

RELATION BETWEEN CANCER INCIDENCE OR MORTALITY AND EXTERNAL NATURAL BACKGROUND RADIATION IN JAPAN

Y. UJENO

Department of Experimental Radiology,
Faculty of Medicine,
Kyoto University,
Kyoto, Japan

Abstract

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Analysis was performed on the relationships between the organ dose-equivalent rate due to natural background radiation (mSv/a) and three parameters of cancer risk: the age-adjusted cancer incidence (patients $\cdot 10^5$ persons $\cdot a^{-1}$) in 13 large areas, the standardized mortality ratio of cancers in 46 large areas, and the cancer mortality in the population aged more than 40 years old (cancer deaths $\cdot 10^5$ persons $\cdot a^{-1}$) in 649 small areas. The age-adjusted liver cancer incidence in males fitted the exponential model significantly ($p < 0.01$) and the relationship of stomach cancer mortality of aged males in small areas fitted the linear model significantly ($p < 0.05$). No relationship was observed with regard to female cancer in either case. The relationships between the three parameters and various other cancers of both sexes were not statistically significant.

1. INTRODUCTION

Understanding the mechanism of cancer induction caused by ionizing radiation is of great importance. Analysis of the dose-response relationship with regard to cancer induction is one approach to this problem. In the laboratory, biological experiments can be carried out to analyse the dose-response relationship at moderate doses or dose rates, but these experiments cannot be readily performed at low doses or dose rates because of various technical difficulties. Furthermore, few experiments have been done at very low doses or dose rate ranges such as those of natural background radiation. The relationships between the epidemiological data on human cancers and the dose-equivalent rate of organs due to natural background radiation are analysed in this study.

Three models are presented to analyse the dose-response relationship: a linear model (L-model), a quadratic model (Q-model) and a linear-quadratic model (LQ-model) [1]. The L-model is stochastic; the other two are non-stochastic. In the

present study, dose-response relationships were analysed according to these three models and an exponential model (E-model), which is non-stochastic. The complex models, such as the LQ-model, were not used.

2. MATERIALS AND METHODS

2.1. Estimation of organ dose-equivalent rate

The data on the exposure rate of external natural background radiation published by the National Institute of Radiological Sciences in Japan [2] were used as the bases for estimating the organ dose-equivalent rate. These exposure rates include almost no exposure from fallout, human bodies or buildings. The dose in each small area received is the mean value of the measured doses in the area. The number of measurement points in an area increases with an increase in population. The dose in each large area received is the mean value of the doses of the small areas which comprise the large area.

For calculating the conversion from the exposure rate ($\mu\text{R}/\text{h}$) to the dose-equivalent rate (mGy/a), the following factors, obtained from published data, were used [3–5]: $D_{\text{air}} = 0.869\dot{X}_{\text{air}}$ (rad/R)¹; q (occupancy factor) = 1.0; g (geometrical factor) = 0.64; sg (for all organs) = 0.7; $C_{\gamma} = 7.7$ (under the assumptions of indoor life of 0.5 and outdoor life of 0.5 taking into account cosmic rays) ($\text{mrad}/\mu\text{rad}$). The q value in Japan is estimated to be slightly less than 1.00 [6]. The fractions of dose of high-LET radiation in the total absorbed dose were estimated as 31% for the lung, 2.1% for the bone marrow, and 1.2% for other organs [7]. The quality factors for high-LET radiation were estimated as 20 for the lung and 10 for other organs [8].

Next, an absorbed dose of internal radiation with a quality factor of 20 was added to the external radiation in the lung. The contribution of this high-LET radiation plus the high-LET radiation with a quality factor of 10 (1.2% of absorbed dose of external radiation) was assumed to be 31% of the total absorbed dose in the lung. In the same manner, the dose-equivalent rate of the bone marrow was calculated. Thus, the present dose-equivalent rates of the lung and the bone marrow contained the dose-equivalent rates of internal and external natural background radiations. In other organs, the addition of internal high-LET radiation was not considered.

The final equations to calculate organ dose-equivalent rate were as follows: \dot{H} (lung) = $0.6531\dot{X}_{\text{air}}$ ($\text{mSv}\cdot\text{a}^{-1}/\mu\text{R}\cdot\text{h}^{-1}$); \dot{H} (bone marrow) = $0.0858\dot{X}_{\text{air}}$ ($\text{mSv}\cdot\text{a}^{-1}/\mu\text{R}\cdot\text{h}^{-1}$); \dot{H} (other organs) = $0.0744\dot{X}_{\text{air}}$ ($\text{mSv}\cdot\text{a}^{-1}/\mu\text{R}\cdot\text{h}^{-1}$); where \dot{H} is the organ dose-equivalent rate ($\text{mSv}\cdot\text{a}^{-1}$) and \dot{X} is the exposure rate ($\mu\text{R}\cdot\text{h}^{-1}$).

