OVERVIEW OF ICRP RESPIRATORY TRACT MODEL*

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Abstract — A special Task Group of the International Commission on Radiological Protection (ICRP) was created to review the dosimetric model of the respiratory tract and propose revisions or a new model. The Task Group directed its efforts toward improving the model used in Publication 30 rather than developing a completely new model. The objective was a model that would (1) facilitate calculation of biologically meaningful doses; (2) be consistent with morphological, physiological, and radiobiological characteristics of the respiratory tract; (3) incorporate current knowledge; (4) meet all radiation protection needs; (5) be user friendly, i.e. not unnecessarily sophisticated; (6) be adaptable to development of computer software for calculation of relevant radiation doses from knowledge of a few readily measured exposure parameters; (7) be equally useful for assessment purposes as for calculating annual limits on intake; (8) be applicable to all members of the world population; and (9) consider the influence of smoking, air pollutants, and diseases on the inhalation, deposition, and clearance of radioactive particles from the respiratory tract. Rather than calculating an average dose to the total lungs, emphasis was given to calculating specific tissue doses that could be used in the ICRP radiation protection system.

INTRODUCTION

The International Commission on Radiological Protection (ICRP) is currently undertaking a number of efforts associated with publication of its 1990 recommendations(1). These efforts include a possible revision of the secondary limits, annual limits on intake for radionuclides (ALI). To support this work, a task group was appointed to review the current lung dosimetry model and, if needed, propose a revised model.

The members of the ICRP Task Group on Human Respiratory Tract Models for Radiological Protection were selected to ensure that the broad spectrum of biological, physiological, chemical, radiological, and health physics aspects of inhaled radioactive aerosols and gases could be competently addressed. The members of the task group are: Michael Bailey, Fredrick Cross, Richard Cuddihy, Peter Gehr, Anthony James, John Johnson, Roland Masse, Monique Roy, Willi Stahlhoven, and William Bair, chairman.

The proposed respiratory tract model described in this and other papers in these proceedings is still in draft form and has not yet been submitted to the ICRP. Therefore, the model currently adopted by the ICRP could be substantially different.

The purpose of a dosimetric model of the human respiratory tract is to provide a qualitative and quantitative understanding of inhalation as a route for radionuclides to enter the body. This is a fundamental requirement for calculating dose equivalents for respiratory tract tissues using information about exposures to airborne radionuclides or from bioassay data. A model that includes a description of the clearance of deposited radionuclides from the respiratory tract and transfer to circulating blood is also necessary to calculate dose equivalents to other body organs and tissues in which the radionuclides may be deposited.

BASIS FOR REVISING MODEL

The proposed model attempts to address the principal inadequacies of the current ICRP model. These include omitting the calculation of radiation doses to the nasal and oral passages; employing the D, W, and Y classification system for clearance of inhaled materials with its attendant deficiencies; averaging the dose over the total lung mass; and not providing for calculation of doses from inhalation of radioactive gases. The revised model incorporates new knowledge about deposition and retention of very small particles (well below 0.1 μm diameter), about regional deposition of inhaled particles, about the distribution and absorption of inhaled gases, and about clearance kinetics for numerous radioactive compounds determined in humans and experimental animals. The model reflects advances in our knowledge of the morphometry and the physiology of the respiratory tract, and of dosimetry modelling concepts and approaches. The major developments in computer technology during the past few years have opened numerous possibilities not only for modelling the intake of radioactive materials but also for using the model for assessment purposes, as well as for calculating ALIs. One of the Task Group's objectives was to construct a model

*This paper reflects changes in the proposed model since the workshop. Some of these changes are in response to comments and suggestions made at the workshop.
consistent with morphological, physiological, and radiobiological characteristics of the respiratory tract. The model is intended to apply to all members of the world’s population, workers and non-workers, including children; it also considers the influence of smoking, air pollutants, and lung disease.

The revised model emphasizes the calculation of doses that are relevant to the biological effects that result from the deposition of radioactive materials in the respiratory tract.

