Acta Physica Universitatis Comenianae
Vol. XLVIII XLIX, Number 1&2 (2007 2008) 133 141

Prediction of Radon Risk by Microdosimetric Models

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Abstract: In the paper the excess risk of lung cancer incidence after radon exposure is analyzed. It was supposed for the evaluation of the radon risk that the depth of the mucose shell of the smokers is greater than that of the non-smokers. For differentiating of the risk between smoking and radon exposure, two calculation models have been used: the additive and multiplicative model. Transformed cells were considered as the radiation risk parameters. It was found as a result of the quantification of the health risk of radon exposure, that the radiosensitivity of basal and secretory cells in the lung tissue is different for smokers and non-smokers. The value of excess relative risk of lung cancer per unit exposure obtained in our study is ERR = (2.1 3.8) 10^{-3} WLM for smokers and ERR = (8.81 13.27) 10^{-3} WLM for nonsmokers (considering the underground medium in mines). Further, our results give an average value of excess relative risk per unit exposure in dwellings ERR = (0.40 0.69) 10^{-3} Bq.m^{-3} for smokers and (1.69 2.61) 10^{-3} Bq.m^{-3} for non-smokers.

1. Introduction

The International Agency for Research on Cancer has classified ^{222}Rn as a primarily human carcinogen on the basis of findings in underground miners exposed to ^{222}Rn progeny. In 1999 the National Research Council of the National Academy of Sciences published the BEIR VI report, which assessed the risks to the U.S. population from radon in homes [1]. The committee concluded that indoor radon is the second leading cause of lung cancer after cigarette smoking. Therefore, in this time great attention is given to the precise quantification of health risk of radon products inhalation in dwellings as well as in working areas. To quantify the possible lung cancer risk from indoor radon exposure three different types of approaches can be taken into consideration:

1. „dosimetric approach“, which proceeds from the observed excess risk of lung cancer among the atomic bomb survivors.
2. results of direct epidemiological studies in population groups exposed residentially,
3. the transfer of exposure risk models using the data from ^{222}Rn exposed miners.

Interaction between two risk factors, smoking and radon exposure, can be assessed using the following models:

Additive risk model

$$rr_A(s,w) \quad r_0 \quad r_0(RR_S \quad 1) \quad r_0(RR_w \quad 1) \tag{1}$$

Multiplicative risk model

Devoted to Prof. Pavel Povinec 65-th anniversary

$$rr_M(s,w) \quad r_0 RR_S RR_w \tag{2}$$

where s number of smoked cigarettes, w radon exposure, rr disease risk, RR_S, RR_w relative risk of lung cancer from smoking and radon exposure, r_0 is the background disease rate in the absence of exposure and smoking.

The relative risk $RR(w)$ of lung cancer is determined by the equation:

$$RR(w) \quad \frac{rr(s,w)}{rr(s,0)} \quad \frac{rr(s,w)}{r_0 RR_S} \tag{3}$$

When the interaction between smoking and radon exposure is additive, it follows for the observed relative risk:

$$RR_A \quad \frac{rr_A}{r_0 RR_S} \quad 1 \quad \frac{RR_w \quad 1}{RR_S} \tag{4}$$

In the case of multiplicative interaction, the following equation is valid

$$RR_M \quad \frac{rr_M}{r_0 RR_S} \quad RR_w \tag{5}$$

2. Materials and method

The geometric model used for the calculation of Lung Cancer Risk is displayed in Fig. 1. Bronchial airways are approximated by a cylinder tube of diameter 4400 m. The alpha activity concentrations of ^{214}Po and ^{218}Po in the different bronchial airways were computed for exposure conditions, which are typical for underground miners, are given by the ICRP Publication 66 Human Respiratory Track Model (HRTM) [2]. ^{214}Po and ^{218}Po alpha particles were emitted isotropically from the mucus/"sol" layer, with exponentially decreasing source distribution (half-value layer 6 m). The thickness of the mucus source shell was 11 m for a non-smoker and 30 m for smokers (Fig. 2) [3]. Energy deposition in the tissue and in the air gap was calculated by the Bethe-Bloch equation. The target nuclei of bronchial epithelium were represented by spheres of 5 m diameter and have been placed in the lung tissue in 5 m steps along the radii of the cylinder. During the simulation of alpha particles interac-

