Journal of Health Physics, **32** (2), 173～184 (1997)

ORIGINAL

First Analysis of Mortality of Nuclear Industry Workers in Japan, 1986–1992

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(Received September 9, 1996)
(Accepted March 26, 1997)

The health effects of low doses and low dose rates exposure to human bodies have not been clarified yet. Under this situation, the Radiation Effects Association entrusted by the Science and Technology Agency of the Japanese Government began a survey entitled "The Epidemiological Study on Nuclear Industry Workers."

The study population consisted of 114,900 workers in the nuclear industry. Their vital status and identification of cause of death were confirmed by residence registration records and by magnetic tapes of National Vital Statistics, respectively. Their dose information was obtained from the Radiation Dose Registration Center for Workers. The total population dose of the study population was 1,598.5 person-Sv, and the mean cumulative dose per individual was 13.9 mSv. The study period was between 1986 and 1992, average follow-up period being 4.6 years. There were 1,758 deaths including 661 of all malignant neoplasms among the population.

The SMR was used to compare mortality among members of the study population and that of Japanese males in general after adjustment for age distribution. Furthermore, members of the population were grouped by cumulative dose groups, and the O/E was calculated to test whether there is a trend for the death rate to increase with dose.

The present study demonstrated no evidence of any effect of low level radiation upon health, particularly upon the cancer mortality.

KEY WORDS: nuclear industry workers, low dose, cancer mortality, standardized mortality ratio (SMR), internal comparison

I INTRODUCTION

In keeping with international efforts to standardize approaches to occupational and public safety, radiation protection guidelines enforced in Japan are based upon the recommendations of the International Commission on Radiological Protection (ICRP). It is known that the dose limits of the ICRP are mainly based on the results of the studies of health effects on the atomic bomb survivors among Hiroshima and Nagasaki who were acutely exposed to high doses of radiation. The ICRP guidelines also assume that health effects of radiation are proportional even at low dose and dose-

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rates of radiation.

Concern over possible effects of low-level radiation in humans has led to the initiation of epidemiological studies in a number of countries such as the United States,[1-3] the United Kingdom,[4-8] and Canada.[9,10] An international collaborative study also is being conducted under the auspices of the International Agency for Research on Cancer, Lyon, France.[11,12]

In these circumstances, an epidemiological study of radiation workers at nuclear power plants and associated facilities had been initiated by the Radiation Effects Association under the trust of the Science and Technology Agency of the Japanese Government.

II SUBJECTS AND METHODS

1. Establishment of study population

From among approximately 230,000 persons registered in the "Radiation Dose Registration Center for Workers" (RADREC) as of March 1989, 181,583 persons excluding the persons with the following criteria were extracted:

a. Persons who had not engaged in actual radiation work even though they were only tentatively listed in RADREC (about 42,000).

b. Persons not of Japanese nationality (about 2,500).

c. Females (about 2,000).

d. Persons who engaged in radiation work only at fuel-processing companies (about 2,800).

Among these persons, their vital status was ascertained through copies of their residence registration record, and some of them were missed. Furthermore, 2,804 persons who vital status happened to be issued even after the legal period of more than 5 years of the record keeping, and 33 persons who are not within the 20- to 85-years-old age range during the follow-up were excluded.

Finally, a study population of 114,900 workers has been analysed based on the vital status of 31 December 1992.

The underlying cause of death was identified by record linkage with the magnetic tapes of National Vital Statistics supplied by the Japanese Ministry of Health and Welfare. This linkage of 1,758 deaths in the population resulted in the identification of the cause of death for 1,748 persons (99.4%). For reference, in the study on agreement between death-certificate and autopsy diagnoses among atomic-bomb survivors, confirmation rates (positive predictive value, i.e., percentage of death-certificate diagnoses confirmed by autopsy) and detection rates (sensitivity, i.e., the percentage of actual cases of a disease listed on death certificates) for neoplasms are 90.9% and 76.7%, respectively based on the atomic bomb survivers data.[13]

2. Radiation dose

The RADREC was established in the Radiation Effects Association in 1978 to register radiation dose and other information for the purpose of individual dose management. Dosimetry record. for the period (back to 1957) before inaugurating registration also have been provided by the respective nuclear facilities. Those records are also included in the RADREC. Therefore, doses associated with radiation work for this study were obtained from the annual dose records for each member of the study population filed in the RADREC from 1957 to 1992. These dosimetry records had been prepared by the respective nuclear facilities for the purpose of radiation protection management and the doses are reported each year as the total doses (mSv), combining the external and internal dose.

