



A Comparative Review of Radiation-induced Cancer Risk Models

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ABSTRACT

Background: With the need for a domestic level 3 probabilistic safety assessment (PSA), it is essential to develop a Korea-specific code. Health effect assessments study radiation-induced impacts; in particular, long-term health effects are evaluated in terms of cancer risk. The objective of this study was to analyze the latest cancer risk models developed by foreign organizations and to compare the methodology of how they were developed. This paper also provides suggestions regarding the development of Korean cancer risk models.

Materials and Methods: A review of cancer risk models was carried out targeting the latest models: the NUREG model (1993), the BEIR VII model (2006), the UNSCEAR model (2006), the ICRP 103 model (2007), and the U.S. EPA model (2011). The methodology of how each model was developed is explained, and the cancer sites, dose and dose rate effectiveness factor (DDREF) and mathematical models are also described in the sections presenting differences among the models.

Results and Discussion: The NUREG model was developed by assuming that the risk was proportional to the risk coefficient and dose, while the BEIR VII, UNSCEAR, ICRP, and U.S. EPA models were derived from epidemiological data, principally from Japanese atomic bomb survivors. The risk coefficient does not consider individual characteristics, as the values were calculated in terms of population-averaged cancer risk per unit dose. However, the models derived by epidemiological data are a function of sex, exposure age, and attained age of the exposed individual. Moreover, the methodologies can be used to apply the latest epidemiological data. Therefore, methodologies using epidemiological data should be considered first for developing a Korean cancer risk model, and the cancer sites and DDREF should also be determined based on Korea-specific studies.

Conclusion: This review can be used as a basis for developing a Korean cancer risk model in the future.

Keywords: Level 3 PSA, Radiation, Health effects, Cancer risk model

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Introduction

A level 3 probabilistic safety assessment (PSA) aims to estimate the environmental and health effects of radiation from nuclear accidents on the public. To this end, various codes have been developed for level 3 PSA: in the U.S., this includes the MELCOR accident consequence code system (MACCS) developed by the Nuclear Regulatory Commission (NRC); in Japan, the off-site consequence analysis of atmospheric releases of radionuclides (OSCAAR); and in the European Commission (EC), the code system from MARIA (COSYMA) [1]. However, there is no level 3 PSA code unique to Korea, and the U.S. NRC code MACCS has been adopted for level 3 PSA.

After the Fukushima nuclear accident in 2011, there has been increasing demand for off-site consequence analyses in terms of the environmental and health impacts of radiation exposure. In Korea, the recent enactment of a new nuclear safety act has obligated relevant organizations to conduct a level 3 PSA, increasing the need to develop a level 3 PSA code specific to Korea.

A level 3 PSA sequentially evaluates the atmospheric dispersion of radioactive material, exposure dose, and public health effects. As well as being an integral component of off-site consequence analyses, assessing the impact of radiation on public health involves quantification of these health effects. Radiation-induced public health effects can be classified as short-term or long-term effects. Short-term effects occur when the body exposed to a large amount of radiation. These effects reveal themselves within a year of exposure and are regarded as deterministic effects associated with exposure more than a threshold dose of radiation. Long-term effects surface several decades after the radiation exposure. They are probabilistic effects that occur without a threshold dose. Examples of long-term effects of radiation are cancer induced by somatic mutations and genetic (i.e., heritable) diseases induced by mutations in reproductive cells [2]. As seen in post-nuclear accidents, chronic exposure is thought to cause long-term health effects, generally cancer; thus, parameters such as the incidence and mortality of cancer are important scales when assessing radiation-induced public health impacts. Accordingly, multiple organizations have developed models estimating radiation-induced cancer incidence and/or mortality, and recently these cancer risk models have been refined using the most recent updates of atomic bomb survivor data from Japan.

In 1972, the U.S. National Academy of Sciences published its initial report on the biological effects of ionizing radiation (BEIR) and developed a risk model for radiation-induced cancer [3]. In its seventh publication, the BEIR VII report in 2006, a new risk model was presented that reflects the latest data from the Japanese atomic bomb database [4, 5]. Similarly, in their 1993 NUREG/CR-4214 report, the U.S. NRC published an updated cancer risk model for exposure to radiation from nuclear accident, which is a revision of the initial model they published in 1985. Later, the U.S. NRC developed an MACCS code as a tool for level 3 PSA, which is built upon the cancer risk model published in NUREG/CR-4214 in 1990 [6-11]. The United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) and the Interna-

tional Commission on Radiological Protection (ICRP) have each developed an updated cancer risk model, which were presented in the UNSCEAR 2006 report and the ICRP 103, respectively [12, 13]. Other models have also been developed and used, for instance by the U.S. Environmental Protection Agency (EPA), which created an improved version of the BEIR VII (2006) model, and by the World Health Organization, which adapted the latest models of UNSCEAR and ICRP to conduct off-site consequence analyses of the Fukushima nuclear accident [14, 15]. These reports indicate that multiple organizations are directing their efforts and resources to develop and enhance models to determine the health effects of radiation and to estimate the associated risks, such as radiation-induced cancer risk.

In advance of developing a model of health risks specific to the Korean population, and thereby a level 3 PSA code specific to Korea, we evaluated the latest cancer risk models of different organizations. We analyzed the methodological approaches employed by each organization to develop these cancer risk models and compared the epidemiological data, dose-response functions, and the selection of cancers across organizations. Recommendations based on our findings are presented with respect to the development of cancer risk models specific to the Korean population.

Materials and Methods

1. Mathematical modeling

The risk of cancer due to radiation can be defined using both multiplicative and additive models. The multiplicative model assumes that radiation-induced excess cancer risk shows a relative increase in risk, or excess relative risk (ERR), in proportion to the baseline rate. The additive model assumes that radiation-induced excess cancer risk shows an absolute increase in risk, or excess absolute risk (EAR) associated with exposure independently of the baseline rate. The radiation-induced excess cancer risk is calculated using the following equations:

$$\text{Multiplicative model: } M(D,e,a,g) = ERR(D,e,a,g) \times \lambda_u(a,g) \quad (1)$$

$$\text{Additive model: } M(D,e,a,g) = EAR(D,e,a,g) \quad (2)$$

$$\text{Weighted arithmetic mean: } M(D,e,a,g) = \omega \times ERR(D,e,a,g) \times \lambda_u(a,g) + (1-\omega) \times EAR(D,e,a,g), \quad 0 \leq \omega \leq 1 \quad (3)$$

Here, $M(D,e,a,g)$ denotes radiation-induced excess cancer risk, with the following functions: dose of exposure (D), age at exposure to radiation (e), attained age of an individual (a), and gender (g). Additionally, $\lambda_u(a,g)$ denotes cancer risk without exposure to radiation.

