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Health Effects of Radon Exposure

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Radon is a naturally occurring radioactive material that is formed as the decay product of uranium and thorium, and is estimated to contribute to approximately half of the average annual natural background radiation. When inhaled, it damages the lungs during radioactive decay and affects the human body. Through many epidemiological studies regarding occupational exposure among miners and residential exposure among the general population, radon has been scientifically proven to cause lung cancer, and radon exposure is the second most common cause of lung cancer after cigarette smoking. However, it is unclear whether radon exposure causes diseases other than lung cancer. Media reports have often dealt with radon exposure in relation to health problems, although public attention has been limited to a one-off period. However, recently in Korea, social interest and concern about radon exposure and its health effects have increased greatly due to mass media reports of high concentrations of radon being released from various close-to-life products, such as mattresses and beauty masks. Accordingly, this review article is intended to provide comprehensive scientific information regarding the health effects of radon exposure.

Key Words: Radon, inhalation exposure, lung neoplasm

INTRODUCTION

Radon is a radioactive gas of natural origin that is formed as the decay product of uranium and thorium found in soil and rocks. As a naturally occurring radioactive material, radon is present everywhere in the air at various concentrations, and radon is estimated to contribute to approximately half of the average annual natural background radiation.[1-3] There are about 40 known isotopes of radon, most of which have short half-lives in the microsecond to millisecond range and have little practical significance. Among them, radon-222 (radon) and radon-220 (thoron) are of practical significance. As the most abundant isotope of radon, radon-222 has a physical half-life of 3.823 days that comes from the decay of radium. Thoron has a physical half-life of 55.6 seconds that comes from decay of thorium. Each of these isotopes undergoes radioactive decay with the emission of alpha particles that change them into different elements, so-called radon progeny. Radon and its progeny can enter the human body when inhaled or swallowed. Most of the inhaled radon is exhaled. However, a small amount of radon and its progeny may remain in the lungs, undergo radioactive decay, and emit alpha particles, leading to lung damage.[4]

In May 2018, there was a news report that radon gas is released from mattresses manufactured by a particular company in South Korea. The problematic mattresses contained monazite, a substance that releases radon gas. Since this news report, other reports of indiscriminate use of monazite in underwear, accessories, beauty masks, and building materials were released, which led to social concerns about the health effects of radon exposure. In this regard, this study will look at the health effects of radon exposure in humans.

HISTORY OF THE RECOGNITION OF THE HEALTH EFFECTS OF RADON EXPOSURE

In the sixteenth century, it was known that some miners in central Europe died in the primes of their life with pulmonary

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symptoms and rapidly progressing cachexia.[5] In 1530, Paracelsus, a Swiss physician, named this lung disease "mala metallorum" in his book. In 1556, Georg Agricola, a German scientist and mineralogist described mala metallorum as a wasting disease of miners and recommended frequent ventilation and maintenance of respiratory protection during their work to prevent mala metallorum in his textbook on mining titled "De Re Metallica." However, over the subsequent few hundred years, it remained unclear as to what mala metallorum was and what caused the disease.

In 1879, Harting and Hesse performed an autopsy on a miner who had died of mala metallorum and identified mala metallorum as lung cancer.[6] Friedrich Ernst Dorn, a German physicist discovered a radioactive substance that was emitted from radium in 1900, later named radon. In 1924, Ludewig, et al. reported that high concentrations of radon in the air were detected at certain mines in Czechoslovakia, where there was a high incidence of lung cancer, which led to the hypothesis that radon exposure could cause lung cancer.[7]

Since the era of the "cold war" in the 1940s, when the "uranium rush" led to the supply of feed material for nuclear weapons production, many uranium mines have been developed all over the world, especially in Germany, Czech Republic, Canada, and the United States of America. Epidemiological studies of miners who worked in these uranium mines revealed that they were more likely to die of lung cancer than the general population. Since the 1950s, the recognition that radon and its progeny can accumulate at high concentrations in homes has led to concern about the potential lung cancer risk associated with domestic indoor exposure in the general population. As a result of this awareness, many epidemiological studies directly concerning the relationship between domestic indoor radon exposure and lung cancer in the general population have been published since the 1980s. Based primarily on studies of underground miners exposed to high levels of radon gas, radon was classified as a carcinogenic agent by the World Health Organization in 1986 and by the International Agency for Research on Cancer in 1988.

