AN NARRATIVE REVIEW: THE RADON GAS EXPOSURE IN THE HOME ON THE RISK OF LUNG CANCER

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ABSTRACT

According to WHO 2009, exposure to radon gas is known to be the second-highest cause of lung cancer. The United States Environmental Protection Agency (U.S.EPA) estimates that 21,000 lung cancer deaths annually result from exposure to radon in the United States. Radon (Rn^{222}) naturally originates in soil and rock and it is the decay of Uranium-238 (U^{238}). This study used a literature review study that aims to review several research journal articles regarding exposure to Radon gas in the home with the risk of lung cancer. The database used to search for research journal articles is Science Direct, PubMed, DOAJ, JSTOR, and Taylor & Francis. The results of this study were: (1) nine out of twelve journal articles described a significant association between Rn in the home (concentration of Rn 37 Bq/m^3 until ≥ 300 Bq/m^3) and the risk of lung cancer; (2) the duration of stay of the occupants in the house lasted from 2-30 years; and (3) eight journal articles presented that the most common lung cancer cell subtype associated with Rn exposure in the home was adenocarcinoma and squamous cell carcinoma. People need to maintain indoor airflow and choose safe building material (not containing Rn).

KEYWORDS

Environment, Indoor, Lung Cancer, Radon.

INTRODUCTION

Common public health problems in this era can include infectious and non-communicable diseases. Cancer is one of the non-communicable diseases which according to WHO (2018), the mortality rate from cancer is the second-highest after cardiovascular disease which reached 9 million cases (22%) in 2016 in the world. The highest death rate in the world due to cancer is lung cancer which reached 18.4% in 2018 [1].

Lung cancer is expected to increase from 14 million cases in 2012 to 22 million cases in the next two decades. Then the incidence of lung cancer in the world in 2020 was 11.4% (2.206.771 new cases) and the mortality rate reached 18% (1.796.144 cases) [2]. In Asia, the incidence of lung cancer is above 13.8% (1.315.136 new cases) and this is followed by a mortality rate of 19.2% (1.112.517 cases) [3]. Then, the incidence of lung cancer in Southeast Asia was 11.2% (123.309 new cases) and the mortality rate was 15.9% (109.520 cases) in 2020 [4].

Exposure to Rn gas is known to be the second-highest cause of lung cancer after smoking. The United States Environmental Protection Agency (U.S. EPA) estimates that there are 21,000 lung cancer deaths per year caused by Rn exposure in the United States [5]. In Indonesia, Radon (Rn^{222}) naturally comes from soil and rock which is radioactive in gaseous form and is a decay of uranium-238 (U^{238}). Rn is odorless, tasteless and colorless. Rn has no commercial uses for human beings, other than as a radiation standard for calibrating Rn monitoring equipment in support of environmental surveys in homes and other buildings [6].

There are 36 types of radioactive isotopes of radon, Rn^{222} and Rn^{220} (Derivative of Th^{232}) are significantly the most frequently found in the human environment. The presence of Rn gas can unconsciously be trapped and accumulated in the house or residence. Generally, Rn is found in homes as a result of poor foundations, cracked floors, basements, building materials (gypsum and concrete), cooking fuel, and homes with poor ventilation or air circulation. In addition, the presence of Rn in the house is also influenced by air temperature, humidity, air pressure, and time factors (season/weather and day/night) [7].

The Rn gas in soil and rocks naturally move into the air through the ground gap. Because of the pressure in the ground, The Rn gas enters the home through the foundation, floor, and wall cracks/holes. Poor ventilation also traps Rn gas inside the home. Other than that, building materials such as gypsum that are usually used for homes building, release the Rn gas inside the home.

There are many factors in how Rn concentrations enter the homes such as house type, design, and construction, geology, soil permeability, etc. Therefore, the responsibility to reduce Rn concentrations in the home rests with the occupants. There are lists to recognize Rn mitigation such as remediation measurement check (Rn homes level before and after remediation), active soil depressurization (ASD), building/house renovations (sealing wall/pipe cracks and adding exhaust ventilation for reducing the negative indoor air pressure), and do water treatment (aeration and filtration) [8].

The process of how Rn exposure can cause lung cancer is because Rn can spontaneously disintegrate or turn into other atoms which can stick to small dust in the air. When dust particles are inhaled, Rn enters the respiratory tract and attaches to the lung epithelium which then settles, and resulting in cell or DNA damage [9]. The amount of Rn concentration in the house and the duration of Rn exposure have an impact on the health risks of residents.

