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**"Considerations of Beta and Electron Transport in
Internal Dose Calculations"**

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INTRODUCTION

Ionizing radiation has broad uses in modern science and medicine. These uses often require the calculation of energy deposition in the irradiated media and, usually, the medium of interest is the human body. Energy deposition from radioactive sources within the human body and the effects of such deposition are considered in the field of internal dosimetry.

Internal dosimetry is usually defined as a process of measurement and calculation which results in an estimate of the absorbed dose to tissues of the body due to an intake of radioactive material. Internal dose calculations are a two-step process as defined in the schema of the Medical Internal Radiation Dose (MIRD) Committee of the Society of Nuclear Medicine. The first step is to model the kinetics of the radionuclide in the body. Here the parameter of interest is the rate at which the radionuclide moves from one organ to another until the nuclide is eliminated from the body or until its residence time in the body exceeds the mean life of the nuclide. Organs of the body are considered to be compartments into which nuclides move in and out. The net movement of the nuclide (including radioactive decay) from a compartment is described by a system of first-order differential equations. The solutions to these equations include constants that depend upon biochemical properties of the organs.

The second part of the internal dose calculation considers the movement (or transport) of radiation from nuclei undergoing radioactive decay to the surrounding tissue. Radiation emitted in these nuclear transformations can be alpha, beta, or gamma radiation. These radiations travel varying distances from the site of their creation before an interaction takes place. The result of an interaction can be a total or partial deposition of the radiation energy. The exact mechanisms of interaction, transport, and energy deposition are described by well-understood physical parameters.

Recent Developments Sponsored by DOE

In July of 1988, a three-year research project was initiated by the Nuclear Engineering Department at Texas A&M University under the sponsorship of the U. S. Department of Energy. The main thrust of the research was to consider, for the first time, the detailed spatial transport of electron and beta particles in the estimation of average organ doses under the MIRD schema. In the MIRD schema, these particles are classified as "non-penetrating" radiations. As a result, their absorbed fraction of energy is considered to equal unity if their production or emission occurs within the target organ of interest; otherwise, the absorbed fraction of energy is zero. As was shown in the initial research

proposal, transport calculations show that absorbed fractions can vary significantly from unity in many situations. This is particularly true for higher energy beta and electron sources within organs with a small mass and a large surface area.

Consequently, a systematic compilation of absorbed fractions for both beta particles and photons (which produce electrons) was initiated. The reference heterogeneous phantom described in MIRD Pamphlet 5 Revised (Snyder 1978) was implemented as a geometry scoring routine within the electron transport code EGS4 (Rogers 1984). This Monte Carlo transport code thus allowed the explicit treatment of electron collisional and radiative energy loss, as well as multiple scattering, in internal dose estimates. An extensive database of electron and revised photon absorbed fractions was compiled for 21 combinations of source-target regions (Akabani and Poston 1990a). Next, this database was used to reevaluate tabulations of S-values for 80 radionuclides of interest in diagnostic and therapeutic nuclear medicine procedures (Akabani and Poston 1990b). Reports for both electron absorbed fractions and the revised S-values are contained in the Comprehensive Report which accompanies this renewal proposal.

In conjunction with this work, revisions were also made to the head and neck region, the gall bladder (Patel et. al 1991a), and the kidney (Patel et. al 1991b) of the MIRD phantom. In the revised kidney model, three subregions were included: the papillae, the medulla, and the cortex. Reports for both the kidney and gall bladder can be found in the Comprehensive Report.

With the capabilities of the EGS4 code, an revised dosimetry model for the circulatory system was initiated within the second year of research. Absorbed fractions of energy were calculated for monoenergetic photons and electrons within infinite cylinders of radius 0.02 to 1.0 cm. The division between the source region (blood) and the target region (blood vessel) were varied so as to simulate the full range of vessels found within the circulatory system. Estimates of the average absorbed dose to blood and the maximum absorbed dose to the vessel walls were made for selected radionuclides and for all vessel sizes (Akabani and Poston 1990c). This effort has been identified by the MIRD Committee as being extremely important to the assessment of dose in nuclear medicine procedures. A report of this work is also included in the Comprehensive Report.

At the present time (December of 1990), research activities are continuing within five areas. Several are new initiatives begun within the second or third year of the current contract period. They include: (1) development of small-scale dosimetry; (2) development of a differential volume phantom; (3) development of a dosimetric bone model, (4) assessment of the new ICRP lung model; and (5) studies into the mechanisms of DNA damage. A progress report is given for each of these tasks within the Comprehensive

Report. In each case, preliminary results are very encouraging and plans for further research are detailed within this document.

Throughout the current contract period (July 1, 1988 - June 30, 1991), direct support has been requested for only one to two graduate students. Nevertheless, the activities performed at Texas A&M under DOE support have been a simulating source of research topics for both master's theses and doctoral dissertations. At present, a total of 13 graduate students have been either directly or indirectly involved in the dosimetry research sponsored by DOE. Six of these students have graduated (5 MS and 1 PhD), two are currently nearing graduation (2 MS), and 5 are currently pursuing their research (2 MS and 3 PhD). Three of the completed master's theses involved tasks related to, but not directly proposed under, the current DOE contract. These studies involved research into: (1) hot particle dosimetry; (2) cavity theory as it relates to TLD design; and (3) nearest-neighbor distributions of free radicals produced within electron and alpha particle tracks. For completeness, a summary of each study is contained in the Comprehensive Report. A list of all students participating in DOE-sponsored research is given below.