The dose records filed in the RADREC reflect changes over time in the definition of radiation quantities and units, technical advances in the method of dosimetric measurements, evaluation of dose, and also reflect methodological differences among the respective nuclear facilities. Thus, it was necessary to consider whether the records were adequately comparable across facilities and time. The investigation and review of these problems were carried out by the Radiation Dosimetry Committee (RDC) of the Radiation Effects Association referring the results of questionnaire survey, on-site inspection survey, radiation control manual of facilities, Japanese Industrial Standard (JIS) and scientific reports.

2.1 Change of definition of radiation quantities and units

In this study, the cumulative dose in a unit of Sv was used, but the dose records were reported in different units chronologically such as biologically effective or "RBE" dose in rem, dose equivalent in rem, effective dose equivalent in Sv. So, it is necessary to confirm the validity of summation of dose in different units. In the energy range of 10 keV-3 MeV of photons, the following relationship is well confirmed in old units, that is, $D=0.96X$, where D(rad) is absorbed dose in tissue and X(R) is exposure. Using this relationship, the dose equivalent, DE(rem), is obtained by the relation of 1 rem = 1 R where we use both approximation of 1 R = 1 rad and the quality factor of 1. The response R_p, of dosimeter measured in a unit of R irradiated with phantom, is very similar to the individual dose equivalent, penetrating, $H_p(10)$ in a unit of Sv. So, the effective dose equivalent in Sv is obtained simply by conversion of rem, $H_p(10)=(1/100)R_p$. For the uniform irradiation of the whole body, the essential difference among these doses is the quality factor for neutrons, because the same quality factor of one for X-, γ-, β-rays and electron is used in these doses. For the biologically effective or "RBE" dose and the dose equivalent, the quality factor was 10 for fast neutron, 3 for thermal neutron and 10 for unknown energy neutron, respectively. These numerical values were obtained from the data of conversion factors from neutron fluence to rem in the national regulations. Conversion factors vary with neutron energy, but fixed values were selected from the view point of simplicity and rather safety assessment of dose. For the effective dose equivalent, conversion factors from neutron fluence to Sv which vary with neutron energy were used instead of the fixed quality factor. The numerical difference between two conversion factors is small, within factor 2 for fast neutron. As a whole, the RDC agreed that the validity and the consistency of summation of dose in different units were confirmed.

2.2 Reliability of dose measured in facilities with different dosimeters

Many types of dosimeters for measurements of external doses were developed and used owing to the diversifying of purposes and the advance of techniques. External doses were measured by film badges and/or thermoluminescent dosimeters used as principal dosimeters. Pocket type dosimeters and thermoluminescent dosimeters were used as a secondary dosimeters for the purpose of daily monitoring and checking in the case of unusual exposure. For X- and γ-ray dose measurements, these dosimeters were calibrated in a unit of R periodically using the national standard ionization chamber maintained at the Electro Technical Laboratory, or the ionization chamber calibrated using the national standard maintained at research institutes and companies.

For neutron dose measurements, the dosimeters were calibrated periodically by the national standard of neutron source of the Electro Technical Laboratory in a unit of neutron fluence and by the moderated neutron field of Japan Atomic Energy Research Institute in a unit of rem. As the result of above investigation, RDC agreed that the doses measured with different dosimeters at various facilities were reliable and traceable to the national standards.

2.3 Characteristics of radiation field and dosimeters

The dosimeters, in general, have the characteristics for type, energy and incident direction of radiations. For measurements of external dose, it is necessary to select appropriate dosimeters reflecting the characteristic of radiation in working environment and geometry. The characteristics of working environment can be grouped as follows: nuclear power plant, nuclear fuel processing facility and nuclear research facility.

