

INDOOR RADON EXPOSURE AND LUNG CANCER RISK ASSESSMENT FOR THE POPULATION OF CLUJ AND BISTRIȚA-NĂȘĂUD COUNTIES

Lucia-Adina TRUTA¹, Werner HOFMANN², Constantin COSMA¹, Liviu SUCIU³

¹*Faculty of Environmental Sciences and Engineering, Babeș-Bolyai University, Cluj-Napoca, Romania,*

²*Division of Physics and Biophysics, Department of Materials Research and Physics, University of Salzburg, Salzburg, Austria,*

³*S.C. ICPE Bistrița S.A., Bistrița-Năsăud, Romania*

Abstract: Interest in estimating lung cancer risk induced by radon and its progeny has been increasing over time, especially in the last decades, because it was shown that, besides acute exposures, low residential exposures to ionizing radiation were also hazardous, exhibiting an elevated cancer risk. The regions investigated in this study were Cluj and Bistrita-Nasaud counties, located in Transylvania, Romania. The present study was conducted from 2005 until 2008 in a sample of 390 dwellings. The current estimates for the two Romanian counties are consistent with that of 2.2-12.4% of lung cancer deaths attributed to indoor radon exposure in France, with that of about of 8.44% in 13 European countries, with that of 11% reported in a recent combined analysis of North American studies and with that of 10-12% in the U.S.

Key words: radon, modeling, lung cancer risk, Cluj, Bistrița-Năsăud.

Introduction

Interest in estimating lung cancer risk induced by radon and its progeny has been increasing over time, especially in the last decades, because it was shown that, besides acute exposures, low residential exposures to ionizing radiation were also hazardous, exhibiting an elevated cancer risk (Kadhim et al., 2006). In the whole world, residential exposure to the short-lived radioactive progeny of the chemically inert gas ²²²Rn is responsible for about half of all non-medical exposures to ionizing radiation because radon concentrations can build up indoors despite low outdoor radon concentrations (Darby et al., 2006). The average annual effective dose from radon and its progeny is responsible for approximately 57% of the total effective dose from all sources of natural radiation to the general population of Romania (Iacob and Botezatu, 2000). Analyses of case-control studies on residential radon and lung cancer risk (Darby et al., 2006) also conclude that great hazards from residential radon have been found, indicating that it is responsible for about 2% of all deaths from cancer in Europe. The US Environmental Protection Agency's updated calculation of a best estimate of annual lung cancer deaths from radon is about 21,000, while the NRC (1999) committee recommended the application of two risk models (exposure-age-duration and exposure-age-concentration models) from which they projected 15,400 and 21,800, respectively, excess lung cancer cases in the U.S. each year (NRC, 1999). Epidemiologic indoor and underground miner studies on radon exposure, as well as the fact that lung cancer is the world's most common cancer, accounting for 1.2 million new cases per year, being the second cause of death after coronary heart disease (Ferlay et al., 2007), prompted the International Agency for Research on Cancer in 1988 to classify radon as a human carcinogen (IARC 1988, 2001).

²²²Rn occurs naturally from the decay of ²³⁸U, which is ever-present in the earth's crust and thus air pollution by radon is ubiquitous (Darby et al., 2006). It has a half-life of almost four days, allowing it to diffuse through soil and into the air before decaying by emission of an alpha particle into a series of short-lived radioactive progeny. Two of these, ²¹⁸Po and ²¹⁴Po, decay by emitting densely ionizing high linear energy transfer (LET) alpha particles. After being inhaled, radon itself is mostly exhaled immediately, but its short-lived progeny tend to deposit on the bronchial epithelium, thus exposing sensitive cells to alpha irradiation (Darby et al., 2006), eventually causing lung cancer. The induction of cancer involves molecular biology phenomena such as interactions with DNA, genetic mutations, chromosomal aberrations, cellular transformation, initiation, cytotoxicity, promotion and progression. With the possible exception of progression, most of these events will depend on the radiation dose delivered at the cellular level, exposure period, dose rate, age at exposure, organ or tissue irradiated, and spatial inhomogeneity of the delivered dose

(Crawford-Brown, 1989). Low dose effects of alpha particles at the tissue level are characterized by a small number of cells traversed by single alpha particles, while most cells in this tissue are not hit at all (Truta-Popa et al., 2008). The dominant role of single hits leads to a linear dose-response relationship at low radon exposure levels. The objectives of the present study were threefold: (i) to assess the lung cancer risk induced by exposure to radon, for the population of Cluj and Bistrita-Nasaud, based on measured radon concentrations; (ii) to predict lung cancer risk for these areas, using two carcinogenesis models based on radiation effects at the cellular level (TF-TR and Darby's model) and (iii) to estimate the fraction of lung cancer cases attributable to radon in each of the two counties.

