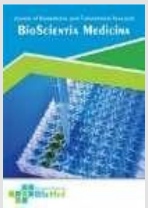
eISSN (Online): 2598-0580



Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Effect of Radon and Lung Cancer Risk: A Narrative Literature Review

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ARTICLE INFO

Keywords:
Carcinogenesis
Lung cancer
Radioactive
Radon
Reactive oxygen species

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All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/bsm.v6i15.669

ABSTRACT

Exposure to cigarette smoke has been known to be a major risk factor for lung cancer. Although smoking has long been considered the main cause of lung cancer, about 5 to 25% of lung cancer cases occur in non-smokers. Radon is said to be the second most important cause of lung cancer after smoking. Radon-222 is a chemical element in the form of a highly radioactive gas that comes from the decay of the parent radioactive element, uranium, which is found in the earth's crust. Inhaled radon gas can adhere to the mucosal lining of the airways and damage the airway epithelium. The process of ionizing radiation by alpha particles due to the decay of radioactive substances can cause mutations and chromosomal aberrations, severance of DNA double chains, and formation of reactive oxygen species. (ROS) that cause cell cycle changes, up-and down-regulation of cytokines, and increased production of proteins associated with cell cycle regulation and carcinogenesis. Research on radon and lung cancer has not been widely conducted in Indonesia. This literature review aims to describe radon and its effects on lung health.

1. Introduction

Lung cancer is cancer originating from the lung parenchyma and is one of the leading causes of death worldwide.[1] In general, exposure to cigarette smoke is considered to be one of the main factors in the occurrence of lung cancer. Although smoking has long been considered the main cause of lung cancer, about 5 to 25% of lung cancer cases occur in non-smokers.[2] Epidemiologically, other factors such as genetic susceptibility, occupational exposure, air pollution, cigarette smoke in the environment, and radon exposure can be independent factors or synergize with tobacco cigarettes in causing lung cancer.[1-5]

Radon is known to increase the risk of lung cancer.[2-6] The link between radon exposure and lung cancer risk dates back to 1924 when an autopsy revealed lung cancer to be the leading cause of death in miners exposed to radon.[5] The United States Environmental Protection Agency (EPA) estimates radon to be the second leading cause of lung cancer in the United States.[2-9] In addition, studies in Europe, North America, and China have confirmed that low radon concentrations, such as those commonly found in residential environments, also pose health risks and contribute to lung cancer worldwide, and this is currently a major concern..[2,6-8] Based on epidemiological studies of radon-induced lung cancer, it is estimated that it ranges from 3% to 14% depending on the average radon concentration and smoking prevalence, whereas in smokers, the risk of radon-induced lung cancer increases.[2,10]

Radon gas is a colorless, odorless, and tasteless noble gas that comes from the radioactive decay of uranium contained in rocks that make up part of the earth's crust.[2,6,12] Radon is classified as a human carcinogen by the International Agency for Research on Cancer (IARC).[1,2,6] Exposure to radon has a relative risk factor of 16% getting lung cancer at a level of 100 Bq/m^3.[3,5] Lung cancer usually appears several years (5-25) after exposure. Exposure to radon can occur in many places, and although the gas is rapidly diluted in the atmosphere, it can still accumulate in large quantities in confined spaces such as homes and workplaces. Radon in indoor air is estimated to cause 21,000 lung cancer deaths in the United States each year. Although this figure does not approach the 480,000 deaths per year caused by smoking, this figure is still significant, so it is said that radon is the leading cause of lung cancer in non-smokers.[6,9-11] This literature review aims to describe radon and its effects on lung health.

Radon and its source

Radon (Rn) was first discovered by Fredrich Ernst Dorn in 1898.[2] Radon is a chemical element in the form of a highly radioactive gas and belongs to the 18 noble gas groups of the periodic table.[6,12] Radon is colorless and odorless, so it cannot be detected by the senses. Radon comes from the decay of the parent radioactive element after emitting alpha and beta particles which then change the composition of the nucleus so that the element turns into another element. According to data from the Michigan Department of Natural Resources and Environment, radon is a product of the natural decay of radium and uranium, which are elements found in the earth's crust (Figure 1).[2,6,12]