HEALTH EFFECT OF RADON EXPOSURE: LUNG CANCER

The relationship between radon exposure and lung cancer risk is described separately for occupational exposure among underground miners and residential exposure among the general population.

Lung cancer risk in underground miners

Since the 1960s, epidemiological studies of lung cancer risk in underground miners have been published. In studies of radon-exposed underground miners, radon progeny concentrations are generally expressed in terms of "working level (WL)" and "working level month (WLM)". WL is defined as any combination of short-lived radon progeny in 1 L of air that results in the ultimate release of 1.3×10^5 MeV of potential energy from alpha particles. WLM is defined as the cumulative exposure of an individual at a concentration of 1 WL for a working month of 170 hours. One WLM is approximately equivalent to the dose received by a person who lives for a year in a dwelling with a radon concentration of 227 Bq/m^3.[8] Table 1 lists the representative studies of radon exposure and lung cancer risk in underground miners with occupational exposure.[9-21]

The first comprehensive study on the relationship between radon exposure and lung cancer risk in underground miners was the Biological Effects of Ionizing Radiations (BEIR) IV report, which included cohort studies of miners in Colorado, Ontario, Eldorado, and Malmberget.[9] According to the BEIR IV report, the excess relative risk per 100 WLM was 1.3 [95% confidence interval (CI): 0.8–2.3]. Five years after the release of the BEIR IV report, the International Commission on Radiological Protection (ICRP) 65 report was published. Some of the epidemiological studies covered in the ICRP 65 report overlapped with those covered in the BEIR IV report (cohorts from Colorado, Ontario, Eldorado, and Malmberget), and some studies were added (from New Mexico, Bohemia, and France). The excessive relative risk per 100 WLM was 1.34 (95% CI: 0.82–2.13), which was similar to the result of the BEIR IV report.[10] In 1999, the BEIR IV report was extended to include 11 cohort studies and more than 60000 miners, resulting in the BEIR VI report, which reported an excessive relative risk per 100 WLM of 0.55 (95% CI: 0.27–1.13).[11] The BEIR VI report also considered the modifying factors of relative risk, such as time since exposure, attained age, and exposure rate. Miners exposed at a younger age and exposed to relatively low radon concentrations had a higher percentage increase in lung cancer death rate per WLM, compared to other miners. After the BEIR VI report, a more extensive and comprehensive study was described in the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) 2006 report.[12] According to the UNSCEAR 2006 report, the excess relative risk per 100 WLM was 0.59 (95% CI: 0.35–1.00). In the ICRP 115 report, the Commission recommended that the detriment-adjusted nominal risk coefficient of 5×10^{-4} per WLM (14×10^{-5} per mJh/m^3) should be used for radon- and radon-progeny-induced lung cancer, and this value was approximately twice the value calculated in the ICRP 65 report. Considering this finding, the recommended maximum reference level of indoor radon was lowered from 600 Bq/m^3 to 300 Bq/m^3, which corresponds to an annual effective dose of 4 mSv at workplace and 14 mSv at home.[8]

After these comprehensive studies, several updated or new cohort studies were published as shown in Table 1. In the near future, a new comprehensive report including these new studies is expected to be reported.

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Table 1. Radon Exposure and Lung Cancer Risk among Underground Miners with Occupational Exposure

Country	Author	Year of publication	Sample size	Person-years of exposure	No. of lung cancers cases	ERR/100 WLM (95% CI)
Combined study	BEIR IV[9]	1988	22562	433019	459	1.3 (0.8, 2.3)
	ICRP 65[10]	1993	31486	635022	1047	1.34 (0.82, 2.13)
	BEIR VI[11]	1999	60606	888906	2674	0.55 (0.27, 1.13)
	UNSCEAR[12]	2009	128634	3246467	5715	0.59 (0.35, 1.00)
	Lane, et al.[13]	2019	Low cumulative radon exposure <100 WLM	394236	408	2.2 (1.3, 3.4)
Canada	Keil, et al.[14]	2015	4124	130000	617	1.17 (1.15, 1.17)
	Navaranjan, et al.[15]	2016	28546	805650	1230	0.64 (0.43, 0.85)
Czech Republic	Tomasek[16]	2012	9978	308910	1141	0.97 (0.74, 1.27)
France	Laborde-Castérot, et al.[17]	2014	5086	153063	159	0.53 (0.19, 1.07)
	Rage, et al.[18]	2018	5400	186994	211	0.73 (0.32, 1.33)
Germany	Walsh, et al.[19]	2010	58987	1997041	3016	0.20 (0.17, 0.22)
	Kreuzer, et al.[20]	2015	5504	158383	159	3.39 (-0.01, 6.78)
Sweden	Jonsson, et al.[21]	2010	5486	170204	122	2.20 (0.23, 3.77)