¹ One rad = 1.00×10^{-2} Gy.

3. CANCER INCIDENCE OR MORTALITY

The present study used the data on the age-adjusted cancer incidence per 10^5 persons per year in 1975 [9], the data on cancer mortality ratio of cancer deaths per 10^5 persons per year standardized to the whole population for 1973–1977 in large areas [10], and the data on cancer deaths per 10^5 persons per year to the population aged more than 40 years old for 1969–1971 in small areas [11]. The world population was used as the standard to calculate age-adjusted cancer incidence [12]. The total population size and total large areas used to calculate age-adjusted cancer incidence were 47 081 026 persons and 148 039 km², respectively. Those used to calculate standardized cancer mortality ratio were 108 135 194 persons and 379 171 km², respectively. Cancers were classified according to the 8th revision of the International Statistical Classification of Diseases and Causes of Death (ICD) [13].

4. RESULTS

4.1. Relationship between age-adjusted cancer incidences and organ dose-equivalent rates of natural background radiation

The relationships for both sexes in 13 large areas were analysed for various types of cancer: oesophagus (ICD No. 150), stomach (151), colon (153), rectum (154), liver (155), pancreas (157), lung (162), breast (174), uterus (180, 181), bladder (188), and leukaemia (204–207).

A statistically significant relationship was observed in the incidence of male liver cancer; results are shown in Fig. 1. The relationship of male liver cancer was expressed by the following equations: $y = -0.8024 + 21.3529x$ (L-model), $y = 4.5046 + 7.1569x + 5.6852x^2$ (LQ-model), and $y = e^{(1.5051 + 1.5888x)}$ (E-model), where y is the age-adjusted cancer incidence and x is the dose-equivalent rate in the liver. The L-model [$r = 0.6594$, $F_s (= 8.4444) > F_{11}^1(0.05) (= 4.84)$] and E-model [$r = 0.6941$, $F_s (= 9.9964) > F_{11}^1(0.01) (= 9.65)$] were significant at the level of 0.05 and 0.01, respectively. However, the LQ- and Q-models were not significant. The statistical significance was analysed according to the F-test.

The incidence of female liver cancer was expressed by the equations $y = 2.1658 + 5.2176x$ (L-model), $y = 3.0301 + 2.7270x + 1.2277x^2$ (LQ-model), and $y = e^{(1.1086 + 0.9002x)}$ (E-model). These equations were not significant.

Stomach cancer had no statistically significant relation.

The following equations were given for the relationship of lung cancer incidence:

for males: $y = 19.6271 + 0.6274x$ (L-model)

$y = 20.0434 + 0.4730x + 0.0056x^2$ (LQ-model)

$y = e^{(2.9979 + 0.0236x)}$ (E-model)

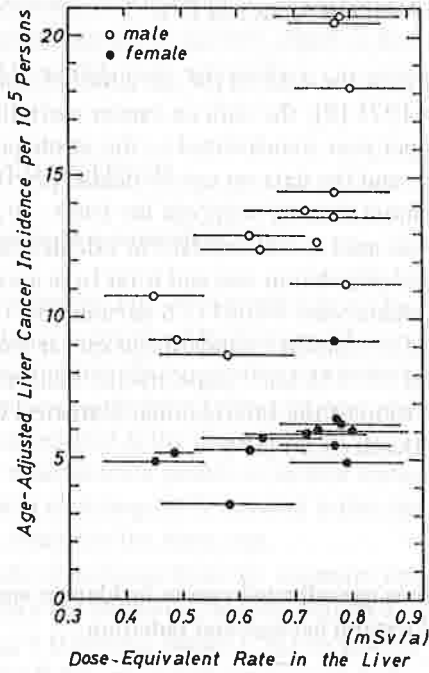


FIG.1. The relationship between the age-adjusted liver cancer incidence per 10^5 persons per year and the liver dose-equivalent rate of the external natural background radiation in large areas of Japan. Horizontal bars show the standard deviations.

for females: $y = 6.0878 + 0.1133x$ (L-model)

$y = 6.1086 + 0.0910x + 0.0007x^2$ (Q-model)

$y = e^{(1.8097 + 0.01489x)}$ (E-model)

These relationships were not significant.

Expressing the relationship of leukaemia according to the L-model, the equations were

for males: $y = 5.4121 - 1.4899x$

for females: $y = 3.7100 - 0.8077x$

Both incidences decreased with the increase in dose-equivalent rate of the bone marrow. These relationships were not significant.

