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Radon and lung cancer: Assessing and mitigating the risk

ABSTRACT

Radon is a naturally occurring radioactive gas. Its progenies emit alpha particles capable of causing tissue damage. Radon exposure is estimated to be the second most common cause of lung cancer in the United States. Management of patients with a history of radon exposure should involve a lung cancer specialist.

KEY POINTS

Radon is a noble gas that occurs naturally as a decay product of uranium 238 and thorium 232.

Radon 222 decays to polonium 218 and then, after several intermediate steps, to polonium 214, both of which emit alpha particles, which are highly effective in damaging tissues.

Radon exposure is associated with increased lung cancer incidence in underground miners. In the general population, it is estimated to be the second most common cause of lung cancer, after cigarette smoking.

There is no evidence yet of a benefit of lung cancer screening based on radon exposure.

IN 1984, A WORKER AT a Pennsylvania nuclear power plant triggered the radiation detector as he was getting ready to go home. This would not be unusual for such a facility, but there was no nuclear fuel on site at the time. The alarm went off every time he left work.

One day, he triggered the alarm as he crossed the detector on arriving at the plant, leading him to suspect that he was bringing radiation from home. He eventually convinced the plant's health physicists to check his home, although at first they were opposed to the idea. The results revealed high concentrations of radon everywhere, especially in his basement.

Radon was already known to be associated with health risks in underground miners at that time. This event revealed that a naturally occurring radioactive gas could be found in households at potentially hazardous concentrations.

The incident captured the public's attention, and the Environmental Protection Agency (EPA) and the US Centers for Disease Control and Prevention (CDC) recommended that nearly all homes be tested.^{1,2} In 1988, the International Agency for Research on Cancer classified radon as a human carcinogen, and Congress passed the Indoor Radon Abatement Act in response to growing concern over health risks.³ This law funded state and federal measures to survey schools and federal buildings for radon levels, to educate citizens, and to develop programs for technical assistance. The long-term goal was to reduce indoor levels nationwide to no more than outdoor levels.

Radon is still considered an important public health hazard. From 15,000 to 21,000

people are estimated to die of lung cancer as a result of radon exposure each year in the United States, making it the second most common cause of lung cancer, behind smoking.⁴

Considering the relevance of this issue, this article will review the unique characteristics of radon as a risk factor for lung cancer.

■ WHAT IS RADON?

Radon is a noble gas that occurs naturally as a decay product of uranium 238 and thorium 232. It is colorless, tasteless, and imperceptible to our senses. Its most common isotope is radon 222 (²²²Rn), which has a half-life of 3.8 days and decays by emitting an alpha particle to become polonium 218. The decay chain continues through several intermediate steps until the stable isotope lead 206 is formed (FIGURE 1). Two of the isotopes in this chain, polonium 218 and polonium 214, also emit alpha particles.⁵⁻⁷

Radon is primarily formed in soil. Its most important precursor, uranium 238, is ubiquitous, found in most soils and rocks in various concentrations. Radon can also be found in surface water, metal mines (uranium, phosphorus, silver, gold), residue of coal combustion, and natural gas.

Outdoor levels are usually much lower than indoor levels, as radon dissipates very quickly. Indoor radon mostly comes from the soil under the house or building, but it can also originate from coal combustion, gas appliances, and water (especially from private wells). In municipal water systems or surface reservoirs, most of the radon dissipates into the air or decays before the water reaches homes.^{8,9}

Radon's only commercial application in the United States is in calibrating measuring instruments. In the past, it was used in radiography and to treat cancer but was later replaced by other radiation sources that cost less and pose less hazard of alpha radiation.¹⁰

■ HOW RADON CAN HARM

Alpha particles, emitted by radon 222 and its progenies polonium 218 and polonium 214, are highly effective in damaging tissues. Al-

though they do not travel far or fast, with their two protons and two neutrons, alpha particles are heavy and therefore can cause considerable damage at short range. Although alpha particles can be stopped by a thin barrier such as a piece of paper or the skin, if the source is inhaled or ingested and lodges against mucosal linings, the alpha particles emitted can destroy cells.¹¹