List of Participating Graduate Students

Graduated

T. Edmond Hui, "A Preliminary Model of the Circulating Blood for use in Radiation Dose Calculations, " Thesis, Texas A&M University, 1986.

Jyoti S. Patel, "A Revised Model of the Kidney for the Calculation of Absorbed Fraction of Various Photon Energies," Thesis, Texas A&M University, 1988.

Donna M. Busche, "A New Approach to Hot Particle Dosimetry Using a Monte Carlo Transport Code, " Thesis, Texas A&M University, 1989.

Mark D. Weyland, "A Look at General Cavity Theory through a Code Incorporating Monte Carlo Techniques," Thesis, Texas A&M University, 1989.

M. Clay Smith, "Nearest-Neighbor Distributions of Free Radicals Produced within Charged-Particle Tracks in Liquid Water," Thesis, Texas A&M University, 1990.

Gamal Akabani, "Internal Dose Calculations for Electrons and Beta Particles," Dissertation, Texas A&M University, 1990.

Completing Research

Joseph Liu, "Internal Beta Dose Calculations Using a Point Kernel Algorithm," Thesis, Texas A&M University, 1991.

Todd A. Shearer, "Assessment of the Dose to Bone Using a Monte Carlo Transport Code," Thesis, Texas A&M University, 1991.

Beginning Research

Oscar Hernandez (MS)

Research Interest: Assessment of New ICRP Lung Model

Judy Hutchings (MS)

Research Interest: Development of a New Brain Model for Internal Dosimetry

How Mooi Lau (PhD)

Research Interest: Mechanisms of DNA Damage

Eun-Hee Kim (PhD)

Research Interest: Microdosimetry of Internal Beta Emitters

Carmin Plott (PhD)

Research Interest: Experiment Determination of Organ Doses from Internal Emitters

List of Research Publications

Akabani, G., J. W. Poston, Sr., and W. E. Bolch, "Estimates of Absorbed Fractions in Small Volumes for Selected Radionuclides", *Journal of Nuclear Medicine* (submitted), 1990a.

Akabani, G. and J. W. Poston, Sr., "Reevaluation of S-Values Considering Electron Transport," *Journal of Nuclear Medicine* (submitted), 1990b.

Akabani, G. and J. W. Poston, Sr., "Absorbed Dose Calculations to Blood and Blood Vessels for Internally Deposited Radionuclides," *Journal of Nuclear Medicine* (submitted), 1990c.

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**Small - Scale Dosimetry Calculation
for
Internally Deposited Radionuclides**

INTRODUCTION

Electron radiations, administered both internally and externally, have become increasingly popular for use in radiation treatment of cancer. Beta emitting nuclides are often used in medicine for therapeutic purpose. The nuclides can be injected into a patient in the form of labeled compounds or can be used as applicators. Uses of electrons or beta-emitting radionuclides is preferred because these radiations exhibit a rapid dose fall-off distal to the treatment volume, thus providing protection to vital healthy tissue. The delivery of radioactive materials to tumor sites using radiolabeled monoclonal antibodies is currently being considered for the treatment of malignant tumors. Beta-emitting radioisotopes can now be attached to proteins that can, with great specificity, bind to tumor cell surfaces. Therefore, a new dimension of therapeutic application of beta emitting nuclides is under development, which necessitate a precise and fast dose calculation. Thus, it is now especially important to be able to calculate the dose distribution in small regions with embedded beta-ray sources.

As far as homogeneous media are concerned, dose calculations are facilitated by the use of beta dose point kernels (BDPK) for the media. To solve the problems of routine dosimetry for heterogeneous media, it is impractical to employ realistic and, in principle, accurate, but tedious Monte Carlo methods. Simpler empirical or semiempirical methods, providing rather fast estimates but of limited accuracy, may be acceptable. Small scale dosimetry, utilizing the results from Monte Carlo calculations and performing straightforward dose calculation, is able to provide rapid estimates of absorbed dose with appropriate accuracy.

In many instances, internal dose assessment has resorted to Monte Carlo calculations to analyze the details of source-target relations and radiation dose. However, such an approach is not always practical, which can be time-consuming and wasteful of computer resources, especially in implementing the approximation encountered in medical internal dosimetry. Considering the feasibility of realistic treatments of beta and electron interactions within tissue, a different approach should be investigated. Small Scale Dosimetry, which incorporates the "once-through" Monte Carlo approach, can be used to analyze the energy deposition in the neighborhood of isotropic point sources, and to make straightforward analytical calculations of absorbed dose. This method makes it possible to calculate absorbed-dose distributions for either homogeneous or inhomogeneous sources by doing simple integrals over point-source distributions. Several computer codes have

been developed to process the data base of energy deposition histories and to implement the absorbed dose calculations by using point kernel algorithm. Conceivably, the Small Scale Dosimetry approach may be extended to be applicable for heterogeneous target tissue compositions, as long as the biological data and physiological information of that organ or tissue are well understood.