Since the various cells and tissues within the respiratory tract vary greatly in sensitivity to radiation exposures, and because there are great differences in the radiation doses received by the various cells and tissues from inhaled radionuclides, averaging the dose over the total respiratory tract or even just over the lungs is often difficult to justify. Therefore, a primary objective was a model that reflected differences in both radiation sensitivities and dose distribution. This led to the identification of anatomical regions within the respiratory tract for which radiation sensitivities could be reasonably distinguished and for which the deposition and residence time of deposited materials could be specified. The model provides for calculation of doses to these several regions.

A major requirement in developing this revised lung model was that the radiation doses calculated must be applicable to the ICRP radiation protection system. This system, as defined in ICRP Publications 60(1) and 30(2), requires a single dose equivalent value for the lungs. To reduce several calculated regional doses to a single value for the lungs, it was assumed that it would be appropriate to adjust each regional dose by the relative radiation sensitivity of the region, to obtain an equivalent dose applicable to the combined thoracic regions.

Similarly, an equivalent dose value can be calculated for the extrathoracic regions. This adjustment of doses is consistent with the ICRP’s use of tissue or organ weighting factors to calculate the effective dose(3).

THE PROPOSED MODEL

Morphometry

The Task Group’s approach was to converge separately developed morphological, radiobiological, physiological, deposition, clearance, dosimetric, and bioassay considerations into a comprehensive multiparameter dosimetric model for the complete respiratory tract. An anatomical representation of the model is shown in Figures 1 and 2. Figure 1 identifies the anatomical regions that can be correlated reasonably well with measurements of deposition, clearance, and retention of inhaled aerosols and with sites of early injury and late-occurring diseases that result from the intake of airborne radioactive materials. Figure 2 further defines these regions and compares them with the subdivision of the current model. The anatomical regions are: the extrathoracic (ET), comprising the anterior nose (ET1) and the posterior nasal passages, larynx, pharynx, and mouth (ET2); the bronchial region (BB), comprising the airway generations 0 through 8 (trachea through the bronchi); the bronchiolar region (bb), comprising the airway generations 9 through 15; and the alveolar interstitial region (AI), comprising the airway generations 16 through 26 (respiratory bronchioles to alveolar sacs). There are two thoracic lymph node regions, LN(ET), draining the extrathoracic region, and LN(TH), draining the bronchial, bronchiolar, and alveolar interstitial regions. For dosimetry purposes, morphological and cytological dimensions are assigned to these regions. To scale for age and gender, the dimensions of the extrathoracic airways are considered to be proportional to the diameter of the trachea. The dimensions of the trachea and bronchi are considered to be related to body height. The dimensions of the respiratory airways can be scaled by the one-third power of the functional residual capacity after age 2 years, when the structure of the lungs is completely developed. The diameter and length of the bronchioles are assumed to decrease exponentially from the 9th to 15th generation. The mass of the alveolar–interstitial region is assumed to vary with age, gender, and race, in proportion to body weight. The thickness and cellular structure of epithelial tissues are considered to be independent of age, gender, and body size.

Physiology

Radiation doses to tissues and cells in the
OVERVIEW OF ICRP RESPIRATORY TRACT MODEL

Physiology

Radiation doses to tissues and cells in the respiratory tract are to a great extent determined by breathing characteristics and certain respiratory parameters that influence the volume and rate of air inhaled and the proportions entering through the nose and mouth. This determines the quantity of radionuclides inspired, the penetration into the respiratory tract, and the quantities deposited. Since breathing characteristics and respiratory parameters vary greatly among the world’s population depending upon body size, level of activity, the presence of respiratory tract diseases and smoking habits, a dosimetric model for the respiratory tract applicable to all populations must allow for these differences. The model will recommend a range of values for the most critical respiratory parameters and give reference values for the adult worker and for members of the general population. The latter will include values for the 3 month old; 1, 5, 10 and 15 year olds; and adult males and females. Reference minute volumes will be recommended for resting and light and heavy activity. For the worker, the volume of air breathed in 8 h will be taken as 13.5 m³ for 7 h at light and 1 h at heavy activity. This compares with 9.6 m³ used in ICRP Publication 30(3).

Breathing only through the nose or mouth and breathing through the nose augmented by mouth breathing are all considered in the model.