In nuclear power plants, BWR, PWR, GCR, dominant radiations for external exposure are relatively high-energy photons emitted from ^{51}Cr, ^{54}Mn, ^{59}Fe, ^{58}Co, ^{60}Co, very high-energy photons from ^{16}N. Film badge dosimeters used as principal dosimeters in nuclear power plants have a good response to photon of wide energy range (20 keV-3 MeV) (JIS 4302, JAERI IV). Thermoluminescent dosimeters used as the principal dosimeter are also have a good response to photons of wide energy

range (25 keV-3 MeV).

In nuclear fuel processing facilities, dominant radiations are rather low-energy photons emitted from ^{238}U, ^{235}U (50 keV-200 keV) and ^{231}Pa (0.8-1 MeV). Film badge dosimeters of wide energy range type (JIS 4323) were used as principal dosimeters, and the choice was appropriate reflecting radiation characteristics in working environment.

In nuclear research facilities, radiations were of various types, such as low, high and very high energy photons, and thermal and fast neutrons originating from accelerator, critical assembly, research reactor and fuel testing facility. Therefore, film badge dosimeter (JAERI IV) is used as a principal dosimeter and additional dosimeters, such as NTA film for fast neutron, pocket type dosimeters for high dose rate environment, are used considering respective radiation characteristics.

As the result of above investigations, RDC agreed that the choices of the dosimeter were appropriate reflecting radiation characteristics throughout in working environment.

2.4 Radiation control criteria

Criteria concerning dose assessment, such as classification of radiation workers, dose limit of worker, condition for wearing personnel dosimeter, are almost the same among nuclear power companies, nuclear fuel processing companies and nuclear research institutes. Furthermore, for example, the same procedure and method were applied for the dose estimation of workers who lost their dosimeters. RDC confirmed the consistency of radiation control criteria and reasonability of procedure, and concluded that methods for dose estimation were reasonably adequate.

Internal doses were estimated by whole body counters and/or by collection and examination of biological specimens. As internal dose was actually negligible in the observed population, we omitted dosimetric investigation.

The results indicated that the quality of the records were appropriate and proper, and it was concluded that the records were adequately consistent for use in this study in all aspects of dosimetry.

To relate the mortality, the cumulative dose was used since the year when the exposure experience began. In the calculation of cumulative dose, it was assumed that the annual dose had been received uniformly over each month. The dose during the year of death was assumed to have been incurred uniformly each month between 1 April to date of death. Doses below the detectable level (X value) were taken to be 0 mSv.

3. Characteristics of the study population

The study population consisted of 114,900 workers. The mean follow-up period was 4.6 years and the total of person-years was 533,168. The distribution of the study population by year of birth is shown in **Fig. 1**. The mode of the year of birth was in the 1950s, and the mean age as of 1986, when follow-up began, was 39 years.

The distribution of the study population by cumulative dose groups is shown in **Table 1**. The mean cumulative dose per individual was 13.9 mSv the total population dose of the study population being 1,598.5 person-Sv.

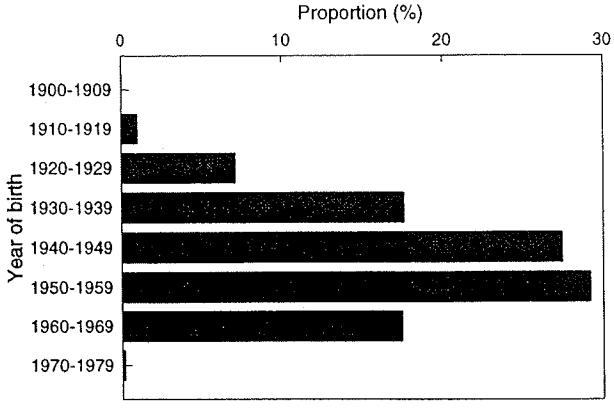

Fig. 1 Distribution of study population by year of birth.

Table 1 Distribution of study population by cumulative dose.