Simply, both ERR and EAR are calculated as the dose-response function, $\rho(D)$, multiplied by the effect modification, $\epsilon(X)$. The basic formula of $\rho(D)$ is a linear, linear-quadratic, or quadratic form and $\epsilon(X)$ has an exponential form with respect to variables such as age at exposure, attained age, and gender. The coefficients of the equation are determined by conducting a regression analysis of the epidemiological data (e.g., of atomic bomb survivor data and medical records/databases) of the exposed population, which are then added to the basic formula of $\rho(D)$ and $\epsilon(X)$ [16, 17].

$$\text{ERR or EAR} = \rho(D) \times \epsilon(X), \tag{4}$$

$$\text{dose-response function, } \rho(D) = \begin{cases} \alpha D \\ \alpha D + \beta D^2 \\ \beta D^2 \end{cases}$$

effect modification, $\epsilon(X) = e^{\theta X}$, θ' = variable factor

The term $\rho(D)$ describes dose-dependent cancer risk, whereas $\epsilon(X)$ adjusts for cancer risk attributed to non-radiological factors such as age at exposure, attained age, and gender under the same dose exposure. Estimates of low-

dose radiation-induced cancer risk are extrapolated from risk models derived from high-dose exposure data, such as the Japanese atomic bomb survivor data. Because the cancer risk in the range of low dose may be overestimated in the linear $\rho(D)$ model, the dose and dose rate effectiveness factor (DDREF) has been used to adjust for this.

2. NUREG model (1993)

The NUREG model assumes that $\rho(D)$ is linear. The DDREF is used for exposure to radiation doses below 0.2 Gy or dose rates below 0.1 Gy·h⁻¹. The term $\epsilon(X)$ is not defined in this model, and risk is adjusted using age group-specific risk coefficients. The excess cancer risk model is shown in Table 1. Further, the cancer risk estimates of the NUREG model use risk coefficients defined in terms of cancer risk per unit of dose calculated in previous studies, such as the BEIR III study.

$$r_k(D) = \left(\frac{1}{DDREF}\right) \times c_k \times D, \tag{5}$$

c_τ = risk coefficient by age group (Gy⁻¹)

The lifetime cancer risk of the population is calculated by multiplying the excess cancer risk over a specific period of time after the initial radiation by population-specific characteristics, such as the distribution of population and survival rates by age group.

Table 1. NUREG Cancer Risk Model

Cancer site	Model/ Sex*	Latency period [yr]	Expression period [yr]	Minimum age [yr]	Risk coefficient†						DDREF
					Morbidity‡			Mortality‡			
					0-19	20-39	40+	0-19	20-39	40+	
Leukemia	A	2	25	0	N/A§	N/A	N/A	4.50 × 10 ⁻⁰⁴	4.50 × 10 ⁻⁰⁴	4.50 × 10 ⁻⁰⁴	2
Thyroid	M	5	∞	0	2.50 × 10 ⁻⁰⁵	1.25 × 10 ⁻⁰⁵	1.25 × 10 ⁻⁰⁵	2.50 × 10 ⁻⁰⁵	1.25 × 10 ⁻⁰⁵	1.25 × 10 ⁻⁰⁵	1
	F	5	∞	0	2.50 × 10 ⁻⁰⁴	2.50 × 10 ⁻⁰⁴	2.50 × 10 ⁻⁰⁴	2.50 × 10 ⁻⁰⁵	2.50 × 10 ⁻⁰⁵	2.50 × 10 ⁻⁰⁵	1
Breast	R	10	∞	30	0.7	0.3	0.1	0.7	0.3	0.1	1
Bone	A	2	25	0	N/A	N/A	N/A	5.00 × 10 ⁻⁰⁶	5.00 × 10 ⁻⁰⁶	5.00 × 10 ⁻⁰⁶	2
Lung	R	10	∞	40	0.6	0.3	0.3	0.6	0.3	0.3	2
Gastrointestinal system	R	10	∞	0	1.2	0.4	0.4	1.2	0.4	0.4	2
Skin	R	10	∞	0	0.5	0.5	0.5	0	0	0	2
Other solid	R	10	∞	0	1.1	0.25	0.25	1.1	0.25	0.25	2
Leukemia from in utero exposure	A	0	12	N/A	N/A	N/A	N/A	2.30 × 10 ⁻⁰²	2.30 × 10 ⁻⁰²	2.30 × 10 ⁻⁰²	1
Solid cancer from in utero exposure	A	0	10	N/A	N/A	N/A	N/A	2.30 × 10 ⁻⁰²	2.30 × 10 ⁻⁰²	2.30 × 10 ⁻⁰²	1
Benign thyroid nodules	M	10	∞	0	9.30 × 10 ⁻⁰⁴	4.65 × 10 ⁻⁰⁴	4.65 × 10 ⁻⁰⁴	0	0	0	1
	F	10	∞	0	9.30 × 10 ⁻⁰⁴	9.30 × 10 ⁻⁰⁴	9.30 × 10 ⁻⁰⁴	0	0	0	1

*A: absolute risk model, R: relative risk model, M: male, F: female; †The unit for EAR is per person-year-Gy and the unit for ERR is per Gy; ‡Individual age at exposure; §Not available.