The main route of radon exposure is by inhalation. Since radon is biologically inert, it is readily exhaled after it reaches the lungs. However, radon's progenies can also be inhaled, either as free particles or attached to airborne particles such as dust, which they tend to attract as a result of their charged state. This attached fraction is believed to be more carcinogenic because it tends to deposit on the respiratory epithelium, notably in the carinae of bronchi. The smaller the dust particle, the deeper it can travel into the lung. The radiation emissions damage the genetic material of cells lining the airways, with the potential to result in lung cancer if the repair process is incomplete.^{5,8,9}

Other routes of exposure include ingestion and dermal exposure. Radon and its progenies can be swallowed in drinking water, passing through the stomach walls and bowels and entering the blood.¹² Dermal exposure is not considered a significant route unless the dermis is exposed, since in usual circumstances the skin protects the body from alpha radiation.¹³

Possible biologic mechanisms by which radon exposure might increase the risk of cancer include gene mutations, chromosome aberrations, generation of reactive oxygen species, up- or down-regulation of cytokines, and production of proteins associated with cell-cycle regulation.¹⁴⁻¹⁶

■ HOW IS RADON MEASURED?

Several devices are commercially available to measure radon levels at home. The most common ones are activated charcoal detectors, electret ion chambers, alpha-track detectors, electronic integrating devices, and continuous monitors. There is no evidence that one device is better than another, but devices that measure radon gas are usually preferred over

Up to 21,000 people die of lung cancer from radon exposure each year in the United States

Radon 222: A risk factor for lung cancer

Radon 222, an odorless, colorless, radioactive gas, decays through several stages in a chain that ends in stable lead 206. Of its progenies, polonium 218 and polonium 214 are particularly dangerous because they can lodge in the lungs and emit alpha particles, with potential for carcinogenesis.

Radon 222 decay process



Radionuclides attach to airborne particles, such as dust, and are inhaled

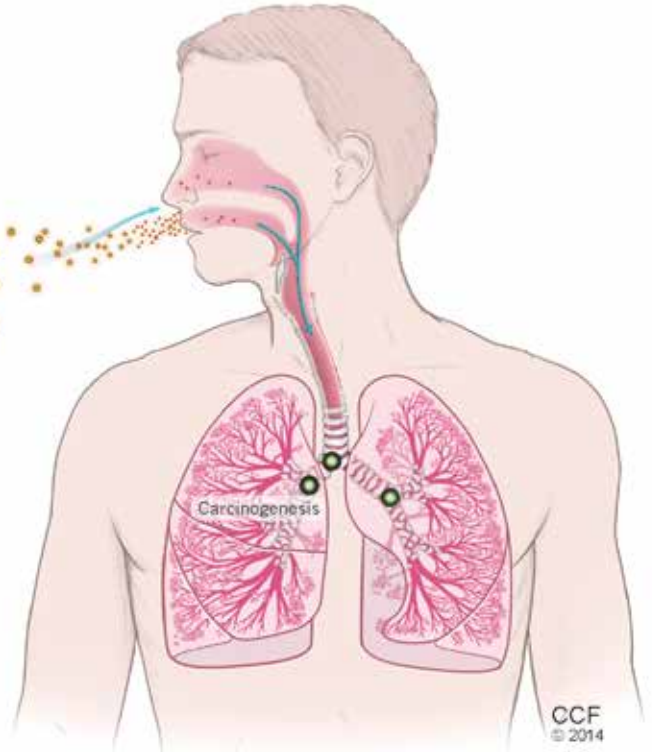


FIGURE 1

those that measure decay products because they are simpler to use and more cost-effective. These devices are divided into those used for short-term testing (2–90 days) and long-term testing (TABLE 1).¹⁷

Radon levels can be expressed as follows:

Working levels. One *working level* (WL) is any combination of radon progeny in 1 L of air that ultimately releases 1.3×10^5 MeV of alpha energy during decay. In studies of miners, the radon progeny concentrations are generally expressed in WL. The cumulative exposure of an individual to this concentration over a “working month” of 170 hours is defined as a *working level month* (WLM).

Picocuries per liter. In the United States,

the rate of decay is commonly reported in picocuries per liter (pCi/L): 1 pCi/L translates to 0.005 WL under usual conditions. The outdoor radon level is normally around 0.4 pCi/L.

Becquerel per cubic meter (Bq/m³) is an International System unit of measure: 1 WL corresponds to 3.7×10^3 Bq/m³, and 1 pCi/L is equivalent to 37 Bq/m³.

