Threshold for Radon-Induced Lung Cancer From Inhaled Plutonium Data

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Abstract
Cohen’s lung cancer mortality data, from his test of the LNT theory, do not extend to the no observed adverse effects level (NOAEL) above which inhaled radon decay products begin to induce excess lung cancer mortality. Since there is concern about the level of radon in homes, it is important to set the radon limit near the NOAEL to avoid the risk of losing a health benefit. Assuming that dogs model humans, data from a study on inhaled plutonium dioxide particulates in dogs were assessed, and the NOAEL for radon-induced lung tumors was estimated to be about 2100 Bq/m³. The US Environmental Protection Agency should consider raising its radon action level from 150 to at least 1000 Bq/m³.

Keywords
radon, inhaled plutonium, radiation hormesis, lung cancer, NOAEL, LNT

Introduction
Indoor radon concentrations, in becquerels (note 1) per cubic metre (Bq/m³), vary widely. While the average radon levels in countries range from 11 Bq/m³ in Australia to 120 Bq/m³ in Finland, maximum values above 50 000 Bq/m³ have been measured.¹ There is fear about the risk of lung cancer due to inhaled radon gas because of the widespread publicity given to the studies that link lung cancer incidence to radon concentration using a linear no-threshold (LNT) model. They predict alarming excess cancers at low radon levels by linear interpolation in the radon range from 0 to high levels (in uranium mines), where excess cancer incidence was observed. Little publicity has been given to the studies that actually measured home radon levels in the range from 50 to 1500 Bq/m³, examined the lung cancer incidence of the residents, and observed a significant decrease below the natural incidence of lung cancer.²-⁴ These observations contradict the predictions made using the LNT dose–response model.

Studies on Inhaled Radon and Plutonium
Cohen⁵ tested the LNT theory by measuring radon levels in counties throughout the United States and correlating them with the lung cancer mortality in each of the counties. His data do not extend to the “no observed adverse effect level” (NOAEL), which is defined in Figure 1. When the concentration reaches the NOAEL, inhaled radon decay products begin to induce excess lung cancer mortality. Since there is a regulatory limit for radon in homes,⁶ it is important to set this limit just below the NOAEL, to avoid the risk of losing an important health benefit.⁷

The Schneeberg Study² identified the NOAEL to be about 1000 Bq/m³. The Worcester County Study concluded that the possibility of a hormetic effect on lung cancer at low radiation doses cannot be excluded.³ The analysis model predicts an adjusted odds ratio of less than 1.0 for radon concentrations up to 545 Bq/m³.⁴ The cases and the controls had similar, relatively low, mean radon exposures of 60.2 and 66.3 Bq/m³, respectively.

Assuming that dogs model humans, many radiation studies are carried out on dogs because their life spans are about 5 times shorter, and the confounding factors can be controlled much better than in human studies. Fisher and Weller⁸ examined the dose–response relationship from studies by Park et al⁹,¹⁰ on lung cancer formation in beagle dogs from inhaled ²³⁹PuO² particulates. These studies were carried out from the mid-1960s through the 1980s. The incidence of lung tumors in the control dog was 18% (5 of 28) and only 16% (7 of 45) in dogs that received lung doses ranging from 8 to 195 cGy. Fisher and Weller⁸ pointed out that the data did suggest a possible

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beneficial health effect—suppression of the high incidence of naturally occurring lung cancer by a low radiation level.

A commentary by Cuttler and Feinendegen supported this observation and drew attention to the overall shape of the dose-response curve by showing, in Figure 2, the cumulative absorbed dose to the lungs on a logarithmic scale. The data contradict the expectation of a strong rise in the incidence of tumors with dose rate, due to the severe DNA damage caused by the $\alpha$-radiation. Reference was made to the large amount of data from a wide variety of medical treatments carried out over the past 120 years that employed low doses of radiation to achieve remarkably beneficial health effects. The biological process of upregulation of the adaptive protection systems by low doses or low dose rates of ionizing radiation was discussed, and the example of a clinical oncology study was given. The commentary identified and discussed several other studies on inhaled $^{239}$PuO$_2$ and other radionuclides that demonstrate longer life times than the controls at low dose rate and a threshold for life span reduction.

A threshold at $\sim$ 0.80 Gy for incorporated plutonium was determined in a multiparametric analysis of lung cancer dose-response relationships for 500 Mayak nuclear workers, 162 cases with cancer, and the control group of 338 workers who did not become ill with cancer in the same period. They were chronically exposed by inhalation to $^{239}$Pu. The data of this clinical-epidemiological, case-control study were subject to confounding factors, and smoking was the major confounding factor. Limitations in the analysis methodology were identified.