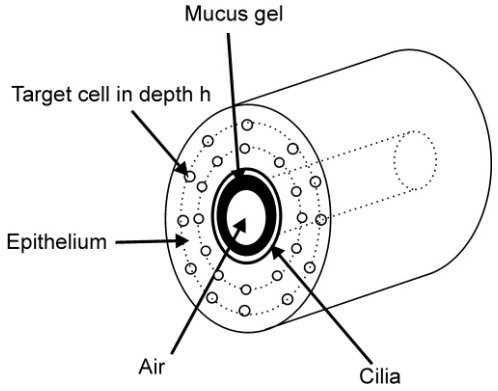

Fig. 1. Geometric model of a bronchial airway used to calculate microdosimetric parameters in target cells.

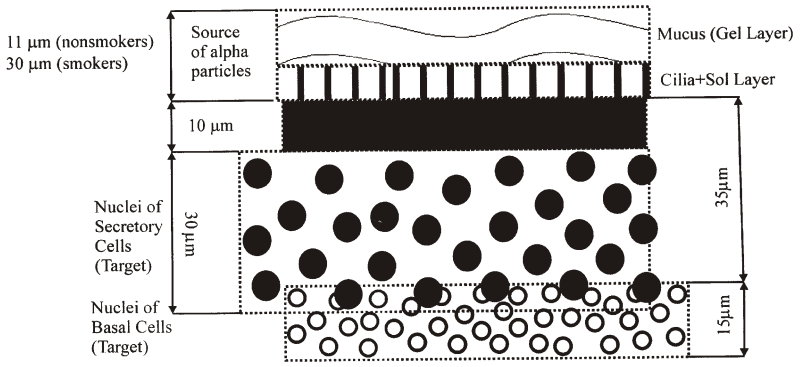

Fig. 2. Model of target cell nuclei (secretory and basal cells) and bronchial wall in the bronchi region.

tion with the lung tissue, specific energies, LET, as well as other characteristics within individual cells (necessary for the calculation of probabilities of biology endpoints), were determined by the geometric model. The detailed description of the biology endpoints calculation by using the microdosimetric models can be found in [4].

For the given thickness of the mucus, the radiation response $R_{mucus}(w)$ (for different cumulative lung exposures w), was obtained by summation of respective probabilities of biological responses over all depths (in 5 m steps) in airway generation:

$$R_{mucus}(w) \qquad p(i)\ TS_{i,mucus} \tag{6}$$

$$i \quad \begin{matrix} 10\ \text{m}, & 15\ \text{m}, & 20\ \text{m}, \\ 25\ \text{m}, & 30\ \text{m}, & 35\ \text{m}, \\ 40\ \text{m}, & 45\ \text{m}, & 50\ \text{m} \end{matrix}$$

where $TS_{i,mucus}$ are the probabilities of cell transformation. In our calculations the heterogeneous depth distributions $p(i)$ [5] of target nuclei were considered.

The thickness of the mucus shell was influenced by the smoking habit (11 m for non-smokers and 30 m for smokers). We inserted the mean cycle time of bronchial cells into the model. The biological response for cohorts Y_{cohort} has been calculated as follows:

$$Y_{cohort}(w) \quad q_N \quad R_{11\ m}\left(w \ \frac{}{exposure}\ 365\right) \quad (1 \quad q_N)\ R_{30\ m}\left(w \ \frac{}{exposure}\ 365\right) \tag{7}$$

and the relative radiation (radon) risk (according to the construction of the response function) is expressed as

$$RR_w(w) \quad 1 \qquad Y_{cohort}(w) \tag{8}$$

where $R_{11\ m}$ ($R_{30\ m}$) are the weighted biological endpoints for the thickness of the mucus source 11 m (30 m); w is the cumulated exposure, $_{exposure}$ is the time of exposure, q_N is the fraction of nonsmokers and is the calibration factor.

