Estimated risks of radon-induced lung cancer by two-mutation model for different exposures in mines and in homes.

Radoslav Böhm [1], Denisa Nikodémová [2], Karol Holý [1]
[1] Faculty of Mathematics, Physics and Informatics of Commenius University, Mlynská dolina F2, 842 48 Bratislava, Slovakia
[2] Institute of Preventive and Clinical Medicine, Slovak Medical University, Limbova 14, 833 01 Bratislava, Slovakia

Introduction

The most recent assessment of lung cancer risks associated with the radon exposure has been undertaken by the US BEIR VI Committee [1]. There the up-to-date data on 11 cohorts of radon exposed underground miners have been used. The Committee gave a preference to two models derived from these data: the exposure-age-duration model and the exposure-age-concentration model. In both the models, the excess relative risk ERR varies as a linear function of the cumulative radon exposure. The ERR is assumed to be the same for both the sexes of all ages at the exposure, and it does not require a modification for the differences between the mining and domestic environments.

The mathematical form for the excess relative risk is:

$$ERR = \beta(w_{5-14} + \Theta_{15-24} w_{15-24} + \Theta_{25+} w_{25+})\varphi_{age}(a)\gamma_Z \qquad (1)$$

where a is the age in years. The parameter β represents the slope of the exposure-risk relationship for the assumed reference categories of the modifying factors. The total exposure can be calculated as the weighted summation of the three time exposure windows, namely: 5-14,15-24, 25 years and more before the age a:

$$W^* = w_{5-14} + \Theta_{15-24} w_{15-24} + \Theta_{25+} w_{25+} \qquad (2)$$

where ($\theta_{5\text{-}14}$, $\theta_{15\text{-}24}$, θ_{25+}) are the weighting factors given in the [1]. ERR declines with the increasing age a, as it is described by the parameter $\theta_{age}(a)$. The parameter $\theta_{age}(a)$ is the step function defined in the three age windows, namely 0-55, 55-65, 75 years and more.

The rate of the exposure also effects the risk through the parameters γ_z. In the exposure-age-duration model the parameter γ_z represents the influence of an exposure duration and in the exposure-age-concentration model it represents the average concentration over the time of the exposure.

The model elaborated by EPA tries to remove the above mentioned differences [2] using the splines to smooth the function $\theta_{age}(a)$ .The EPA radon risk model is a simple model giving the risk values midway between those obtained from the two BEIR VI preferred models.

Methods

For a prediction of the radon risk we have used a modified two-mutation model [3]. The two-mutation model is a quasi-biological model of carcinogenesis, which describes the interaction of smoking and radiation for the induced lung cancer. This model is based on the assumption that the normal somatic cell must pass through two mutations to become malignant. The number of normal (stem) cells $N(t)$ is assumed to be deterministic and increases linearly at a young age and becomes constant from the age of 20 years. In the calculations, a heterogeneous distribution of the target cells was considered according to Mercel [4]. The thickness of the mucus source shell was 11μm for a non-smokers and 30 μm for smokers [5].

Results and discussion

Shorttime exposures – MINE environment

In our calculations, we supposed that the miners started to work in the mine at the age of 30y, there were about 80% smokers in the chosen cohort and a mean exposure time was 6 year. Generally it can be assumed that a miner starts to smoke at the age of 18 and he smokes about 18 cigarettes per day. The calculated values of the relative risk RR from the exposure $RR_{radiation}$ (W) are shown in figures 1. The calculated dependence is compared with two preferred models of BEIRVI and Lubin epidemiological data [6]. In the range of medium and high exposures the performed calculations give the same radon risk RR (within the statistical errors).

More significant differences are occurred mainly in the range of low exposures, which is important for the risk estimation in dwellings.

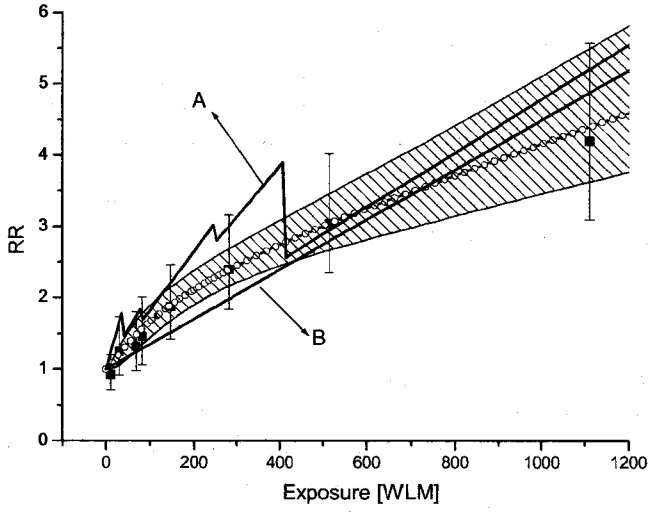

Figure 1. The relative risk of lung cancer (A - exposure-age-concentration model, B- exposure-age-duration model, ○ - Two-mutation model calculations). The lines represent the 95% confidence limit (upper, lower) interval.