There are inconsistent research results regarding exposure to Rn gas with the risk of lung cancer, as several research results belonging to Brauner, et al. (2012) [10] and Wilcox, et al. (2008) [11], which shows the Incidence Rate Ratio (IRR) 1.04 (95% CI: 0.69–1.56) at the concentration of Rn in the house of 100 Bq/m^3 in Denmark and the Estimated Odds Ratio (EOR) 0.05 (95 % CI: 20.14 to 0.56) at the same concentration in New Jersey. The study concluded that there was no significant relationship between exposure to Rn gas and the risk of lung cancer. However, several studies in different countries showed significant results between exposure to Rn gas and the risk of lung cancer as the research of Pisa, et al. (2001) [12], in Italy showed an OR of 2.0 (95% CI: 1.0 - 3.9) for a concentration of Rn 40 – 76 Bq/m^3. Then research belonging to Kreienbrock, et al. (2001) [13], in Germany showed RR 1.93 (95% CI: 1.19 - 3.13) for a concentration of Rn 80–140 Bq/m^3.

From these studies, the geographical conditions of each country or residential area and the concentration of Rn in the house affect the results of the study. Research courtesy of Cong Li, et al. (2020) [7] in Spain, explained that the concentration of Rn in residential areas was higher in new homes compared to traditional houses. Then the concentration of Rn was found to be higher in newly renovated traditional houses compared to traditional houses that were not renovated. Several studies in Korea related to Rn in the house were assessed based on location or area, length of construction, and season. These factors affect the concentration of Rn in the house.

The colorless, tasteless, and odorless characteristic of Rn makes it difficult for people to detect it if they do not use a tool. The presence of radon exposure in the house on the risk of lung cancer can be detected by using a radon detector to determine its concentration. From some of these studies, the geographical conditions of each country or residential area and the concentration of Rn in the house affect the results of the study. The types of cancer cells that develop in each of the research respondents also have variations. Therefore, further studies and research are needed on Rn exposure in the home with the risk of lung cancer.

MATERIALS AND METHODS

This study uses 12 (twelve) journal articles (Table 1). There are several steps in searching for journal articles on the topic of exposure to Rn gas in the home on the risk of lung cancer. The first step is to use the PICO (Problem, Indicator, Comparison, Outcome) framework to formulate the problem. In addition, PICO is used to determine inclusion and exclusion criteria, as well as an aid in determining keywords to make it easier to search for articles. Keywords that are relevant to related topics are 'Radon residential', 'Radon exposure', 'Radon homes', 'indoor radon', 'Rn exposure', 'Rn homes', 'Indoor Rn', ' 'or', 'and ', 'non-small cell lung cancer', 'adenocarcinoma', 'squamous cell carcinoma', 'large cell carcinoma', 'small cell lung cancer', and 'lung cancer risk'.

The next step is to search for research journal articles using a database portal (search engine) for online journals, namely *Science Direct* (3 journal articles), *PubMed* (4 journal articles), *Directory Open Journal Access (DOAJ)* (2 journal articles), *JSTOR* (2 journals articles), and *Taylor & Francis* (1 journal article), by entering keywords that have been determined. Keywords are entered regarding the available 'or' and 'and' and activating the 'journal article', 'free full text', 'content I can access', 'articles', and 'full text' options contained in each database. Then filtering is carried out based on the title of the journal article and the inclusion & exclusion criteria that have been previously determined using the PICO framework. The inclusion criteria based on the PICO framework are (P) radon in the house, (I) radon gas, (C) radon gas concentration and duration of exposure, (O) lung cancer risk. Other inclusion criteria are journal articles that have a publication year between 1993-2020 and are international journal articles that are written in English. Journal articles outside of these criteria will be excluded.

Screening related to research methods in journal articles that will be reviewed is using a case-control study design. Because many international journal articles with related topics (Indoor Radon and Lung Cancer Risk) were found using a case-control study design. The case-control study design is most appropriate for causal research. In addition, taking several journal articles with only one type of study design makes it easier for authors to compare one journal article with another.

There are several limitations found in writing this narrative review. First, the number of research journal articles with related topics is limited because they are not full-text articles and open access journals, so they cannot be accessed. Second, how to enter keywords that are still manually one by one. Then, the search for journal articles by researchers with related topics starts from October 19, 2020, to February 18, 2021. After passing that date, the researcher no longer searched for journal articles.