ERR, excess relative risk; WLM, working level month; CI, confidence interval; BEIR, Biological Effects of Ionizing Radiations; ICRP, International Commission on Radiological Protection; UNSCEAR, United Nations Scientific Committee on the Effects of Atomic Radiation.

Lung cancer risk in the general population with residential exposure

With the identification of an increased risk of lung cancer due to occupational radon exposure in miners, residential exposure in the general population is also be expected to yield an increased risk of lung cancer. However, it should be taken into account that there is a substantial uncertainty to directly extrapolate the results of the underground miners, since the special nature of the cohort of underground miners and the propensity of the cohort of the general population may differ in their smoking habits and exposure to other harmful substances, such as arsenic and quartz, which can also cause lung cancer.

Epidemiological studies regarding residential radon exposure and the risk of lung cancer in the general population usually use the average concentration of radon gas per cubic meter (Bq/m^3 or pCi/L, where 1 pCi/L is equal to 37 Bq/m^3) of indoor air over the period of individual residence.

Table 2 shows the case-control studies that have reported on residential radon exposure and lung cancer risk.[22-29] While some of these studies have reported an increased risk of lung cancer in proportion to radon exposure dose, some studies did not report statistically significant results. The observation that many studies regarding residential exposure of the general population showed statistical insignificance, compared to occupational exposure among miners, could be explained by the smaller cohorts and the relatively lower levels of exposure to radon than among miners. Accordingly, several reports that collected single cohort studies and carried out combined analyses were published, and representative combined studies are shown in Table 3.[30-36] Most combined studies reported a statistically significant increase in lung cancer risk in proportion to radon exposure. Among them, in a collaborative study from 13 European case-control studies, the risk of lung cancer increased by 16% (95% CI: 5–31) per 100 Bq/m^3 after correction for random uncertainties in measuring radon concentrations. The absolute risk of lung cancer by age 75 years at usual radon concentrations of 0, 100, and 400 Bq/m^3 would be about 0.4%, 0.5%, and 0.7%, respectively for lifelong non-smokers and about 25 times greater (10%, 12%, and 16%) for cigarette smokers. That study also concluded that the dose-response relation seemed to be linear, with no threshold dose, and there was a significant dose-response relation even at low doses.[34]

Considering the epidemiologic studies regarding the relationship between radon exposure and lung cancer risk so far, the majority of studies of underground miners and most combined studies of the general population have reported that the risk of lung cancer increases statistically significantly in proportion to radon exposure. The World Health Organization considers that radon exposure is the second most common cause of lung cancer after cigarette smoking.[37] Moreover, since even low concentrations of radon exposure can also result in a small increase in the risk of lung cancer, a national radon policy is needed to reduce the risk of lung cancer and raise public awareness.

HEALTH EFFECTS OF RADON: DISEASES OTHER THAN LUNG CANCER

There are many pieces of scientific evidence indicating that radon exposure can cause lung cancer; however, it is unclear whether radon can cause diseases other than lung cancer. Due to the unique biokinetics of radon inhalation in the body, the effective radiation doses reaching specific organs are much lower than that received by the lungs.[38] Since radon mainly affects the human body by releasing alpha particles, it hardly causes health problems by external exposure. Therefore, when assessing a possible association between radon exposure and diseases other than lung cancer, the rationale for such a relationship is weak.