Cumulative dose groups (mSv)	Number of workers (%)	Mean cumulative dose (mSv)
<10	81,169 (70.6)	1.7
10-	12,044 (10.5)	14.4
20-	12,494 (10.9)	31.8
50-	6,085 (5.3)	69.9
100+	3,108 (2.7)	149.6
Total	114,900 (100.0)	13.9

4. Statistical analysis

4.1 Method of handling person-years at risk, follow-up period, and latency period

Person-years were calculated for each subject as the denominator for calculation of the death rate. The beginning date for calculation of person-years (the beginning date of follow-up) was April 1 of the year when the doses were first recorded, or the date 5 years preceding the issuance date of the copy of the residence registration record, whichever was the latest, because information on vital status preceding the issuance date of residence registration records by 5 years were not used in this study. The closing date for calculation of person-years (the date of completion of follow-up) was the issuance date of the residence registration records for survivors, the date of migration for migrants, and the date of death for the deceased. However, since mortality tapes were available only to the end of 1992, person-years were not calculated beyond 1 January 1993. Thus, although the follow-up period from the beginning date to closing date of follow-up differs among the subjects, all of the follow-up periods fall into the period between November 1986 (5 years preceding the date when a residence registration record had been first issued) and 31 December 1992 (the final date of record on the mortality tapes).

Furthermore, analyses were conducted using cumulative doses calculated both with and without "lagging" to account for disease latency. In the analysis, a 2-year lag was used for leukemia, and a 10-year lag for neoplasms other than leukemia.[14] By using lagging, the radiation dose received during the latent period is excluded from calculation of the cumulative dose.

4.2 External and internal comparisons

For external comparison, the cause-specific death rate by 5-year age groups for Japanese males in general for the period 1986-1992, in accordance with the total follow-up period in this study, was taken to be the standard death rate for this purpose. Significance tests for the SMR (Standardized Mortality Ratio) were calculated in two tailed.

For internal comparison, the subjects were grouped into 5 dose categories by cumulative dose, i.e., less than 10, 10-, 20-, 50- and 100 mSv or more. The expected number of deaths, E, that would be expected in each group was calculated on the assumption that deaths would occur at the age-specific death rate by 5-year age groups for the population as a whole. Thus, the ratio of the actual observed number of deaths, O to expected deaths, i.e., the O/E ratio, was obtained. Further, one-tailed p values were calculated using score test statistics[15] to test for any trend of an increase in death rate with cumulative dose. In the calculation of score test statistics, the mean cumulative dose was used to represent each dose group.

III RESULTS

1. External comparison

Table 2 shows the observed deaths according to the code numbers of the International Classification of Diseases, Injuries, and Causes of Death (ICD9th).[16] The results of the external analysis are shown in **Tables 3** and **4**. The SMR of all causes of death is 0.83 (95% confidence interval: 0.79-0.87), and that for non-cancer 0.72 (95% confidence interval: 0.67-0.77). For all neoplasms including benign neoplasms and neoplasms of an unspecified nature, the SMR was 0.89 (95% confidence interval: 0.82-0.96) without lagging and 0.92 (95% confidence interval: 0.84-1.01) on a 10-year lag. The SMR of stomach cancer was 0.79 (95% confidence interval: 0.63-0.97) on a 10-year lag. The SMR was not significant for any of the other neoplasms.

2. Internal comparison

Shown in **Tables 5** and **6** are the results of the internal analyses. Examination of deaths by cumulative dose groups showed no statistically significant difference for any cause of death. One-tailed p values calculated for tests of trend are shown in **Tables 5** and **6**. p value was 0.539 for all causes of death and 0.888 for non-cancer excluding external causes. For all neoplasms, the p value was 0.315 without lagging and 0.692 on a 10-year lag. As for the specific neoplasm site, p value for neoplasm of the pancreas was 0.043 on a 10-year lag.

IV DISCUSSION

This was the first major epidemiological study to

Table 2 Number of deaths by cause of death.

Cause of death	ICD9 Code no.	Observed number of deaths
All causes of death		1758 [2]
Non-cancer (excluding external causes)	1-26, 39-89 [1]	726
All neoplasms	140-239	679
All malignant neoplasms	140-208	661
By site		
Oral cavity and pharynx	140-149	8
Esophagus	150	25
Stomach	151	149
Colon	153	51
Rectum	154	35
Liver	155	111
Gallbladder	156	18
Pancreas	157	40
Lung	162	117
Prostate	185	7
Bladder	188	9
Kidney and other and unspecified urinary organs	189.0-189.2	10
Neoplasms of brain and nervous system [3]	191, 225, 237.5, 237.6, 239.6	11
Lymphatic and haematopoietic tissue		
Leukemia	204-208	23
Leukemia other than chronic Lymphoid leukemia [4]	204-208 except 204.1	23
Non-Hodgkin's lymphoma	200, 202.0-202.3, 202.5-202.9	18
Multiple myeloma	203	6
Malignant neoplasms other than leukemia	140-203	638

1) Codes of the simplified classification
2) Includes 10 individuals for whom the cause of death could not be identified
3) Malignant and unspecified nature of the brain neoplasms
No nervous system neoplasms
4) No cases of chronic lymphoid leukemia

Table 3 Standardized mortality ratio (SMR) by cause of death (with no lag).