Note: Mathematical model

$$RISK_k(D) = \left(\frac{1}{DDREF}\right) \times c_k \times D, \quad c_\tau = \text{risk coefficient, D=dose}$$

$$R(D) = \sum_{\tau} R(\tau, D) = \sum_{\tau} \sum_k f_k \times S_k(\tau) \times r_k(\tau, D) \tag{6}$$

Here, $R(\tau, D)$ denotes the mean cancer risk from exposure to radiation over a certain period of time after the initial radiation (τ). The population-specific factors f_k and $S_k(\tau)$ denote the population distribution by age group (k) and the survival rate of the age group (k) during this time (τ), respectively [9]. Because the MACCS code, which is the adopted code in Korea, calculates lifetime cancer risk using an $R(D)$ equation based on data from the US National Census in 1980, estimating the cancer risk in Korean populations with the MACCS code may lead to errors [10].

3. BEIR VII model (2006)

The BEIR VII model is developed based on epidemiological data from radiation-exposed populations, and aims to estimate cancer risk induced by exposure to low-linear energy transfer radiation. Risk models for cancer incidence and mortality have been developed for leukemia and for solid cancers. Models for solid cancers were further developed according to site (stomach, colon, liver, lung, breast, prostate, ovary, bladder, thyroid, and others). The risk model for leukemia was derived from the Japanese atomic bomb mortality data from the period 1950-2000 [18], and that for the solid

cancers from the Japanese atomic bomb cancer incidence data from the period 1958-1998 [17]. Cancer risks are predicted as weighted means of the ERR and EAR estimates and adjusted for age at exposure, attained age, gender, and time after initial exposure (t). The leukemia model has a linear-exponential $\rho(D)$ term and a latency period of 2 years. The solid cancer model has a linear $\rho(D)$ term with an estimated DDREF of 1.5 and a latency period of 5 years. The ERR and EAR models are shown below, and the coefficients of the BEIR VII model are presented in Table 2.

$$\text{Leukemia: } ERR \text{ or } EAR = \beta_g (1 + \theta D) \times e^{[\gamma e^* + \delta \log(\frac{t}{25}) + \phi e^* \log(\frac{t}{25})]} \tag{7}$$

$$\text{Thyroid cancer: } ERR = \beta_g D \times e^{\gamma e^*} \tag{8}$$

$$\text{Breast cancer: } EAR = \beta_g D \times e^{[\gamma \frac{(e-25)}{10}]} \times (\frac{a}{50})^\eta \tag{9}$$

$$\text{Other solid cancers: } ERR \text{ or } EAR = \beta_g D \times e^{\gamma e^*} \times (\frac{a}{60})^\eta, e^* = \frac{\min(e, 30) - 30}{10} \tag{10}$$

Although the equations for ERR and EAR are identical for risk models of cancer incidence and mortality, the risk of cancer mortality is calculated by multiplying the risk of cancer incidence by the ratio of the baseline rate of cancer mo-

Table 2. Coefficients of the BEIR VII Cancer Risk Model

Cancer site	Weighting factor for ERR (ω)	ERR				EAR			
		β_{M^*}	β_{F^*}	γ^{\dagger}	η	$\beta_{M^{\ddagger}}$	$\beta_{F^{\ddagger}}$	γ^{\dagger}	η
Leukemia	0.7	1.1 $\delta = -0.48$	1.2 $\delta = 0.42$	-0.4 $\delta = 0.87$	N/A [¶]	1.62 $\delta = -0.48$	0.93 $\delta = 0.56$	0.29 $\delta = 0.88$	N/A
Thyroid [§]	1	0.53	1.05	-0.83	N/A	No model			
Breast [§]	0	No model				N/A	9.9	-0.51	3.5 1.1
Stomach	0.7	0.21	0.48	-0.30	-1.4	4.9	4.9	-0.41	2.8
Colon	0.7	0.63	0.43	-0.30	-1.4	3.2	1.6	-0.41	2.8
Liver	0.7	0.32	0.32	-0.30	-1.4	2.2	1.0	-0.41	4.1
Lung	0.3	0.32	1.40	-0.30	-1.4	2.3	3.4	-0.41	5.2
Prostate	0.7	0.12	N/A	-0.30	-1.4	0.11	N/A	-0.41	2.8
Uterus	0.7	N/A	0.055	-0.30	-1.4	N/A	1.2	-0.41	2.8
Ovary	0.7	N/A	0.38	-0.30	-1.4	N/A	0.70	-0.41	2.8
Bladder	0.7	0.50	1.65	-0.30	-1.4	1.2	0.75	-0.41	6.0
Other solid	0.7	0.27	0.45	-0.30	-2.8	6.2	4.8	-0.41	2.8

*The unit for ERR is per Sv, M: male, F: female; [†]The unit is per decade; [‡]The unit for EAR is per 104 person-year-Sv, M: male, F: female; [§]The dose unit is Gy; ^{||}If attained age is below 50, η is 3.5. Otherwise, η is 1.1; [¶]Not available. Note: Mathematical models

$$\text{Leukemia: } ERR \text{ or } EAR = \beta_g (1 + \theta D) \times e^{[\gamma e^* + \delta \log(\frac{t}{25}) + \phi e^* \log(\frac{t}{25})]}$$

$$\text{Thyroid cancer: } ERR = \beta_g D \times e^{\gamma e^*}$$

$$\text{Breast cancer: } EAR = \beta_g D \times e^{[\gamma \frac{(e-25)}{10}]} \times (\frac{a}{50})^\eta$$

$$\text{Solid cancer: } ERR \text{ or } EAR = \beta_g D \times e^{\gamma e^*} \times (\frac{a}{60})^\eta, e^* = \frac{\min(e, 30) - 30}{10}$$

ality, $\lambda_m(a)$ to the baseline rate of cancer incidence of the unexposed population, $\lambda_i(a)$.