Many studies regarding the relationship between radon exposure and hematological cancers have been reported, and these studies are shown in Table 4.[39-48] Although some studies have suggested that radon may cause leukemia, many other studies did not show statistical significance. Some studies[39,44] even reported negative correlations; thus, the opinion that radon exposure may cause leukemia is generally not accepted as a scientific fact. However, it is thought that a combined report

Table 2. Case-Control Studies Regarding the Relationship between Residential Radon Exposure and Lung Cancer Risk

Country	Author	Year of publication	Study design	Sample size (Case/Control)	Grouping (Bq/m^3)	Risk estimate (95% CI)
China	Wang, et al.[22]	2002	Case-control	768/1659	100	OR 1.19 (1.05, 1.47)
Czech Republic	Tomasek[23]	2013			100	ERR
			Case-control	370/1399		0.14 (0.03, 0.39)*
			Never smoker	58/670		0.73 (0.02, 1.90)*
			Ever smoker	312/729		0.14 (0.02, 0.30)*
France	Baysson, et al.[24]	2004	Case-control	486/984	100	ERR 0.04 (-0.01, 0.11)
Spain	Barros-Dios, et al.[25]	2012	Case-control	349/513		OR
					<50	1.00
					50–00	1.87 (1.21, 2.88)
					101–147	2.25 (1.32, 3.84)
					>147	2.21 (1.33, 3.69)
	Torres-Durán, et al.[26]	2014	Case-control Never smoker	192/329		OR
					≤100	1.00
					101–147	0.80 (0.43, 1.50)
					148–199	1.16 (0.64, 2.11)
					≥200	2.42 (1.45, 4.06)
UK	Darby, et al.[27]	1998	Case-control	982/3185	100	ERR 0.12 (-0.05, 0.33)
USA	Sandler, et al.[28]	2006	Case-control	1474/1811	100	ERR 0.002 (-0.21, 0.21)
	Wilcox, et al.[29]	2008	Case-control	651/740	100	OR 1.05 (0.86, 1.56)

CI, confidence interval; OR, odds ratio; ERR, excess relative risk; UK, United Kingdom; USA, United States of America.
*90% confidence interval.

Table 3. Pooled Studies Regarding Residential Radon Exposure and Lung Cancer Risk

Author	Year of publication	No. of studies	Sample size (Case/Control)	Grouping (Bq/m^3)	Risk estimate (95% CI)
Lubin, et al.[30]	1997	8	4263/6612	150	ERR 0.14 (0.0, 0.3)
Pavia, et al.[31]	2003	17	NR		Adjusted OR
				50	1.07 (1.04–1.11)
				100	1.15 (1.07–1.24)
				150	1.24 (1.11–1.38)
				200	1.33 (1.15–1.354)
				250	1.43 (1.19–1.72)
Lubin, et al.[32]	2004	2	1050/1996	100	OR 1.33 (1.01, 1.36)
Krewski, et al.[33]	2005	7	3662/4966	100	OR 1.11 (1.00, 1.28)
Darby, et al.[34]	2006	13	7148/14208	100	ERR 0.08 (0.03, 0.16)
Zhang, et al.[35]	2012	22	13380/21102	100	ERR 0.07 (0.04, 0.10)
Lorenzo-González, et al.[36]	2019	Never smokers in Spain	523/892		OR
				≤100	1.00
				101–147	1.14 (0.80, 1.64)
				148–199	1.25 (0.85, 1.85)
				≥200	1.73 (1.27, 2.35)

CI, confidence interval; ERR, excess relative risk; NR, not reported; OR, odds ratio.

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Table 4. Epidemiologic Studies Regarding the Relationship between Radon Exposure and Hematologic Cancer Risk

Country	Author	Year of publication	Type of leukemia	Sample size (Case/Control)	Grouping (Bq/m^3)	Risk estimate (95% CI)
Sweden	Stjernfeldt, et al.[39]	1987	ALL, AML	7/7	-	Case 156 Bq/m^3 Control 333 Bq/m^3
USA	Lubin, et al.[40]	1998	ALL	281/281 (matched) 505/443 (unmatched)	>148 vs. <37	ERR: 0.02 (-0.5, 1.0) ERR: 0.44 (-0.1, 1.3)
Germany	Kaletsch, et al.[41]	1999	Acute leukemias	82/209	> 70 vs. <70	OR 1.30 (0.32, 5.33)
Canada and USA	Steinbuch, et al.[42]	1999	AML	173/254	>100 vs. <37	OR 1.1 (0.6, 2.0)
UK	Law, et al.[43]	2000	Acute leukemias	578/983	>200 vs. <25	OR 0.90 (0.31, 2.62)
UK	UK Childhood Cancer Study Investigators[44]	2002	ALL Other leukemias	805/1306 146/232	>30 vs. <8	OR: 0.77 (0.61, 0.99) OR: 0.71 (0.43, 1.19
Denmark	Raaschou-Nielsen[45]	2008	ALL ANLL Chronic leukemias	860/1720 150/300 143/286	>178 vs. <52 (for 5 yr-old child)	ERR: 0.63 (0.05, 1.53) ERR: -0.40 (-0.75, 0.41) ERR: 0.36 (-0.52, 2.83)
Switzerland	Hauri, et al.[46]	2013	All leukemias ALL	283 (cohort) 225 (cohort)	≥139.9 vs. <77.7	HR: 0.95 (0.63, 1.43) HR: 0.90 (0.56, 1.43)
Norway	Del Risco Kollerud, et al.[47]	2014	All leukemias	431 (cohort)	<50 50–100 >100 Per 100	HR 1.00 1.05 (0.82, 1.33) 1.06 (0.82, 1.39) 0.99 (0.86, 1.13)
USA	Teras, et al.[48]	2016	All hematologic cancers	1308 (women's cohort)	<74 74–<100 100–124 125–148 >148 Per 100	HR 1.00 0.97 (0.78, 1.21) 1.37 (1.07, 1.75) 1.39 (0.96, 2.02) 1.63 (1.23, 2.18) 1.38 (1.15, 1.65)