Different areas have different radon levels

The Indoor Radon Abatement Act of 1988 helped identify areas in the United States that have the potential for elevated indoor radon levels. An estimated 6 million homes have concentrations greater than 4 pCi/L.

TABLE 1

Radon measuring devices and their sampling periods

Type of detector	Sampling period	Short-term	Long-term
Activated charcoal	2–7 days	x	
Electret ion chamber	5 days–1 year	x	x
Alpha-tracking	1–2 months	x	
Electronic integrating device	2 days–years	x	x
Continuous	1 hour–years	x	x

To assist in implementing radon-reducing strategies and allocation of resources, the EPA has created a map (FIGURE 2) that classifies counties according to the predicted indoor level.¹⁸

WHAT IS THE RELATIONSHIP BETWEEN RADON AND LUNG CANCER?

Determining the degree to which radon exposure contributes to lung cancer is a complex task. Radon can be found nearly everywhere, and there are diurnal, seasonal, and random year-to-year variations in the concentration of radon in indoor air.

A minority view

Not everyone agrees that radon is completely bad. For centuries, people have flocked to spas to “take the waters,” and the water at many of these spas has been found to contain radon. In the early 20th century, radiation was touted as having medicinal benefits, and people in many places in the world still go to “radon spas” (some of them in abandoned uranium mines) to help treat conditions such as arthritis and to feel invigorated and energized.

In 2006, a report by Zdrojewicz and Strzelczyk¹⁹ urged the medical community to keep an open mind about the possibility that radon exposure may be beneficial in very low doses, perhaps by stimulating repair mechanisms. This concept, called *hormesis*, differs from the mainstream view that cancer risk rises linearly with radiation dose, with no minimum threshold level (see below).

Risk in miners

As early as in the 16th century, metal miners in central Europe were noted to have a high rate of death from respiratory disease. Radon was discovered in 1900, and in the 20th century lung cancer was linked to high levels of radon detected in uranium mines.

Several small studies of underground miners exposed to high concentrations of radon consistently demonstrated an increased risk of lung cancer.

The Committee on the Biological Effects of Ionizing Radiation (BEIR VI 1999) reviewed 11 major cohort studies of miners. The studies included more than 60,000 miners in Europe, North America, Asia, and Australia, of whom 2,600 died of lung cancer. Lung cancer rates increased linearly with cumulative radon exposure, and the estimated average increase in the lung cancer death rate per WLM in the combined studies was 0.44% (95% confidence interval [CI] 0.20–1.00%). The percentage increase in the lung cancer death rate per WLM varied with time since exposure, with the highest increase in risk during the 5 to 14 years after exposure.^{4,17} Furthermore, the increase in risk was higher in younger miners, who were exposed to a relatively low radon concentration.

Risk in the general population

The magnitude of the risk in miners led to concern about radon exposure as a cause of lung cancer in the general population. Statistical models were generated that suggested a causal link between radon exposure and lung cancer. Although extrapolation of the results from miners caused controversy, the BEIR VI estimation of risk was validated by studies in the general population.^{7,20–23}

Since the 1980s, several small case-control studies with limited power examined the relationship between indoor radon and lung cancer in the general population. In these studies, individuals who had developed lung cancer were compared with controls who had not developed the disease but who otherwise represented the population from which the cases of lung cancer came.

To improve the statistical power, the investigators of the major studies in Europe, North America, and China pooled the results

