Multistage model description of French and Czech miner data: implications for radon-induced lung cancer risks

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Body of Abstract: Biologically based models are useful tools for analysis of radiation-induced carcinogenesis. They can make a valuable contribution to quantification of the risk of lung cancer from radon at low exposure rates, which remains an important challenge in radiation protection research. In the present work, a two-mutation carcinogenesis model has been applied to two miner cohorts with low exposure levels and a long follow-up. The aim was to derive radon-induced lung cancer risk estimates from a biologically based model solution that is consistent with both data sets and with previous model analyses of animal and human epidemiological data.

The modelled data includes 5098 and 5002 individuals from the French and Czech cohorts of uranium miners, with 125 and 449 observed lung cancer deaths respectively. For each miner the annual radon exposure has been reconstructed for the period of the (often long-lasting) occupation. The corresponding mean total cumulative exposure levels are 37 and 57 working level month (WLM) for the two cohorts respectively.

A two-mutation carcinogenesis model with clonal expansion of cells in the intermediate stage has been fitted to the individual miner data. The baseline lung cancer risk (from other causes than radon exposure) is described with background values for the model parameters. The effect of radon is modelled with linear dose-effect relationships for the two mutational steps, based on radiobiological information and on previous modelling of animal data. Joint fits of the French and Czech miner cohorts have been made using the same multiplicative radon effect on the mutation rates for the two cohorts.

The fitted linear radon effect on the first mutational step is one order of magnitude larger than that of the second mutational step, in agreement with previous model analyses of animal and human epidemiological data. The baseline lung cancer risk in the Czech miner cohort is considerably higher than that of the French miners, which results in significantly different background parameter values. Both data sets can, however, be described with the same parameter values for the relative effect of radon on the mutation rates. Incorporation of effects of decreased cellular proliferation at very advanced ages and/or birth-year effects improves the model fits by a better description of the baseline lung cancer risk, but does not lead to significant changes in the estimated radiation parameters.

The uniform description of the effect of radon for the two miner cohorts with distinctly different baseline lung cancer risks demonstrates the possibility of using the model for risk transfer across populations. In addition, the biologically based model implicitly describes age and dose-rate effects and thereby allows for extrapolation to lifetime exposures to low-level radon concentrations. Lifetime risks were calculated for a 75-year continuous exposure to 1 WLM/y (~256 Bq/m3). The lifetime excess relative risk calculated from the model solution is 1.1 for both cohorts. The lifetime excess absolute risks depend on the background parameter values, and result in 0.09 for the French and 0.23 for the Czech miner baseline risk. The uncertainties in the risk estimates will be discussed.