Indoor Rn exposure is known as the presence of radon gas in the house which is inhaled by the occupants. In this study, two risk factors contribute to Rn gas exposure and the risk of lung cancer: 1) the indoor Rn concentration level and 2) the duration of stay of the occupants in the house. This study also mentioned the most common lung cancer cell subtype. Afterward, there is still no study about the differences of the symptom of lung cancer caused by Rn with any else.

RESULTS AND DISCUSSION

In writing this narrative review, the PRISMA flow chart diagram (Figure 1) is used to explain the flow or stages in the search for journal articles. The PRISMA flow chart diagram explains the identification, screening, and eligibility stages of a journal article, and the last stage is selected journal articles that meet the inclusion criteria. Twelve journal articles match the inclusion criteria for writing this narrative review. Meanwhile, three types of researchtypes of research Sobue, et al. 2000 [14]; Kreuzer, et al. 2003 [15]; and Wilcox, et al. 2008 [11], from twelve research journal articles, showed insignificant results between exposure to Rn at home and the risk of lung cancer. The twelve journal articles and their variables are explained simply in table 1.

Based on table 1, it is known information from each journal article and the results of different studies regarding the concentration of Rn gas with the risk of lung cancer. However, there is one journal article [16] that does not discuss the variable duration/residence years of the householder/respondent in the house which is detected to have a concentration of radon. In addition, one journal article, Pisa, et al. 2001 [12], did not discuss the variable types of lung cancer that developed in respondents due to Rn exposure at home.

Indoor Radon Concentration

Based on nine journal articles reviewed, it shows that a large range of Rn concentrations that have a risk of lung cancer is ranging from 37 Bq/ Bq/m^3 to ≥ 300 Bq/m^3. Meanwhile, the limit for Rn concentration that has been set by WHO (2009) [8] is 100 Bq/m^3 which aims to reduce the dangers of public health risks due to exposure to Rn in the house. The risk of exposure to Rn concentrations at the level of 100 Bq/m^3 (over the limit determined by WHO) on the risk of lung cancer is also influenced by the duration of stay/residence years of householders exposed to Rn. The method of measuring Rn concentration using an Rn detector is by hanging or placing the device in a predetermined room (in the bedroom and family room) with a distance approximately 60 cm – 180 cm above the floor surface, not exposed to strong wind gusts, 15 cm from the walls of the room and far from windows or ventilation. Measurements are carried out at a minimum of 1-12 months.

