radiation were taken from MIRD pamphlet 11 (*7*).

RESULTS

Initial deposition within the respiratory tract has been normalized to 1 mCi delivered through the glottis.

Table 1 summarizes the calculated dose to the lungs, given separately by generation number for the first 95 μm of ciliated epithelium and also for the lung parenchyma.

In Table 2, the radiation doses from the radioaerosol procedure are compared with those from Xe-133 ventilation tests (*30,31*).

Figure 1 gives time-activity curves for the trachea (generation 0), generation 2 (in which the maximum dose occurred), generation 3 (in which the initial relative surface concentration of particles is highest), and generation 15 (the last ciliated generation).

DISCUSSION

Let us compare the various doses to different organs as shown in Table 2. Note, however, that different approaches were used for the tracheal dose calculations. The value of 1.1 rads for Xe-133 was not calculated as a mean dose over a thickness of epithelium as ours was, but rather as the surface epithelial dose assuming a 5-μm thickness of mucus (*30*). Perhaps a more valid comparison for the tracheal epithelial dose would be the value suggested by Lassen (*32*) who calculated the mean dose to the first 100 μm of tracheal epithelium from Xe-133 to be about half that shown in Table 2.

It has been suggested that the radiation dose for xenon gas decreases in proportion to airway diameter (*30*), whereas for the radioaerosol the relationship presented in Table 1 is not so simple.

In a disease state the relative doses will change. In abnormal lungs, fractional deposition in the large airways may be much greater than predicted due to turbulence. Therefore, doses to the large airways, stomach, and intestine will be larger and the fraction deposited in some alveolar regions reduced, leading to smaller doses there.

Disease and smoking can also affect clearance, especially mucociliary clearance (*33–35*), in which case it is difficult to predict what will occur because of complicating factors such as coughing. Nevertheless, the dose

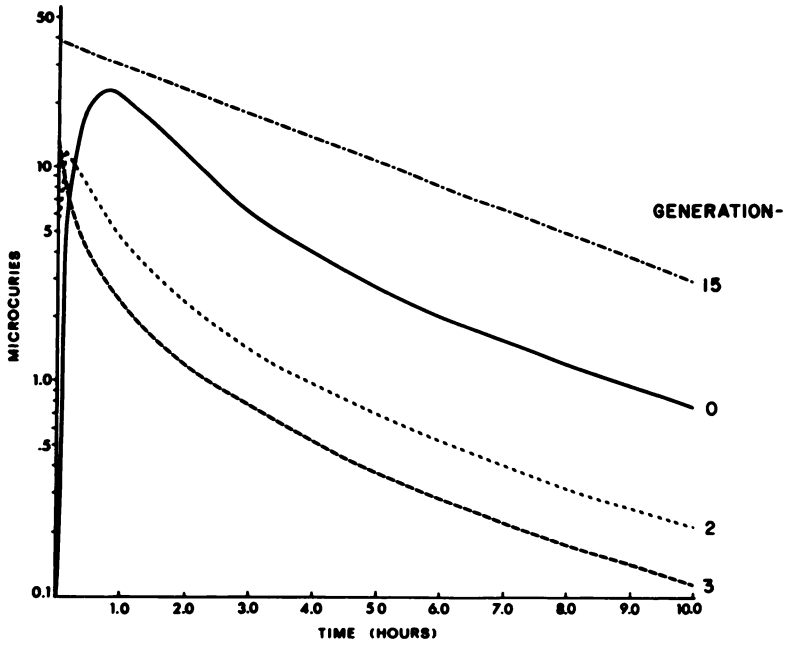

FIG. 1. Semilogarithmic time-activity curves in airway generations 0, 2, 3, and 15 for initial deposition of 1 mCi within lungs.

to the small airways will probably be increased since the particles may not clear as quickly from these regions as in normal subjects.

The radiation dose to the ciliated epithelium can be diminished by reducing the particle size of the radioaerosol to below 1 μm (*12*), but under such conditions the alveolar dose would increase.

As anticipated, the dose to the lung parenchyma is similar to that calculated for 1 mCi of Tc-99m macroaggregated albumin (*36*), and is appreciably higher than that for the inert-gas procedure. It remains for the physician to decide whether the increased information resulting from the radioaerosol study justifies the increased radiation dose.

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APPENDIX

Derivation of electron dose data. The time-activity curves for the intestines, the stomach, and the 16 ciliated airways were calculated using the deposition model of Gerrity et al. (*9*) and a set of Bateman equations taken from Lee et al. (*14*). Their equations can be represented as:

$$N_{\alpha\beta}(t) = \begin{cases} N_\beta(0)\left\{\sum_{j=\alpha}^{\beta}\left\{\prod_{\substack{k=\alpha \\ k\neq j}}^{\beta}\right][(\lambda_k-\lambda_j)\right\}^{-1}\cdot\exp(-\lambda_j\cdot t)\right\}\prod_{m=\alpha+1}^{\beta}\lambda_m & (\text{for } \alpha<\beta) \\ N_\beta(0)\cdot\exp(-\lambda_\beta\cdot t) & (\text{for } \alpha=\beta) \\ 0 & (\text{for } \alpha>\beta) \end{cases} \quad (6)$$

The constant λ_i equals the average transport rate of mucus in generation i divided by length of this generation. Therefore, Eq. (6) represents the total number of particles at any time t in generation α due to deposition in airway β.

