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Microdosimetric calculation of absorption fraction and the resulting dose conversion factor for radon progeny

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Abstract It is an established fact that radon progeny can induce lung cancers. However, there is a well-known discrepancy between the epidemiologically derived dose conversion factor for radon progeny (4 mSv/WLM) and the dosimetrically derived value (15 mSv/WLM) (mSv is a unit of the dose while WLM is a unit of exposure to radon progeny). Up to now there is no satisfactory explanation to this. In the present study we propose that microdosimetry will help reduce the discrepancy significantly. The ICRP Human Respiratory Tract Model (HRTM) has been applied to calculate the effective dose conversion factor. All parameters have been kept at their best estimates. Modifications were made in the calculation of the absorbed fractions of alpha particles. In contrast to the ICRP approach where the energy has been considered to be deposited in the layer containing the sensitive cells, we used a microdosimetric approach in which the alpha particles deposit their energy only in the nuclei of sensitive cells. This modification alone has lowered the dose conversion factor by about one-third (from 15 mSv/WLM down to approximately 10 mSv/WLM).

Introduction

A number of previous investigations have determined the dose conversion factor (DCF), which is defined as the ratio of effective dose in human lung (in mSv) and the total exposure to radon progeny (in WLM) [1, 2, 3, 4, 5]. A major milestone regarding this field in the last decade was the publication of the report of the task group of the International Commission on Radiological Protection (ICRP) in 1994 [6], known as ICRP Publication 66. This extensive report describes in detail the dosimetric model of the human respiratory tract model (HRTM), which consists of a few sub-models, such as the morphometric and the deposition models, models for clearance and translocation of radioactive materials in the lung, etc.

The ICRP calculation procedure [6] is outlined as follows: (a) The number of emitted alpha particles, N_α, for a given exposure condition and time is first calculated – this phase of calculations requires computer programs to simulate deposition and clearance in various regions of the HRTM. (b) The number of emitted alpha particles is multiplied by the alpha particle energy, E_α, and the absorbed fraction (AF) of alpha particles in the targets, which gives the energy absorbed in that target. (c) The absorbed energy is divided by the mass of the target to give the absorbed dose. The absorbed doses are calculated separately for different targets, namely the layers containing basal and secretory cells in the bronchial region (generations 1–8, symbolized as BB in ICRP [6]), i.e., $D_{BB,bas}$ and $D_{BB,sec}$, respectively, and for the layer containing secretory cells in bronchiolar region (generations 9–16, symbolized as bb in ICRP [6]), i.e., $D_{bb,sec}$. (d) The calculated doses are weighted as follows. First, the average dose in BB, D_{BB}, is found as

$$D_{BB} = 0.5D_{BB,bas} + 0.5D_{BB,sec} \quad (1)$$

where the same weighting factor 0.5 is adopted for basal and secretory cells. Such a weighting assumes equal radiation sensitivities of basal and secretory cell populations, which is of course not necessarily true. Second, the doses in BB and bb are weighted by the factor 0.333, i.e.:

$$D_{T\text{-}B} = 0.333D_{BB} + 0.333D_{bb,sec} \quad (2)$$

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In the original ICRP report, there is a third term contributed by the alveolar-interstitial region (AI) also with a weighting factor 0.333, but AI is not considered here due to its much smaller dose. Finally, the effective dose is given by:

$$E = 20 \times 0.12 \times D_{T\text{-}B} \quad (3)$$

where 0.12 is a tissue weighting factor for the lung according to ICRP Publication 60 [7] and 20 is a radiation weighting factor for alpha particles, also according to ICRP 60 [7]. The effective dose thus obtained is divided by the corresponding potential alpha energy concentration (PAEC, in WLM) employed above for the calculation of N_α, and the final DCF is given in units of mSv/WLM.

