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Radon exposure: a major cause of lung cancer in nonsmokers

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ABSTRACT

Exposure to radon can impact human health. This is a nonsystematic review of articles written in English, Spanish, French, or Portuguese published in the last decade (2013-2023), using databases such as PubMed, Google Scholar, EMBASE, and SciELO. Search terms selected were radon, human health, respiratory diseases, children, and adults. After analyzing the titles and abstracts, the researchers initially identified 47 studies, which were subsequently reduced to 40 after excluding reviews, dissertations, theses, and case-control studies. The studies have shown that enclosed environments such as residences and workplaces have higher levels of radon than those outdoors. Moreover, radon is one of the leading causes of lung cancer, especially in nonsmokers. An association between exposure to radon and development of other lung diseases, such as asthma and COPD, was also observed. It is crucial to increase public awareness and implement governmental control measures to reduce radon exposure. It is essential to quantify radon levels in all types of buildings and train professionals to conduct such measurements according to proven efficacy standards. Health care professionals should also be informed about this threat and receive adequate training to deal with the effects of radon on human health.

Keywords: Radon; Lung neoplasms; Risk factors.

INTRODUCTION

Radon is a colorless and odorless radioactive gas that has a half-life of 3.83 days. It is formed from the radioactive decay of uranium from groundwater, soil, or rocks, and Its products are also colorless, tasteless, and odorless.[1,2]

Indoor (houses and buildings) radon concentrations vary and are influenced by several conditions: (a) geological characteristics of the site (permeability of the rocks, uranium content, and type of soil where the building is located); (b) the pathways that radon finds to infiltrate residences and commercial or noncommercial buildings; (c) the emanation of radon from building materials and ornamentation (such as granite floors and walls); (d) air exchange rate between interior and exterior areas, which depends on the type of building, ventilation systems, and how airtight (sealed) the building is.[3]

Nonspecific symptoms experienced by occupants due to the time spent in a building with poor indoor air quality are collectively designated "sick building syndrome."[4] Radon is harmful to the health of individuals exposed to it. Knowing the risks of such exposure is essential to prevent health damage.[5]

Radon seeps into buildings through cracks in floors or wall joints, gaps around pipes or cables, small pores in walls made of hollow concrete blocks, and open walls or ceilings. It usually reaches higher concentrations in cellars and living spaces in direct contact with the ground, but significant concentrations can also be found above the ground floor.[3] These concentrations can vary between adjacent buildings and within the same structure from one day to the next, or even within hours.[3]

The unit of measurement of radon is the Becquerel per cubic meter (Bq/m^3),[6] and the average concentration of radon in open air ranges from 5 Bq/m^3 to 15 Bq/m^3; however, it is higher in enclosed spaces, especially if they are poorly ventilated. In buildings such as schools, offices, and homes radon concentrations range from 10 Bq/m^3 to over 10,000 Bq/m^3.[7,8]

The WHO recommends that indoor radon concentrations should not be higher than 100 Bq/m^3.[4] It is adivisible that the reference level should not be higher than 300 Bq/m^3.[7,8] According to the International Commission on Radiological Protection,[9] the global effective dose attributed to this type of radiation is estimated to be 2.4 mSv/year. The sum of equivalent doses in the tissues or organs is the effective dose.

The *Projeto Planalto de Poços de Caldas* (Poços de Caldas Plateau Project),[10] a pioneering initiative in Brazil, aims to provide reliable, technically accurate, and ethically safe information to alert health professionals and the population about the effects of radon radiation on health. The study identified three sites with average doses above 10 mSv/year, namely: Morro do Ferro (in the rural zone in the city of Poços de Caldas), Morro do Taquari, and in a uranium mine (both in the rural area in the city of Caldas).[10]

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The second part of that project (2004-2013) identified that 21% of the households surveyed had a radon concentration higher than 200 Bq/m³, pointing to the need for the implementation of a permanent model for surveillance of exposure to natural radiation.[11]

In many countries, drinking water is obtained from underground sources, such as springs and wells. Often, these sources have higher concentrations of radon than does surface water from reservoirs, rivers, or lakes. Radon dissolved in drinking water is released into the indoor air; thus, the amount inhaled by breathing is more significant than that ingested from drinking water.[3]