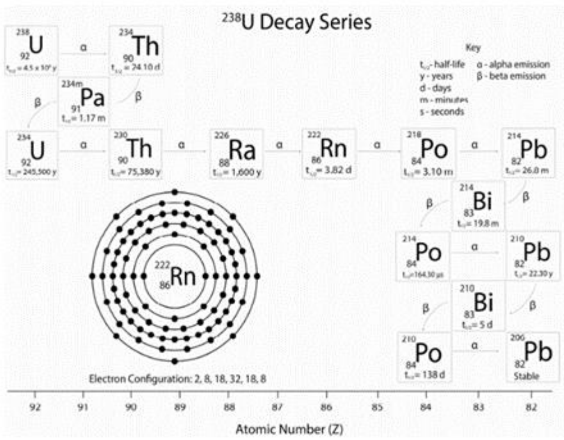

Figure 1. The decay series of uranium-238 and its products.[12]

Radium-226 has a half-life of about 1600 years, after which it decays into radon (Rn-222) with a half-life of 3.8 days and thoron (Rn-220) with a half-life of 55.6 seconds.[7,12] The derivatives of radon are polonium-218, lead-214, bismuth-214, and polonium 214. These are chemically active solids that can be found in an environment together with radon, which cannot be detected by the human senses. Although radon isotopes are short-lived, they can bind and fly with dust in the environment. The Argonne National Laboratory states that if radon gas is inhaled, it can stick to the mucosal lining of the respiratory tract, and even radon that is not bound with dust can enter deeper into the lungs. Likewise, the alpha particles emitted by radon can damage the airway epithelium.[2,7,12]

Alpha particles are the most widely emitted form of radiation as a result of radon decay. Although their ability to penetrate into tissues is very limited, alpha particles can cause very significant biological damage because they have a relatively high biological effect. Beta and gamma particles are also emitted during the decay of radon, but their biological effects are relatively lower than that of alpha particles. Alpha particles consist of a helium nucleus (2 protons and 2 neutrons) and have the potential to store large amounts of energy, and have high linear energy transfer (LET). Ionizing radiation caused by alpha particles can cause mutations and chromosomal aberrations, cleavage of DNA double chains, and formation of reactive oxygen species. (ROS) that cause cell cycle changes, up-and down-regulation of cytokines, and increased production of proteins associated with cell cycle regulation and carcinogenesis.[2,6,12]

Radon in nature is found underground, in rocks containing uranium, in hot springs, and indoors. Radon can accumulate in underground structures such as mines. There is a lot of convincing evidence that radon gas has carcinogenic properties, namely through epidemiological studies of underground mining workers.[2]

The process of formation of radon can be explained from its source, namely uranium. All rocks contain some elemental uranium, although most are only in small amounts - roughly 1 ~ 3 parts per million (ppm) of uranium. In general, the uranium content in the soil is approximately the same as the uranium content of the original rock. Several types of rock with higher than average uranium content, including; granite, phosphate sedimentary rock, light-colored volcanic rock, shale rock that contains a lot of organic material, and metamorphic rock from the four previous rock types. The decay of uranium produces radon gas, which makes it easier for radon to escape through rock fractures and the pore spaces between soil grains. This is what affects the level of radon levels that enters the house. The speed of radon transfer through the soil is controlled by factors of physical properties (water content, porosity, soil permeability) and meteorological factors (barometric pressure, wind, relative humidity, rainfall). Radon travels faster through permeable soils (which consist of sand and gravel) than through impermeable soils (clay).[7]

Radon produced in the soil can dissolve and accumulate in water from underground sources such as wells. And in many cases, the risk of radon entering the home through the water is much lower than if it enters through the soil. The concentration of radon in groundwater is highly dependent on the characteristics of the rock through which the groundwater passes.[13] One of the cities famous for its water sources that contain a lot of radium that produces radon is the city of Misasa, Japan.[2,6]

Radon is also found indoors or in homes. For most people, the greatest exposure to radon occurs in the home, where people spend most of their time rather than in the workplace.[2,6,7,10,11] The main source of radon in the home is ground gas that enters from below and surrounding structures.[6] The air pressure inside the house is lower than the pressure in the soil surrounding the foundation of the house. This pressure difference can draw air and other gases in the soil, including radon, into the house. Potential entry routes for radon in homes include cracks in foundation concrete in basements, cracks in areas with exposed soil or rock, pumps, drainage, holes around pipes or cables, and water from wells, as shown in Figure 2 and Figure 3.[9,13]