A life span study of female Wistar rats, exposed to $^{239}$PuO$_2$ aerosol, focused on survival and lung cancer. There were 1052 sham-control rats and 2105 in the exposed groups. The rats were also exposed to 1 to 2 mGy of $\gamma$-radiation from $^{169}$Yb that was incorporated in the aerosol particulates. Survival was significantly reduced only in rats with lung doses $>30$ Gy. One adenocarcinoma was found in the controls, and only 4 adenomas were seen in the exposed rats at lung doses $<1.5$ Gy. The lowest doses at which lung tumors appeared were 1.5 Gy, for squamous cell carcinoma. The incidence of all lung tumors was 0.095% in control rats, 0.21% in 1877 rats with lung doses $<1$ Gy, and 41% in 288 rats with doses $>1$ Gy, the threshold lung dose.

**Protection Against Lung Cancer by $\gamma$-Radiation**

Low dose rate $\gamma$-radiation, from inhaled particulate radionuclides, stimulates protective processes that prevent lung cancer, while high dose rate radiation inhibits these processes. The low-level radiation stimulates the signaling that leads to activated natural protection (ANP). $\gamma$-radiations from inhaled $\alpha$ emitters (and $^{169}$Yb, when present) activate the ANP, which suppresses both naturally occurring lung tumor incidence (18% in the control dogs) and the $\alpha$-radiation–induced tumors, in the low dose rate range. However, as the plutonium lung burden increases, a level is reached at which the $\alpha$-radiation overwhelms or inhibits the ANP. It can no longer suppress the formation of lung tumors. The NOAEL is the dose rate level at which the lung tumor incidence rises back to the natural incidence level. Figure 2 indicates that the NOAEL for inhaled $^{239}$PuO$_2$ in dogs occurs at a cumulative absorbed dose to the lungs of about 60 cGy.

After many studies on beagle dogs, Raabe discovered that it is the dose rate, not the cumulative dose, that determines the radiation-induced cancer risk. Since the average life span of beagle dogs is about 5000 days, and since the inhalation occurred at 550 days, therefore the duration of the exposure at the NOAEL was about 4450 days or 12 years. This corresponds to an average dose rate of about 60 $\div$ 12 = 5.0 cGy/year.

**Estimating the NOAEL for Inhaled Radon**

Can the NOAEL for inhaled radon in humans be estimated, based on the NOAEL for inhaled $^{239}$PuO$_2$ in dogs? There is evidence that low-dose $\gamma$-radiation protects against lung cancer formation in rats and humans inhaling $^{239}$PuO$_2$ particles. Inhalation of residential radon, which emits $\alpha$- and $\gamma$-radiations, may also protect against lung cancer. Radiation hormesis is induced by low-level radon radioactive progeny (decay products) for the ANP against lung cancer.

It should be noted that the spatial and temporal dose distribution patterns are different for inhaled radon and inhaled $^{239}$PuO$_2$ particles. The pattern for inhaled $^{241}$Am and $^{244}$Cm oxides are more like radon, since the particles are soluble with rapid clearance and provide a more homogeneous dose pattern. (Radon is continuously replenished.) The widely varying dose patterns in the lung from inhaled $^{239}$Pu, $^{241}$Am, and $^{244}$Cm oxides in the rat did not result in significant differences in lung tumor formation at lung doses of less than 1.0 Gy.

International Commission on Radiological Protection Publication 115 on human lung cancer risk from radon and progeny determined that 17 mSv is the annual effective dose for the reference radon level of 300 Bq/m$^3$, with a 0.4 equilibrium factor and a 80% occupancy. Since the effective dose uses the $\alpha$-radiation and lung tissue weighting factors of 20 and 0.12,
respectively, the mean absorbed dose rate that corresponds to 300 Bq/m$^3$ is $17 \div (20 \times 0.12) = 7.1$ mGy/year. Therefore, the radon level that corresponds to the 60 cGy NOAEL for inhaled $^{239}$PuO$_2$ in dogs is $300 \times 5.0 \div 0.71 = 2100$ Bq/m$^3$. This radon level is shown in Figure 3, along with the Cohen radon data.\textsuperscript{5}
Many other studies reviewed by Cuttler and Feinendegen show that there is a threshold in the region of about 100 cGy in the lung dose required to induce cancer in that organ.\textsuperscript{11} This suggests that the estimated NOAEL of 2100 Bq/m$^3$ for radon in this article is low and could be at least 50\% higher.

**Conclusion**

The EPA action level for reducing radon in homes\textsuperscript{6} is 4 pCi/L (150 Bq/m$^3$). This limit is 14 times lower than the NOAEL of 2100 Bq/m$^3$ estimated in this article. The very low action level has been causing undue fear and unwarranted costs to many homeowners as well as a reduction in the market prices of their radon-stigmatized homes. It should also be noted that radon remediation significantly increases lung cancer mortality, as shown in Figure 3. To dispel the fear and eliminate this economic burden, the action level should be raised by a factor of at least 7 to about 1000 Bq/m$^3$ (27 pCi/L), where the health benefit is near optimum.

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**Note**

1. Becquerel (Bq) = disintegrations per second is the SI unit for rate of decay of a radioactive substance.

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