These data are confirmed by a study carried out in Porto Alegre, Brazil, that determined the concentrations of radon in water samples obtained from (precambrian fractured and cenozoic porous) aquifers that feed that city; it was found that more than half of the samples analyzed reached up to 500 BqL,[12] which is above the maximum limit determined as safe by the WHO.[3]

According to radon properties, all buildings are potential sources of this gas, and its concentration is unique to each environment. People living or working in these buildings might be exposed to very high levels, which makes the problem more complex and difficult to address.[6]

IMPACTS OF RADON EXPOSURE ON HUMAN HEALTH

Exposure to radon inside the home can potentially lead to serious health problems. Lopez et al. have shown that radon concentrations can be higher in residential than in public buildings.[13]

Indoor air renewal in residential buildings may only occur for a short period of time since poor ventilation might occur at night, during winter, or during the day when people are away on business. This was confirmed when determining radon concentrations in Canadian homes: they were up to three times higher than in school buildings, 4.7 times higher than in other public buildings and indoor workplaces, and 12 times higher than in the air outdoors.[14]

School children exposed to median concentrations equal to, or greater than the recommended concentrations of fine particulate matter, benzene, limonene, ozone, and radon in a school environment significantly had more frequent systemic, ocular, and upper/lower airway symptoms (sick school syndrome) when compared with unexposed subjects.[4,15]

In children's schools, indoor radon concentrations are also influenced by ventilation types, attendance regime, and building characteristics.[16] Davis et al. found that classroom radon concentrations decreased when school ventilation systems were on.[17] Branco et al. reported that radon concentrations in daycare centers and elementary schools in Portugal were related to the year of construction of the buildings.[18]

Several factors have been identified as capable of interfering with indoor radon concentrations: number of occupants, ventilation, room location in the building,[19] and construction-related factors, since constructions located on the same geological substrate but with different types of building materials may present different indoor radon concentrations.[20,21] In addition, the duration of exposure to radon also has essential relevance. Children, for having a longer life expectancy, if exposed continuously, have a higher lifetime risk of developing cancer.[22,23]

Another topic recently highlighted is the occupancy bias within the residential environment. Newly built houses are mainly inhabited by younger people, who appear to be exposed to higher radiation rates (5.01 mSv/year). In contrast, homes built many years ago are occupied by older people who are exposed to lower radiation rates (3.45-4.22 mSv/year).[24] This observation is important and reinforces the previous citation that exposure to radon at a younger age may represent an increased lifetime risk of health problems.[22,23]

A study conducted in the metropolitan region of Recife, Brazil, found that radon concentrations ranged from 2 to 1,174 Bq/m³ in residences in areas of uraniferous phosphorite outcrops, increasing by 10-16% the risk of developing radon-related pulmonary neoplasia.[25] The authors found that most households evaluated had habits that contributed to indoor gas accumulation, such as keeping windows closed for many hours during the day.[25]

High levels of radon have also been documented in large cities, leading to greater exposure for a broader population.[8] A survey by Petroni & Lima[26] in 35 air-conditioned commercial and residential buildings in the city of São Paulo, Brazil, indicated that 3% of those had radon concentrations above the WHO recommendations.[3] That study found the presence of radon (above 4 mSv/year) in some buildings.

The population must be aware of the health impacts related to home exposure to radon. Health professionals must encourage access to information about the health hazards resulting from such exposure and inform about the monitoring of home radon levels provided by public agencies.[27]

LUNG CANCER AND RADON

Lung cancer is the leading cause of death from cancer in the world, as well as a public health problem. Smoking is identified as the main risk factor for pulmonary cancer and accounts for about 80% of cases, while radon is the main factor among nonsmoker individuals, affecting between 10% and 15% of this population, and increases the 25-fold risk among active smokers when compared with nonsmokers.[8,28,29]

Studies on cancer have classified radon as a grade-1 human carcinogen, also called low grade or well differentiated, because it causes cancerous cells to be a little different from normal cells, which makes the neoplasm slowly progress. A relationship between exposure to radon and increased risk of pulmonary cancer in the general population has been established.[8,30] However, the consequences of this contribution vary among different studies.[31,32]