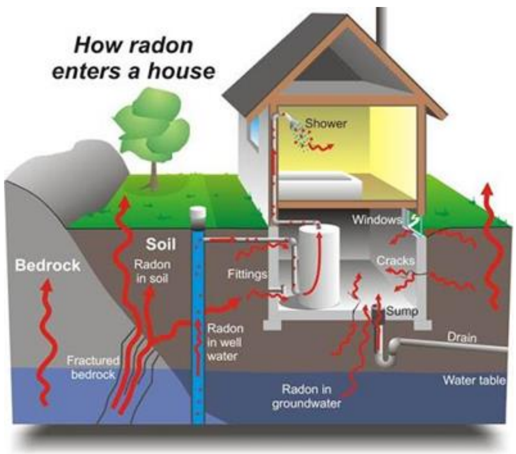

Figure 2. Sources of radon in the house.[9]

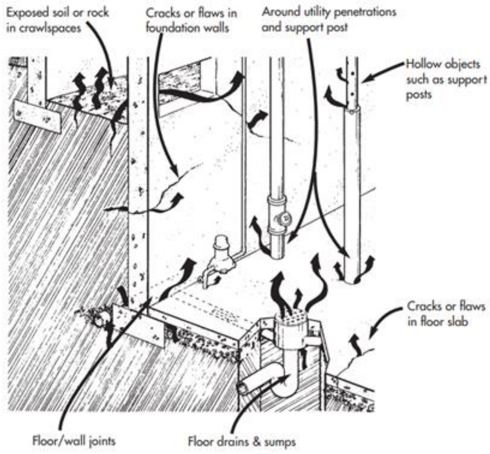

Figure 3. Typical radon entry routes in cast concrete foundation walls and floors.[13]

The concentration of radon in a building depends on the local geology, for example, the uranium content and permeability of the underlying rock and soil, the routes available for radon entry from the soil into the building, the condition and shape of the home or office building, and ventilation. Houses that have insufficient air ventilation or houses that have a closed air circulation system can cause the concentration of radon in them to be relatively higher than houses that have an open circulation system.[2,9,11,13]

The concentration of radon gas in the room is not only caused by groundwater, rocks, and soil around the house environment but is also strongly influenced by the type of basic building material of the house. Research on the concentration of radium in building materials conducted in developed countries such as England, America, Germany, and others has shown that building materials such as bricks, wallboards, or concrete can emit radon gas into the air. Once inside a room, radon gas will accumulate in the air, especially in poorly ventilated buildings.[2,5,7,9]

Surveys of indoor radon concentrations in the United States and many other countries have shown that radon is ubiquitous indoors, usually at concentrations of only one-hundredth to one-tenth of those found in underground mines, and have been shown to be associated with lung cancer. For a survey conducted by the EPA in the United States, a rough distribution of concentrations was obtained; the mean concentration was about 46.25 Bqm-3 (1,25 pCiL-1).[6]

Risk of lung cancer due to radon

Workers in uranium, tin, silver, coal, and other underground mines are the group with higher radon exposure.[2.6] The Committee on the biological effects of ionizing radiation (BEIR VI 1999) conducted a study of mining workers exposed to radon in 1990. There were eleven cohort studies evaluated. The total number of mining workers was 60,000 people from Europe, North America, Asia, and Australia. Among these 60,000 people, 2600 people died from lung cancer. It was found that the number of lung cancers generally increased with increasing accumulation of radon exposure, and the subjects developed lung cancer after 5-14 years of radon exposure.[2.6] Grosche et al. conducted a cohort study in Germany with a total number of 59,001 subjects who worked at the East German Wismut company. Among these subjects, there were 2388 cases of death due to lung cancer, and the incidence of lung cancer increased after 15-24 years of exposure.[2]

Everyone has the same risk of being exposed to radon, but there are some populations who are at high risk of radon exposure and have a greater risk of developing lung cancer from radon exposure. Radon is the second leading cause of death of lung cancer in smokers, but in the non-smoker group, radon exposure is the leading cause of lung cancer death. About 6 million homes in America have radon levels above 4 picocuries per liter (pCi/L), which is the EPA's recommendation for radon levels in indoor air. While the standard emission of radon -222 into the air is 20 pCi/m^2/sec.[6.16]

The World Health Organization (WHO) estimates that 14% of the 300,000 cases of lung cancer each year in the United States are related to radon. The Environmental Protection Agency *(EPA)* determined that a radon level of 4 pCi/L has a 1% risk of lung cancer in non-smokers, 3% in former smokers, and 5% in smokers. These estimates are subject to change based on factors affecting the population. Researchers suggest not only paying attention to the concentration of radon in assessing the risk of lung cancer but also paying attention to work history and lifestyle. Many factors can influence the incidence of lung cancer in people exposed to radon, including age, length of exposure, cigarette smoke, daily activities, water sources, climate, and so on.[2,6,11]