Deposition

The proposed revised model addresses inhalability of aerosols (which is dependent upon particle size but largely independent of breathing rate) as well as deposition in extrathoracic tissues (such as the nose, nasal passages, pharynx, and larynx). Deposition in the thoracic BB and the bb regions is assumed to include material rapidly cleared essentially by particle transport from airway generations 0 through 15. Deposition in the Al region includes material slowly cleared from airway generations 16 through 26 by both particle transport and solubilisation processes, as well as material infinitely retained, such as in lymphatic tissues. Calculations of the deposition of particles in these regions are based on morphometric models and experimental data from human subjects inhaling test aerosols over a broad range of particle sizes.

Particles are largely deposited at two sites in the

<table>
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<th>Function</th>
<th>Cytology (Epithelium)</th>
<th>Histology (Walls)</th>
<th>Generation Number</th>
<th>Anatomy</th>
<th>Compartments</th>
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<td>Air Conduction; Gas Exchange, Size Particle Clearance</td>
<td>Goblet Cells; Stratified Cells with Squamous Cells on Top</td>
<td>Mucous Membrane, Respiratory Epithelium, Clara Cells, Glands</td>
<td>0</td>
<td>Trachea</td>
<td>ET₁</td>
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<td>1</td>
<td>Main Bronchi</td>
<td>ET₂</td>
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<td>No Goblet Cells, Cell Types (All Respiratory Epithelium)</td>
<td>Goblet Cells</td>
<td>Mucous Membrane, Respiratory Epithelium, Clara Cells, Glands</td>
<td>2-6</td>
<td>Bronchi</td>
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Figure 2. Proposed subdivision of the respiratory tract compared with the current ICRP model.
ET₂ region, the posterior nasal passages and the larynx. The model assumes that during nasal breathing, deposition of particles is half in ET₁ and half in ET₂; during mouth breathing, deposition of particles occurs only in ET₂. Deposition efficiencies for the BB, bb and AI regions are calculated for both aerodynamic and thermodynamic processes over the particle size range of 0.0005 μm activity median thermodynamic diameter (AMTD) to 100 μm activity median aerodynamic diameter (AMAD). Reference values of regional deposition are provided, and guidance is given for extrapolation to specific individuals and populations.

Clearance

The proposed model describes four clearance pathways. Material deposited in ET₁ is removed by extrinsic processes, such as nose blowing. For the other regions, clearance of inhaled material occurs by particle transport processes (such as macrophage uptake and transport in fluids over airway surfaces by ciliary action) to the G₁ tract and to lymph nodes and by absorption into blood. It is assumed that clearance of inhaled material by these two processes, particle transport and absorption, is competitive. It is also assumed to be non-linear, with excretion a time-varying factor of the residual amount. Since it is assumed that clearance by particle transport is the same for all materials, a single model is proposed. Rates for particle transport were derived from studies with human subjects. Absorption into blood is material-specific, acts in all regions except region ET₁, and is assumed to occur at the same rate from all regions. Absorption into the blood is essentially a two-stage process:

1. the dissociation of the particles into material that can be absorbed into the blood (dissolution), and
2. the absorption into blood of inhaled soluble material and of material dissolved from particles.

The model will use observed rates of absorption for compounds for which reliable human data exist or for which data can be extrapolated with confidence from animal experiments. The absorption rates of other compounds will be specified as ‘fast’, ‘moderate’, or ‘slow’. Initially these will be based primarily on their current D, W, and Y classification, but eventually will be replaced since this classification system combines clearances by both particle transport and absorption processes.

Dose calculations

Mathematical models for calculating radiation doses to various tissues of the respiratory tract incorporate expressions describing the deposition and retention of radionuclides. Rather than treat the lung and lymph nodes as a single organ and calculate an average dose, as in the current ICRP model, the revised model provides for calculating doses to tissues in anatomical regions identified in Figures 1 and 2.

The calculation of doses follows the method of ICRP 30(2), in which the committed equivalent dose in a target tissue is determined by the energy absorbed per unit mass from the radiation emitted from a source organ. Compared with the current model, the proposed model is expected to simplify calculating respiratory tract doses from bioassay data. Computer software will facilitate, but not be necessary for, using the revised dosimetric model for the respiratory tract.

Among target tissues of the respiratory tract selected for dose calculation are those identified as the most sensitive to radiation-induced cancer as well as those that have been observed in humans and experimental animals to receive the highest doses. These are:

keratinised epithelium of the anterior nasal passages, ET₁,
stratified squamous epithelium of the naso-oropharynx and larynx, ET₂,
ciliated epithelium of the bronchi containing secretory and basal cells, BB,
ciliated epithelium of the bronchioles containing secretory cells, bb,
alveolar-interstitium, AI,
extrathoracic and thoracic lymph nodes, LN₄ and LN₇₁.