ICRP does not give DCFs for radon progeny calculated with the HRTM. Recently, Marsh and Birchall [5] used the program RADEP which was developed based on ICRP Publication 66 [6] and gave a DCF of about 15 mSv/WLM. On the other hand, ICRP [6] explicitly expressed that "the Commission does not recommend the assessment of risk from calculation of equivalent doses to respiratory tract tissues... the use of the respiratory tract model to calculate equivalent dose to lungs may be helpful in comparing those lung doses that result form different exposure condition." Instead, the epidemiologically derived dose conversion factor for radon progeny is 4 mSv/WLM [8].

Up to now, such a large discrepancy between the dosimetrically and epidemiologically determined DCF values has not been satisfactorily resolved. One of the proposals to reconcile the differences is to lower the value for the radiation weighting factor for alpha particles w_R=20. However, this value is based on the relative biological effectiveness (RBE), although a large range of values has been measured for RBE.

In the recent publication by Marsh and Birchall [5], a sensitivity analysis has been performed in a way that all parameters were kept at their best estimates, except one at a time which was varied in a reasonable range. By varying the various parameters they found DCFs to range from about 10 mSv/WLM up to more than 33 mSv/WLM. If all the parameters are kept at their best estimates, the DCF is 15 mSv/WLM. However, these authors, as well as ICRP Publication 66, assumed that the lung could be represented as compartments for dosimetric purposes and did not involve the abundance and distribution of sensitive-cell nuclei in the wall of the airway tubes in the dosimetric calculations. The present work is a microdosimetric approach which takes these factors into account, and considers energy deposition of alpha particles only in the nuclei of sensitive cells. The corresponding change in the DCF will also be determined.

Methodology

Our present work has different phases. The first one will aim to reproduce the DCF of about 15 mSv/WLM given by ICRP [6]. To achieve this objective, of course, we have to adopt the concepts introduced by ICRP, and we have to adopt the method of AF calculations as used in their publication 66 [6]. The reproduction of the DCF has at least the following significance: [1] its success would serve as a validation of our calculations, and [2] some intermediate results in the course of the DCF calculations (which are not available when using the programs RADEP or LUDEP [9]) can be utilized for our analyses. For this purpose, a number of programs were created in order to calculate the following items:

- Deposition of monodispersed aerosols in different deposition regions of the HRTM according to the algebraic model of ICRP Publication 66 [6]
- Total deposition of polydispersed aerosols for given exposure conditions, where summations were carried out assuming log-normal distributions of aerosols
- Equilibrium activities of radon progeny in different regions of the HRTM, and the total number of emitted alpha particles for given exposure conditions and exposure time (here a set of differential equations describing different processes in each clearance compartment has been developed)
- Absorbed energies by multiplying $N_\alpha E_\alpha$ with AF
- Absorbed doses and their weighted values according to Eqs. 1, 2, and 3

A FORTRAN computer program LUNGDOSE.F90 has been developed to perform the above calculations. Some of the results are given in Table 1 and compared with those given by Marsh and Birchall [5]. All calculations have been performed with the best estimates for the input of the model. One can see excellent agreement in the BB region (for both basal and secretory cells). There is a discrepancy in the bb region of about 14% and the reason for this is not clear. When calculating the values in

Table 1 Absorbed dose per WLM in different targets of HRTM according to Marsh and Birchall [5] and to the present work

Target tissue	Absorbed dose/mGy	
	Marsh and Birchall [5]	Present work
Bronchial basal cells, $D_{BB,bas}$	5.4	5.4
Bronchial secretory cells $D_{BB,sec}$	12.4	12.5
Bronchial dose ($0.5D_{BB,bas}$+0.5 $D_{BB,sec}$)	8.9	9.0
Bronchiolar D_{bb}	9.2	10.5
Thoracic	123 mSv/WLM	130 mSv/WLM
Total DCF	15 mSv/WLM	16 mSv/WLM

Table 1, the AF values originating from ICRP Publication 66 were used.