Inhaled radon decay products emit radiation associated with high cytotoxic and genotoxic effects, causing lesions in the respiratory epithelium, damaging DNA, and potentially causing lung cancer.[33]

Mechanisms of action

Carcinogenesis by radiation is a complicated process and subject to the effects of different environmental agents, as well as genetic factors.[34] The carcinogenic effect induced by inhaled radon, particularly for the bronchial epithelium and especially in the bifurcations of the airways, is mainly due to the progenies of radon, mainly polonium 214 and 218, which emit high-energy alpha particles as the predominant form of radiation. Despite their limited ability to penetrate tissues, alpha particles can damage exposed tissues due to their high biological efficacy through various cytogenetic effects.[34]

Some of these effects include expression of pathogenic variants, chromosomal aberrations, generation of reactive oxygen species, modification of cell cycles, and increased production of proteins associated with cell cycle regulation and carcinogenesis.[35] In addition, there is evidence suggesting that residential exposure to radon is capable of inducing the expression of pathogenic *EGFR* variants, *ALK* translocations,[31] and an increased risk of small cell lung cancer among all histological types.[36,37]

Non-small cell lung cancer shows molecular alterations, such as somatic mutations (*EGFR*, *BRAF*, *HER2*, *MET*) or chromosomal rearrangements (*ALK*, *ROS1*, *RET*, *NTRK*) mainly in nonsmokers, suggesting an association between radon exposure and non-small cell lung cancer in nonsmokers.[29]

Epidemiology

Epidemiological studies have established an important association between exposure to radon and pulmonary cancer,[33,38-40] confirmed by the higher frequency of pulmonary cancer among uranium miners exposed to radon.[41,42]

A recent meta-analysis of 13 studies documented a direct relationship between the level of radon in households and the risk of developing lung cancer. Based on this information, the authors estimated that exposure to radon could be responsible for up to 2% of deaths from lung cancer in Europe.[43]

The risk of pulmonary cancer increases with the level of exposure to radon. An association was documented between exposure to radon above 50 Bq/m^3 and lung cancer.[44] Individuals exposed to concentrations greater than 200 Bq/m^3 had a 2.06-fold higher risk (95% CI, 1.61-2.64) than did those exposed to concentrations ≤ 50 Bq/m^3. Among active smokers, the risk increased more markedly with increasing exposures to radon, reaching up to 29.3 times higher (95% CI, 15.4-55.7) for heavy smokers exposed to concentrations greater than 200 Bq/m^3.[44]

A meta-analysis evaluated indoor exposure to radon and its effects on health and showed an increase in the relative risk for pulmonary cancer in China of 1.01 (95% CI, 1.01-1.02) for each increment of 10 Bq/m^3 in indoor radon concentrations.[45]

A systematic review followed by a meta-analysis[34] evaluated the association between residential radon exposure and lifetime risk of pulmonary cancer in never smokers. Those exposed to radon concentrations ≥ 100 Bq/m^3 presented with an excess relative risk of 15% of developing lung cancer, especially men.

Another meta-analysis studied the relationship between residential exposure to radon and histological types of pulmonary cancer.[46] High residential exposure to radon was associated with an increased risk of pulmonary cancer (OR = 1.48; 95% CI, 1.26-1.73). All histological types of pulmonary cancer were associated with residential radon exposure. The strongest association was observed with small cell lung cancer (OR = 2.03; 95% CI, 1.52-2.71), followed by adenocarcinoma (OR = 1.58, 95% CI, 1.31-1, 91), other histological types (OR = 1.54, 95% CI, 1.11-2.15), and squamous cell carcinoma (OR = 1.43, 95% CI, 1.18-1.74). With the elevation of residential levels of radon above 100 Bq/m^3, the risk of pulmonary cancer, small cell lung carcinoma, and adenocarcinoma increased by 11%, 19%, and 13%, respectively.[46]

Home exposure

Residential exposure to radon is a major contributor to pulmonary cancer mortality, although this contribution is highly variable across different countries, indicating the need for targeted prevention policies. The correction of estimates for dwelling height is essential to provide reliable estimates of mortality attributable to radon.[31]