Excess cancer incidence risk:

$$M_i(D, e, a) = \begin{cases} EAR(D, e, a), & EAR \text{ model} \\ ERR(D, e, a) \times \lambda_i(a), & ERR \text{ model} \end{cases} \quad (11)$$

Excess cancer mortality risk:

$$M_i(D, e, a) = \begin{cases} EAR(D, e, a) \times \frac{\lambda_m(a)}{\lambda_i(a)}, & EAR \text{ model} \\ ERR(D, e, a) \times \lambda_m(a), & ERR \text{ model} \end{cases} \quad (12)$$

The lifetime risk of cancer of the exposed population is calculated using the lifetime attributable risk (LAR), which describes the accumulated risk from the initial radiation. When calculating the LAR of solid cancers, excluding thyroid and breast cancers, and of leukemia, the weighted geometric mean is utilized (L = latency, $S(a)$ = survival rate by age group of the study group) [5].

$$LAR = \int_{e+L}^{100} M(D, e, a) \times \frac{S(a)}{S(e)}, \quad (13)$$

$$\text{Weighted geometric mean: } LAR = (LAR_{ERR})^\omega \times (LAR_{EAR})^{1-\omega} \quad (14)$$

4. UNSCEAR model (2006)

Risk models for the incidence and mortality associated with radiation exposure were developed for leukemia and solid cancers by UNSCEAR. These cancer risk models were derived through regression analyses of the Japanese atomic bomb survivor cancer mortality data from the period 1950-2000 and of Japanese atomic bomb survivor cancer incidence data from the period 1958-1998. The risk models for mortality from leukemia and solid cancers have a linear-quadratic $\rho(D)$ term, and the sites of solid cancers are not specified. The risk model for the incidence of solid cancers is linear and was developed for various cancer sites (Table 3). Only the $\rho(D)$ of risk models for incidence of bone cancer and non-melanoma skin cancer have a linear-quadratic function and a quadratic-exponential function, respectively. For leukemia, the risk models for cancer incidence and mortality are the same. The DDREF was presented as 2 and the ERR and EAR estimates were adjusted via $\epsilon(X)$ with respect to age at exposure, attained age, and gender.

Table 3. Coefficients of the UNSCEAR Solid Cancer Risk Model

Cancer site	ERR								EAR					
	α^*	β^{\dagger}	γ	κ_1	κ_2	κ_3	κ_4	α^{\ddagger}	β^{\S}	γ	κ_1	κ_2	κ_3	κ_4
Thyroid	3.81×10^4	0	0	0	0	-2.20	-0.44	2.63×10^{-4}	0	0	1.36	0	0	-0.39
Breast	1.49×10^4	0	0	0	0	-2.30	0	1.94×10^{-5}	0	0	0	1.09	0	0
Esophagus	0.53	0	0	0	0	0	0	1.45×10^{-5}	0	0	0	0	0	0
Stomach	4.03×10^3	0	0	0	0	-2.25	0	3.97×10^{-7}	0	0	0	0	1.83	0
Colon	1.48×10^5	0	0	0	0	-3.53	0	2.88×10^9	0	0	0	0	3.20	0
Liver	3.95×10^{-1}	0	0	0	0	0	0	1.04×10^{-10}	0	0	0	0	3.48	0
Lung	3.18×10^{-1}	0	0	1.48	0	0	0	1.01×10^{-11}	0	0	0.40	0	4.21	0
Bone	0	6.90×10^7	0	0	0	-4.47	0	0	9.33×10^{-6}	0	0	0	0	0
Skin	0	2.62×10^3	-0.27	0	3.20	-4.60	0	0	5.25×10^{-9}	-0.27	0	2.89	0	0
Bladder	8.99×10^{-1}	0	0	0	0	0	0	6.14×10^{-15}	0	0	0	0	5.75	0
Brain and central nervous system	7.43	0	0	0	0	0	-0.99	4.92×10^{-5}	0	0	0	0	0	0
Other solid	1.43×10^2	0	0	0	1.65	-2.94	0	2.21×10^{-7}	0	0	0	2.16	0	0

*The unit is per Sv; [†]The unit is per Sv²; [‡]The unit is per Sv·a; [§]The unit is per Sv²·a; ^{||}Skin cancer is limited to non-melanoma skin cancer.

Note:

1) Mathematical model

$$\text{Solid cancer (morbidity): } ERR \text{ or } EAR = (\alpha D + \beta D^2) \times e^{\gamma D} \times e^{\kappa_1 \cdot 1_{g=female} + \kappa_2 \ln(a-e) + \kappa_3 \ln(a) + \kappa_4 \ln(e)}$$

2) Other models

$$\text{Solid cancer (mortality): } ERR = (\alpha D + \beta D^2) \times e^{\kappa_1 \cdot 1_{g=female} + \kappa_2 \ln(a-e)}$$

$$\alpha = 408.29 \text{ Sv}^{-1}, \frac{\beta}{\alpha} = 0.29 \text{ Sv}^{-1}, \kappa_1 = 0.66, \kappa_2 = 0.99, \kappa_3 = -2.64$$

$$EAR = (\alpha D + \beta D^2) \times e^{\kappa_1 \ln(a-e) + \kappa_2 \ln(a)}$$

$$\alpha = 7.75 \times 10^{-9} \text{ Sv}^{-1}, \frac{\beta}{\alpha} = 0.40 \text{ Sv}^{-1}, \kappa_1 = 0.66, \kappa_2 = 2.34$$

$$\text{Leukemia: } ERR = (\alpha D + \beta D^2) \times e^{\kappa_1 \ln(a)}, \alpha = 864.55 \text{ Sv}^{-1}, \frac{\beta}{\alpha} = 1.18 \text{ Sv}^{-1}, \kappa_1 = -1.65$$

$$EAR = (\alpha D + \beta D^2) \times e^{\kappa_1 \cdot 1_{g=female} + \kappa_2 \ln(a-e)}, \alpha = 7.52 \times 10^{-4} \text{ Sv}^{-1}, \frac{\beta}{\alpha} = 1.04 \text{ Sv}^{-1}, \kappa_1 = -0.53, \kappa_2 = -0.61$$

Risk model for the incidence of and mortality from leukemia:

$$ERR = (\alpha D + \beta D^2) \times e^{\kappa_1 \ln(a)} \tag{15}$$

$$\alpha = 864.55 \text{ Sv}^{-1}, \frac{\beta}{\alpha} = 1.18 \text{ Sv}^{-1}, \kappa_1 = -1.65$$

$$EAR = (\alpha D + \beta D^2) \times e^{\kappa_1 \cdot 1_{g=female} + \kappa_2 \ln(a-e)} \tag{16}$$

$$\alpha = 7.52 \times 10^{-4} \text{ Sv}^{-1}, \frac{\beta}{\alpha} = 1.04 \text{ Sv}^{-1}, \kappa_1 = -0.53, \kappa_2 = -0.61$$