Figure 1. PRISMA Flow Chart Diagram

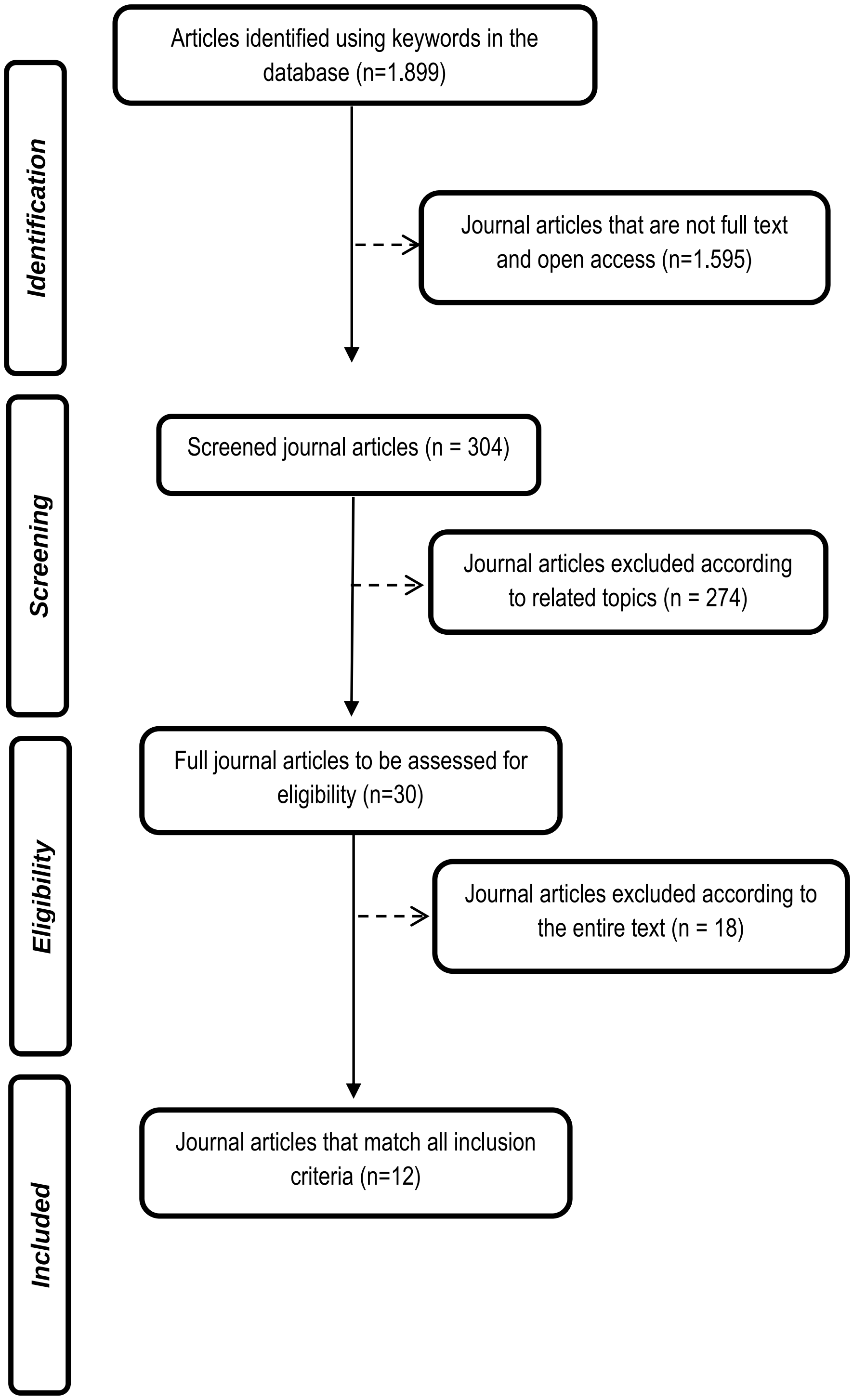

Table 1. Journal Articles used in This Narrative Reviews

No	Author and Years	Setting and Sample	Result		
			Rn Concentration	**Duration/Residence Years**	**Lung Cancer Subtype**
1	(Biberman, et al. 1993)	*Israel.* 35 (Case) 35 (Control)	OR 5.2 (90% CI: 1.1 – 24.9) radon > 1 pCi/l	± 10 years	*Small Cell Lung Cancer* (SCLC)
2	(Sobue, et al. 2000)	*Misasa, Japan.* 28 (Case) 36 (Control)	OR 0.25 (95% CI: 0.03–2.33) radon ≥ 100 Bq/m^3.	± 30 years	-
3	(Pisa, et al. 2001)	*Rendena Valley, Italy.* 138 (Case) 291 (Control)	OR 2.0 (95% CI: 1.0 - 3.9) radon 40 – 76 Bq/m^3.	± 10 years	-
4	(Kreienbrock, et al. 2001)	*Germany.* 365 (Case) 595 (Control)	RR 1.93 (95% CI: 1.19 - 3.13) radon 80–140 Bq/m^3.	± 23 years	- *Adenocarcinoma* - *Squamous Cell Carcinoma*
5	(Kreuzer, et al. 2003)	*Thuringia, Germany.* 1.192 (Case) 1.640 (Control)	OR 1.30 (95% CI: 0.88 – 1.93) radon >140 Bq/m^3.	± 21 years	*Small Cell Lung Cancer* (SCLC)
6	(Bochicchio, et al. 2005)	*Lazio, Italy.* Sampel: 384 (Case) 404 (Control)	OR 1.48 (95% CI: 1.08 –2.02) radon 100 – 199 Bq/m^3.	25 years	*Adenocarcinoma*
7	(Wilcox, et al. 2008)	*New Jersey, US.* 651 (Case) 740 (Control)	EOR 0.05 (95% CI: -20.14 - 0.56) radon 100 Bq/m^3.	≥ 2 years	- *Small Cell Lung Carcinoma* - *Adenocarcinoma*
8	(Duran, et al. 2014)	*Galicia, Spain.* 192 (Case) 329 (Control)	OR 2.42 (95% CI: 1.45–4.06) radon ≥ 200 Bq/m^3.	30 years	- *Adenocarcinoma* - *Squamous Cell Carcinoma*
9	(Barros-Dios, et al. 2012)	*Galicia, Spain.* 349 (Case) 513 (Control)	OR 2.21 (95% CI, 1.33–3.69) radon ≥ 148 Bq/m^3.	>5 years	*- Small Cell Lung Cancer* *- Adenocarcinoma*
10	(Gonzales, et al. 2019)	*Galicia, Spain.* 523 (Case) 892 (Control)	OR 1.73 (95%CI: 1.27–2.35) radon ≥ 200 Bq/m^3.	± 30 years	- *Adenocarcinoma* - *Squamous Cell Carcinoma*
11	(Mourino, et al. 2020)	*Galicia, Spain.* 369 kasus	HR 1.42 (95%CI 1.06–1.90) radon ≥ 300 Bq/m^3.	-	*Adenocarcinoma*
12	(Park, et al. 2020)	*South Korea.* 519 (Case) 519 (Control)	OR 1.56 (95% CI: 1.03–2.37) radon ≥ 100 Bq/m^3.	>2 years	*Non – Small Cell Lung Cancer*