METHODOLOGY

There are three major steps in the assessment of radiation absorbed doses to small volumes or regions of the body. First, it is necessary to establish the fundamental understanding of interactions between beta radiation and human tissue. The energy deposition in concentric tissue rings is studied. As shown in Fig.1 is the target tissue domain used for energy deposition study, which has radius equal to 1.2 times the R_{csda} (Continuous Slowing Down Approximation Range) and subdivided into 100 concentric shells. A Monte Carlo transport code EGS-4 (Electron Gamma Shower) is used to trace the electron histories and score the energy deposition in each shell. The calculation of Absorbed Fraction (AF), Specific Absorbed Fraction (SAF) and Scaled Dose Kernel ($F(r/R)$) are performed following Eq. 1, 2 and 3 to establish the data base of monoenergetic electrons, which will be applied for subsequent absorbed dose calculations.

$$AF = \frac{\text{energy deposited in target region}}{\text{energy emitted in source region}} \quad \text{Eq.1}$$

$$SAF = \Phi = \frac{AF}{\text{mass of target}} \quad \text{Eq.2}$$

$$F(r/R_{csda}) = \frac{\delta E(r)/E_0}{\delta r/R_{csda}} \quad \text{Eq.3}$$

where

$\delta E(r)$ is the energy deposition in a shell with distance r from the center of sphere;

E_0 is the average energy of electron or beta-particle;

δr is the thickness of each concentric ring; and

R_{csda} is the Continuous Slowing Down Approximation range.

Fig. 1. The tissue sphere with 100 concentric rings used in the energy deposition study. Monte Carlo method is used to trace the electron transportation in each skeletal muscle shell.

Secondly, the advent of radiolabeled monoclonal antibodies (MAB's) has elicited much interest in the possibility of developing cancer cell specific radiopharmaceuticals for therapeutic purpose. In the context of radioimmunotherapy of cancer, there is a need for continued improvement of dosimetry of radionuclides localized in tumors. Therefore, instead of using monoenergetic electrons as the sources, beta radiations from radionuclides with spectral energy emission will be the focus of study. Composite scaled dose kernel, $F(r/R)$, will be generated for the following radionuclides: P-32, Y-90, Cu-67 and I-131, which are the potential candidates for tumor treatment. Dose profile for each radionuclides will be performed to study the therapeutic effect of administration of these radionuclides.

At last, absorbed dose calculation will be performed by selecting thyroid, ovary and kidney as the target organs and using P-32, Y-90, Cu-67 and I-131 as source radionuclides. Mathematical description of the target organs as used by MIRD Committee (Snyder et al. 1969) is employed to define the target domain. Scaled dose kernels obtained from procedure (3) is utilized to calculate the absorbed dose by administrating of these four radionuclides in the selected organs. Then, the absorbed dose is calculated by the equation

$$\text{Dose} = E_{av} \frac{F(r/R_{csda})}{4 \pi r^2 \rho R_{csda}} \quad \text{Eq.4}$$

where

$F(r/R_{csda})$ is the scaled dose kernel of that given energy;
 r is the distance from source to target;
 ρ is the density of target material.

The isodose profiles at different plane of interest are plotted to represent the results of absorbed dose calculations.

CURRENT PROGRESS

The proposed procedure discussed above have completely fulfilled. A FORTRAN program has been generated to process the database of monoenergetic electrons and produce scaled dose kernel of any radionuclide by giving the atomic number, end-point energy and branching ratio of that radionuclide. As shown in Fig.2 and Fig.3 are the scaled dose kernel profiles for P-32 and Y-90 in skeletal muscle (ICRP1975).

Fig. 2. The scaled dose kernel profile of P-32 in skeletal muscle. The R_{csda} associated with 1.71 MeV electron in skeletal muscle is about 0.794 cm.

Fig. 3. The scaled dose kernel profile of Y-90 in skeletal muscle. The R_{csda} associated with 2.273 MeV electron in skeletal muscle is about 1.107cm.

The absorbed dose distribution in thyroid by uniformly administrating 1 Bq of P-32 is plotted by a series of isodose contour lines, as shown in Fig.4. The 100% dose point or the maximum dose point in this plot is equal to $3.743\text{E-}2$ MeV/g. From this plot, the capability of small scale dosimetry is clearly stated and the dose calculation algorithm of small scale dosimetry is sufficiently accurate to analyze the dose distribution of human organ when deposited with radionuclide.

Fig. 4. The isodose contour lines of thyroid by administrating 1 Bq of P-32.

**ASSESSMENT OF THE DOSE TO BONE
USING A MONTE CARLO TRANSPORT CODE**

INTRODUCTION

The study of the toxicity of bone-seeking radionuclides has shown that the soft tissues within spaces in trabecular bone are especially vulnerable to malignant changes induced by radiation. There are three cell populations associated with this soft tissue that are suspect to carcinogenic risk. These are (1) haematopoietic marrow, (2) osteogenic tissue, particularly on the endosteal surfaces, and (3) the reticulo-endothelial tissues in the trabecular spaces (ICRP 1968). Dosimetry for the haematopoietic marrow and the reticulo-endothelial tissues can be considered together since the relevant dose is the mean absorbed dose to the soft tissues in the trabecular cavities. The relevant dose to the osteogenic tissue is the mean dose to a layer of cells of 10 μm thickness lining the marrow cavities (Sissons 1970, Vaughan 1970). Thus, the relevant dose to calculate when considering the effects of radionuclides in bone are the mean absorbed dose to the marrow cavities, and the mean absorbed dose to a 10 μm thick endosteal layer of cells lining the marrow cavities.

Radionuclides that are deposited in the bone ("bone-seekers") are separated into two categories. Radionuclides that are taken up in high concentrations in the bone where active mineralization is taking place are known as "volume seekers". These radionuclides also are distributed diffusely in low concentrations throughout the bone mineral. The ICRP, in their most recent model, assumed uniform concentration of a volume-seeker throughout mineral bone (ICRP 79).

Radionuclides of concern in this situation are calcium, radium, strontium, and barium. These are alkaline earth elements and it was thought originally that they would replace the calcium in the bone mineral. This may be true after a short period of time, but there are important differences in how these chemical analogs behave in the skeleton. Their metabolic behavior is different and so is their pattern of distribution. This is seen at least a

short time after the radionuclide reaches the blood stream, such as, for the radionuclide Ca-45. This radionuclide is shown to be taken up immediately after injection and is concentrated on all bone surfaces. Within days after injection it is diffusely distributed throughout mineral bone.