Risk model of mortality from solid cancers:

$$ERR = (\alpha D + \beta D^2) \times e^{\kappa_1 \cdot 1_{g=female} + \kappa_2 \ln(a-e)} \tag{17}$$

$$\alpha = 408.29 \text{ Sv}^{-1}, \frac{\beta}{\alpha} = 0.29 \text{ Sv}^{-1}, \kappa_1 = 0.66, \kappa_2 = 0.99, \kappa_3 = -2.64$$

$$EAR = (\alpha D + \beta D^2) \times e^{\kappa_1 \ln(a-e) + \kappa_2 \ln(a)} \tag{18}$$

$$\alpha = 7.75 \times 10^{-9} \text{ Sv}^{-1}, \frac{\beta}{\alpha} = 0.40 \text{ Sv}^{-1}, \kappa_1 = 0.66, \kappa_2 = 2.34$$

Risk model for incidence of solid cancers:

$$ERR \text{ or } EAR = (\alpha D + \beta D^2) \times e^{\gamma D} \times e^{\kappa_1 \cdot 1_{g=female} + \kappa_2 \ln(a-e) + \kappa_3 \ln(a) + \kappa_4 \ln(e)} \tag{19}$$

The lifetime risk of cancer of the population is derived from parameters such as excess cancer death and risk of ex-

Table 4. Coefficients of the ICRP 103 Leukemia Risk Model

Sex	EAR*								
	0-19 [†]			20-39 [†]			40+ [†]		
	α	β	κ_1	α	β	κ_1	α	β	κ_1
Male	0.33	0.26	-0.17	0.48	0.38	-0.43	1.31	1.03	-0.07
Female	0.66	0.52	-0.07	0.97	0.77	-0.03	2.64	2.09	-0.03

*The unit is per 10⁴ person-year·Sv; [†]Age at exposure.

Table 5. Coefficients of the ICRP 103 Solid Cancer Risk Model

Cancer site/sex*	ERR						EAR		
		g_s^{\dagger}	g_e			g_s^{\ddagger}	g_e		
			g_e	g_a	g_e		g_a		
Thyroid	M	0.53				0.69			
	F	1.05	0.056	0		2.33	0.024	0.01	
Breast	M	N/A [§]	N/A	N/A		N/A	N/A	N/A	
	F	0.87	0	-2.26		10.9	0.039	3.5 1.0	
Stomach	M	0.23				6.63			
	F	0.38	0.017	-1.65		9.18	0.024	2.38	
Colon	M	0.68				5.76			
	F	0.33	0.017	-1.65		2.40	0.024	2.38	
Liver	M	0.25				4.18			
	F	0.40	0.017	-1.65		1.30	0.024	2.38	
Lung	M	0.29				6.47			
	F	1.36	-0.017	-1.65		8.97	-0.001	4.25	
Ovary	M	N/A [§]	N/A	N/A		N/A	N/A	N/A	
	F	0.32	0.017	-1.65		1.47	0.024	2.38	
Bladder	M	0.67				2.00			
	F	1.10	0.017	-1.65		2.77	0.011	1.38	
Esophagus	M	0.40				0.48			
	F	0.65	0.017	-1.65		0.66	-0.064	1.38	
Other solid	M	0.22				7.45			
	F	0.17	0.017	-1.65		10.45	0.024	2.38	

*M: male, F: female; [†]The unit is per Gy; [‡]The unit is per 104 person-year·Gy; [§]Not available; ^{||}If attained age is below 50, g_a is 3.5. Otherwise, g_a is 1.1.

Note: mathematical model

Leukemia: $EAR = (\alpha D + \beta D^2) \times e^{\kappa_1 \ln(a-25)}$

Solid cancer: $ERR \text{ or } EAR = g_s D \times e^{-g_e \cdot (e-30) + g_a \cdot \ln(\frac{a}{70})}$

posure-induced death [12].

5. ICRP 103 model (2007)

The ICRP 103 presents models for cancer incidence. With improved outcomes of cancer treatment, radiation-induced health effects are emphasized in connection with the incidence of cancer, instead of cancer-related mortality. The model for leukemia incidence is based on the Japanese atomic bomb survivor data from the period 1950-1987 [19], and the model for solid cancer incidence is based on the Japanese atomic bomb survivor data from the period 1958-1998. It is assumed that the $\rho(D)$ term is linear-quadratic for leukemia and linear for solid cancers (with a DDREF of 2). The lifetime risk for cancer is calculated using the LAR and the weighted arithmetic mean, using the LARs of ERR and EAR. In the ICRP 103 model, solid cancers are divided into the following sites: thyroid, breast, esophagus, stomach, colon, liver, lung, ovary, bladder, and others. The two models estimating cancer incidence are shown below, and their coefficients are presented in Table 4 and 5 [13].

$$\text{Leukemia: } EAR = (\alpha D + \beta D^2) \times e^{\kappa_1 \cdot \ln(a-25)} \quad (20)$$

$$\text{Solid cancers: } ERR \text{ or } EAR = g_s D \times e^{-g_e \cdot (e-30) + g_a \cdot \ln(\frac{a}{70})} \quad (21)$$

6. U.S. EPA model (2011)

The U.S. EPA developed risk models for cancer incidence and mortality, using the same models as the BEIR VII model. Additionally, they developed new risk models for thyroid cancer and mathematical models for kidney, bone, and skin cancers. It is assumed that the cancer risk model for thyroid cancer has a linear $\rho(D)$ term, and this model is defined using $\epsilon(X)$ related to age at exposure and time after exposure. The cancer risk model for kidney cancer is defined as the EAR per unit of dose by multiplying the solid cancer model of the BEIR VII model by the incidence rate of kidney cancer, $\lambda_{i,kidney}$, divided by the incidence rate of other solid cancers, $\lambda_{i,residual}$. The cancer risk model for bone cancer is based on statistics on alpha radiation-induced bone cancer and for skin cancer, on tinea capitis cohort data.