Cause of death (ICD9 code no.)	Observed number of deaths	Expected number of deaths [1]	SMR (95% CI)		p value of two-tailed test
All causes of death	1758	2116.2	0.83	(0.79-0.87)	0.000
Non-cancer (excluding external causes) (1-26, 39-89) [2]	726	1011.4	0.72	(0.67-0.77)	0.000
All neoplasms (140-239)	679	766.0	0.89	(0.82-0.96)	0.002
All malignant neoplasms (140-208)	661	744.8	0.89	(0.82-0.96)	0.002
By site					
Oral cavity and pharynx (140-149)	8	13.9	0.58	(0.25-1.14)	0.150
Esophagus (150)	25	37.1	0.67	(0.44-0.99)	0.057
Stomach (151)	149	177.2	0.84	(0.71-0.99)	0.038
Colon (153)	51	42.6	1.20	(0.89-1.57)	0.226
Rectum (154)	35	34.8	1.01	(0.70-1.40)	0.966
Liver (155)	111	128.9	0.86	(0.71-1.04)	0.125
Gallbladder (156)	18	23.3	0.77	(0.46-1.22)	0.321
Pancreas (157)	40	41.5	0.96	(0.69-1.31)	0.878
Lung (162)	117	124.9	0.94	(0.78-1.12)	0.511
Prostate (185)	7	8.2	0.85	(0.34-1.76)	0.806
Bladder (188)	9	7.1	1.26	(0.58-2.39)	0.611
Kidney and other and unspecified urinary organs (189.0-189.2)	10	11.3	0.89	(0.43-1.63)	0.822
Neoplasms of the brain and nervous system [3] (191, 225, 237.5, 237.6, 239.6)	11	13.2	0.84	(0.42-1.50)	0.647
Lymphatic and haematopoietic tissue					
Leukemia (204-208)	23	25.5	0.90	(0.57-1.35)	0.695
Leukemia except chronic lymphatic leukemia [4] (204-208, except 204.1)	23	25.2	0.91	(0.58-1.37)	0.738
Non-Hodgkin's lymphoma (200, 202.0-202.3, 202.5-202.9)	18	19.1	0.94	(0.56-1.49)	0.893
Multiple myeloma (203)	6	5.4	1.12	(0.41-2.44)	0.951
All malignant neoplasms except leukemia (140-203)	638	719.3	0.89	(0.82-0.96)	0.003

1) Expected number of deaths: Number of deaths that would be expected in the study population assuming that deaths would occur at the death rate for Japanese males in general.
2) Codes of simplified classification
3) Malignant and unspecified nature of the brain neoplasms. No nervous system neoplasms
4) No cases of chronic lymphatic leukemia

be undertaken in Japan with regard to radiation workers at nuclear facilities for the purpose of obtaining scientific information on the effects of low-level radiation exposure in humans. The objective of this 5 year project was not only the conduct of a mortality survey, but also the development of the basis for future studies. Efforts also were directed at the development of methodology for this

Table 4 Standardized mortality ratio (SMR) by cause of death (based on a 2-year lag for leukemia and a 10-year lag for other neoplasms).