CI, confidence interval; ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; USA, United States of America; ERR, excess relative risk; OR, odds ratio; UK, United Kingdom; ANLL, acute nonlymphocytic leukemia; HR, hazard ratio.

of all case-control studies will be needed.

According to the Cancer Prevention Study II, which was a prospective trial conducted in the United States of America, radon exposure was significantly associated with chronic obstructive pulmonary disease (COPD) mortality (hazard ratio per 100 Bq/m^3, 1.13; 95% CI: 1.05–1.21), suggesting that residential radon exposure may increase the mortality rate due to COPD.[49] More studies regarding the relationship between radon exposure and benign lung disease are thought to be needed.

The relationship between radon exposure and central nervous system tumors is also inconclusive. According to a systematic review performed by Ruano-Ravina et al.,[50] among 18 studies, some studies showed an association with radon and cancers of the central nervous system, while the majority did not show any effect. The relationship between radon exposure and thyroid cancer;[51,52] skin cancer;[53-55] head and neck cancer;[56-58] stomach cancer;[59] heart disease;[60] and reproductive, fetal, and hereditary effects[61] have also not been scientifically proven for the same reason.

DISCUSSION AND CONCLUSION

It has been scientifically proven that exposure to radon can cause lung cancer. Diseases other than lung cancer, however, seem to be unrelated, and the relationship with some diseases, especially leukemia and COPD, remains controversial. Nevertheless, as interest among the public increases in the event of nuclear or radiation-related issues and causes excessive concern, passing on scientifically unproven information recklessly to the general public will lead to its acceptance as the truth, regardless of its authenticity. Therefore, mass media and related experts need to deliver accurate information continuously to the general public based on scientific evidence. When mass media or related experts communicate information to the public, there is a need for a balanced view supported by many studies, rather than focusing on one or two studies.

There have been many commercial advertisements recently for air purifiers, foods, and drugs that can remove radon from the air or the body. For now, scientific evidence regarding their health effects is insufficient, and these should be elucidated clearly. Based on the misunderstanding that anions can have a beneficial health effect, a monazite-containing substance that could release anions was added to bed mattresses, and this resulted in the radon bed mattress incident in Korea. Thus, if products that are scientifically not validated are sold commercially through false or exaggerated advertisements, consumers could be deceived twice. Hence, attempts to further spread public fear of radon for commercial purposes and economic gains should be eradicated.

It is difficult to accurately assess by how much the risk of lung cancer would increase among customers who used radon-releasing mattresses based only on the report regarding the concentration of radon in a specific mattress model announced by the Korean government. Furthermore, because the occurrence of lung cancer due to radon exposure is a stochastic effect, this would need to be observed through long-term follow-up (for several years to several decades). Some experts argue for epidemiological investigations regarding the radon mattress incident; however, in order to carry out an accurate epidemiological study, more precise individual data (e.g., duration of radon-releasing bed mattress use, sleeping habits, and sleep posture) need to be collected.

In conclusion, it is scientifically proven that radon exposure can cause lung cancer, whereas its relation with diseases other than lung cancer remains controversial. Mass media and related experts need to communicate accurate information to the general public, and it is necessary to maintain a balanced view supported by many studies when providing information to the general public.

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AUTHOR CONTRIBUTIONS

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