The other category of bone-seekers is known as the "surface-seekers". These are radionuclides that concentrate on bone surfaces, but do not distribute throughout the mineral. The ICRP model assumes these radionuclides remain on the bone surfaces for extended periods (ICRP 79). Radionuclides of concern in this case are plutonium, americium, thorium, cerium, californium, and yttrium. Variations in the way these radionuclides are distributed have important implications for assessment of the radiation dose they will deliver to the sensitive tissues. All of these are surface seekers, but do not distribute themselves on the surfaces in the same manner. Of these radionuclides, plutonium and americium present the greatest practical hazard in the workplace.

Many approaches have been made to the assessment of dose to bone and its radiosensitive cells. All theoretical approaches involve physical assumptions and approximations which are necessary to obtain expressions capable of numerical solution.

BACKGROUND

Two types of structures are found in the skeleton: (1) hard cortical bone found in the shafts of long bones and the plates of flat bones, and (2) trabecular, spongy or cancellous bone contained in the ends of long bones, in the thin-walled vertebrae and between the plates of the flat bones. Three types of bone cells are recognized: osteoblasts, osteocytes, and osteoclasts. These cells perform five functions in the bone. They produce the protein in the bone, stimulate the mineralization of the protein in bone, maintain the bone tissue, resorb bone, and play an active role in mineral physiology. The bone itself serves at least four functions: (1) facilitates mobility and stability, due to muscular attachments, (2) protects vital organs - central nervous system, heart, lungs, liver, and to some extent the female genital system, (3) serves as a storehouse for essential minerals, such as calcium, and wastes such as lead and plutonium, (4) encloses hematopoietic tissue, bone marrow.

Cortical bone consists of a mineralized matrix made up of a mosaic of small units called osteons. These are from 200 to 400 μm in diameter and through them run the Haversian canals carrying nutrients from the arteries. These arteries feed the bone cells, the osteocytes, that reside in small lacunae in the surrounding matrix, connected to the nutrient artery and to each other by extremely fine canaliculi. The Haversian canals are from 20 to 100 μm in diameter and are themselves lined with cells, the osteoblasts and the osteoclasts, which can build up or resorb the bone matrix, respectively. These cells, the nutrient arteries and the osteocytes together are the soft tissue component of cortical bone; they maintain the bone and damage to them may result in bone death.

Trabecular bone consists of a fine network of interlacing thin lamella of hard bone which forms a system of interconnecting cavities of various sizes and shapes. The lamellae, or trabeculae, include some osteocytes but, having a thickness of only 100 μm , they do not normally need blood vessels to nurture them as in the osteons of cortical bone. The surface of the trabeculae, the endosteal surfaces, are lined with osteoblasts, osteoclasts and their precursors whose function is bone growth and remodeling. Behind them are primitive bone cells, the osteoprogenitor cells, from which the osteoblasts and osteoclasts develop. The cavities in the trabecular network contain the bone marrow consisting of the red and white cells and their precursors and the stromal cells and their precursors.

The detailed structure of bone varies from bone to bone in both man and animals and indeed varies within a single bone. Whereas the trabeculae do not vary greatly in thickness, the marrow cavities often vary greatly from bone to bone.

OBJECTIVES

This proposal describes an approach to dosimetry of the bone using a Monte Carlo transport code. This code can be used to determine effectively the energy deposited in the bone marrow, the trabeculae, and the cells on bone surfaces, the endosteal layer. To accomplish this assessment, a precise model is needed. Because the structure of the trabecular bone is complex, it cannot be described by simple geometric shapes. Previous work done by Chen and Poston (1982) describe a distribution function of the trabeculae throughout a cross section of bone. This distribution function is based on the mean cavity size that contains the red marrow. The objectives of this proposal can be summarized as follows:

1. Generate a bone model using a trabecular distribution function and compare this computer generated picture with that of an actual bone.
2. Effectively use the Monte Carlo computer code Electron Gamma Shower (EGS4) to estimate absorbed fractions of energy deposited in the bone marrow, trabeculae, and the endosteal layer of the bone.
3. Calculate S-factors for several different radionuclides of interest in the dosimetry of bone.
4. Compare the results with other techniques to assess the accuracy of the bone model developed.

Figure 1. Possible track lengths through a cross section of trabecular bone.

Figure 1 shows a enlarged section of bone for which the paths of the particles will be followed. The path of the particle may traverse the structures as shown, i.e. bone, endosteal layer, marrow, etc. However, this is not the only option. It is also shown that a particle may traverse through the trabeculae and never cross the marrow cavity, thus reducing the dose to that tissue.

METHODOLOGY

The following steps outline the proposed procedure for bone dosimetry using the EGS4 Monte Carlo transport code.

(1) Since the specific absorbed fraction, $\Phi(r,E)$, is an essential element in internal dose estimation, it must be estimated as accurately as possible. This will be done using a Monte Carlo transport code, Electron Gamma Shower (EGS4), to generate the specific absorbed fractions within the tissues of the bone. The database will cover those radionuclides which are bone-seeking β -emitters including P-32, Ca-45, Sr-89, Sr-90, and Y-90.

The EGS4 code system can be used to simulate the coupled transport of electrons and photons in an arbitrary geometry for particles ranging in energy from a few keV to several TeV. EGS4 can be used to follow each particle throughout the tissue of interest. A preliminary evaluation shows that 50,000 histories must be followed to show satisfactory results with acceptable uncertainties.