4.2. Relationships between standardized cancer mortality ratio (SMR) and dose-equivalent rate

As the relationship between the bone marrow dose-equivalent rate and leukaemia incidence was unusual, the relationship between SMR of leukaemia for leukaemia incidence and bone marrow dose-equivalent rate were analysed in 46

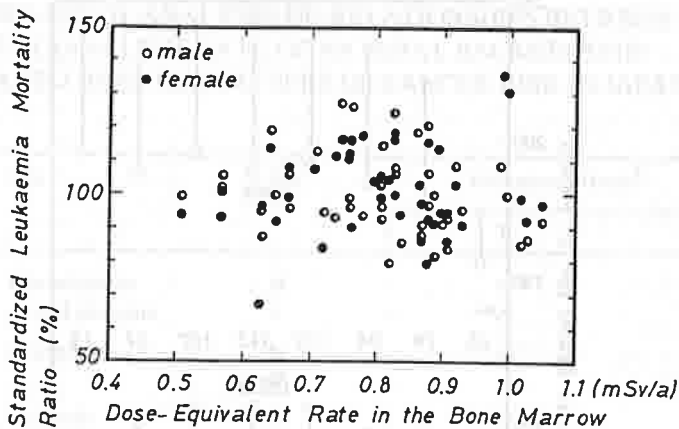


FIG.2. The relationship between the standardized leukaemia mortality ratio (SMR) and the bone marrow dose-equivalent rate of the natural background radiation in large areas of Japan.

large areas, because leukaemia is a fatal disease. The results are shown in Fig. 2. No significant relationship was observed. That is,

$$\text{for males: } y = 117.0866 - 20.0730x$$

$$r = -0.2112, F_s = 2.0542 < F_{44}^1 (0.05) (= 4.06)$$

$$\text{for females: } y = 93.2608 + 11.2376x$$

$$r = 0.1096, F_s = 0.5350 < F_{44}^1 (0.05) (= 4.06)$$

No significant relationship was observed for cancer of bucca and pharynx (140–149), oesophagus (150), stomach (151), intestine (152–153), rectum (154), liver (155), biliary passages (156), pancreas (157), larynx (161), trachea, bronchus and lung (162), bone (170), skin (172, 173), breast (174), uterus (180–182), ovary (180.3), prostate (185), urinary bladder (188), or kidneys (189.0, 189.1).

4.3. Relationships between cancer mortality of population more than 40 years old and dose-equivalent rate

These relationships were analysed in 649 small areas; that of stomach cancer was expressed as follows:

$$\text{for males: } y = 148.3821 + 49.4883x \text{ (L-model)}$$

$$\text{for females: } y = 92.7982 + 9.7209x \text{ (L-model)}$$

where x is the middle value in each 0.1 mSv/a range of stomach dose-equivalent rate. The equation for male stomach cancer [$r = 0.8020, F_s (= 10.8162) > F_6^1 (0.05) (= 5.59)$] was significant ($p < 0.05$) but that for female stomach cancer was not. These results are shown in Fig. 3. No significant relationship is observed for cancer of the oesophagus (150), large intestine (153), rectum (154), pancreas (157), lung (162), breast (174), or uterus (180, 181).

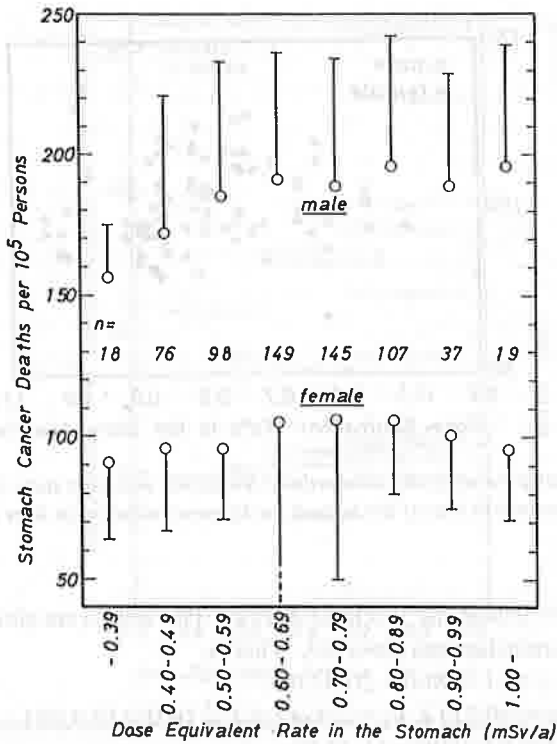


FIG. 3. The relationship between stomach cancer mortality per 10^5 persons per year in the population aged more than 40 years old and the stomach dose-equivalent rate of the external natural background radiation in small areas of Japan; "n" is the number of small areas in each dose-equivalent rate range. Vertical bars show the standard deviations.

5. DISCUSSION

There are always many assumptions in epidemiological analyses and various uncertainties are unavoidable in epidemiological data. For example, the effects of other carcinogens and the effects of ionizing radiation combined with the effects of other carcinogens could be analysed in the present study. In consideration of these points the present data should be discussed.