Thyroid cancer:

$$ERR = \alpha D \times A(e) \times T(t), \quad (22)$$

$$\alpha = 10.7 \text{ Gy}^{-1}, A \begin{cases} 1.0, & e < 5 \\ 0.6, & 5 \leq e \leq 9 \\ 0.2, & 10 \leq e \leq 14 \\ 0.2e^{-0.083(e-15)}, & 15 \leq e \end{cases}$$

$$T(t) = \begin{cases} 0, & t < 5 \\ 1.15, & 5 \leq t \leq 14 \\ 1.9, & 15 \leq t \leq 19 \\ 1.2, & 20 \leq t \leq 24 \\ 1.6, & 25 \leq t \leq 29 \\ 0.47, & 30 \leq t \end{cases}$$

Kidney cancer:

$$EAR_{kidney} = \frac{\lambda_{i,kidney}}{\lambda_{i,residual}} \times EAR_{residual} [Gy^{-1}] \quad (23)$$

Bone cancer:

$$EAR = \alpha D \times g(e) \times h(t), \quad (24)$$

$$g(e) = e^{-0.0532(e-30)},$$

$$h(t) = (2\pi\sigma^2)^{-0.5} \times e^{-\frac{[\ln(t)-\ln(t_0)]^2}{2\sigma^2}} \times \frac{1}{t}$$

$$\alpha = 178 \times 10^{-3} \text{ Gy}^{-1}, t_0 = 12.72, \sigma = 0.61$$

$$\text{Skin cancer: } ERR = 0.2D \times 0.88^{e-7} \quad (25)$$

The lifetime risk of cancer in the radiation-exposed population is calculated using LAR, as in the BEIR VII model. Although the BEIR VII model sets the upper range of age at 100 years, the U.S. EPA model sets it to 110 years and computes the risk as a weighted arithmetic mean of the ERR and EAR estimates [14].

Results and Discussion

In advance of the development of a Korean health risk assessment model, we examined the preexisting cancer risk models used by nuclear- and radiation-related organizations worldwide. With improved cancer treatment rates, radiation-derived cancer risk generally refers to the risk of cancer incidence rather than the risk of cancer mortality. Thus, each organization analyzed in this study has developed risk models for cancer incidence as well as cancer mortality. Current mathematical models for cancer risk distinguish the risk of leukemia from that of solid cancers. Furthermore, risk models for solid cancers specify the site of cancer, as shown in Table 6. Of the risk models, the U.S. EPA model describes the most number of models for cancer (15 cancers, excluding only esophageal cancer and brain and central nervous system [CNS]-related cancers). Table 7 compares the risk models by organization. These models can be categorized into 2 groups according to the methodology of how they were de-

veloped: (1) those based on epidemiological data to develop ERR and EAR (the BEIR VII, UNSCEAR, ICRP, and U.S. EPA models), and (2) the NUREG model, which uses risk coefficients derived from preexisting studies and determines radiation-induced cancer risk by multiplying these risk coefficients by the exposure dose. Additionally, the BEIR VII UNSCEAR, ICRP, and U.S. EPA models use a modification function to adjust for the effects of age at exposure, attained age, and gender on cancer risk under the same exposure conditions, but the NUREG model does not. Instead, modification calculations are possible using a set of different risk coefficients that can be applied to different subgroups of gender and age.

The epidemiological data that have been applied to the BEIR VII, the UNSCEAR, the ICRP, and the U.S. EPA models are mostly derived from Japanese atomic bomb survivor data. From this dataset, the cancer mortality data until 2000 and the cancer incidence data until 1998 were used. The models also include epidemiological finding incorporating medical exposure data, although to a lesser extent. Thus, the resulting model may differ depending on the combination of other radiation exposure data used, even if the major epidemiological data in all models are the Japanese atomic bomb survivor data.

Ideally, risk models should be developed using arbitrarily sampled epidemiological data from radiation exposure data

Table 6. Cancer Sites in Cancer Risk Models

Cancer site	NUREG (1993)*		BEIR VII (2006)		UNSCEAR (2006)		ICRP 103 (2007)†		U.S.EPA (2011)	
	Morbidity	Mortality	Morbidity	Mortality	Morbidity	Mortality	Morbidity	Mortality	Morbidity	Mortality
Leukemia	o	o	o	o	o	o	o	x	o	o
Thyroid	o	o	o	o	o	x	o	x	o	o
Breast	o	o	o	o	o	x	o	x	o	o
Stomach	o	o	o	o	o	x	o	x	o	o
Colon	o	o	o	o	o	x	o	x	o	o
Liver	x	x	o	o	o	x	o	x	o	o
Lung	o	o	o	o	o	x	o	x	o	o
Prostate	x	x	o	o	x	x	x	x	o	o
Uterus	x	x	o	o	x	x	x	x	o	o
Ovary	x	x	o	o	x	x	o	x	o	o
Bladder	x	x	o	o	o	x	o	x	o	o
Kidney	x	x	x	x	x	x	x	x	o	o
Bone	o	o	x	x	o	x	x	x	o	o
Skin	o	o	x	x	o	x	x	x	o	o
Esophagus	x	x	x	x	o	x	o	x	x	x
Brain and central nervous system	x	x	x	x	o	x	x	x	x	x
Other solid	o	o	o	o	o	o	o	x	o	o

*The risk model for the stomach and colon is equivalent; †ICRP 103 only developed a cancer incidence model. A cancer mortality model was developed in ICRP 60.