An estimated 6 million homes have concentrations > 4 pCi/L

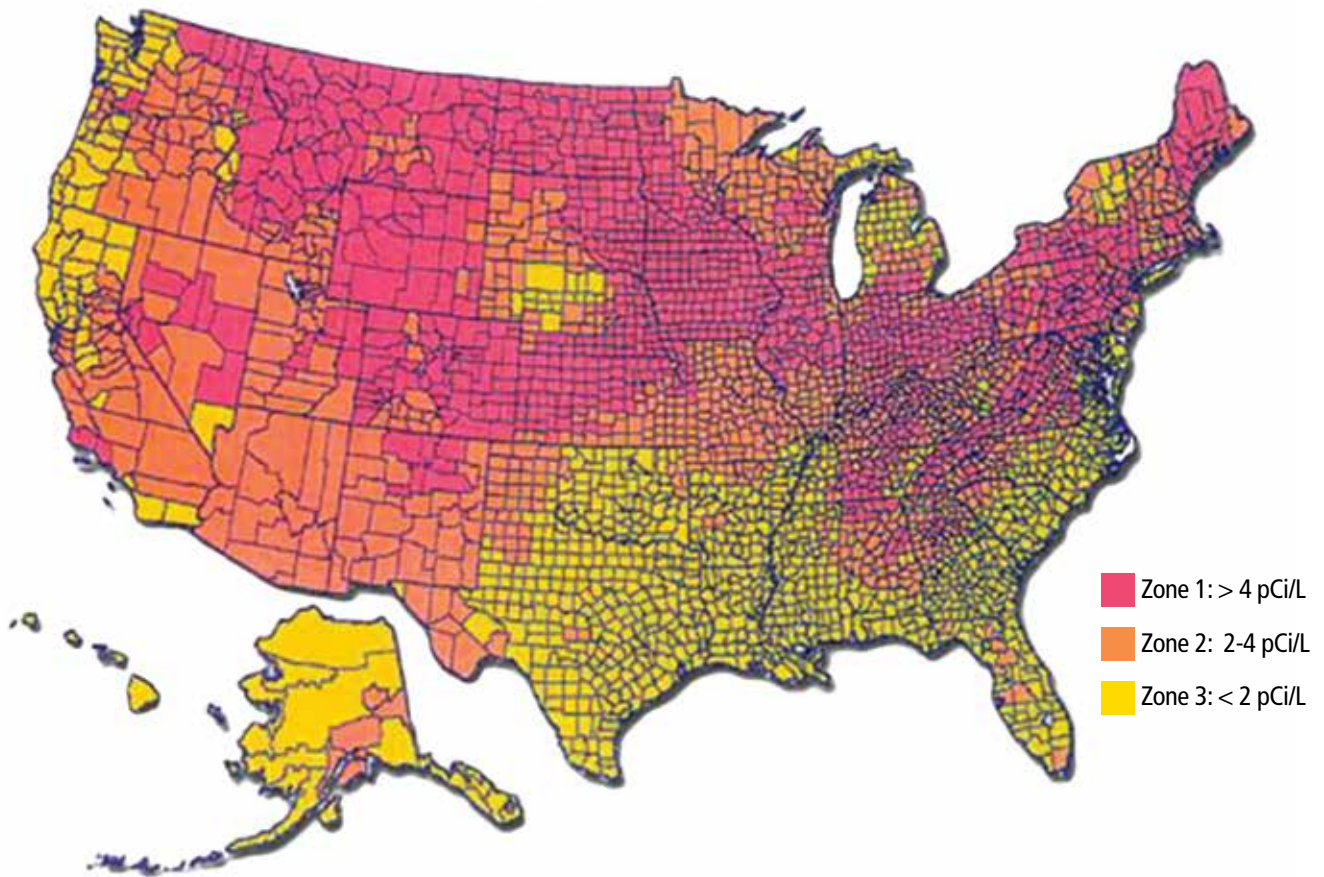


FIGURE 2. Radon distribution in the United States with zone classification according to the predicted indoor level.

FROM THE US ENVIRONMENTAL PROTECTION AGENCY. WWW.EPA.GOV/RADON/.

in separate analyses (TABLE 2).^{7,20–23} The average radon concentration to which each individual had been exposed over the previous decades was estimated by measuring the radon concentration at their present and previous homes. On the basis of information from the uranium miners, these studies assumed that the period of exposure was the 30 years ending 5 years before the diagnosis or at death from lung cancer.

The results provided convincing evidence that radon exposure is a cause of lung cancer in the general population and substantiated the extrapolation from the studies of miners. Further, the results of all three pooled analyses were consistent with a linear dose-response relationship with no threshold, suggesting an increased risk of lung cancer even with a radon level below 4 pCi/L (200 Bq/m³), which is the concentration at which mitigation actions

are recommended in many countries.¹⁷

The North American pooled analysis included 3,662 cases and 4,966 controls from seven studies in the United States and Canada. When data from all studies were combined, the risk of lung cancer was found to increase by 11% per 100-Bq/m³ (about 2.7-pCi/L) increase in measured radon concentration (95% CI 0%–28%). The estimated increase in lung cancer was independent of age, sex, or smoking history.^{7,20}

The Chinese pooled data²² demonstrated a 13% (95% CI 1%–36%) increased risk per 100 Bq/m³.