A crucial step in dose calculations is the computation of the absorbed fraction AF, which is the subject of the present work. Absorbed fractions for alpha particles for various combinations of sources and targets were calculated through Monte Carlo methods and given by ICRP in their publication 66, however, ICRP did not describe in detail the program that was used, but the concept of a target was a cylindrical layer containing the sensitive cells. We prepared an independent program also based on the Monte Carlo method for AF calculations. In this program a very large number of alpha particle histories are generated, and both the input energies E_{input} and output energies E_{output} in the sensitive layer are determined. The absorbed energy for a particular history in the corresponding sensitive layer is then given by $E_{abs}=E_{input}-E_{output}$, and the average absorbed energy E_{abs} is determined. The absorbed fraction is then found as the ratio $AF = E_{abs}/E_{\alpha}$. The particular cases where the alpha particles were stopped inside the sensitive layer were also taken into account.

The stopping powers of alpha particles in striated tissue published in ICRU Report 49 [10] were used in our calculations. Another independent check of the AF values was also carried out through a semianalytical approach based on the numerical solution of a triple integral and the calculation of imparted energy in a small test sphere. Details of these calculations will be published separately. All the AF results obtained by our programs (both the Monte Carlo simulations and semi-analytical solutions) are consistent with the ICRP Publication 66 values with an agreement better than 3%. Up to this point the calculations of AF did not take into account the distribution or any possible structure of sensitive cells in the layer. Only the energies input into and output from the layer of interest were considered.

It is apparent that the nuclei of sensitive cells occupy only a relatively small volumetric fraction of the layer, so only a relatively small proportion of cell nuclei are hit by alpha particles, and the majority of the cells do not receive any dose and will remain intact. In other words, most alpha particles miss the sensitive targets and dissipate their energies in the insensitive tissue in the layer containing the sensitive cells. On the other hand, it is also an established fact that the dose from an alpha particle is mainly localized along its track, and the nuclei of cells hit by alpha particles receive very high doses that can lead to lethality by inactivation of the cells or can induce some transformations. Under these considerations, it is important to understand how the absorbed fraction in the whole layer containing sensitive nuclei is relevant to dose calculations.

In the present study we propose to adopt the microdosimetric approach and to calculate the dose only in the nuclei of sensitive cells. For this purpose the volume abundance and density distribution of the sensitive-cell nuclei, as well as other data about their shape and size, are needed. The cell abundance and volumetric distribution data that are adopted here were provided by Mercer et al. [11] who also calculated the absorbed doses in different types of cells (both for cytoplasm and nuclei) in humans and rats, but no effective doses were given.

Model

A mathematical model of an airway tube has been developed for the simulations and calculations. The model follows the one proposed by ICRP [6] and NRC [12] except that we consider cell nuclei instead of sensitive layers. The wall of the airway tube in BB comprises 5 μm of mucus, 6 μm of cilia, 10 μm of tissue without sensitive cells, 30 μm of a layer containing secretory cells, and 15 μm of a layer containing basal cells (this layer is partially overlapped with the secretory-cell layer by 5 μm). The tube wall in bb comprises 2 μm of mucus, 4 μm of cilia, 4 μm of insensitive tissue, and 8 μm of a layer with secretory cells (and there are no basal cells in bb). Simulations of alpha particle trajectories have been performed with the following steps:

Step 1

In contrast to ICRP, we considered a structure of a certain number of sensitive-cell nuclei in the layer which was considered sensitive in the ICRP Publication 66 scheme. The centers of the nuclei were chosen randomly and the total volume of all nuclei was calculated. The nuclei were chosen to be spherical, with a diameter of 9 μm in BB and 8 μm in bb, after Hofmann et al. [13]. The nuclei were added one by one until the volume abundance given by Mercer et al. [11] was achieved. The height of the tube was 2 mm so the end effect was negligible. All the sampled nuclei are in the layer designated as sensitive by ICRP. The volumetric density of nuclei was chosen to be uniform, which has been achieved by (a) sampling the random radius of a nucleus center in the cylindrical coordinate system as $r_{random}=r_1+(r_2-r_1)\gamma^{0.5}$, where γ is a uniform random number between 0 and 1, and r_1 and r_2 are radii of the cylinders which are boundaries of the sensitive layer, (b) sampling the cylindrical coordinate φ by $\varphi_{random}=2\pi\gamma_1$, and (c) sampling the altitude by $z_{random}=h\gamma_2$ (h=2 mm is the height of the cylinder). Overlapping of nuclei is theoretically possible, however, this was avoided by choosing distances between neighboring nuclei to be larger than one nucleus radius.