The values for λ_i in Eq. (6) were obtained by assuming that in the ciliated airways there is no net absorption or secretion of mucus, that the mucus blanket is of constant thickness, and that the clearance rate in the trachea was consistent with known values (*14*), i.e., 5.5 mm/min. Their equations were then extended to include the stomach ($\alpha = -1$), the small intestine ($\alpha = -2$) and the large intestine ($\alpha = -3$), where it was assumed that there was no initial deposition in these organs and the clearance constants were 3.47/hr, 0.347/hr and 0.0289/hr, respectively. Thus the 19 time-activity curves were calculated using Eqs. (6), (1), and (2).

The next stage in the calculation for the ciliated airway was to determine for the 95-μm epithelium layer of the airway the value of $\Sigma_i\phi_i\Delta_i$ for the electron radiation. Since a 5-μm layer of mucus was assumed to line the mucosal surface of the ciliated airways, only absorption fractions (ϕ_i) for 140-keV and 120-keV electrons had to be determined. From Eq. (4), the calculated absorption fractions were 0.7047 for the 140-keV electrons and 0.7957 for the 120-keV electrons. These were then combined with the decay data supplied by MIRD (*29*) and a value of 0.024 g-rad/μCi-hr for $\Sigma_i\phi_i\Delta_i$ was calculated. This value was then multiplied by the integral of the time-activity curve for each ciliated airway, then divided by the mass of each ciliated airway epithelium to obtain the electron dose given in Table 1.

Derivation of data for total radiation dose. Total dose for trachea was estimated as the sum of doses from electron and photon radiation taken from Table 1. This was necessary since there are no available "S" values for the trachea.

For all other organs, total dose was calculated using the following MIRD formula:

TABLE 3. CONTRIBUTION IN RADS OF SOURCE ORGAN TO TARGET ORGAN

Target organ	Source (with values of $\tilde{A}_h$) Lung 7154.12 μCi · hr	Stomach content 46.54 μCi · hr	Small intestine 349.061 μCi · hr	Large intestine 837.598 μCi · hr	Total dose
Lung	(5.2×10^{-5})	(1.7×10^{-6})	(2.2×10^{-7})	(1.7×10^{-7})	
	3.72×10^{-1}	7.9×10^{-5}	7.7×10^{-5}	1.4×10^{-4}	0.371
Total body	(2.0×10^{-6})	(1.9×10^{-6})	(2.4×10^{-6})	(2.25×10^{-6})	
	1.43×10^{-2}	8.9×10^{-5}	8.38×10^{-4}	1.88×10^{-3}	0.016
Testes	(7.9×10^{-9})	(5.1×10^{-8})	(3.1×10^{-7})	(1.0×10^{-6})	
	5.6×10^{-5}	2.37×10^{-6}	1.05×10^{-4}	8.2×10^{-4}	0.00098
Ovaries	(9.4×10^{-8})	(5.0×10^{-7})	(1.1×10^{-5})	(1.5×10^{-5})	
	6.7×10^{-4}	2.33×10^{-5}	3.8×10^{-3}	1.26×10^{-2}	0.017
Stomach wall	(1.8×10^{-6})	(1.3×10^{-4})	(3.7×10^{-6})	(2.8×10^{-6})	
	1.28×10^{-2}	6.05×10^{-3}	1.29×10^{-3}	2.34×10^{-3}	0.022
Small intestine	(1.9×10^{-7})	(2.7×10^{-6})	(7.8×10^{-5})	(1.32×10^{-5})	
	1.38×10^{-3}	1.09×10^{-4}	2.7×10^{-2}	1.1×10^{-2}	0.039
Large intestine	(1.45×10^{-7})	(2.35×10^{-6})	(1.56×10^{-5})	(1.6×10^{-4})	
	1.0×10^{-3}	1.1×10^{-4}	5.44×10^{-3}	1.34×10^{-1}	0.14

$$D_{(r_k)} = \sum_h \tilde{A}_h \cdot S\,(r_k \leftarrow r_h), \qquad (7)$$

where $\tilde{A}_h$ is the cumulated activity in source organ r_h, and r_k is the target organ.

Cumulated activity for the whole lung was taken as the sum of cumulated activities from each ciliated airway generation (from 0 to 15), and this was added to the cumulated activity of the parenchymal region.

The "S" value for the large intestine was taken as the average of "S" values for the upper and lower large intestine as provided by MIRD (*7*).

Table 3 shows the contributions, in rads, of each source organ to the target organ. The "S" values used in the calculations are in parentheses and were obtained from MIRD (*7*). Selected values from Table 3 are listed in Table 2.

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