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Methodology Issues in Risk Assessment for Radon

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The alpha dose per unit radon daughter exposure in mines and homes is comparable at about 5 mGy/WLM. This means that excess lung cancer risk determined in follow-up studies of miners should be valid to extrapolating to environmental populations. There are several models currently used for risk projection to estimate lung cancer in the U.S. from indoor radon exposure. The accuracy of the estimates depends upon the quality of the exposure data and the models. Recent miner epidemiology confirms that excess lung cancer risk decreases with time subsequent to cessation of exposure. The most rigorous ecological study, to date, shows a persistent negative relationship between average measured indoor radon in U.S. counties and lung cancer mortality. A model for lung cancer risk is proposed that includes smoking, urbanization, and radon exposure. The model helps to explain the difficulties in observing the direct effects of indoor radon in the environment.

Introduction

Lung cancer as a consequence of radon daughter exposure at relatively high exposure rates is well documented (*1–5*). Follow-up studies of many types of underground mining cohorts indicate that radon daughter exposure is the common factor in producing lung cancer above expectations. These miners were exposed to a broad spectrum of concomitant airborne pollutants. Although the inhaled minerals and dusts undoubtedly have some carcinogenic potential, their effects appear small compared with the radon exposure itself.

The underground miner epidemiology began to show the trend between exposure and lung cancer response in the late 1960s (*1*). Occupational guidelines were reevaluated and, in the U.S., were lowered to the present annual occupational limit of 4 WLM/year in 1971.

Because of its natural origin, radon is present in every environment. In the early 1980s, environmental measurements in homes showed that high radon concentrations were not found exclusively in underground mines. At this juncture, environmental research concerning radon exposure at home accelerated and, within the past 4 years, an enormous number of measurements have been made for various purposes (*6,7*).

It is useful to introduce certain dosimetric aspects of radon daughters early. The significant radiation dose does not arise from inhalation of radon gas (3.82 day half-life) but from deposition of its particulate, short-lived alpha-emitting daughters, ^{218}Po and ^{214}Po (30-min effective half-life). It was not fully appreciated that the occupational limit of 4 WLM delivers an annual dose equivalent to cells in the bronchial epithelium of 0.4 Sv (40 rem) (*8*). Because some homes attain this value, the environmental lung dose to a fraction of the population is of this order of magnitude, compared with the natural whole-body gamma-ray dose of 0.1 rem per year.

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Some states, such as Pennsylvania and New Jersey, for example, have mounted programs dedicated to finding extraordinarily high radon levels in homes to reduce the exceptional lung cancer risk (EPA, unpublished data).The Environmental Protection Agency (EPA) has conducted state surveys to try to identify regions within states which have the potential for high radon concentration in homes (EPA, unpublished data). The Department of Energy has initiated a radon program to attempt to better understand the reasons for the high radon concentrations in homes with a view to overall radon exposure reduction. Their program is also supporting studies bearing on the fundamental mechanisms of radon carcinogenesis (*9*).

Risk assessment is tied to exposure estimation and the projection models. This paper brings some of the modeling and measurement information together to attempt to show the difficulties in assessing the true lung cancer risk from environmental radon exposure and proposes a methodology which may have validity.

The Problem

Four factors are required to determine the environmental lung cancer risk from radon exposure: exposure-response relationship, radiation dose versus exposure for mining versus environmental populations, relevant exposure of the population, and risk projection models to estimate the effects in the population. Although the emphasis of this manuscript concerns the relevant exposure of the population, the dosimetry and the risk projection models will be mentioned briefly.

Table 1 shows the exposure of five mining populations used for risk projection. The occupational exposure duration was short compared with environmental exposure which occurs over a lifetime. Table 2 shows the results of some of the existing measurements in homes as of the date of this writing. Many of these surveys were performed for particular purposes and may not be valid estimates of average exposure. The measurements

Table 1. Lung cancer deaths in five major mining cohorts, 1976–1982, the date of the last follow-up.

Cohort	Total number[a]	Mean age	Mean WLM	Lung cancer Observed	Lung cancer Expected
Colorado (U.S.)	3,360	57	800	256	59
Ontario (Canada)	10,661	50	37	87	37
Eldorado (Canada)	6,847	43	22	65	29
Czechoslovakia	3,043	60	226	484	98
Malmberget	1,292	67	94	51	15

[a]Number of total miners in the study.

Table 2. Estimates of the distribution of radon in U.S. living area.

Reference	Average, pCi/L	Percent > 4 pCi/L
(*13*)	1.0	3
(*7*)	1.5	7
(*15*)	7.0	23
(B. L. Cohen, unpublished)	3.3	19

in Table 2 were selected as living areas, not basements. In general, the values in Table 2 may overestimate the true average exposure in the U.S. because they are not truly random surveys. The definitive study of exposure of the U.S. population awaits action.