(2) Table 1 (Chen and Poston 1982) shows the physical characteristics of bone at different locations throughout the skeleton. It is difficult to calculate the absorbed dose in trabeculae, marrow or the endosteal layer without knowing the geometry or location of the marrow cavities. Chen and Poston (1982) introduced a function that describes the distribution of marrow throughout a cross section of bone. The distance traveled by a charged particle through marrow is given by the chord length rather than the cavity size. The chord length distribution function, $P(l)$, may be expressed such that:

$$P(l) = \frac{1}{M^2} \exp - \left(\frac{l}{M} \right)$$

where: M = The most probable chord length which is approximately equal to the mean cavity size divided by two.

l = chord length, $0 < l < l_m$.

Using the data in Table 1, the distribution function given above, and the computer graphics package "DISSPLA", a computer generated picture of the bone will be produced. A comparison between the computer generated picture and a actual picture of a cross-section of bone will demonstrate the accuracy of the distribution function.

(3) Use the Monte Carlo Transport Code (EGS4) to calculate the specific absorbed fractions of energy for monoenergetic electrons over a range of energies.

(4) Using the specific absorbed fractions, calculate S-factors for selected radionuclides.

(5) Verify results of energy deposited, specific absorbed fractions, and S-factor calculations and compare results with other techniques.

The method described will enable more precise calculations of the absorbed dose for particles of any range crossing the irregular and interpenetrating systems of bone trabeculae, marrow cavities, and the endosteal layer. This method may be compared to earlier methods with very simple geometries.

Table 1. Physical characteristics of bone at different location throughout the skeleton.

Bone Region	Red Marrow 1.028 g/cm ³		Bone Mass (g)	Trabecular Mass	Trabeculae 1.92 g/cm ³		Yellow Marrow 0.983 g/cm ³		Mean Cavity Size (mm)
	Mass	Vol			Mass	Vol	Mass	Vol	
Arms:									
Upper	28.5	27.7	474	20	94.8	49.38	9.5	9.7	0.84
Lower			520	15	78	39.27	389	395.7	0.84
Clavicle	24	23.3	49.2	6	2.95	1.54	8	8.1	0.8
Legs:									
Upper	57	55.4	2036	33	671.8	349.9 4	19	19	0.84
Lower			1588	25	397	206.7 7	461	469	0.84
Pelvis	543	528.2	177	25	44.25	184.1	181	184.1	0.58
Ribs	153	148.8	688	6	40.25	204.5	201	204.5	0.72
Scapulae	72	70	206	6	12.36	24.4	24	24.4	0.8
Skull:									
Cranium	178.5	173.6	557	5	27.85	60.5	59.5	60.5	0.72
Mandible	18	17.5	439	5	21.95	6.1	6	6.1	0.72
Spine:									
Upper	51	49.6	130	75	97.5	17.3	17	17.3	0.99
Middle	211.5	205.7	533	75	399.8	71.7	70.5	71.7	0.99
Lower	163.5	159	87.8	66	57.95	55.4	54.4	55.4	0.99

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**Assessment of the New
ICRP Lung Model**

INTRODUCTION

Within both the fields of nuclear medicine and radiation protection, there is the need to assess the activity concentration of inhaled radioactive material in the different regions of the respiratory system. So far, it has been shown that the lung, together with the gonads, breast, and red bone marrow, are the more radiosensitive organs within the human body (NCRP 1987). In addition, the lung is one of the more difficult organs to model in that its dynamic behavior requires simultaneous simulation of physical, biological, and biochemical processes.

Physical processes account for the deposition of aerosol particles within the irregular diameters and lengths of the tracheobronchial tree. Biological processes include the mechanical clearance and epithelial absorption resulting in the removal of deposited material from the inner regions of the lung to the circulatory system. These occur in a competition with alveolar absorption of inhaled material.

The use of compartmental analysis has shown to be a simple, yet powerful, mathematical tool in assessing the distribution and retention of radioactive material in the different regions of the respiratory system. Therefore, biokinetic assessment of retention functions for inhaled aerosols are commonly used to calculate absorbed doses to target cells at risk following the inhalation of alpha- and beta-emitting radionuclides. Moreover, dynamic modeling of the distribution and retention of inhaled aerosols in the lung might also be applied in assessing lung burdens of other industrial chemical pollutants.

So far, modeling of the lung has been based on an analytic solution of linear chains of compartments representing the main three physiological regions of the respiratory system (ICRP 1979). In this analysis, the transfer rates between compartments are assumed to be constant. This simplified representation of the respiratory system, however, does not take into account the full range of biological processes which govern the translocation of material within the lung. These processes are more correctly represented as time-varying functions involving nonlinear parameters.

At present, a task group of the ICRP has undertaken an extensive revision of the ICRP Lung Model for use in radiation protection guidance. In this new model, new experimental values are considered for clearance rates, solubility rates, and deposition fractions for a variety of inhaled materials. These parameters are time dependent and, as a result, steady-state solutions to the system can be extremely difficult to obtain. As a result, the task group chose to simplify their system by subdividing the main regions of the new lung model into additional compartments. This process results in, once again, a linear

chain of compartments with time-independent transfer rates. Although this approximation does assure a stable system, it does not reflect the real dynamical behavior of the biological and physico-chemical processes of material translocation in the human lung.