For calculation of the relative risk RR, we receive the following equations for the additive and multiplicative models:

$$RR_A \quad \frac{rr_A}{r_0 RR_S} \quad 1 \quad \frac{}{RR_S} Y_{cohort}(w) \tag{9}$$

$$RR_M \quad \frac{rr_M}{r_0 RR_S} \quad 1 \quad Y_{cohort}(w) \tag{10}$$

Both equations have the same linear shape :

$$RR(w) \quad 1 \quad Y_{cohort}(w) \tag{11}$$

The values of beta are: RR_S for the additive model and for the multiplicative model.

The parameters of were obtained by fitting equation (11) on the epidemiological Lubin's data [1, 6] using the weighted least squares method (as the weight the reciprocal value of square deviation was used).

2.1 The risk estimation for smokers and non-smokers

The relative risks RR of miners have been calculated through the calibration constant for various types of models and for various smoking habits:

• for the multiplicative risk model (nonsmokers):

$$R_{M,N} \quad 1 \quad R_{11\ \mathrm{m}}(w) \tag{12}$$

• for the multiplicative risk model (smokers):

$$RR_{M,S} \quad 1 \quad R_{30\ \mathrm{m}}(w) \tag{13}$$

• for the additive risk model (nonsmokers):

$$R_{A,N} \quad 1 \quad RR(s_{cohort}) R_{11\ \mathrm{m}}(w) \tag{14}$$

• for the additive risk model (smokers):

$$RR_{A,S} \quad 1 \quad \frac{RR_S(s_{cohort})}{RR_S(s_{smoker})} R_{30\ \mathrm{m}}(w) \tag{15}$$

where s_{cohort} presents the average number of smoked cigarettes in the cohort used for calibration purposes and s_{smoker} is the average number of smoked cigarettes by smokers.

The ratio between excess relative risk at WLM (ERR/WLM) of nonsmokers (N) and smokers (S) depends on different risk models used and it can be expressed by the following equations:

$$\frac{(ERR/WLM)_N}{(ERR/WLM)_S}_{M} \quad \frac{\dfrac{dRR_{M,N}}{dw}}{\dfrac{dRR_{M,S}}{dw}} \quad \frac{\dfrac{d}{dw} R_{11\ \mathrm{m}}(w)}{\dfrac{d}{dw} R_{30\ \mathrm{m}}(w)} \tag{16}$$

$$\frac{(ERR/WLM)_N}{(ERR/WLM)_S}_{A} \quad \frac{\dfrac{dRR_{A,N}}{dw}}{\dfrac{dRR_{A,S}}{dw}} \quad RR(s_{smoker}) \frac{\dfrac{d}{dw} R_{11\ \mathrm{m}}(w)}{\dfrac{d}{dw} R_{30\ \mathrm{m}}(w)} \tag{17}$$

$$RR(s_{smoker}) \quad \frac{(ERR/WLM)_N}{(ERR/WLM)_S}_{M}$$

One WLM is defined as the exposure to 1 WL concentration of radon progeny potential alpha energy in air for 170 h (1 working month). The WL is defined as any combination of radon (or thoron) progeny in air that ultimately releases 1.3 10^5 MeV of alpha energy during the decay.

It can be stated from Equation (16, 17) that the ratio RR_S (s_{smoker}) is greater for the additive risk model than for that multiplicative model. The value of RR_S (s_{smoker}), depends on the number of smoked cigarettes per day s_{smoker} in the miners cohorts. According to the published data in BEIR VI, it could be supposed for smokers nowadays that RR_S 22 and RR_S 9.4 for the smoking miners in the past.