Dosimetry and Risk Projection Models

It is worthwhile to indicate that studies of the dose delivered to cells in bronchial epithelium lining the airways have been published by several investigators (*8,10*). Although conditions differ in mines and homes with regard to particle size of the atmospheric aerosol, breathing rate, unattached fraction of the radon daughters, etc., the radiation dose per unit in mines and homes is similar due to compensating factors among the variables. That is, the dose is about 5 mGy/WLM (0.5 rad/WLM) regardless of whether this exposure took place in a mine or in a home. The dose per unit exposure is about the same for men and women and is somewhat higher for children, but this occurs only over a short interval at around age 10. Given the risk reduction with time from exposure and the fact that lung cancer is rare before age 40, this higher dose to the child lung for a short interval is not thought to be of particular significance. EPA and the International Commission on Radiation Protection (ICRP) have considered the lung cancer risk from radon to children to be three times higher than that for adults. ICRP has modeled lifetime risk of lung cancer incorporating a risk coefficient three times higher for persons 0 to 20 years old (*11*). There is, as yet, no justification for this assumption.

The models used for risk projection to environmental situations have generally been of two types, absolute and relative risk models. It has become evident in the past few years that neither model is correct but that modified versions of the usual models are necessary. Excess lung cancer risk diminishes with time from exposure, and some data show that the excess risk may disappear completely in 30 to 40 years subsequent to a single exposure (*12*).

The National Council on Radiation Protection and Measurements (NCRP) model was the first to include the risk reduction with time from exposure (*13*). It is a modified absolute risk projection model, with risk expression beginning at age 40 to follow the natural disease mortality, a 5-year minimum latent interval, and an exponential reduction of excess risk following each (single year's) exposure. In this way, continuous exposure can be modeled by the appropriate summations and correction for competing causes of death. The NCRP model of lung cancer following a single exposure is shown below.

$$CA(t) = \sum_{t_0}^{85} RC\, D \exp[-\lambda(t - t_0)]$$

where CA is the lung cancer mortality at age t, following an exposure at age t_0. CA $(t) = 0$ for $t < 40$; RC is the risk coefficient, 10 lung cancers per year per million persons per WLM; λ is the falloff rate for risk, $t_{1/2} = 20$ years; D is the exposure at t_0 in WLM; t is the age specified; and t_0 is the age at exposure.

The National Academy of Sciences (*14*) used a modified relative risk projection model with a 5-year minimum latency and a step function reduction in excess risk following exposure. At 15 years subsequent to exposure, the relative risk coefficient (increase in baseline lung cancer rate per WLM exposure) becomes one-half that at times from 5 to 15 years following exposure. In this model, risk is also reduced with attained age such that after age 65 the risk coefficient is 0.4 of the value at age 55 to 64.

The BEIR IV model of lung cancer following a single exposure is shown below.

$$r(a) = r_0(a)\,[1 + 0.025\,\gamma(a)\,(W_1 + 0.5\,W_2)]$$

where $r(a)$ is the age-specific lung cancer mortality rate; $r_0(a)$ is the background lung cancer mortality rate; $\gamma(a)$ is the correction for attained age: $<54 = 1.2$, $55–64 = 1.0$, $>65 = 0.4$; W_1 is the WLM exposure between 5 and 15 years before age a; and W_2 is the WLM exposure 15 years or more before age a.

Although the BEIR IV committee analyzed the data from four mining cohorts and found diminishing risk of lung cancer following cessation of exposure in all of the groups, the model developed assumed a step function with reduced risk after 15 years remaining constant to the end of life. Data from the Czech uranium miner cohort indicate that continuing the excess risk to end of life is not appropriate and that excess risk from radon exposure persists only for about 35 years (*12*).

These models may be used to sum the excess risk over a full lifetime or to calculate the number of lung cancers seen annually in a population with a particular age composition. The lifetime risk and annual risk are calculated for various models in Table 3. If the BEIR IV model is corrected so that risk following each annual exposure persists for 35 years, rather than for full life, the lifetime lung cancer risk is almost halved.

Table 3. Lung cancer risk for continuous exposure to 1 WLM/year (4 pCi/L) as predicted by various models.

Reference	Lifetime risk	Model type	Comment
(*13*)	0.9	Modified absolute	Risk decreases with time from exposure
(*12*)	1.6	Constant relative	
	1.1	Constant additive	
(*16*)	1.3-5.0	Constant relative	Exposure for 70 years 75% of time
(*14*)	3.4 (2.2)[a]	Modified relative	Risk decreases with time from exposure
	1.4 (0.9)[a]		

[a]BEIR IV values modified to express risk for 35 years after exposure rather than for entire lifetime.

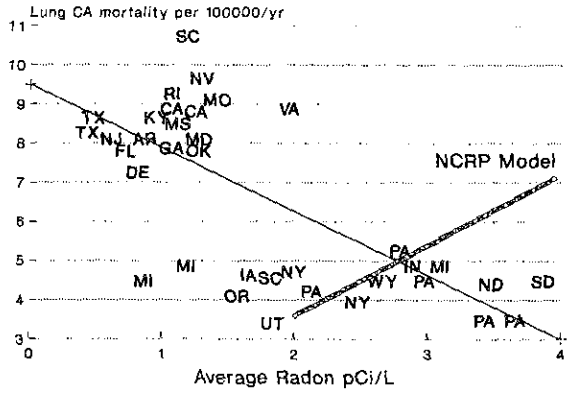

FIGURE 1. Radon exposure versus white female lung cancer mortality (1950–1959). Data from B. Cohen (unpublished).