In the European study, the risk of lung cancer increased by 8% per 100 Bq/m³ (95% CI 3%–16%). The European investigators repeated the analysis, taking into account the random year-to-year variability in measured radon concentration, finding the final

TABLE 2

Pooled analyses of case-control studies of radon exposure in the general population

Geographic area	Studies	Cases	Controls	Risk^a
North America ⁷	7	3,662	4,966	11 (0–28)
Europe ²¹	13	7,148	14,208	8 (3–16)
China ²²	2	1,050	1,995	13 (1–36)

^aPercent increase in lung cancer risk per 100-Bq/m³ increase in the radon concentration and the 95% confidence interval

Risk in miners led to concern about radon as a cause of lung cancer in the general population

estimated risk was an increase of 16% per 100 Bq/m³ using long-term average concentration.²¹

The combined estimate^{21,24} from the three pooling studies based on measured radon concentration is an increased risk of lung cancer of 10% per 100 Bq/m³.

Synergistic risk with smoking

Radon exposure was independently associated with lung cancer, and the relationship with cigarette smoking is believed to be synergistic. The radon progeny particles attach themselves to smoke and dust and are then deposited in the bronchial epithelium.²⁵

In the pool of European case-control studies, the cancer risk for current smokers of 15 to 24 cigarettes per day relative to that in never-smokers was 25.8 (95% CI 21–31). Assuming that in the same analysis the lung cancer risk increased by 16% per 100 Bq/m³ of usual radon concentration regardless of smoking status, the cumulative absolute risk by age 75 would be 0.67% in those who never smoked and 16% in smokers at usual radon levels of 400 Bq/m³ (11 pCi/L).²¹

Rates of all lung cancer subtypes increased

Radon exposure is not associated with a specific histologic subtype of lung cancer. It has been speculated that the incidence of the small-cell subtype might be slightly increased because radon tends to deposit in the more central bronchial carinae.^{20,21} However, all subtypes have been described in association with radon, the most common being adenocarcinoma and squamous cell carcinoma.^{26–28}

EFFECT OF MITIGATION MEASURES

The US Surgeon General and the EPA recommend that all homes be tested.¹⁸ Short-term tests should be used first, keeping in mind that diurnal and seasonal variations may occur.

The World Health Organization has proposed a reference level of 100 Bq/m³ (2.7 pCi/L) to minimize health hazards from indoor radon exposure.¹⁷ If this level cannot be reached under the country-specific conditions, the chosen reference level should not exceed 300 Bq/m³ (8 pCi/L).

In the United States, if the result of home testing is higher than 4 pCi/L, a follow-up measurement should be done using a different short-term test or a long-term test. If the follow-up result confirms a level of more than 4 pCi/L, mitigating actions are recommended. The goal is to reduce the indoor radon level as much as possible—down to zero or at least comparable to outdoor levels (national average 0.4 pCi/L).¹⁸

A variety of radon mitigation strategies have been used, with different rates of efficacy (TABLE 3). The optimal strategy depends on the likely source or cause, construction characteristics, soil, and climate.²⁹ TABLE 4 lists resources for the general public about testing and mitigation measures.

How beneficial is radon mitigation?

Although it is logical to try to reduce the indoor radon concentration, there is no strong evidence yet that this intervention decreases the incidence of lung cancer in the general population.

Using the BEIR VI risk model, Méndez et al³⁰ estimated a 21% reduction in the an-

nual radon-related lung cancer mortality rate by 2100 if all households were compliant with government recommendations (mitigation actions at levels of 4 pCi/L) and assuming that the percentage of cigarette smokers remained constant.

On the other hand, if the number of smokers continues to decline, the benefits from radon mitigation may be less. The expected benefit from mitigation in this scenario is a reduction of 12% in annual radon-related deaths by the year 2100.³⁰ However, it will be challenging to determine whether the expected decline in the incidence of lung cancer and lung cancer deaths is truly attributable to mitigation measures.

MANAGING PATIENTS EXPOSED TO RADON
Screen for lung cancer in smokers only

The National Lung Screening Study (NLST) was a large multicenter trial of annual low-dose computed tomography (CT) to screen for lung cancer in a cohort at high risk: age 55 to 74, at least a 30 pack-year history of smoking in a current smoker, or a former smoker who quit within the past 15 years. The trial demonstrated a 20% reduction in lung cancer deaths in the CT screening group.³¹

Since the publication of the NLST results, many societies have endorsed screening for lung cancer with low-dose CT using the study criteria. The National Comprehensive Cancer Network (NCCN) expanded these criteria and has recommended screening in patients over age 50 who have a history of smoking and one additional risk factor, such as radon exposure.