3. Results and discussion

3.1 Calibration of Microdosimetric Models

From the equation representing the calibration (11) the relative risk distribution has been estimated for miners, supposing that the proliferation time has 3 values: = 30 d, = 100 d, = 180 d [1, 7]. One can conclude from the obtained results that the optimal value of the proliferation time is = 180 d. This value was used in our further considerations. The multiplicative risk model allowed us to determine, from the calibration Equations(12) and (13), the distribution of *RR* for miners-smokers and miners-nonsmokers. The results were compared with available epidemiological data (Fig. 3) and they are summarised in Table 1. The risk rapidly increases in the region of low exposures, but saturation can occur in the region of intermediate and high exposures. In the whole investigated range the risk of non-smokers is higher than that of smokers.

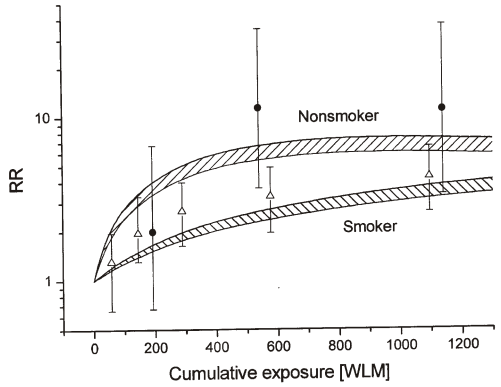

Fig. 3. Relative risk of lung cancer for smokers ( ) and nonsmokers (•) from epidemiologic data of Lubin and assessment from two-mutation model (hatched sections). The lines represent the 95 % confidence limit (upper, lower) interval.

We have derived the excess relative risk per unit of exposure ERR/WLM from these results. The predicted values are comparable with the epidemiological data in the range of the supposed uncertainties (Table 1). It follows from Table 1 that tha ratio of excess relative risk to WLM (ERR/WLM), between the non-smokers (N) and smokers (S) groups is:

$$\frac{(ERR/WLM)_N}{(ERR/WLM)_S}_M \quad 3 \quad 5 \tag{18a}$$

for multiplicative model and

$$\frac{(ERR/WLM)_N}{(ERR/WLM)_S}_A \quad \frac{(ERR/WLM)_N}{(ERR/WLM)_S}_M \quad RR(s_{smoker}) \quad 30 \quad 50 \tag{18b}$$

for additive model.

Table 1. The values of excess relative risk ERR per WLM for nonsmokers, smokers and miners.

Status	ERR/WLM [10^{-3}]			
Type of smoking status	Our			Lubin [6]
	LET model	Threshold specific energy model	Track model	
Smoker	2.11 (1.64 2.58)	2.44 (1.94 2.93)	3.76 (2.99 4.53)	4.80 (1.80 12.70)
Nosmoker	10.12 (7.86 12.37)	8.81 (7.02 10.61)	13.27 (10.55 16.00)	10.20 (1.50 71.80)
All	3.71 (2.88 4.54)	3.71 (2.96 4.47)	5.66 (4.50 6.82)	

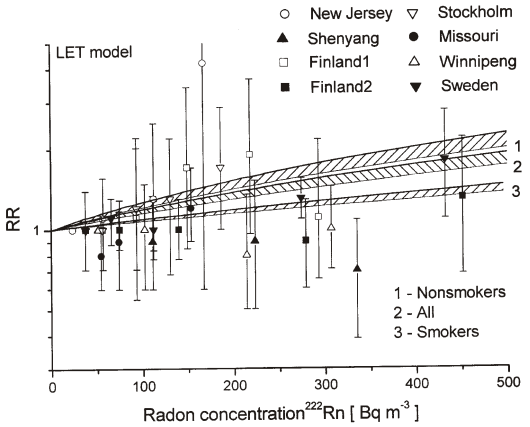

Fig. 4. Relative risk of cancer induction in smoker (3), nonsmoker (1) and normal (2) population calculated by microdosimetric models. The data are compared to control studies of residential radon [10]. The lines represent the 95 % confidence limit (upper, lower) interval.