Cause of death (ICD9 code no.)	Observed number of deaths	Expected number of deaths[1]	SMR (95% CI)	p value of two-tailed test
All neoplasms (140-239)	439	476.3	0.92 (0.84-1.01)	0.092
All malignant neoplasms (140-208)	428	463.7	0.92 (0.84-1.01)	0.102
By site				
Oral cavity and pharynx (140-149)	6	8.3	0.72 (0.27-1.57)	0.534
Esophagus (150)	18	23.4	0.77 (0.46-1.22)	0.311
Stomach (151)	87	110.4	0.79 (0.63-0.97)	0.029
Colon (153)	33	26.4	1.25 (0.86-1.76)	0.234
Rectum (154)	24	21.2	1.13 (0.72-1.68)	0.623
Liver (155)	69	78.2	0.88 (0.69-1.12)	0.324
Gallbladder (156)	9	15.3	0.59 (0.27-1.12)	0.140
Pancreas (157)	26	26.3	0.99 (0.65-1.45)	0.963
Lung (162)	83	82.2	1.01 (0.80-1.25)	0.971
Prostate (185)	5	6.0	0.83 (0.27-1.94)	0.832
Bladder (188)	7	4.8	1.45 (0.58-2.99)	0.426
Kidney and other and unspecified urinary organs (189.0-189.2)	8	7.1	1.13 (0.49-2.23)	0.869
Neoplasms of the brain and nervous system [2] (191, 225, 237.5, 237.6, 239.6)	7	7.2	0.98 (0.39-2.01)	0.901
Lymphatic and haematopoietic tissue				
Leukemia (204-208)	23	24.8	0.93 (0.59-1.39)	0.794
Leukemia except chronic lymphatic leukemia [3] (204-208, except 204.1)	23	24.5	0.94 (0.59-1.41)	0.839
Non-Hodgkin's lymphoma (200, 202.0-202.3, 202.5-202.9)	12	11.3	1.07 (0.55-1.86)	0.942
Multiple myeloma (203)	5	3.5	1.45 (0.47-3.38)	0.529
All malignant neoplasms except leukemia (140-203)	411	450.1	0.91 (0.83-1.01)	0.069

1) Expected number of deaths: Number of deaths that would be expected in the study population assuming that deaths would occur at the death rate for Japanese males in general.
2) Malignant and unspecified nature of the brain neoplasms. No nervous system neoplasms
3) No cases of chronic lymphatic leukemia

study, including the confirmation of vital status by use of residence registration records and the identification of causes of death by record linkage with magnetic tape transcripts of National Vital Statistics.

In the present study, the study population (114,900) reduced to 63% from the original nuclear worker population (181,583). However, it was found that a larger proportion of workers of the study population had higher cumulative doses than workers of the original population, and that retrospective confirmation of vital status was more difficult for workers with low cumulative doses. Judging from these reasons, a possibility of the

Table 5 Observed number of deaths (O) and expected number of deaths (E) by cause of death and cumulative dose group, and test of trend (with no lag).

Cause of death (ICD9 code no.)	Cumulative dose groups (mSv) <10 O/E [1]	10- O/E	20- O/E	50- O/E	100+ O/E	Test of trend (one-tailed p value)
All causes of death	1290 / 1301.2	186 / 169.3	170 / 171.7	74 / 77.8	38 / 38.1	0.539
Non-cancer (excluding external causes) (1-26, 39-89) [2]	549 / 540.9	77 / 68.9	62 / 69.4	24 / 31.3	14 / 15.4	0.888
All neoplasms (140-239)	502 / 506.1	64 / 63.7	66 / 65.1	31 / 29.4	16 / 14.8	0.315
All malignant neoplasms (140-208)	488 / 492.8	62 / 61.9	64 / 63.4	31 / 28.6	16 / 14.3	0.259
By site						
Oral cavity and pharynx (140-149)	6 / 5.9	2 / 0.8	0 / 0.8	0 / 0.4	0 / 0.2	0.796
Esophagus (150)	22 / 18.7	0 / 2.3	1 / 2.4	2 / 1.1	0 / 0.5	0.754
Stomach (151)	105 / 110.9	16 / 14.0	16 / 14.3	9 / 6.5	3 / 3.3	0.255
Colon (153)	44 / 38.0	1 / 4.8	3 / 4.9	2 / 2.2	1 / 1.1	0.774
Rectum (154)	31 / 25.9	2 / 3.3	1 / 3.4	1 / 1.6	0 / 0.8	0.944
Liver (155)	77 / 82.4	14 / 10.4	12 / 10.7	4 / 4.9	4 / 2.5	0.199
Gallbladder (156)	11 / 13.6	2 / 1.6	3 / 1.7	1 / 0.7	1 / 0.4	0.073
Pancreas (157)	27 / 30.2	4 / 3.7	5 / 3.7	3 / 1.6	1 / 0.8	0.144
Lung (162)	93 / 88.5	6 / 10.6	11 / 10.8	4 / 4.7	3 / 2.3	0.509
Prostate (185)	4 / 5.3	1 / 0.6	2 / 0.6	0 / 0.3	0 / 0.1	0.444
Bladder (188)	6 / 6.7	2 / 0.9	0 / 0.9	1 / 0.4	0 / 0.2	0.509
Kidney and other and unspecified urinary organs (189.0-189.2)	8 / 7.4	1 / 1.0	1 / 1.0	0 / 0.5	0 / 0.2	0.779
Neoplasms of the brain and nervous system [3] (191, 225, 237.5, 237.6, 239.6)	8 / 8.3	1 / 1.0	1 / 1.0	0 / 0.5	1 / 0.2	0.163
Lymphatic and haematopoietic tissue						
Leukemia (204-208) [4]	14 / 16.5	3 / 2.4	3 / 2.4	3 / 1.2	0 / 0.6	0.294
Non-Hodgkin's lymphoma (200, 202.0-202.3, 202.5-202.9)	15 / 13.3	0 / 1.7	3 / 1.8	0 / 0.8	0 / 0.4	0.816
Multiple myeloma (203)	5 / 4.6	1 / 0.5	0 / 0.6	0 / 0.2	0 / 0.1	0.767
All malignant neoplasms except leukemia (140-203)	474 / 476.3	59 / 59.6	61 / 60.9	28 / 27.4	16 / 13.8	0.291

