Radiation Protection Dosimetry (2006), Vol. 122, No. 1–4, pp. 534–536 doi:10.1093/rpd/ncl493
Advance Access publication 8 January 2007

KILLING OF TARGET CELLS DUE TO RADON PROGENY IN THE HUMAN LUNG

B. M. F. Lau[1], D. Nikezic[1,2] and K. N. Yu[1,*]
[1]Department of Physics and Materials Science, City University of Hong Kong, Tat Chee Avenue, Kowloon Tong, Hong Kong
[2]Faculty of Science, University of Kragujevac R. Domanovic 12, 34000 Kragujevac, Serbia and Montenegro

The dose conversion coefficient (DCC) is used to assess the risk due to inhaled radon progeny in the human lung. The present work uses the microdosimetric approach and determines the linear energy transfer in the target cell nuclei. Killing of target cells was also taken into account through an effect-specific track length model. To focus on the relevant part of the absorbed dose in the cell nuclei, the absorbed dose, which causes cell-killing is discarded in the final calculations of the DCC. Following this approach, the calculated DCC has become 3.4 mSv WLM^{-1} which is very close to the epidemiologically derived value of ~4 mSv WLM^{-1}.

INTRODUCTION

To calculate the absorbed dose in the human respiratory tract (HRT) due to inhaled radon progeny, ICRP66[(1)] made use of the absorbed fraction (AF) which is the average energy of alpha particles absorbed in layers containing the target cells. The AF for a given combination of a source and a target is then multiplied with the number of alpha particles emitted in that source to give the energy absorbed in the target. ICRP66 considered the layers containing the target cells, i.e. the basal and secretory cells. The dose conversion coefficient (DCC) thus calculated is ~15 mSv WLM^{-1} (see Table 1).

A well-known paradox is the significant discrepancy between the DCC calculated as described above and the epidemiologically derived value of ~4 mSv WLM^{-1}[(2)] and 2.7–6.2 mSv WLM^{-1}[(3)]. Our group has previously made different recalculations of the DCC in order to explain/alleviate this discrepancy, including those based on different lung morphometry models[(4)], different ethnic groups[(5)], different deposition models[(6)], bifurcation of the human tracheo-bronchial tree[(7,8)] and micro-dosimetry[(9)]. Although narrowing of the gap between the two DCC values has been achieved for some approaches, the calculated DCC has not come close to the epidemiological value. There are also efforts from other groups who have explored the reconciliation of the discrepancy. For example, Marsh *et al.*[(10)] found that, according to their uncertainty analyses, it was unlikely to obtain a calculated DCC for exposures in home as low as 4 mSv WLM^{-1}. Hofmann *et al.*[(11)] suggested that a radiation weighting factor of 10 might be more realistic than that of 20 for alpha particles. Stather[(12)] adopted the radiation weighting factor for alpha particles as 10 and determined the DCC for exposures in home as 7.5 mSv WLM^{-1}.

In the present work, the micro-dosimetry approach will be further developed. It is established that the target cells irradiated by alpha particles can be killed[(13–15)], which has not been taken into account in our previous investigations using the micro-dosimetry approach[(9)]. To actually focus on the relevant part of the absorbed dose in the cell nuclei, i.e. the part involved in carcinogenesis, the absorbed dose, which causes cell-killing should be discarded in the final calculations of the DCC. The present paper will take into account the probabilities for cell-killing by applying the effect-specific track length model[(13–15)] in determining the DCC and other related parameters.

DCC CALCULATIONS ACCORDING TO ICRP66 MODEL

The procedures for DCC calculations according to ICRP66 can be briefly summarised as follows:

(1) The first step is the calculation of the absorbed dose D in the target, where $D = N\alpha \times E\alpha \times \mathrm{AF\ m^{-1}}$, N$\alpha$ is the number of alpha particles emitted for a given exposure condition and time, $E\alpha$ is the alpha particle energy, AF is the absorbed fraction in the target and m is the mass of target. In the ICRP66 model, the targets are layers containing the sensitive cells.
(2) The second step involves weighting of the calculated doses as follows. First, the average dose in the bronchial (BB) region, 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 employed for the dose $D_{BB,bas}$ in basal cells and the dose

*Corresponding author: peter.yu@cityu.edu.hk

Table 1. The absorbed dose (mGy WLM^{-1}) and the total DCC (mSv WLM^{-1}) calculated for layers that contain the basal and secretory cell nuclei (ICRP66 approach) and for the cell nuclei themselves (present work).

Absorbed dose (mGy WLM^{-1})	Layers	Cell nuclei
Bronchial basal cells ($D_{BB,bas}$)	5.15	0.578
Bronchial secretory cells ($D_{BB,sec}$)	11.7	1.45
Bronchial dose ($0.5D_{BB,bas} + 0.5\ D_{BB,sec}$)	8.42	1.01
Bronchiolar (D_{bb})	10.4	3.18
Total DCC (mSv WLM^{-1})	15.1	3.35

$D_{BB,sec}$ in secretory cells. Second, the doses in BB region and the bronchiolar (bb) region are weighted by the factor 0.333 to give the dose in the tracheo-bronchial (T-B) tree, i.e.,

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

The contribution to the total dose from the AI region is neglected here.

(3) The third step calculates the effective dose as

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

where 0.12 is a tissue weighting factor for the lung and 20 is a radiation weighting factor for alpha particles. The effective dose obtained by Equation 3 is then divided by the corresponding potential alpha energy exposure (in the unit of working level month (WLM)) employed above for the calculation of $N\alpha$, and finally the DCC (in the unit mSv WLM^{-1}) is obtained.