Step 2

The alpha particle sources are in the fast or slow clearance mucus. Trajectories of alpha particles were simulated in the system of airway tubes (tissue+air). For each particle, we determined whether it hits any of the nuclei constructed in step 1 (see above). If a nucleus is hit, the

energy imparted to it is calculated based on the particle energy incident on the nucleus and the path length of particle through the nucleus. If no nucleus is hit, the process is repeated by choosing a new particle history.

Step 3

When the number of hits achieves the preset number of successful simulations, the total energies absorbed in the cell nuclei are summed up and then divided by the total mass of sensitive cell nuclei (regardless whether they were hit or not) to give the absorbed dose in sensitive cells. This absorbed dose is further divided by the number of emitted alpha particles, which is equal to the total number of simulations, to give the absorbed dose per alpha particle.

Step 4

The program also enables us to calculate the microdosimetric quantity, specific energy, z, and its distribution. Continuous slowing down approximation (CSDA) was used in these calculations.

The data on volume abundance of sensitive cells and their depth distribution were given by Mercer et al. [11]. They were recently employed by Hofmann et al. [13] who made a linear fit to them with steps of 5 μm. The original data by Mercer et al. [11] were given for the large bronchi (diameters 3–5 mm), small bronchi (diameters 1–3 mm) and bronchiole (diameter <1 mm). It is noted that the starting and ending depths of sensitive cell nuclei given by Mercer et al. [11] did not match completely with those given by ICRP [6], and it is difficult to completely incorporate their data in the ICRP Publication 66 scheme. We therefore adopted completely the epithelium model proposed by ICRP66, but instead of a sensitive layer, we considered randomly distributed cell nuclei with an average volume abundance as was given by Mercer et al. [11]. According to their Tables 1–3, the percent values in average abundance of the cell nuclei were: 5.8% and 4.5% for basal-cell nuclei in large and small bronchi (average 5.25%), 1.2% and 0.8% for secretory-cell nuclei in large and small bronchi (average 1%) and 10.3% in bronchiole. These average values have been used in constructing the cell nuclei along the airway tube as described above.

Results

The input parameters for the program LUNGDOSE.F90 are: breathing rate=0.78 m^3/h; tidal volume=0.866 l/breath; functional residual capacity=3300 ml; equilibrium factor F=0.395; unattached fraction of PAEC f=8%; density of unattached particles=1 g/cm^3; density of attached particles=1.4 g/cm^3; shape factors equal 1 and 1.1 for unattached and attached particles, respectively; median diameters (with geometrical standard deviations given in brackets) are 0.9 (1.3) nm, 50 (2) nm, 250 (2) nm and 1500 (1.5) nm for unattached, nucleation, accumulation and coarse modes, respectively.

Table 2 Number of emitted alpha particles in different regions of the HRTM (in disintegration/μm^3 per 1 WLM)

Alpha particle source	Disintegrations/μm^3	
	^{218}Po (6 MeV)	^{214}Po (7.69 MeV)
Bronchi fast (BB1)	2.352×10^{-5}	7.270×10^{-5}
Bronchi slow (BB2)	2.022×10^{-5}	6.771×10^{-5}
Bronchioles fast (bb1)	1.523×10^{-5}	8.845×10^{-5}
Bronchioles slow (bb2)	0.777×10^{-5}	4.811×10^{-5}

The intermediate results from the program utilized for further calculations are the volumetric activity (in disintegrations/μm^3) of radon progeny in different sources. Table 2 shows the results that are given for an exposure of 1 WLM. These results can be used for calculating the absorbed doses in different regions of the HRTM (given in Table 1). The results in Table 1 were derived from the figures in Table 2 by using data about the total surface area of BB and bb and the thickness of the sources and targets given in ICRP Publication 66, as well as the data for AF also given in ICRP Publication 66. On the other hand, with the figures in Table 2, we can also calculate the dose values in units of mGy/WLM.