The discrepancies shown in the results with regard to three epidemiological parameters emphasize the importance of choosing reasonable parameters to fit the purpose of the study. The age-adjusted cancer incidence is the most reasonable parameter with regard to radiation carcinogenesis. Among the many cancers analysed in the present study, only the incidence of male liver cancer was significantly dependent upon the organ-equivalent rate in the E- and L-models. The incidence of liver cancer ranks third among male cancers in Japan [14]. The role

TABLE I. SUMMARY OF ANALYSES OF RELATIONSHIPS BETWEEN ORGAN DOSE-EQUIVALENT RATE OF NATURAL BACKGROUND RADIATION AND THREE PARAMETERS OF CANCER RISK IN JAPAN

ICD ^a	Site	Sex	Biological effects ^b		
			I	II	III
140	Buccal cavity and pharynx	M	—	n ^c	—
-149		F	—	n	—
150	Oesophagus	M	—	n	n
		F	—	n	n
151	Stomach	M	n	n	S* ^d
		F	n	n	n
152	Intestine	M	—	$\begin{bmatrix} n \\ n \end{bmatrix} \left[\begin{array}{c} 152+153 \end{array} \right]$	—
		F	—		—
153	Colon	M	n	—	n
		F	n	—	n
154	Rectum	M	n	n	n
		F	n	n	n
155	Liver	M	S ^e	$\begin{bmatrix} n \\ n \end{bmatrix} \left[\begin{array}{c} 155.0 \\ 197.7 \\ 197.8 \end{array} \right]$	—
		F	n		—
156	Biliary tract	M	—	n	—
		F	—	n	—
157	Pancreas	M	n	n	n
		F	n	n	n
161	Larynx	M	—	n	—
		F	—	n	—
162	Lung	M	n	n	—
		F	n	n	—
170	Bone	M	—	n	—
		F	—	n	—
172	Skin	M	—	n	—
-173		F	—	n	—
174	Breast	M	n	n	n
		F	n	n	n
180	Uterus	F	n	n	n
-182					
183	Ovarium	F	—	n	—
185	Prostate	M	—	n	—

TABLE I (cont.)

ICD ^a	Site	Sex	Biological effects ^b		
			I	II	III
188	Bladder	M	n	n	—
		F	n	n	—
189.0 -189.1	Kidney	M	—	n	—
		F	—	n	—
200 -202	Lymph node	M	—	n	—
		F	—	n	—
204 -207	Leukaemia	M	n	n	—
		F	n	n	—

^a ICD: ICD, 8th Revision [13].

^b Biological effects I: Age-adjusted cancer incidence. II: Standardized cancer mortality ratio. III: Cancer mortality in the population aged more than 40 years old.

^c n: Not significant (L-model).

^d S*: Significant (5% level) (L-model).

^e S: Significant (1% level) (E-model).

of hepatitis B virus in the induction of liver cancer is well known [15], and ionizing radiation might accelerate the viral induction of liver cancer. The reasons for the sex differences in the dose-response relationship of liver cancer are unclear. The slope of the equation of the L-model for male liver cancer incidence, $21.35 \cdot 10^5$ persons/mSv \cdot a⁻¹ corresponds to $2135 \cdot 10^6$ persons/rem \cdot a⁻¹, which is much larger than the value recommended in BEIR III [16]. This difference might be due to the differences in dose rate used in these two reports. The theoretical dose-response curve drawn in regard to carcinogenesis in the low dose range suggests this possibility [17].

Neither stomach cancer, which has the highest incidence in Japan [14], nor lung cancer with the second highest [14], has a significant relationship with each organ dose-equivalent rate. Cancer of the pancreas, which has been noted in Hanford workers [18], also had no significant relationship. The negative association of leukaemia with the organ dose-equivalent rate was unusual. However, some similar data have been summarized on other effects including cancer induction [19, 20]. This negative tendency should be further analysed. It is pointed out by Sakka [21] that the significant relationship between stomach cancer mortality in the population aged more than 40 years old and the stomach dose-equivalent rate

reported in Ref. [22] is based on the fact that non-adjusted stomach cancer mortality was used in the analyses. The same indication could be available in the present results, because the same material data were used in both previous and present studies. In the present study, the medical exposure, estimated to be $0.579 \text{ mGy} \cdot \text{person} \cdot \text{a}^{-1}$ in Japan [23], was not taken into consideration. This exposure should be included in future studies.

The present results are not always consistent with the data published in Ref. [24], which shows the difficulties in this field of study. At present, it is essential not to use the published epidemiological data but to collect worthwhile epidemiological data. The present study suggests that the incidence of male liver cancer is positively associated with the liver dose-equivalent rate; results are summarized in Table I.

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