A major study on radon in the home environment and lung cancer was conducted in Europe by Darby et al. They drew on data from 13 European studies on the association of radon in the home with lung cancer risk. The study subjects were at least 150 subjects with lung cancer and 150 controls without lung cancer who came from the same population and recorded the smoking history of all subjects. They measured radon concentrations in all subjects' residences for the past 15 years or more. In total, all subjects were more than 7000 cases of lung cancer, and more than 14000 controls were included in the study analysis. The result of the study was that the risk of lung cancer increased by 8% per 100 Bq/m^3 increase in radon concentration. The increase was not influenced by age, gender, and smoking history.[2.6]

In research in North America conducted by Krewski et al. there were 3662 cases of lung cancer and 4996 controls from 7 studies in the United States and Canada. The method used is similar to the method used in research in Europe. The results showed that the risk of lung cancer increased by 11% for every 100 Bq/m^3, but the increased risk of lung cancer was not affected by age, gender, and smoking history.[2,6,13]

Pathogenesis of lung cancer due to radon

Radon causes the effects of cell damage, DNA damage, chromosomal changes, gene mutations, and genetic instability due to α particle radiation released during the decay of radioactive substances originating from uranium-238.[2,6,12,16] Figure 4 shows the concept of cell biology that develops into a tumor due to α particle radiation produced by the decay of radioactive substances. These processes include a series of radiation-induced molecular alteration events, the effect of gene regulation on normal cell function, genetic instability, loss of normal cells, tissue hemostasis, and progression to malignant cells.[2.16]

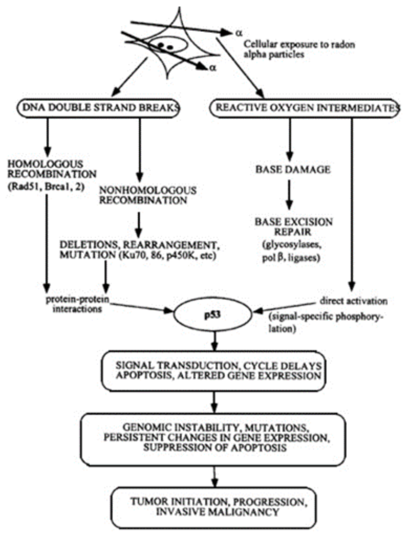

Figure 4. The concept of cell biology develops into a tumor due to α particles.[6]

One of the pathways for tumor formation begins with radiation-induced DNA damage to cells. α Particles can directly recognize the cell nucleus and can damage DNA strands by emitting energy to a number of ions and causing a number of DNA double chains to break. These events are known as multiply locally damaged sites (MLDSs). A broken DNA chain is the most prominent form of DNA damage caused by radiation by radon α particles. The broken DNA chain can be repaired by pairing again with homologous or non-homologous chains. Homologous repair, rad51-like protein pairs and associated modulator proteins, terminal DNA pairs with complete DNA. The p53 protein that regulates cell cycle control, apoptosis, and transcription of various genes will interact with rad51 and suppress the formation of DNA pairs by rad51. Meanwhile, in the non-homologous pathway, DNA repair was mediated by Ku87 protein, p450 kinase, and DNA ligase IV. Under ideal conditions, the broken DNA strands can return to normal, and cell function will also return to normal. However, under certain conditions, errors can occur in the repair of damaged DNA strands. The end result of incomplete DNA repair can be deletions, insertions, or rearrangements of genetic material that can remain in the next generation. If genetic damage occurs in key genes in the growth cycle and other important cellular systems, then the potential for cell transformation into cancer is enormous.[2,6,12,15]

The ionizing radiation that does not directly cause DNA damage can produce reactive oxygen intermediates that affect the stability of p53, which can disrupt cell regulation. Reactive oxygen intermediates can cause oxidative damage to DNA and mutations during DNA replication. This damage can also be repaired via glycosylase, β polymerase, and ligase. Cellular changes through DNA damage or through reactive oxygen intermediates can cause p53 age to increase, and one of the subsequent consequences is slowing the cell cycle and inhibiting apoptosis. Cells that have a long life but have damaged genetic material, such as gene deletion, rearrangement, amplification, and persistent gene instability, have the potential to become uncontrolled growth. This can lead to abnormal cell growth and can develop into malignant cells.[2,6,12]