For example, the dose in secretory cell nuclei in the BB fast region for 6 MeV is 20.28 Gy/(disintegration/μm^3) (see Table 3). This was multiplied with the number of disintegrations/μm^3 per 1 WLM given in Table 2 (2.352×10^{-5}) to give the absorbed dose in cell nuclei as 0.477 nGy/WLM. Table 3 presents a summary of the results.

The values in the fifth and sixth columns of Table 3 can also be calculated in another independent way. In the course of Monte Carlo simulations, the specific energy z was calculated for each hit of a cell nucleus and the distribution of z was established. The mean value of z, z_{av}, is equal to the dose in cell nuclei hit by alpha particles. The dose in the cell nuclei can generally thus be found as a product of z_{av} and the fraction f of hit nuclei. Such calculations were performed separately and close agreement was obtained.

From the results for the absorbed dose in sensitive-cell nuclei given in Table 3 (fifth and sixth columns), the total doses in BB from all sources are 0.477+0.708+2.760+3.451=7.396 mGy/WLM for secretory-cell nuclei, and 0.002+0.084+1.604+1.982=3.672 mGy/WLM for basal-cell nuclei, respectively. Therefore, the dose in BB (according to the weighting procedures described above) is D_{BB}=(7.396+3.672)/2=5.534 mGy/WLM. The dose in bb (only secretory cells are present) is given by D_{bb}=0.545+0.610+3.266+3.672=8.093 mGy/WLM. Therefore, the DCF is found as

DCF=20×0.12×0.333×(5.534+8.093)=10.89 mSv/WLM

Table 3 Results of Monte Carlo calculations for absorbed dose (third and fourth columns: in Gy per unit volume activity of alpha particle emitters in sources; fifth and sixth columns: in mGy per 1 WLM)

Source	Target	Absorbed dose per disintegration per unit volume		Absorbed dose per WLM	
		6 MeV $Gy \cdot \mu m^{-3}$	7.69 MeV $Gy \cdot \mu m^{-3}$	6 MeV mGy/WLM	7.69 MeV mGy/WLM
BB fast	secretory	20.28	37.96	0.477	2.760
BB slow	secretory	35.01	50.97	0.708	3.451
BB fast	basal	0.085	22.06	0.002	1.604
BB slow	basal	4.15	29.27	0.084	1.982
bb fast	secretory	35.78	36.92	0.545	3.266
bb slow	secretory	78.5	76.32	0.610	3.672

Table 4 Absorbed dose per WLM calculated for layers containing sensitive cells (Layer) and for sensitive-cell nuclei using the microdosimetric approach (Nuclei)

Target tissue	Absorbed dose/WLM mGy	
	Layer	Nuclei
Bronchial basal cells, $D_{BB,bas}$	5.4	3.7
Bronchial secretory cells $D_{BB,sec}$	12.5	7.4
Bronchial dose ($0.5D_{BB,bas}+0.5\ D_{BB,sec}$)	9.0	5.5
Bronchiolar D_{bb}	10.5	8.1
Total DCF	16 mSv/WLM	11 mSv/WLM

which is significantly smaller than 15.58 mSv/WLM (about 30%) obtained when the dose is calculated for the entire layer (ICRP Publication 66 approach). These values are shown in Table 4 together with the values calculated for layers containing sensitive cells for comparison.

In conclusion, the present work shows that the determination of the absorbed fraction of alpha particles can be a crucial factor in calculating the dose conversion factor. ICRP [6] and NRC [12] defined the targets as layers containing sensitive cells. However, a more precise definition of the targets seems to be necessary for a more accurate dosimetric model of the human respiratory tract. By using a microdosimetric approach, i.e., the targets are defined to be the nuclei of the sensitive cells, the dose conversion factor is decreased by about 30%. This shows that the microdosimetric approach alone can already significantly reduce the gap between the two approaches.

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