Materials and methods

The regions investigated in this study were Cluj and Bistrita-Nasaud counties, located in Transylvania, Romania. The present study was conducted from 2005 until 2008 in a sample of 390 dwellings. Information about the dwellings (area, number of rooms, building materials, ventilation, etc.) was collected using questionnaires. Indoor radon measurements were performed using CR-39 Radosys detectors placed for about 3 months in the most populated sites of the buildings, such as bedrooms and living-rooms, at 1-1.5 m height from the floor, both during summer and winter time, according to the NRPB Measurements Protocol. The information regarding the detectors, measurement technique, calibration, quality assurance and quality control, development process and calculation of radon concentration was detailed elsewhere (Truta-Popa et al., 2010). The mean measured radon concentration values (C_{Rn}) were corrected for seasonal variations, depending on the time when detectors were exposed during the course of a year (Cosma et al., 2009).

Lung cancer risk models

A biologically-based Transformation Frequency–Tissue Response (TF-TR) carcinogenesis model, based on experimentally observed cellular transformation and survival functions, was applied to simulate the dose-effect curve at low doses. In this model (Truta-Popa et al., 2011) lung cancer risk $R(D)$ is expressed as the product of the transformation frequency (TF) and the tissue response (TR) functions, while dose is expressed in terms of single and multiple alpha particle hits. Measured radon concentrations expressed in Bq/m^3 were converted to exposure by using the conversion $1 \text{ WLM} \cong 230 \text{ Bq}/m^3$ (ICRP 65, 1994) and then to absorbed dose with the relationship $1 \text{ WLM} = 5 \text{ mGy}$. Lung cancer risk simulated by the TF-TR model is given by:

$$R(D) = C \cdot \sum_{i=1}^n TFS(D_n) \cdot \exp(-\gamma \cdot D_n) \cdot \{\lambda_1 + \lambda_2 \cdot p \cdot [1 - \exp(-\gamma \cdot D_n)]\} / \lambda_1 \cdot P_n \quad (1)$$

where $D_n = n \cdot \overline{D_c}$ ($\overline{D_c} = 0.33 \text{ Gy}^{-1}$ for cells with a nuclear diameter of $9 \mu\text{m}$ and an LET of $130 \text{ keV } \mu\text{m}^{-1}$), and C is a constant scaling factor relating the number of transformed cells at dose D to the occurrence of an observable bronchial tumor, derived from epidemiological studies, γ represents the cell killing probability, λ_1 is the normal mitotic rate of lung cells, equivalent to a cycle time of 30 days, which may increase to λ_2 , the rate of division under conditions of extensive tissue damage and cellular replacement, corresponding to a cycle time of approximately one day, and p denotes the probability that a progenitor cell will divide as a direct result of the inactivation of an adjacent epithelial cell (Truta-Popa et al., 2011). It was assumed here that $p = 1$, i.e. each dead epithelial cell would force a stem cell to divide. The TF-TR model is a relatively simple mechanistic model that is described in more detail elsewhere (Truta-Popa et al., 2011). For continuous low-level exposures, it was assumed that cancer induction is related to the cycle time of an irradiated cell, thus exhibiting a distinct dose-rate effect. Model predictions were compared with epidemiologically observed lung cancer risk, indicating excellent agreement in the low dose region.

For indoor radon concentrations, the dose-effect relationship is linear as illustrated by many epidemiological studies. The collaborative analysis on residential radon from 13 European countries of Darby et al. (2006) is such an example. Their results were based on a linear model for the

relationship between the time-weighted average observed radon concentrations and the risk of lung cancer, described as:

$$RR=1+\beta x \quad (2)$$

where β is the excess relative risk of lung cancer per 100 Bq m⁻³ increase in the time-weighted average observed radon concentration (x), estimated after stratification by study, age, sex, region of residence and smoking history. The equation for the fitted model was $RR=1+0.000844x$, with 95% confidence interval, where x represents the measured radon concentration.