In Canada there are no "radon-free" areas, and radon is responsible for 16% of deaths from lung cancer, 20% of homes exceed the guideline of 200 Bq/m^3, and 47.5% exceed the reference level recommended by the WHO (100 Bq/m^3).[47-49]

Long-term inhalation of alpha particles increases the risk of pulmonary cancer by 16% for each 100 Bq/m^3 increment and has a synergistic effect with other risk factors for pulmonary cancer.[47] When levels reach the limit set by the Canadian guideline, that is, above 200 Bq/m^3, the lifetime risk of pulmonary cancer is 17% for active smokers and 2% for nonsmokers.[47,50] These data reinforce those observed by a North American study in which a 3% increase in the incidence of pulmonary cancer was observed for each increase of 100 Bq/m^3 in radon exposure.[51]

Kurkela et al.[52] estimated that (at least) 3% to (at most) 8% of all pulmonary cancers were attributable to residential radon exposure. The proportion of small cell carcinoma cases attributable to radon was 8-13%. Among smokers, most radon-related cases were attributable to the combined effect of radon and smoking, and the authors concluded that reducing radon exposure to an action level of 100 Bq/m³ would eliminate approximately 30% of radon-attributable lung cancer cases.[52]

Hadkhale et al.[53] observed an increased risk of pulmonary cancer in a population-based study in Finland in hospital districts with high radon exposure when compared with those with lower exposure. The authors reported that exposure to radon from groundwater would also be associated with an increased risk of pulmonary cancer.[53]

One study in Thailand reported significant differences in household levels of radon between lung cancer patients and healthy controls and estimated that 26% and 28% of deaths from lung cancer in men and women, respectively, were attributable to indoor radon exposure in that country. Other factors were identified as capable of interfering with the indoor radon levels, such as characteristics of the residence and its ventilation. The window-to-wall ratio was negatively associated with indoor radon levels.[54]

An ecological study evaluated the increased risk of pulmonary cancer mortality due to exposure to radon indoors in Mexico.[55] The mean indoor radon concentrations ranged from 51 to 1,863 Bq/m³, the highest mean exposure dose found was 3.13 mSv/year in the north of the country (Chihuahua), and the excess mortality from pulmonary cancer in the country was 10.0 ± 1.5 deaths per 10^5 population. The highest values were found in the north of the country, where there are numerous uranium deposits, followed by Mexico City, the most populous and polluted area in the country.[55]

Torres-Durán et al.[56] evaluated 829 patients with lung cancer, 56.7% of whom were smokers or former smokers. There was no association of indoor radon concentrations with age, sex, histological type, or tumor staging at diagnosis. Median indoor radon concentrations increased with age at diagnosis in men but not in women. When analyzing participants exposed to more than 1,000 Bq/m³, a predominance of small cell lung cancer and a more significant presence of advanced stages (IIIB and IV) were observed.[56]

Rodríguez-Martínez et al.[37] evaluated, in a multicenter case-control study, the effect of residential exposure to radon on the risk of small cell lung cancer in the general population. There was a statistically significant association for those exposed to concentrations above the permitted level (OR = 2.08; 95% CI, 1.03-4.39) in relation to those exposed to concentrations below 50 Bq/m³.[37]

Maggiore et al.[57] assessed the risk of radon exposure and lung cancer incidence/mortality in southeastern Italy. In that study the authors pointed out that the risk of exposure to radon should be better studied to evaluate the causes of the higher lung cancer mortality and incidence rates in the Salento area as compared with national average rates. For these reasons, the Local Health Authority of Lecce, in cooperation with the Regional Agency for Protection and Prevention of the Environment in Puglia and the National Research Council Institute of Clinical Physiology, has included the monitoring of individual concentrations of radon indoors in the protocol of a case-control study intended to investigate the role of different personal and environmental risk factors for lung cancer in the Salento area.[57]