Table 7. Summary and Comparison of Cancer Risk Models

	NUREG (1993)	BEIR VII(2006)	UNSCEAR(2006)	ICRP 103 (2007)	U.S.EPA (2011)
Data	N/A†	· Leukemia: Japanese atomic bomb survivor mortality data from the period 1950-2000 · Solid cancer: Japanese atomic bomb survivor morbidity data from the period 1958-1998	· Japanese atomic bomb survivor mortality data from the period 1950-2000 · Japanese atomic bomb survivor morbidity data from the period 1958-1998	· Leukemia: Japanese atomic bomb survivor morbidity data from the period 1950-1987 · Solid cancer: Japanese atomic bomb survivor morbidity data from the period 1958-1998	· Leukemia: Japanese atomic bomb survivor mortality data from the period 1950-2000 · Solid cancer: Japanese atomic bomb survivor morbidity data from the period 1958-1998
Dose-response model	Linear	· Leukemia: linear-quadratic · Solid cancer: linear	· Leukemia: linear-quadratic · Solid cancer: linear-quadratic (mortality), linear (morbidity)*	· Leukemia: linear-quadratic · Solid cancer: linear	· Leukemia: linear-quadratic · Solid cancer: linear
Modification function	N/A	Exposure age, attained age, sex	Exposure age, attained age, sex	Exposure age, attained age, sex	Exposure age, attained age, sex
DDREF	1 or 2	1.5	2	2	1.5

*Exceptionally, the dose-response models for bone cancer and non-melanoma skin cancer are a linear-quadratic function and a quadratic-exponential function, respectively; †Not available.

that are not derived from specific nations or populations. However, currently available large-scale radiation exposure data are restricted to data from a specific population (i.e., the Japanese atomic bomb survivors); therefore, applying risk models derived from such country/population-specific data to other countries or populations can lead to errors. Thus, in numerous organizations, geometric and arithmetic means, which take into account the weighted factors of ERR and EAR, are used to offset the potential errors. Despite these precautions, limitations and uncertainties associated with the epidemiological data, which are currently heavily restricted to the Japanese population, still remain, and the Korean cancer risk model will share the same difficulties. Further, the Japanese atomic bomb survivor data generally reflect acute, high-dose exposure to high-energy radiation, meaning that estimating the risk associated with low-dose and low-dose-rate radiation and different types of radiation may be difficult.

The DDREF, initially adopted by the ICRP, complements the limitations of the high dose and dose-rate exposure data and allows the estimation of risk from low dose and dose-rate exposures. These DDREF values are derived from life span study data and from animal experiment findings. Although the use of DDREF is a simple and practical way of estimating low dose and dose-rate risk, the effectiveness of DDREF for extrapolating risk from the high dose and high

dose-rate exposure effects is still under question. Representative cell biology findings that purport to support the DDREF are vague and obscure, and whether the findings of animal experiments can be translated to humans remains debatable. Recently, the German Radiation Protection Committee argued that the use of the DDREF can no longer be justified [20]. Thus, prior to developing a Korean risk model, an evaluation of the limitations of the Japanese atomic bomb survivor data and of the effectiveness of the DDREF should be carried out.

Through the comparison of the current cancer risk models, we analyzed the factors that must be taken account when developing a Korean cancer risk model. First, the risk models that have been developed calculate the risks for the following 17 types of cancers: leukemia, thyroid cancer, breast cancer, stomach cancer, colon cancer, liver cancer, lung cancer, prostate cancer, uterine cancer, ovarian cancer, bladder cancer, renal cancer, bone cancer, skin cancer, esophagus cancer, brain and CNS-related cancers, and other solid cancers. The Korean cancer risk model should include the most prevalent cancers among the Korean population. According to the 2013 national cancer incidence statistics, cancers with a 5-year cancer incidence greater than 3% included solid cancers in regions including the thyroid, stomach, large intestine, lung, breast, liver, and prostate. Thus, the Korean cancer risk model should include these cancers, as well as leukemia.

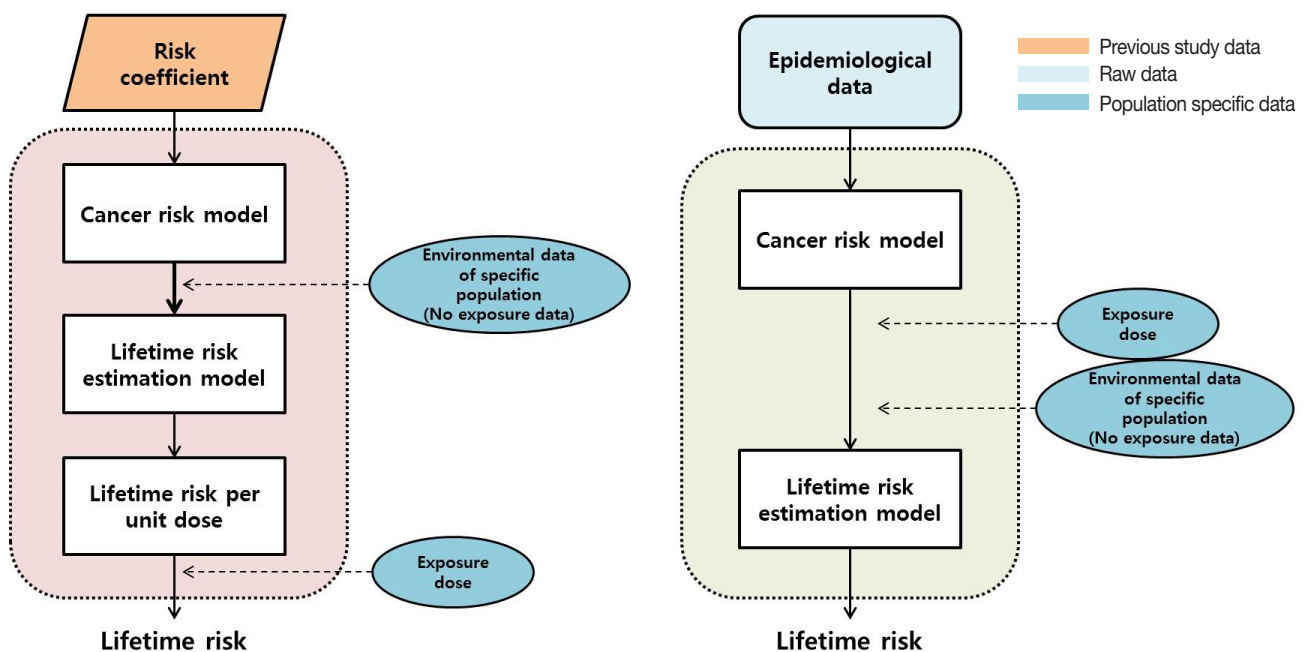


Fig. 1. Development methodology of risk model – NUREG model (left), BEIR VII, UNSCEAR, ICRP and U.S. EPA model (right).