Prediction of lung cancer cases due to radon

The number of total lung cancer deaths due to indoor exposure to ²²²Rn ($N_{Rn,a}$) was estimated with the following relation, derived from the other available studies (Catelinois et al., 2006):

$$N_{Rn,a} = \frac{(RR-1)}{RR} \cdot N_{T,a} \quad (3)$$

where $\frac{(RR-1)}{RR}$ is the fraction of risk attributed to radon (FRA), a is the area where population is exposed, RR is the relative risk, predicted by the model based on radon concentration and frequency of measurements in defined exposure intervals, and $N_{T,a}$ is the total, average annual number of lung cancer deaths in the area a , where Rn-222 concentrations were measured (Table 1). These demographic data were provided by the National Institute of Statistics (INSSE, 2009) Romania, for each county. For these calculations, it was assumed that the populations of the different regions as well as the measured sites were homogeneously distributed among these regions.

Fraction of lung cancers due to radon exposure

The percentage of lung cancers attributable to radon is a more relevant parameter to express the lung cancers attributed to radon exposure, since it implies a comparison with the total lung cancers, while the absolute number does not have this advantage. The formula proposed in this study for calculating this percentage (Eq. 4) was derived from Eq. 3 and has the great advantage that it requires only the RR value, so the demographic data are no longer necessary. In case that the number of annual lung cancers is not available for administrative units (regions) smaller than counties, then the percentage of lung cancers due to exposure to radon (%LC_{Rn}) could simply be calculated from the fraction of risk attributable to radon (FRA) with the following formula:

$$\%LC_{Rn} = (FRA) \times 100 \quad (4)$$

Thus, the quantitative estimates of the lung cancer risk caused by radon will no longer be influenced by the uncertainties associated with the demographic and lung cancer data from the National Institute of Statistics for the area under study. This is particularly relevant in cases where the lung cancer data are difficult to get from medical records or National Institutes of Statistics, or where not all persons who die of lung cancer are registered accordingly, especially in the rural sites. Hence, the quantitative estimates of the lung cancer risk caused by radon will no longer be affected by the uncertainties from the demographic and lung cancer data, a fact that is really important in using the risk projections as a basis for making risk-management decisions (NRC, 1999).

Results and discussions

Table 1 summarizes the mean measured radon concentrations in defined exposure intervals as well as the mean, weighted annual radon concentration in the two counties. The mean measured values were corrected for the seasonal variation as mentioned above.

Table 1

Measured radon concentrations in the two counties and mean annual radon concentrations (Truta-Popa et al., 2010)

County	Range of measured values	Mean measured radon concentrations [Bq/m ³]	Frequency [%]	Mean annual Rn concentration [Bq/m ³]	RR _{Rn} for non-smokers predicted with TF-TR model	RR _{Rn} for non-smokers predicted with Darby's model
Cluj	<25	20	10	114	1.08	1.10
	25-49	38	23			
	50-99	69	32			
	100-199	140	20			
	200-399	266	11			
	400-799	592	4			
Bistrita-Nasaud	<25	16	15	71	1.05	1.06
	25-49	38	33			
	50-99	69	30			
	100-199	128	16			
	200-399	250	6			

Based on the radon concentration measurements in the two counties, lung cancer risk model predictions were: 1.08 for Cluj and 1.05 for Bistrita-Nasaud using TF-TR model and 1.10 for Cluj, 1.06 for Bistrita-Nasaud using Darby's model, values summarized in Table 1. In this study, we investigated only the case for lifetime non-smokers, but it is worth to specify that the RR for smokers is about 25 times greater than that for lifetime non-smokers (Darby et al., 2006) and that the effect of radon exposure and cigarette smoking is synergistic, more than additive and less than multiplicative (NRC, 1999).

Percentage of lung cancer cases due to radon

The percentages of lung cancer deaths attributed to radon exposure were derived at first from the total, average annual number of lung cancer deaths for the areas where Rn-222

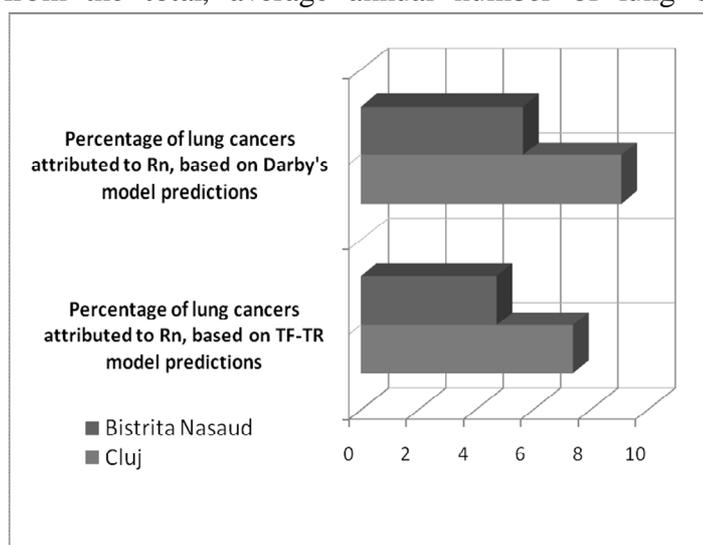


Fig. 1. Percentage of lung cancers attributed to radon, from all lung cancer cases, for lifetime non-smokers, based on the RR predictions with the TF-TR and Darby's model, for both investigated counties.