In this research task, a detailed assessment of the new ICRP Lung Model will be made in which all transfer rates in the model will be treated, not as constants, but as time-varying parameters. A dynamic simulation of the lung model will be accomplished using the computer code SAAM (Simulation Analysis and Modeling) developed by Berman and Weiss (1978). Comparisons will subsequently be made of both lung and organ committed dose equivalents following the inhalation of radioactive material as given by both the present and the proposed implementation of this new ICRP Lung Model.

THE NEW ICRP LUNG MODEL

Four main factors have to be considered in modeling the lung. These factors include: (1) breathing rates and volumes of inhaled air in the different regions of the lung during complete breathing cycles; (2) the fraction of inhaled aerosols deposited in the different regions of the lung through the physical processes of inertial impaction, sedimentation, and diffusion; (3) biological clearance processes such as mechanical mucociliary transport of inhaled dust in the tracheobronchial tree, and phagocytosis by alveolar macrophages; and (4) the absorption of soluble (and sometimes "insoluble") material to blood from the extrathoracic, tracheobronchial, and pulmonary regions.

Following this approach, a Task Group of the ICRP has proposed a new compartmental distribution to represent the respiratory system as shown in Fig. 1 (Johnson 1989). It consists of three main regions of interest: an extrathoracic region, a fast-clearing thoracic region, and a slow-clearing thoracic region. The extrathoracic region includes and represents the clearance and deposition of materials in the nose, mouth, pharynx, and larynx. In this region, material is cleared by mucociliary transport, sneezing, nose wiping and blowing, and dissolution (for soluble particles). Most of the information on nasal deposition comes from experimental work. Mathematical modeling of particle deposition is complicated by the irregular geometry of nasal and mouth passageways (Guilmette et. al 1989) and the resulting uncertainties in aerosol flow patterns (Bowes and Yu 1989).

The two thoracic compartments representing the tracheobronchial (T-B) and parenchymal-nodular (P-N) regions are called the fast and slow translocation compartments, respectively. The fast translocation compartment includes airways 0-16 of the tracheobronchial region. In this region, radioactive inhaled material is deposited by the physical processes of impaction, sedimentation, and diffusion (Hoffmann and Martoneen

1989). At the same time, radioactive material is absorbed to the blood and cleared to the gastrointestinal tract by solubility transport of material through the bronchial epithelium, and by mechanical mucociliary transport by the combined action of mucus-secreting cells, and bronchial glands and ciliated cells. These processes are mathematically represented by exponential time-varying functions illustrated as $B(t)$ and $G_f(t)$ in Fig. 1.

In the slow translocation compartment representing airways 17-23 (bronchioles, alveolar sacs, and thoracic lymph nodes), radioactive material is slowly cleared by competitive processes of mechanical transport and solubilization (Cuddihy and Yeh 1988). Mechanical nonabsorptive processes are controlled by alveolar macrophages. These cells move freely on the epithelium and phagocytize, transport, and detoxify deposited material they contact. Solubilization mechanisms involves dissolution. Particles that dissolve in the alveolar fluid can diffuse through the epithelium and interstitium into the lymph or blood, and those translocated and trapped in interstitial sites may be absorbed. Once again, these processes are simulated by the exponential time-varying functions that are represented in Fig. 1 as $G_s(t)$ and $B(t)$.

Figure 1. Compartmental distribution of the proposed new ICRP Lung Model.

When all these biological and physicochemical factors are taken into account, the activity of inhaled material distributed in the different lung regions is given by the numerical solution of a mass balance equation describing the compartmental distributions of Fig. 1. Therefore, the concentration of radioactive material in each compartment is given by the solution of a set of coupled, differential equations:

$$\begin{aligned}\frac{dq_{E-T}(t)}{dt} &= \dot{I}(t)D_{E-T} - [B(t) + G_{E-T}(t) + \lambda_R]q_{E-T}(t) \\ \frac{dq_{T-B}(t)}{dt} &= \dot{I}(t)D_{T-B} + G_s(t)q_{T-B}(t) - [B(t) + G_f(t) + \lambda_R]q_{T-B}(t) \dots\dots\dots(1) \\ \frac{dq_{P-N}(t)}{dt} &= \dot{I}(t)D_{P-N} - [B(t) + G_s(t) + \lambda_R]q_{P-N}(t)\end{aligned}$$

where:

$q_{E-T}(t)$, $q_{T-B}(t)$, $q_{P-N}(t)$ are the activities of an inhaled radionuclide in the different regions of the lung.

$\dot{I}(t)$ = Rate of inhalation of activity of the radionuclide.

$B(t) = \sum_{i=1}^n A_i e^{-\lambda_i t}$ with A_i and λ_i constants is a solubility function calculated from experimental fitting processes.

D_{E-T} , D_{T-B} , D_{P-N} are the total deposition fractions of inhaled material in the different regions of the lung.

$G_s(t)$ = Slow clearance rate function (same form as $B(t)$).

$G_{E-T}(t)$, $G_f(t)$ = Extrathoracic and fast clearance rates.

CURRENT PROGRESS

Presently, a FORTRAN program is being developed for assessing the total deposition fraction of inhaled and exhaled aerosols of varying aerodynamic diameters for the different regions of the lung. This program will consider values of breathing frequencies and tidal volumes, reported by Hoffman and Martoneen (1989), for a 20-year-old at different levels of physical activity. Deposition fractions of inhaled material in the extrathoracic region are assumed for an individual working at a light activity level with a breathing frequency of 15 breath/min and a breathing flow rate of 15 liter/min. Therefore, the fraction of inhaled

material deposited in the nasopharyngeal region is first intended to be calculated from the following equation (ICRP 1966):

$$D_{E-T} = -0.62 + 0.475 \log (D_a^2 Q_a),$$

where

D_a = aerodynamic diameter of the particle

Q_a = breathing flow rate (liter/min).