However, radon exposure has not been incorporated into a lung cancer risk-prediction model, and there is no empirical evidence suggesting that people who have such a history would benefit from screening.^{32,33} The joint guidelines of the American College of Chest Physicians and American Society of Clinical Oncology recommend annual low-dose CT screening only for patients who meet the NLST criteria.³⁴

What to do about indeterminate lung nodules

The widely used guidelines from the Fleischner Society³⁵ on how to manage small lung

TABLE 3

Radon mitigation techniques and their estimated reduction of indoor radon levels

Technique	Indoor radon reduction
Subslab suction	50%–99%
Passive subslab suction	30%–70%
Drain-tile suction	50%–99%
Block-wall suction	50%–99%
Sump-hole suction	50%–99%
Submembrane depressurization	50%–99%
Natural ventilation	Variable
Basement pressurization	50%–99%
Aeration of private water well	95%–99%
Activated charcoal for private water well	85%–99%
Sealing of entry routes	Must be combined with another mitigation measure

BASED ON INFORMATION IN REFERENCES 17 AND 29.

nodules stratify patients into groups at low and high risk of developing lung cancer on the basis of risk factors. The guidelines apply to adults age 35 and older in whom an indeterminate solid nodule was recently detected.

If a patient is at high risk, the recommended approach includes follow-up in shorter intervals depending on the nodule size. History of smoking is recognized as a major risk factor, and the statement also lists family history and exposure to asbestos, uranium, and radon.³⁵

Although the association of radon with lung cancer has been shown in epidemiologic studies, radon exposure has not been included in validated statistical models that assess the probability that an indeterminate lung nodule is malignant. We would expect the risk to be higher in miners, who suffer a more intense exposure to higher levels of radon, than in the general population, which has a low and constantly variable residential exposure. Furthermore, there are no data to support a more aggressive follow-up approach in patients with indeterminate lung nodules and a history of radon exposure.

An estimated 6 million homes have a radon concentration above 4 pCi/L

TABLE 4

Radon resources for the general public

US Environmental Protection Agency

www.epa.gov/radon/pubs/citguide.html

A citizen's guide to radon

National Radon Hotline

1-800-SOS-RADON (1-800-767-7236)

Purchase radon test kits by phone

National Radon Helpline

1-800-55RADON (1-800-557-2366)

Live help for radon questions

National Radon Fix-It Line

1-800-644-6999

General information about fixing or reducing the radon level at home

Safe Drinking Water Hotline

1-800-426-4791

For information on radon in water

Radon has not been incorporated into a lung cancer risk-prediction model

■ RADON AND OTHER CANCERS

When a person is exposed to radon, the bronchial epithelium receives the highest dose of ionizing radiation, but other organs such as the kidneys, stomach, and bone marrow may receive doses as well, although lower. Several studies have looked into possible associations, but there is no strong evidence to suggest an increased mortality rate related to radon from cancers other than lung.^{24,36} However, there seems to be a positive association between radon and the incidence of lymphoproliferative

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disorders in uranium miners.^{37,38}

Radon can be measured in drinking water, and a few studies have looked at a possible association with gastrointestinal malignancies. The results did not reveal a consistent positive correlation.^{39,40} The risk of cancer from exposure to radon in the public water supply is likely small and mostly from the transfer of radon particles into the air and not from drinking the water. On the other hand, the risk could be higher with private wells, where radon levels are variable and are possibly higher than from public sources.⁴¹

■ DATA ARE INSUFFICIENT TO GUIDE MANAGEMENT

Radon is a naturally occurring and ubiquitous radioactive gas that can cause tissue damage. Cohort and case-control studies have demonstrated that radon exposure is associated with increased risk of lung cancer. It is recommended that radon levels be measured in every home in the United States and mitigation measures instituted if levels exceed 4 pCi/L.

There are insufficient data to help guide the management of patients with a history of radon exposure, and prospective studies are needed to better understand the individual risk of developing lung cancer and the appropriate management of such patients.

Smoking cessation is an integral part of lung cancer risk reduction from radon exposure. ■

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