From all the research journal articles, there are 41.67% of studies used the CR-39 type Rn detector, and 16.7% of the studies used the LR115 type detector for Rn measurement. It is known that the CR-39 type Rn detector is often compared to the LR115. This is because the Rn detector type LR115 is widely used by laboratories and Rn security institutions such as the United States of America - Environmental Protection Agency (US-EPA) and the United Kingdom - National Radiological Protection Board (UK-NRPB). LR115 proved to be more effective than CR-39 [17].

Based on the research belonging to Mirsch, et al. (2020)[18], explained that in one hour with a concentration of Rn 44 kBq/m^3 or equivalent to a full year's exposure with an exposure concentration of Rn 50 Bq/m^3, it can cause DNA damage in experimental mice. The absorbed dose induced by Rn exposure is 10 mGy (milligray) in the lung. It is known that 1 mSv is produced by exposure to radiation of 1 mGy. The International Commission on Radiological Protection (ICRP) sets the maximum effective dose per unit of Rn exposure in the house per year alike 3-10 mSv. An understanding of the dangers of Rn exposure can be found if the householder is exposed to an Rn concentration level of 50 Bq/m^3, for one-year exposure duration (365 days/24 hours) it is estimated that it can lead to induction in the lungs with an absorbed dose of Rn of 10 mGy. The concentration of Rn 50 Bq/m^3, can be said to be less than the reference value set by WHO which is 100 Bq/m^3, but due to the long duration of exposure, the risk of lung cancer may increase [8]. The indoor Rn gas concentration shows higher values in the autumn and winter season when the outdoor temperature is low, doors and windows remain closed most of the time[19]. From twelve journal articles obtained that the country which shows the most dominant indoor Rn concentration and the risk of lung cancer was Spain. Countries in Europe show the highest value of Rn concentration other than another country.

Duration/Residence Years of the Occupants

Nine research journal articles showing an association with lung cancer risk, the average duration of stay in the house of the respondent with various Rn concentrations, starting from> 2 years (Park, et al. 2020 [20]); 2 years (Wilcox, et al. 2008 [11]); > 5 years (Barros-Dios, et al. 2012 [21]); ± 10 years (Pisa, et al. 2001[12]. & Biberman, et al. 1993 [22]); and between 20 – 30 years (Gonzalez, et al. 2019 [23]; Duran, et al. 2014 [24]; Kreienbrock, et al. 2001 [13]; Bochicchio, et al. 2013 [25]). Measurement of the respondent's residence years for at least the last 15 years is urgently needed. The average duration of the respondent's stay is 23 years and if necessary, it is adjusted to changing seasons, so that each measurement of radon concentrations at home for one full year can be said to be representative [8].

From several reviewed journal articles, there is the age of the occupants which shows between 25-75 years old. The explanation can be supported by the calculation of environmental health risk analysis (EHRA) which predicts the estimated level of carcinogenic risk of a toxic agent can start from the duration of exposure of 30 years (residential / settlement) [26]. However, there is one research journal article that belongs to Park, et al. (2020) [27], who explained that there was a significant relationship between Rn exposure and the risk of lung cancer with the duration of residence of the occupants of the house, which was > 2 years and the Rn concentration of 100 Bq/m^3. This study provides another fact that the duration of exposure to Rn in the house to cause a risk of lung cancer in residents, may occur in the range of > 2 years of stay with Rn concentrations that exceed the WHO reference limit of 100 Bq/m^3 [27] .