According to the *Instituto Nacional do Câncer* (Brazilian National Cancer Institute) data, lung cancer was responsible for 28,620 deaths in Brazil in 2020, has been one of the leading causes of preventable death, and is, respectively, the third and fourth most common type of cancer in men (17,760 new cases) and women (12,440 new cases).[58] In addition, lung cancer is the first and third most common type regarding incidence among men and women worldwide, respectively.[59]

Cigarette smoking is the most critical risk factor for developing pulmonary cancer. Other risk factors cited by the *Instituto Nacional do Câncer*, besides radon, are occupational exposure to chemical or physical agents (asbestos, silica, uranium, chromium, alkylating agents, among others); drinking water containing arsenic, and high doses of beta-carotene supplements in smokers and former smokers. Radon is the main factor for pulmonary cancer in people who are nonsmokers (around 10-15%, with small variations).[58]

Lorenzo-González et al.[60] claimed that health professionals neglect residential radon and that it is rarely considered a variable in lung cancer risk scoring. Discussions with young adults can be valuable as they make long-term plans to settle into a home and work.[47] Family physicians play a crucial role in informing their patients about the health risks of radon exposure and in recommending proactive actions to reduce their exposure.[61]

From a clinical point of view, when nonsmokers are diagnosed with pulmonary cancer, radon should be considered as a potential cause.[34,62] From a public health point of view, residential radon should be considered an important factor for predicting the risk of pulmonary cancer, especially among smokers due to the synergistic effect of radon and tobacco smoke. Smoking cessation should be one of the main health priorities.[34]

There is a need to raise awareness among health professionals, legislators, policymakers, and the population so that necessary measures can be taken to reduce this harmful exposure, particularly in radon-prone areas, thus preventing a significant proportion of cancer deaths.[63]

Tables 1 and 2 show the risk of pulmonary cancer according to the level of radon exposure and smoking habit.[64]

PREVENTION AND MITIGATION

The following measures should be observed so that exposure to radon has a less destructive potential or even does not occur[3,65]:

a. For risk reduction in the general population, strategies are needed both for the prevention of radon release (in new housing) and mitigation (in preexisting housing)

b. Periodic radon measurements should be carried out so that the effectiveness of the measures adopted for radon prevention and mitigation can be verified
c. Professionals in the construction sector are key players in preventing and mitigating radon exposure. They need to be trained to ensure their competence in this area

IDEAL RADON CONTROL PROGRAM

The following are characteristics and needs that a national radon exposure control program should have to be effective[3]:

a. National radon control programs should aim to reduce the risk for the general population, especially for individuals living in environments with high concentrations of this gas
b. To limit the risk, a national reference exposure level of 100 Bq/m³ should be established. If it is not possible to use this reference level, levels ≥ 300 Bq/m³ should be avoided
c. To reduce the risk to the general population, building codes should be implemented to require radon measurements in houses under construction
d. Radon measurements are necessary because building codes alone cannot guarantee that concentrations will be below the reference level
e. An effective national radon control program requires input from multiple agencies in the same country. One agency should lead implementation and coordination and ensure linkage with tobacco control, and one should lead health promotion programs

EXAMPLES OF ACTIONS

National Radon Action Plan—2021-2025

The U.S. National Radon Action Plan—2021-2025[66] goals are to find, correct, and prevent elevated levels of radon in eight million buildings by 2025 and to prevent 3,500 lung cancer deaths annually. Under this plan, leaders from various sectors work together to plan, guide, and sustain national actions to prevent radon exposure[66]:

a. To eliminate preventable lung cancer from radon by expanding protections for all communities and buildings
b. The only way to determine home radon levels is through testing
c. Qualified professionals can install a system that informs when high levels of radon are accumulating inside the building
d. New buildings should be designed and constructed using radon-resistant construction techniques in order to save lives now and in the future
e. Since low-income individuals and families are less likely to have their homes tested for radon levels, government awareness of this type of problem is needed
f. Some people do not know that indoor radon exposure can cause lung cancer, so there is a dire need for more disclosure
g. Some renters, or even homeowners, may challenge these provisions to protect their homes because they cannot afford the cost of radon testing and mitigation
h. Because reducing high radon concentrations in homes and other buildings is expected to result in important health benefits, access to life-saving radon protections should be more equitable across social groups

NEW SPANISH REGULATIONS FOR PROTECTION FROM RADON EXPOSURE

The Spanish Royal Decree No. 1029/2022 of December 20, 2022, establishes that the reference level for radon concentration in indoor areas is 300 Bq/m³ in terms of the annual average concentration of radon in the air in residences, public access buildings, and workplaces.[67]

Table 1. Risk of cancer from radon exposure for smokers.