A home written program LUNGDOSE was applied to calculate the DCC values for the following sets of the input parameters. The first set of parameters was related to the indoor room atmosphere: ventilation rate $\lambda_v = 0.55$ h^{-1}; attachment rate $\lambda_a = 50$ h^{-1}; deposition rate of unattached progeny $\lambda_d^u = 20$ h^{-1}; deposition rate of attached progeny $\lambda_d^u = 0.20$ h^{-1}; recoil factor = 0.83. The attached progeny were assumed to distribute in three modes, namely, nucleation, accumulation and coarse modes, with the following fractions 0.28, 0.70 and 0.02, respectively[16]. These parameters were used in the Jacobi parametric room model, which gave the ratios of progeny to radon concentration. These were used as the input data for the LUNGDOSE program. The total equilibrium factor was $F = 0.372$ and the unattached fraction was $f = 0.0655$. Other aerosol characteristics included: median diameters (with geometrical standard deviations in brackets) are 0.9 (1.3), 50 (2), 250 (2) and 1500 (1.5) nm for the unattached, nucleation, accumulation and coarse modes, respectively. The density of the unattached progeny was taken as 1 g cm^{-3}, while that of the attached progeny as 1.4 g cm^{-3}; the shape factors taken as 1 and 1.1 for unattached and attached progeny, respectively; and hygroscopic growth factors as 1 and 1.5 for unattached and attached progeny, respectively. The subject-related parameters were: breathing rate = 0.78 m^3 h^{-1}; tidal volume = 0.866 l per breath; functional residual capacity = 3300 ml; breathing frequency = 15 min^{-1}. The half-life for transfer to blood was taken as 600 min. Other parameters that were not mentioned here were simply adopted as recommended in ICRP66. The DCC was found to be 15.1 mSv WLM^{-1} (also given in Table 1). This agrees well with the DCC of 15 mSv WLM^{-1} calculated by other groups[17].

MICRODOSIMETRY WITH CELL-KILLING

For the microdosimetric calculations, the program LUNGDOSE was modified as follows. The absorbed doses were only calculated for the nuclei of sensitive cells. According to the ICRP66 model, basal cells exist only in the first eight generations of the HRT (BB region). The diameters of the nuclei of spherical basal and secretory cells in BB and secretory cells in bb were taken as 9 and 8 μm, respectively[11]. The abundance of basal and secretory cells was taken from Mercer *et al.*[18]. The nuclei of basal cells and secretory cells were chosen to be spherical. Cylindrical geometry was adopted for the airway tubes as was proposed in ICRP66. Other elements of calculations were the same as those in our previous papers[7–9] and will not be repeated here in detail. The difference was that very long tubes (10 mm) were considered here instead of the 2 mm tubes considered in previous works.

The effect-specific track length model[13–15] and the concept of the probability per unit track length (PPUTL) for cell-killing are adopted in the present study. For a given linear energy transfer (LET, in keV μm^{-1}), the probability for cell-killing by an alpha particle traversing the cell nucleus is given by the product of the PPUTL at that LET multiplied by its track length in the nucleus (chord length)[14]. The PPUTL for cell-killing (PD) of C3H 10T1/2 mouse embryo cells as a function of LET was given by[14]

$$\mathrm{PD} = 10^{-0.14+2.03\log10(\mathrm{LET})-0.21(\log10(\mathrm{LET}))^2} \quad (4)$$

In the present study, the LET for each hit cell nucleus was determined in order to calculate PD. The product of PD and the chord length in the hit cell nucleus then gave the probability for cell-killing. The latter was employed to decide whether the cell was killed or survived after the alpha particle traversed the nucleus by comparing with a generated random number. If the cell was killed, the absorbed dose in that cell nucleus would be discarded from our calculations. At the same time, the cell-death rates in different regions were obtained as the total

number of killed cells divided by the total number of hit cells.

RESULTS AND DISCUSSION

The cell-death rates in the BB region for alpha particle energies 6 and 7.69 MeV were ~72–81 and 75–80%, respectively; those in the bb region for alpha particle energies 6 and 7.69 MeV were ~69 and 58%, respectively. The ranges of the cell-death rates rise as a result of different positions of the deposited radon progeny. The smaller cell-death rates in the bb region were expected because the incident energies on the target cell nuclei in the bb region were in general larger than those in the BB region. The stopping power relevant to our discussions increases with decreasing energy, so most of the hit cell nuclei in the BB region were killed by the alpha particles due to the high stopping power.

The specific energy distribution and hit frequency were calculated for all combinations of different sources and targets. From these, the mean specific energy was calculated. The product of specific energy and hit frequency gives the absorbed dose D. The doses were weighted according to Equation 1–3 and the DCC values (in the unit mSv WLM^{-1}) are given in Table 1. Table 1 also gives the doses in layers that contain the basal and secretory cell nuclei and the corresponding DCC, which is actually the ICRP66 approach. The DCC value obtained for cell nuclei was 3.35 mSv WLM^{-1}, which was significantly less than the value obtained using the ICRP66 approach. We conclude that by using the micro-dosimetry approach and by only concentrating on the relevant dose which does not kill the hit cells, the calculated DCC value (3.4 mSv WLM^{-1}) can become very close to the epidemiologically derived value of ~4 mSv WLM^{-1}.

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