At the same time, these deposition fractions will be compared with the experimental results of Bowes and Yu (1989) which are represented by the following relationship:

$$DF = 0.153 + 0.0422 \frac{d_a}{(\mu m)},$$

where

DF = deposition fraction

d_a = mass median aerodynamic diameter.

Deposition fractions in the tracheobronchial and pulmonary regions are calculated under the assumption that the solution of the Navier-Stokes equations is in the region of linearity, the settling velocity of an aerosol particle follows Stoke's law. Moreover, it is also assumed that settling velocities are corrected for slip when inertial impaction and sedimentation processes are considered. Therefore, deposition fractions at the different generations of the tracheobronchial and pulmonary regions are calculated as:

$$F = 1 - (1-I)(1-S)(1-D),$$

where

F=Total deposition fraction

I= impaction deposition probability

S= sedimentation deposition probability

D= diffusion deposition probability.

Since values of I, S, and D are dependent upon parameters such as the gravity and branching angles of the airways, as well as the diameters lengths of the airways. Morphometric calculations of the tracheobronchial tree reported by Weibel (1963) have been improved in the design of this program by the substitution of values reported by

Phalen et. al (1985) for generations (0-15) and by Dunnill (1962) for generations (16-22). As a result, the program will be designed accommodate of any change in parameter values.

Concurrent with this program development, the computer code SAAM (Simulation Analysis and Modeling) is being tested in the simulation and acquisition of numerical solutions of the mass balance equations shown in the previous section. At this point, the code has demonstrated excellent agreement between analytical and numerical solutions for the case of linear chains of compartments with constant transfer rates.

The stability of linear dynamical equations like Eq. 1 will depend on the existence of a steady-state solution of the system; this means that if the system is perturbed from the equilibrium state by an impulsive or periodic input function (sudden or periodic inhalation of radioactive material), then the system will return to the same or another equilibrium state as the time tends toward infinity. In attempting to solve the dynamic system of Eq. 1, the steady-state solution becomes important, since the general solution for the time-varying case can always be decomposed into the zero-input response and the zero-state response:

$$\mathbf{q}(t) = \phi(t; t_0, \mathbf{q}_0, \mathbf{0}) + \phi(t; t_0, \mathbf{0}, \mathbf{u})$$

where $\mathbf{q}(t)$ = is the vector of solutions in the different regions of the lung

$\mathbf{q}_0$ = is the vector of initial conditions of the system

$\mathbf{u}$ = is the vector of inputs of the system.

$\phi(t; t_0, \mathbf{q}_0, \mathbf{u})$ = is the transition solution of the system and depends on the temporal integration of the compartmental matrix and the initial conditions.

Since a system's steady-state is a particular solution of the zero-input response, the first step in the numerical solution of a dynamical system like Eq. 1 is to find the steady-state solution of the system to guaranty the stability of the solutions. At this point, SAAM has been tested by calculating the steady-state solution of a two-compartmental distribution representing the metabolism of an arbitrary compound in a turnover study. Simulation of an experiment in the steady-state is carried out by the injection of compound X as a bolus in plasma. Blood samples are collected every hour after injection. The objective is to estimate the steady-state mass distribution among the compartments in a proposed two linear chain of compartments. Figure 5.2 shows a comparison of the simulated solution calculated by SAAM and the experimental blood sample readings. Fitting of the numerical solution with the experimental points was carried out by the use of the optimization and least-squares subroutines of SAAM. The error between the numerical solution and the experimental measures was reduced to be less than 2%. Figures 5.3 and 5.4 show a comparison between the numerical transient solutions calculated from another SAAM

model code and the steady-state solution within the different compartments. They also show how the transient solutions always tend toward the steady-state solution at infinite times, presuming the system remains stable.

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—◆— Numerical
□ Experimental

Figure 2.
Steady state solution.

○ Transient solution.
 ◇ Steady state sol.

Figure 3.
Solutions for the first
compartment.

○ Transient solution.
 ◇ Steady state sol.

Figure 4.
Solutions for the second
compartment.

**DEVELOPMENT OF A DIFFERENTIAL
VOLUME PHANTOM**

INTRODUCTION

In 1964 the Society of Nuclear Medicine formed a committee to fulfill the needs of the nuclear medicine community to determine the radiation absorbed dose to patients who are administered radiopharmaceuticals. The objectives of the Medical Internal Radiation Dose (MIRD) Committee were to provide the best possible estimates of the absorbed dose to the patients resulting from the diagnostic or therapeutic use of internally administered radiopharmaceuticals. Data required to achieve these objectives were:

- 1) radiological parameters;
- 2) anatomical and physiological data for patients of various ages and physiognomies, and
- 3) metabolic distribution data for radiopharmaceuticals.

Uncertainties associated with these data will be propagated in absorbed dose calculations. Although, relevant radiological transformation characteristics of radionuclides are well known, uncertainties in physiological aspects, such as variance in organ morphology and metabolic aspects, e.g., variance in organ uptakes, contribute the greatest sources of errors.

In 1978 a reference heterogeneous phantom was described by MIRD in Pamphlet 5 Revised (Snyder et. al. 1978). This mathematical phantom was used as a model upon which internal absorbed dose calculations were based. The phantom provided an approximately correct anatomical representation of the human body based on ICRP Publication 23 (1975) which described a reference man. The organs in the phantom were described geometrically by mathematical equations. Several revisions and improvements have been made to represent populations of different ages and gender (Cristy et. al. 1987).