There is a study from Chen, et al. (2019) [28] on measuring the risk of lung cancer due to exposure to Rn at home. Because Rn is present in many places and various concentrations, the time data regarding daily activity is a key component of exposure assessment. For example, the measurement of the duration of household occupants in Canada where about 70% of the total activity time is spent indoors and the concentration of Rn in the home is higher (three times) compared to school and office buildings. Based on these data, the study explained that exposure to Rn in the home accounts for 90% of the risk of lung cancer.

The duration of exposure to Rn in the house on the risk of lung cancer can be related through the calculation of the effective radiation dose that can be received per year (365 days) which is 3-10 mSv based on ICRP. ICRP also establishes a maximum indoor Rn exposure level of 7,000 hours or the equivalent of 292 days with a maximum Rn concentration of 200-600 Bq/m^3 [6]. It means that exposure to Rn with concentrations up to 600 Bq/m^3 (passing the WHO reference ≤ 100 Bq/m^3) for less than a year can increase the risk of lung cancer.

Subtypes of Lung Cancer

Based on each journal article used in this narrative review, there are six journal articles [13], [16], [21], [23], [24], and [25], explained that the type of lung cancer cells with certain subtypes that mostly developed in respondents due to exposure to Rn was Adenocarcinoma. Then followed by another type of lung cancer, namely Squamous Cell Carcinoma which is found in three research journal articles [13], [23], [24], and Small Cell Lung Cancer found in two research journal articles [21], [22]. One article journal explained the types of lung cancer cells due to exposure to Rn were found to be Non-Small Cell Lung Cancer with stage I-IIIA [27].

Types of cancer found in the central part of the lung, are divided into two types, namely squamous cell carcinoma (SCC) and small cell lung cancer (SCLC). SCC is histologically defined as a malignant epithelial cell tumor showing keratinization and/or intercellular bridges. There are four variants of SCC, namely papillary, clear cell, basaloid, and small cell variants. While small cell lung cancer (SCLC) or small cell lung cancer is defined as a non-malignant epithelial tumor consisting of small cells with little cytoplasm, then unclear cell boundaries, finely granular nuclear chromatin, and no nucleus showing nuclear prints. Macroscopically, SCLC is brownish-white, smooth, and brittle at the area of necrosis [29].

he peripheral of the lung is divided into two lung cancer types, namely adenocarcinoma, large cell carcinoma, and adenosquamous carcinoma. Histologically, adenocarcinoma is defined as a malignant epithelial tumor showing glandular differentiation or mucin production in an acinar, papillary, bronchoalveolar cell, or solid pattern with mucinous growth or a mixture of these. Macroscopically, adenocarcinoma of the lung is gray-white in color, often with central fibrosis that causes shrinkage of the pleura and can lead to necrosis [29]. The type of lung cancer cell, large cell carcinoma, is an epithelial malignant neoplasm that lacks cytology, with characteristics such as small cell carcinoma and glandular or squamous differentiation. In general, tumors are peripheral except for the basaloid form. In this tumor, there is a prominent cell nucleus that is different from small cell carcinoma. Rn gas can be inhaled or entered into the inhalation channel through the nose as a portal of entry, and the particles are in the respiratory tract and then go to the lungs. Furthermore, biological interactions occur in lung epithelial tissue or cells and then precipitate [8].

The deposition of solid alpha particles can cause DNA damage to cells. DNA damage caused by these alpha particles can also cause gene mutations. As a result of cell damage, cell growth becomes irregular, causing malignancy or cancer in lung tissue. Alpha particles that can cause DNA damage and genetic mutations give the possibility that DNA damage can occur due to Rn concentrations at each exposure level (low to high) [9]. In general, lung cancer has symptoms such as a chronic cough with or without phlegm. Then most of them have a cough with bloody sputum or hemoptysis. Symptoms of lung cancer are then followed by tightness or pain in the chest and around the ribs to the spine[29].

CONCLUSIONS AND SUGGESTION

Several journal articles in this study explained that there was a significant relationship between the concentration of Rn in the house and the risk of lung cancer with the duration of exposure/residence years of the occupants, which was between 2-30 years (median: 17 years). The indoor Rn gas concentration shows higher values in the autumn and winter season. Then the types of lung cancer cells that developed the most were adenocarcinoma and squamous cell carcinoma. Therefore, people need to maintain the indoor airflow by opening windows/ventilation routinely and using an exhaust fan/fan, for reducing the concentration of Rn that may exist in the house. Measurement of Rn gas concentration can be carried out routinely using an Rn detector.

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