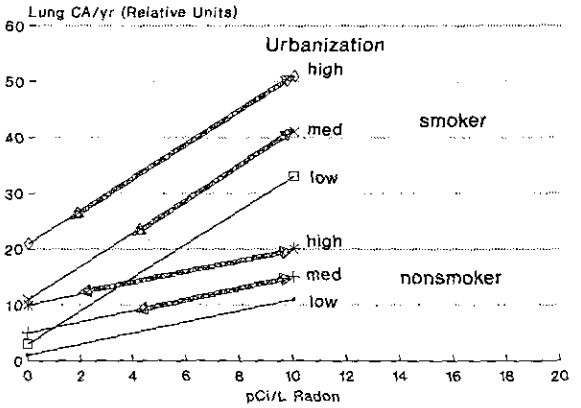

FIGURE 2. Model predictions of lung cancer as a function of radon, urbanization, and smoking.

The EPA used a constant relative risk model and the ICRP both a constant relative and additive risk model. These are not as faithful to the time pattern of appearance of lung cancer following exposure, and the numerical results (with the exception of the upper range of the EPA model) differ by a factor of 3. Thus, until better information on the actual temporal pattern of appearance in miner or environmental populations is available, the uncertainty in the models remains about a factor of 3.

Proposed Methodology

Figure 1 is taken from Bernard Cohen's studies to show the negative correlation that he finds between measured average radon exposure in U.S. counties and lung cancer mortality. This negative relationship persists in all of his data so far. The large variation in lung cancer mortality rate with geographic location at the same radon concentration in Figure 1 is indicative that a lung carcinogen other than radon predominates. The present radon risk projection models suggest that a baseline mortality rate of less than 7 per year per 100,000 for a true long-term radon exposure of 4 pCi/L is impossible. Cohen's data show mortality rates generally less than 5×10^{-5} for this exposure (unpublished manuscript), a clear inconsistency. It is possible that either the models are wrong or the true radon exposure of persons in these counties over the last 30 to 40 years is incorrectly assessed by the current measurements.

In an attempt to examine qualitatively the relationship between exposure and other factors bearing upon lung cancer risk, the following stylistic model is proposed. Three factors appear to be the dominant factors in lung cancer mortality: urbanization, smoking, and radon exposure. Further, some interaction between (or among) factors is likely.

Alpha radiation from radon daughters can transform cells that may later proliferate due to (perhaps) nonspecific stimulation or promotion from smoking or urban pollution. These transformed cells apparently disappear with time due to cell death, so that the effect of a given radon exposure lasts for 30 to 40 years. It is proposed that the total annual lung cancer mortality rate is proportional to the three factors plus their interactions. It is doubtful that multiplicativity of the factors is correct, but the numerical results are manipulated this way to examine the maximum effects upon an exposed population. Such a model might be

$$\text{Annual Lung Cancer} = K_1X_1 + K_2X_2 + K_3X_3 + K_4X_1X_2 + K_5X_1X_3 + K_6X_2X_3$$

where X_1 is the urbanization factor (1, 5, 10 for cities $<$100,000, 500,00, 1,000,000 population); X_2 is the smoking factor (0, 1 for nonsmoker or smoker); X_3 is the radon factor (1, 4, 10 for 1, 4, 10 pCi/L); and $K_{1\text{-}6}$ are the coefficients related to the magnitude of their impact (assumed here to equal 1).

Figure 2 is a plot of this model for a wide range of the three variables. The dashed portions of the lines indicate situations that have never been observed in the environment, namely, high radon in a large city.

From Figure 2, it is clear that if this form of model were actually to apply to lung cancer mortality, the impact of high and low radon exposure could be easily obscured by smoking or urbanization. For example, nonsmokers exposed at 10 pCi/L (2 WLM/year) in a low urbanization setting could have lower lung cancer mortality than nonsmokers in a highly urban setting, regardless of radon exposure. A study comparing low and high radon exposure in these differing urbanization settings would not be able to detect an effect from radon. Similarly, smoking can overwhelm the effect of radon exposure.

If radon-related lung cancer is to be investigated in the environment, a study methodology is needed to account for urbanization and smoking as well as radon exposure history. Smoking can be accounted for if adequate smoking history is available, but very little is known concerning the effects of urbanization on lung cancer except that it is a positive variable.

Studies where very different urbanization exists, but are assumed to be comparable, seem doomed to fail. If a highly urban location with high radon existed, this would provide a sensitive indicator of radon effects, but such a city has not been identified.

Urbanization is one term used as a variable in the model. In fact, urbanization as a surrogate for air pollution may not be

appropriate and may depend upon local factors such as the particular industries in an area, etc. A study in areas with low urbanization remains as one hope of resolving any identifiable effects. Smoking may be accounted for if sufficient smoking history is available. If the true effects of environmental exposure to radon can be deduced in a population, it is then possible to calculate more reliable estimates of radon-induced lung cancer in the entire U.S.

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