New nuclear medicine procedures, such as positron-emission tomography and other imaging techniques, radiation therapy procedures, and blood-flow studies require precise a-priori estimates of absorbed dose to specific organs or precisely defined tissue regions. Consequently, inadequacies in the description of these regions will contribute to errors in absorbed dose calculations. Therefore, certain organs and regions must be more accurately described.

OBJECTIVES

At the present time, a basic variable is used in nuclear medicine procedures to assess the energy per unit mass given to an organ or tissue of the human body for either external beam therapy or internally deposited radionuclides. This variable is the average absorbed dose; which conveys only information concerning the whole tissue or tissues based on a uniform distribution of the radionuclide. However, it does not convey information related to the spatial dose distribution inside a tissue, nor the doses to other healthy tissues near the region of interest. Moreover, the effectiveness of a procedure is not simply based on average absorbed doses but also on the spatial distribution of energy due to different types of radiations (related to the Linear Energy Transfer, LET).

Absorbed dose calculations for internally deposited radionuclides are based on a mathematical phantom which is a gross representation of a reference man. Today's nuclear medicine procedures require better estimates of absorbed doses for the human body. These estimates are of extreme importance due to the sensitivity of certain regions (such as the brain) for the correct planning and delivery of absorbed doses. The correct visualization or representation of regions of the human body will provide a more accurate estimate of the absorbed dose and its distribution throughout an organ or tissue. This representation is based upon improved modeling of an organ or tissue in the human body and also an estimate of the distribution of the radionuclide through the region itself.

Taking the above into consideration, a new differential volume phantom was designed to study the possibilities of generating new information concerning dose volume distributions and radionuclide distribution in the human body (dynamic processes are included). This new phantom is constructed based on physiological, anatomical and metabolic variables obtained from an individual patient which generates a specific phantom that simulates only one specific patient. Such data is obtainable from MRI studies and easily reconstructed to be used as geometrical input for new calculations.

This new phantom required further work to consolidate the concept. A variety of tests were made to assess the feasibility of the original idea.

First Test:

The first step made was to use of the old mathematical phantom described in MIRD Pamphlet 5 Revised and translated into a non-mathematical representation, then the data

was superimposed into a three-dimensional boxel arrangement which provided the location or region of the boxel with respect to an organ or tissue of the body.

Second Test:

This test consisted in extracting information on regions and tissues of the phantom which were defined by the user. The information extracted was the average absorbed dose, isodose curves, the spatial absorbed dose, the dose volume distribution and blood-tissue dose ratio. These variables are not the only ones used but many other can be extracted such as LET spectra distribution (if more than one type of radiation is used.)

Several other tests are now being carried out and results are still not available for commentary and discussion.

METHODOLOGY

The mathematical phantom used in MIRD Pamphlet 5 Revised was reconstructed into a non-mathematical form. Figure 1 shows a representation of cross sections of the mathematical phantom by the planes $z = 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10$ and 11 cm. These non-mathematical representations of a phantom were used to reconstruct a three-dimensional representation of the phantom shown in Figure 2. This anatomical representation was then coupled with the Monte Carlo transport code Electron Gamma Shower (EGS4) to assess energy deposition patterns in different regions of the human body.

The identification of regions or tissues in this new mathematical phantom are left to the user. It is possible to assess the dose volume histogram of any region by selecting in the physical boundaries of the region. As an example, Figure 3 shows the main results of the variance of energy deposition throughout the liver itself containing a uniform distribution of ^{99m}Tc . This pictorial result conveys more information concerning the tissue than just having the average absorbed dose. As an example, Figure 4 shows the isodose contours superimposed with the different organs; the source region was defined as the cortex of the kidney and the radionuclide used was ^{99m}Tc . Similar results were obtained in a three-dimensional representation.

Task 1:

The first task consists of construction of the phantom using MRI images obtained from an specific patient. The images should be processed in such a form that they can be used for Monte Carlo transport. The implementation of such images should require the use of digitizers to locate regions of the body in which the radionuclide is concentrated. This will allow the assessment of the radionuclide distribution inside different organs of the body, as well as calculation of retention times and other metabolic parameters. This process is tedious and requires large blocks of computer time to process; however, once done it is a single step to obtain absorbed doses for the regions of interest in the human body.

Task 2:

The second task consists of the determination of regions of the human body which are of importance for medical procedures (e.g., the brain). Then it is necessary to determine the different physiological and metabolic parameters to be used in the phantom. The objective is to locate the radionuclide distribution throughout the phantom itself and, therefore, assess the distribution in different regions and tissues of the body. This will allow the correct sampling of the radionuclide distribution rather than just assuming a uniform distribution. Having located and excluded the regions of interest, the code EGS4 will be used to asses energy deposition patterns in the body (as shown in figures 3 and 4). The results obtained will allow a complete state of the-art treatment planning for abnormal regions of the human body.

Figure 1. Schematic representation of the mathematical phantom. The cross sections were used to generate a non-mathematical phantom to be used in transport calculations.

Figure 2. Consolidation of two dimensional cross sections to generate a three dimensional view of the non-mathematical phantom. This configuration was used to obtain information of different regions and tissues of the human body.

Figure 3. Energy - Volume histogram for the liver for ^{99m}Tc uniformly distributed in the liver. As can be seen the distribution is wide; the dose-volume distribution will be similar, however, the shape of the distribution will be the same.

Figure 4. Superposition of a dose contour and a cross section of the phantom at $z = 35.0$ cm. The source region was the cortex of the kidneys with a uniform distribution of ^{99m}Tc . This plot allows the visualization of the isodose curves superposed with the different regions and organs of the phantom.

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