Second, we make methodological suggestions for the development of a Korean risk model. As shown in Figure 1, pre-determined risk coefficients were used to develop the NUREG model, along with unexposed population data, to calculate the lifetime risk per unit dose. The BEIR VII, UNSCEAR, ICRP, and U.S. EPA models were derived from epidemiological data. These models calculate lifetime risk by age at exposure, attained age, and gender. Both methodologies provide advantages when developing a Korean risk model: the risk coefficient-derived methodology is a relatively simplified process of creating a mathematical model, while the epidemiological data-based methodology allows the latest data to be incorporated. Further, because both methods use unexposed population data, national census data can be used, allowing the contextualization of the model to the Korean characteristics. Further, because the development of the Korean risk model will employ the latest datasets of the Japanese atomic bomb survivor data (up to 2009), in contrast to the current risk models that have used data up to 2000, we will be able to create the most up-to-date risk model. Thus, the methodology of the Korean risk model development should prioritize collecting and using the latest Japanese atomic bomb survivor data.

Finally, each organization applied a different DDREF value, meaning that a DDREF value for the Korean risk model is also needed. We suggest that this DDREF value should be determined on the basis of recent studies regarding low dose and low-dose-rate radiation exposure-dependent cancer risk. Because studies evaluating the effectiveness of the DDREF have not been extensively conducted in Korea, future studies are required concerning this widely employed factor.

Conclusion

In advance of the development of a health risk assessment model specific to the Korean population, and thereby a level 3 PSA code specific to Korea, we evaluated the latest cancer risk models used by organizations worldwide. The following cancer risk models were evaluated: the NUREG model (1993), the BEIR VII model (2006), the UNSCEAR model (2006), the ICRP 103 model (2007), and the U.S. EPA model (2011). In this study, the methodological approaches and the epidemiological data of these models were comparatively analyzed, and the different cancer sites of each model were summarized.

Through a comparative analysis of existing cancer risk

models, we determined important factors that must be considered in order to develop a Korean cancer risk model. We suggest that the Korean cancer risk model should be developed on the basis of the latest epidemiological data and should include the following key cancer sites: the thyroid, stomach, large intestines, lung, breast, liver, prostate, and other solid cancers, as well as leukemia. These cancer sites are suggested on the basis of the cancer incidence statistics data in Korea from the previous 5 years. In order to develop an up-to-date model, we also suggest that the Japanese atomic bomb survival data for the period up to 2009 should be used. In conclusion, the findings of this study are expected to serve as the basis for future studies on the development of a Korean cancer risk model.

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References

1. Korea Atomic Energy Research Institute. Development of computing code system for level 3 PSA. KAERI/RR-1758/96. 1997;3-7.
2. International Commission on Radiological Protection. Recommendations of the international commission on radiological protection. ICRP Publication 60. 1991;11-25.
3. National Academy of Sciences. The effects on populations of exposure to low levels of ionizing radiation: BEIR I. 1972;85-91.
4. National Academy of Sciences. Health risks from exposure to low levels of ionizing radiation: BEIR V. 1990;161-176.
5. National Academy of Sciences. Health risks from exposure to low levels of ionizing radiation: BEIR VII-Phase 2. 2006;259-282.
6. Evans JS, Moeller DW, Cooper DW. Health effects model for nuclear power plant accident consequence analysis. Part I: Introduction, Integration, and Summary. Part II : Scientific basis for health effects models. NUREG/CR-4214. 1985;123-135.
7. Evans JS. Health effects models for nuclear power plant accident consequence analysis. Rev. 1 PART I. NUREG/CR-4214. 1990; I26-I42.
8. Abrahamson S, Bender MA, Boecker BB, Gilbert ES, Scott BR. Health effects models for nuclear power plant accident consequence analysis. Rev. 1 Part II. NUREG/CR-4214. 1991;45-46.
9. Evans JS, Abrahamson S, Bender MA, Boecker BB, Gilbert ES, Scott BR. Health effects models for nuclear power plant accident consequence analysis. Rev. 2 PART II. NUREG/CR-4214. 1993;

- 26-44.
10. Jow HN, Sprung JL, Rollstin JA, Ritchie LT, Chanin DI. MELCOR Accident Code System (MACCS) model description. Vol. 2. NUREG/CR-4691. 1990;6.8-6.10.
 11. Takahara S, Iijima M, Shimada K. Application of health effect model of NUREG/CR-4214 to the Japanese population and comparison with a latest model. *Jpn. J. Health Phys.* 2015;50(3): 172-181.
 12. United Nations Scientific Committee on the Effects of Atomic Radiation. Effect of ionizing radiation: Volume 1 with Scientific Annex A. UNSCEAR 2006 report. 2008;123-138.
 13. International Commission on Radiological Protection. Recommendations of the international commission on radiological protection. ICRP Publication 103. 2007;173-200.
 14. U.S. Environmental Protection Agency. EPA radiogenic cancer risk models and projections for the U.S. population. EPA Report 402-R-11-001. 2011;16-48.
 15. World Health Organization. Health risk assessment from the nuclear accident after the 2011 great east Japan earthquake and tsunami based on a preliminary dose estimation. 2013;125-129.
 16. Thompson DE, et al. Cancer incidence in atomic bomb survivors. Part II: Solid tumors, 1958-1987. *Radiat. Res.* 1994;137:S17-S67.
 17. Preston DL, Ron E, Tokuoka S, Funamoto S, Nishi N, Soda M, Mabuchi K, Kodama K. Solid cancer incidence in atomic bomb survivors: 1958-1998. *Radiat. Res.* 2007;168:1-64.
 18. Preston DL, Pierce DA, Shimizu Y, Cullings HM, Fujita S, Funamoto S, Kodama K. Effect of recent changes in atomic bomb survivor dosimetry on cancer mortality risk estimates. *Radiat. Res.* 2004;162:377-389.
 19. Preston DL, et al. Cancer incidence in atomic bomb survivors. Part III: Leukemia, Lymphoma and Multiple Myeloma, 1950-1987. *Radiat. Res.* 1994;137:S68-S97.
 20. Werner R, et al. Dose and dose-rate effects of ionizing radiation: a discussion in the light of radiological protection. *Radiat. Environ. Biophys.* 2015;54:379-401.