The value predicted by multiplicative model is comparable with the published epidemilogical data in BEIR VI:

$$\frac{(ERR/WLM)_n}{(ERR/WLM)_s}_{BEIRVI} \quad 2 \tag{19}$$

For this reason the additive model has been rejected.

3.2 The estimation of lung cancer incidence relative to the risk for normal population

Some typical exposure conditions in dwellings (ICRP66) [2] were simulated using the presented model assuming that 35 % of population are smokers. In Fig. 4 dependences of the *RR* as a function of exposure for dwellings [8] are shown. The calculated average value for population is *ERR* 0.15 per radon activity of 100 Bq.m ^{3}.

Similar values have been published by Lubin and Boice [9], analysing the epidemiological data of lung cancer incidence in the cohorts of population exposed in dwellings in various parts of world (Canada, China, Finland, Sweden and USA). Combination of the results from all published data allowed Lubin to confirm the trend of increase of the cancer risk with the radon exposure. He postulated for the volume activity of radon equal to 100 Bq.m ^{3}, the value of *ERR* 0.9 (0.01 0.20) per radon activity of 100 Bq.m ^{3}.

The other source of information about *RR* were the epidemiological studies of more than 7000 lung cancer cases reported from 14 European countries compiled by Darby et al. [10]. The excess relative to the risk from this source gives the value of *ERR* 0.17 (95 % CI: 0.03 0.37) per radon activity of 100 Bq.m ^{3}.

The results from both sources give comparative results with our values of *ERR* per radon activity of 100 Bq.m ^{3}, taking into account the uncertainties by the estimation of the volume activities of radon. Table 2 shows estimated excess relative to the risk for lung cancer by categories of smoking status.

Table 2. The predicted average excess relative risk for lung cancer per 100 Bq.m radon concentration for smokers, nonsmokers and population.

Model	ERR/WLM 10^{-3} $Bq^{-1}.m^{3}$		
	Smoker	Nonsmoker	All
Boundary	0.5 (0.4 0.6)	1.9 (1.7 2.2)	1.4 (1.3 1.6)
LET	0.4 (0.4 0.5)	2.3 (2.0 2.25)	1.6 (1.4 1.8)
Track	0.5 (0.5 0.6)	2.0 (1.7 2.2)	1.5 (1.3 1.6)

The most significant source of information for the radiation risk estimation from radon and radon decay products inhalation in dwellings still remains on the epidemilogical data from the studies of lung cancer incidence in uranium mines.

3.3 Radiosensitivity of basal and secret cells

The ratio between radiosensitivity of basal and secretory cells was determined also by microdosimetric models usig Equation (20):

$$P \quad \frac{\overline{T}_{bazal}}{\overline{T}_{sekre}} \tag{20}$$

where $\overline{T}_{bazal}, \overline{T}_{sekret}$ represent the mean value of probability with which the basal or secretory cells with exposure lower than 100 WLM are transformed. The results of calculation are presented in Table 3, where the mean value of $\overline{P}$ is estimated for the range with exposure lower than 100 WLM from equation:

$$\overline{P} \quad \frac{1}{100} \int_0^{100} P(W)dW \tag{21}$$

It follows from these analyses that ERR of basal cells is 4.3–6.3 times higher than the risk of secretory cells. The basal cells absorb approximately 2 times lower dose than the secretory cells. It is supposed from this reason that the radiosensitivity of basal cells per unit of absorbed dose is by 8 12 times greater than radiosensitivity of secretory cells per unit absorbed dose.

Table 3. The ratio of sensitivity of basal and secretory cells for smoker and nonsmoker status.

Model	Status	
	Nonsmoker	Smoker
Border energie	4.1	3.8
LET	3.6	2.9
Track	5.6	3.7

Our results agree with the published data by Hofmann [11], where the ratio of probability of transformation of basal cells to transformation of secretory cells reached the value of 2.4 for ^{218}Po and the value 5.4 for ^{214}Po for exposure of 20 WLM.