The tissue masses used to calculate dose are defined by the surface area and the target cell depth specified for each region. These regional doses are adjusted by the relative radiation sensitivity and summed to obtain a single value of committed equivalent dose for the extrathoracic tissues and another for the thoracic tissues.

Considerations of radiation detriment

The ICRP(1) focuses on protection of workers and the public from the total radiation detriment. This detriment includes the probability of attributable fatal and non-fatal cancers, hereditary effects, and length of life lost if harm occurs. For the purpose of this lung model, it is assumed that the relative sensitivities of the various tissues of the respiratory tract to all radiation-induced deleterious effects are the same as for cancer and that all regions of the respiratory tract are susceptible, but not equally. Since data are inadequate to provide risk estimates for each region or tissue, it was further assumed that
induction of cancer by radiation is proportional to the spontaneous incidence in each region and that the relative distribution of spontaneous regional cancers in unexposed persons reflects relative sensitivities of the regions to radiation-induced cancer. A major uncertainty in this approach is the effect of cigarette smoking and other inhaled toxic materials on the distribution of ‘spontaneous’ cancers among the regions of the respiratory tract.

After reviewing data on cancers of the human respiratory tract, the relative sensitivity of each region and tissue was estimated and the radiation detriment partitioned among the regions as shown in Table 1.

It is proposed, then, that committed equivalent doses, adjusted for radiation detriment, be calculated for the extrathoracic and thoracic regions as follows:

\[ H_T(ET) = H_{T,ET1} A_{ET1} + H_{T,ET2} A_{ET2} + H_{T,LNET} A_{LNET} \]

and

\[ H_T(TH) = H_{T,BB} A_{BB} + H_{T,bb} A_{bb} + H_{T,AL} A_{AL} + H_{T,LTH} A_{LTH} \]

where \( H_T(ET) \) and \( H_T(TH) \) are detriment adjusted equivalent doses for the extrathoracic and thoracic regions, respectively; \( H_{T,ET1} \), etc. are equivalent doses for tissues in the extrathoracic regions; and \( H_{T,BB} \), etc. are equivalent doses for tissues in the thoracic regions; and \( A_{ET1} \), etc. are factors for apportionment of radiation detriment from Table 1 for the extrathoracic region and \( A_{BB} \), etc. for the thoracic regions.

The above partitioning of detriment is consistent with observations in experimental animals following inhalation of insoluble alpha emitters, which irradiate mainly the alveolar-interstitial region where nearly all cancers occur and the lymphatic region where cancers have been very rare. There are no contra-indications among workers who have inhaled insoluble alpha emitters.

As noted previously, the partitioning of detriment is influenced by the exposures to cigarette smoke and other airborne toxic materials that occurred in the populations on which the apportionment is based. Thus, the partition of detriment for the respiratory tract tissues may not apply to all people equally. However, there is no reason to believe that use of the proposed apportionment for radiation protection purposes and for calculating effective doses to most populations would underestimate the risk. Where more precise information is available for specific populations, it is recommended that the apportionment of detriment be adjusted accordingly. The ICRP tissue weighting factors appropriate for the extrathoracic tissues and for the thoracic tissues (lungs) can be applied to these two values of committed equivalent dose for calculating the effective dose for the individual as described in ICRP Publication 60(1).

**SUMMARY**

The respiratory tract model to be proposed to the ICRP is based on the premise that because of the large differences in radiation sensitivity of the various tissues in the respiratory tract and because doses received by these tissues can vary substantially, depending upon the characteristics of the intake, calculating doses to these specific tissues is more relevant for radiation protection purposes than the current practice of calculating an average dose for the total lung mass. The model required for these dose calculations is more complex than the current lung model because it must describe the deposition of inhaled radioactive material in, and the clearance from the several tissues and regions of, the respiratory tract. It must also be applicable to the worldwide population of both workers and the general public. The model provides for use of the calculated doses in the ICRP radiation protection system.

**ACKNOWLEDGEMENT**

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REFERENCES