concentrations were measured (N_T) and the number of lung cancers deaths attributed to radon, for lifetime non-smokers, and then, calculated with Eq. (4). The results are the same, with the specification that RR values used within the two methods should have exactly the same values. For Cluj county, the National Institute of Statistics reported in 2007 a population of 689523 inhabitants and had a number of 267 lung cancer deaths due to lung cancer for the respective year, while for Bistrita-Nasaud the population was 317685 inhabitants and had a number of 92 lung cancer deaths (INSSE). The RR estimated with the TF-TR model, for never smokers, based on the measured radon concentrations and frequency of measurements in defined exposure intervals, was 1.08 for Cluj and

1.05 for Bistrita-Nasaud county.

Thus, the percentage of lung cancer deaths attributed to radon, based on TF-TR model predictions and equation (3), (4), in case of lifetime non-smokers will be 7.4% for Cluj and 4.76% for Bistrita-Nasaud county. In the same manner, we estimated a percentage of 9.09% and 5.66% of lung cancers attributed to radon, from the total lung cancers for Cluj and Bistrita counties, respectively, for non-smokers, based on the RR values predicted with Darby's model (i.e. 1.10 and 1.06) (see Figure 1).

It could be observed that the proposed method (Eq. 4) has more advantages, and it is much more simple and efficient than the laborious method, eliminating the errors related to the demographic data. Nevertheless, both methods require a precise estimation of RR values, and represent a basic, efficient tool for quantitative lung cancer risk estimations that underlie decisions for risk management. On the other hand, it could also be observed that RR values predicted with the TF-TR model are in good agreement with the ones predicted with Darby's model, although a little bit smaller (with 1% to 2%). Risk estimated with both models suggest that the percentage of lung cancers attributed to residential radon, out of the total lung cancers range between 7- 9% for Cluj and between 4- 6% for Bistrita-Nasaud county.

Conclusions

Data from epidemiologic studies provide convincing evidence that residential radon is an important cause of lung cancer, the most common type of fatal cancer in Europe in the general population (Ferlay et al., 2007). The current estimates for the two Romanian counties are consistent with that of 2.2-12.4% of lung cancer deaths attributed to indoor radon exposure in France (Catelinois et al., 2006), with that of about of 8.44% in 13 European countries (Darby et al. 2006), with that of 11% reported in a recent combined analysis of North American studies (Field et al. 2006) and with that of 10-12% in the U.S. (Lubin and Steindorf, 1995). Policies regarding exposure to this form of natural radiation were developed and refined so as to reduce the percentage of deaths from lung cancer. The European Commission issued recommendation 90/143/Euratom, in 1990, defining 400 Bq m^{-3} as the level for considering remedial action in existing dwellings, and 200 Bq m^{-3} as the reference level for new dwellings (CEC, 1990). So far, only a few responsible authorities developed detailed legislation specifying levels above which financial support for mitigation will be provided. The International Radon Project set up by the WHO in 1995 (WHO, 2007) will provide evidence-based recommendations for radon policies and promote programmes that reduce the health impact of radon in countries.

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Contact data

Lucia-Adina TRUTA: Faculty of Environmental Sciences and Engineering, Babes-Bolyai University, Fantanele Street, No. 30, 400294 Cluj-Napoca, Romania, e-mail: luciadinapopa@yahoo.com

Werner HOFMANN: Division of Physics and Biophysics, Department of Materials Research and Physics, University of Salzburg, Helbrunnerstrasse 34, Salzburg, 5020, Austria, e-mail: Werner.Hofmann@sbg.ac.at

Constantin COSMA: Faculty of Environmental Sciences and Engineering, Fantanele Street, No. 30, 400294 Cluj-Napoca, Romania, e-mail: constantin.cosma@ubbcluj.ro

Liviu SUCIU: S.C. ICPE Bistrita S.A., 7 Parcului Street, 420035 Bistrita, Romania, e-mail: liviu.suciu@yahoo.com