The decrease of the excess lung cancer risk per unit exposure predicted by the two-mutation model at the intermediate and high exposure levels is consistent with the epidemiological evidence in the cohort of uranium miners and with the results obtained by the French and American rat inhalation studies [1]. Suchlike behaviour is influenced by the inverse dose-rate (protraction enhancement) effect - a trend towards the increasing tumor risk with the decreasing exposure rate.

In contrast, there is no evidence of an inverse exposure-rate effect at low exposure levels. Recent studies on the radon inhalation by rats support the hypothesis that at low doses the risk of lung cancer is proportional to the exposure rate. This result is in a good agreement with the prediction of the two-mutation model.

Longterm exposures – HOME environment

Some typical exposure conditions in dwellings [5] were simulated using the presented model assuming that 35% of population are smokers. In the figure 2 there is shown the dependence of the RR on the exposure in dwellings.

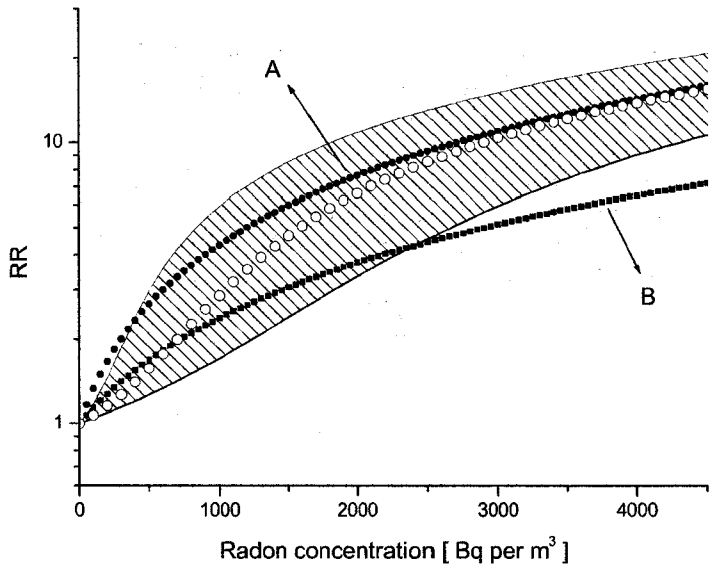

Figure 2. Relative risk of cancer induction in normal population calculated by two-mutation model. (A - exposure-age-concentration model, B- exposure-age-duration model, ○ - Two-mutation model calculations). The lines represents the 95% confidence limit (upper, lower) interval.

From the obtained results it can be concluded that for concentrations up to 500 Bq per m^3 the two-mutation model predicts the risk more corresponding to the exposure-age-duration model. The exposure-age-concentration model is more convenient for higher radon concentrations. Moreover, in the range of low concentrations the excess relative risk dRR per unit of the radon concentration increases with the increase of the radon concentration. It is in a good agreement with the experimental results obtained during an irradiation of rats at the low concentrations. The inverse dose rate effect occurs only in the case of an irradiation with higher concentrations, about 1500 Bq per m^3.

Conclusions

In this work, the two-mutation model has been applied and compared with BEIR VI models for a prediction of the radon risk in various environments. The obtained results can be summarised into several points.

The values of risk from the radon exposure predicted by the two-mutation model are comparable with the results obtained by BEIR VI for the short-time as well as for the long-time exposures. In the range of low exposures is this agreement of the results closer to the risk values assessed by the exposure- age-concentration model. In the range of higher exposures the results are closer to the values based on the age-duration model.

The two-mutation model predicts the increase of dRR/dC with the increase of the radon concentration in the range of low concentrations. According to our results the inverse effect occurs only when the radon concentrations reach the value of 1500 Bq per m^3.

The two-mutation model can be taken as an universal model for the risk calculation in different environments, and for various smoking status. This model makes possible to analyse the influence of the fractionalisation of the exposure on the resulting RR.

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