According to ICRP 66 [2] the dose deposited in lung tissue can be calculated as an arithmetic mean of dose in basal and secretory cells. This method has been chosen namely because of supposing equal radiosensitivity of both types of cells. By the analyses described in this work the sensitivity of basal cells per unit absorbed dose is 8 12 times higher compared to the sensitivity of secretory cells. This would need revaluation of the values of weighting coefficients of target cells in the Recommendation of ICRP in the future.

4. Conclusion

- The value of excess relative risk is (ERR/WLM) = (2.1 3.8) 10^{-3} WLM^{-1} for smokers and that of the nonsmokers is (ERR/WLM) = (8.8 13.3) 10^{-3} WLM^{-1}, considering the underground medium.
- The average value of excess relative risk per unit exposure in dwellings is ERR = 0.04 (0.04 0.05) per 100 $Bq.m^{-3}$ for smokers and for nonsmokers ERR = 0.51 (0.19 0.23) per 100 $Bq.m^{-3}$.
- The sensitivity of basal cells per unit absorbed dose is 8 12 times higher compared to the sensitivity of secretory cells. This would need revaluation of the values of weighting coefficients of target cells in the Recommendation of ICRP in the future.

- Microdosimetric models give adequate descriptions of radiation response lung tissue under the influence of significant effects (time since exposure, inverse efect …). For this reason the model is suitable for risk prediction in dwellings and working sites. Microdosimetric models are very helpful and suitable for prediction of the radon risk for underground conditions, as well as for indoor radon risk evaluation, and they are also able to take into account the influence of the smoking habit.

Acknowledgements

This study was funded by the Scientific Grant Agency of the Ministry of Education of the Slovak Republic (VEGA project No. 1/3046/06) and ESF project NO. JPD 3BA-2005/1-034.

References

[1] National Research Council, Committee on Health Risks of Exposure to Radon, Health Effects of Exposure to Radon (BEIR VI). National Academy Press, Washington, DC, 1999.
[2] Human Respiratory Tract Model for Radiological Protection, ICRP66, 1994.
[3] D. Brenner, R. C. Miller, Y. Huang, E. J. Hall: The Biological Effectiveness of Radon-Progeny Alpha Particles., Radiation Research **142** (1995) 61 69.
[4] R. Böhm, D. Nikodemová, K. Holý: Use of Various Microdosimetric Models for the Prediction of Radon Induced Damage in Human Lungs, In: Radiat. Prot. Dosim. **104** (2) (2003) 127 137.
[5] R. Mercer, M. L. Russel, J. D. Crapo: Radon Dosimetry Based on the Depth Distribution of Nuclei in Human and Rat Lungs. In: Health Physics **61** (1) (1991) 117 13
[6] J. H. Lubin, Jr. J. D. Boice, Ch. Edling, R. W. Hornung, G. R. Howe, G. R. Kunz, R. A. Kusiak, H. I. Morrison, E. P. Radford, J. M. Samet, M. Tirmarche, A. Woodward, S. X. Yao, D. A. Pierce: Lung Cancer in Radon-Exposed Miners and Estimationof Risk from Indoor Exposure. In: Journal of the National Cancer Institute **87** (11) (1995) 817 827.
[7] W. Hofmann: Microdosimetry and Cellular Radiation Effects of Radon Progeny in Human Bronchial Airways. In: Radiation Protection Dosimetry **52** (1 4) (1994) 381 385.
[8] D. Krewski, J. H. Lubin, J. M. Zielinski, M. Alavanja, V. S. Catalan, R. W. Field, J. B. Klotz, E. G. Letourneau et al.: Residential Radon and Risk of Lung Cancer. Epidemiolgy **16** (2) (2005) 137 145.
[9] J. H. Lubin, J. D. Boice: Lung Cancer Risk from Residential Radon: Meta-analysis of Eight Epidemiologic Studies. Journal of the National Cancer Institute **89** (1) (1997) 49 57.
[10] S. C. Darby, D. C. Hill: Health effects of residential radon: A European Perspective at the End of 2002, Radiat. Prot. Dosim. **99** (2003) 265 268.