Radon level	If 1,000 people who smoked were exposed to this level over a lifetime[a]. . .	The risk of cancer from radon exposure compares to[b]. . .	What to do: stop smoking and. . .
20 pCi/L	About 260 people could get lung cancer	< 250 times the risk of drowning	Fix your home
10 pCi/L	About 150 people could get lung cancer	< 200 times the risk of dying in a home fire	Fix your home
8 pCi/L	About 120 people could get lung cancer	< 30 times the risk of dying in a fall	Fix your home
4 pCi/L	About 62 people could get lung cancer	< 5 times the risk of dying in a car crash	Fix your home
2 pCi/L	About 32 people could get lung cancer	< 6 times the risk of dying from poison	Consider fixing your home if levels are 2-3.9 pCi/L
1.3 pCi/L	About 20 people could get lung cancer	(Average indoor radon level)	(Reducing radon levels below 2 pCi/L is difficult)
0.4 pCi/L	-	(Average outdoor radon level)	

Adapted from the U.S. Environmental Protection Agency.[64] [a]If you are a former smoker, your risk may be lower. [b]Comparison data calculated using the 1999-2001 National Center for Injury Prevention and Control Report by the Centers for Disease Control and Prevention.

Table 2. Risk of cancer from radon exposure for never smokers.

Radon level	If 1,000 people who never smoked were exposed to this level over a lifetime[a]. . .	The risk of cancer from radon exposure compares to[b]. . .	What to do:
20 pCi/L	About 36 people could get lung cancer	35 times the risk of drowning	Fix your home
10 pCi/L	About 18 people could get lung cancer	20 times the risk of dying in a home fire	Fix your home
8 pCi/L	About 15 people could get lung cancer	4 times the risk of dying in a fall	Fix your home
4 pCi/L	About 7 people could get lung cancer	< the risk of dying in a car crash	Fix your home
2 pCi/L	About 4 people could get lung cancer	< the risk of dying from poison	Consider fixing your home if levels are 2-3.9 pCi/L
1.3 pCi/L	About 2 people could get lung cancer	(Average indoor radon level)	(Reducing radon levels below 2 pCi/L is difficult)
0.4 pCi/L	-	(Average outdoor radon level)	

Adapted from the U.S. Environmental Protection Agency.[64] Note: If you are a former smoker, your risk may be higher. [a]Lifetime risk of lung cancer deaths according to the U.S. Environmental Protection Agency Assessment of Risks from Radon in Homes (EPA 402-R-03-003). [b]Comparison data calculated using the 1999-2001 National Center for Injury Prevention and Control Report by the Centers for Disease Control and Prevention.

The new Spanish regulation establishes the obligation to perform radon measurements in all public access buildings, businesses, and residences, especially in areas with high radon levels. If high levels of this gas are detected, measures must be taken to reduce and mitigate exposure (for example, installation of radon reduction systems).[67]

FINAL CONSIDERATIONS

According to Stanifer et al.,[68] home radon testing is a primary lung cancer prevention strategy. Due to the high prevalence of smoking in adults and the high incidence of lung cancer, this measure can benefit these populations by providing more preventive interventions and adopting smoke-free and radon control policies. Thus, reducing the risk of radon exposure will be integrated with smoking cessation messages and lung cancer screening programs.

The key steps to reduce lung cancer deaths induced by radon exposure are to increase the awareness of population and health professionals of this threat, measure radon levels in all types of new buildings, build a workforce of qualified professionals who can solve radon-related problems using proven standards, and ensure that adequate funding is available to cover the costs of testing and repair.

AUTHOR CONTRIBUTIONS

All authors equally contributed to this work and approved the final version of the manuscript.

CONFLICTS OF INTEREST

None declared.

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