Efforts to prevent and educate about radon in the community

About 1 in 15 homes is considered to have high levels of radon. Since this odorless and invisible gas causes no immediate symptoms, the only way to tell if a residential home is affected by radon is to have a residential radon test done.[2,6,13] About 6 million homes in America have radon levels above 4 picocuries per liter (pCi/L), which is the EPA-recommended dangerous limit.[2.9]

Research on radon is advised not only to pay attention to radon concentrations in assessing the magnitude of the risk of lung cancer but also to pay attention to a person's work history and lifestyle. Many factors can influence the incidence of lung cancer in people exposed to radon, including age, length of exposure, cigarette smoke, daily activities, water sources, climate, and so on.[2,5,6,13]

People in developed countries, such as Canada, have paid attention to the problem of radon in their environment, so they carry out testing efforts by providing detectors that can be purchased by themselves or by hiring professional testers.[10] The Canadian Ministry of Health recommends measuring radon concentrations by placing at least one long-term measuring detector in the home for a minimum of 3 to 12 months. The tools used in long-term measurements include an alpha track detector, an electret ion chamber, and a digital detector (Figure 5). The detector is placed on the lowest level of the house where homeowners spend at least 4 hours a day, such as in bedrooms, living rooms, and play rooms. The detector is placed at a height of 0.8 meters to 2 meters from the floor but at least 50 cm from the ceiling and 20 cm from other objects to provide normal airflow around the detector.[2.13]

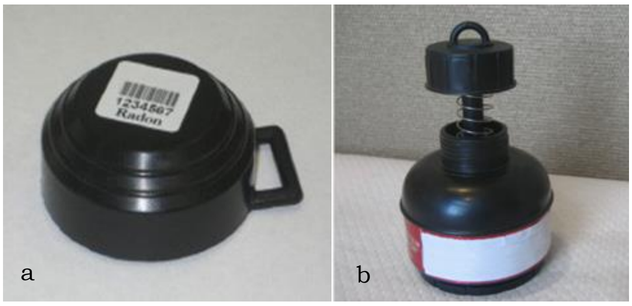

Figure 5. a. Alpha track detector. b. electret ion chamber.

The 3-month time test is considered representative of a person's annual average exposure. Then the detector is sent to the laboratory once every 3 months for testing. The units used to measure the concentration of radon are Becquerel per cubic meter (Bq/m^3) and picoCuries per liter (pCi/L), 5.4 pCi/L equals 200 Bq/m^3. If high radon levels are found in the home, steps can be taken to reduce radon levels, such as the most common method of installing a ventilation pipe and fan system, which draws radon from under the house and then releases it to the outside. Radon can also enter homes through the water supply, although the risk is much lower than that of entering through the soil. Likewise, if there is a private well in the house, it can be tested for radon levels so that the water supply can be regulated and radon can be removed before entering the house.[13]

The amount of radon in a home depends on many factors, including soil characteristics, type of construction, foundation conditions, occupant lifestyle, and weather. The concentration of radon can vary greatly depending on the uranium content in the soil. In addition, radon flows more easily through some types of soil than others, such as sand, than clay. The type of housing and its design also affects the amount of soil contact and the number and size of radon entry points. Foundation conditions with many cracks and openings have more potential entry points for radon. Us*ing* exhaust fans, windows and fireplaces, for example, affects the pressure difference between the house and the ground. This pressure difference can attract radon in the room and affect the rate of air exchange outside and inside. Weather variations (e.g., temperature, wind, barometric pressure, precipitation, etc.) can affect the amount of radon that enters your home.[13]

There is no specific examination to determine the extent to which a person has been exposed to radon, but if a person feels that he or she has been exposed, he or she can perform regular health checks and pay attention to symptoms such as shortness of breath, chronic cough, chest pain, hoarseness. , and others for early detection of lung cancer symptoms.[13]

2. Conclusion

Radon gas has carcinogenic properties that not only cause lung cancer in underground mining workers but can also cause lung cancer in the general population due to exposures that occur in homes or other buildings. Radon is a highly radioactive gas originating from the decay of uranium that escapes the earth's crust naturally, emitting alpha particles that are very dangerous and can cause DNA damage. Alpha particles can induce lung cancer through the p53 protein pathway. Radon mitigation and education about radon in the community are needed regarding its potential as a cause of lung cancer.

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