1) Expected number of deaths: Number of deaths calculated for each cumulative dose group using the age-specific death rate of the study population
2) Codes of simplified classification
3) Malignant and unspecified nature of the brain neoplasms. No nervous system neoplasms
4) No cases of chronic lymphatic leukemia

Table 6 Observed number of deaths (O) and expected number of deaths (E) by cause of death and cumulative dose group, and test of trend (based on a 2-year lag for leukemia and a 10-year lag for other neoplasms).

Cause of death (ICD9 code no.)	Cumulative dose groups (mSv) <10 O/E [1]	10- O/E	20- O/E	50- O/E	100+ O/E	Test of trend (one-tailed p value)
All neoplasms (140-239)	349 /349.7	39 /40.1	41 /35.5	8 /10.7	2 /3.1	0.692
All malignant neoplasms (140-208)	339 /341.0	39 /39.0	40 /34.6	8 /10.4	2 /3.0	0.654
By site						
Oral cavity and pharynx (140-149)	5 /4.8	1 /0.6	0 /0.5	0 /0.1	0 /0.0	0.718
Esophagus (150)	15 /14.3	0 /1.6	2 /1.5	1 /0.4	0 /0.1	0.418
Stomach (151)	68 /69.3	9 /7.9	7 /7.1	3 /2.1	0 /0.6	0.533
Colon (153)	26 /26.3	3 /3.0	4 /2.7	0 /0.8	0 /0.2	0.680
Rectum (154)	22 /19.1	1 /2.2	1 /2.0	0 /0.6	0 /0.2	0.899
Liver (155)	52 /54.8	10 /6.4	6 /5.6	0 /1.7	1 /0.5	0.459
Gallbladder (156)	6 /7.2	2 /0.8	0 /0.7	1 /0.2	0 /0.1	0.238
Pancreas (157)	17 /20.8	2 /2.3	5 /2.1	2 /0.6	0 /0.2	0.043
Lung (162)	72 /66.4	3 /7.4	6 /6.6	1 /2.0	1 /0.6	0.712
Prostate (185)	3 /4.0	1 /0.4	1 /0.4	0 /0.1	0 /0.0	0.370
Bladder (188)	4 /5.6	2 /0.7	1 /0.6	0 /0.2	0 /0.1	0.396
Kidney and other and unspecified urinary organs (189.0-189.2)	6 /6.3	1 /0.8	1 /0.7	0 /0.2	0 /0.0	0.550
Neoplasms of the brain and nervous system [2] (191, 225, 237.5, 237.6, 239.6)	6 /5.6	0 /0.6	1 /0.5	0 /0.2	0 /0.0	0.609
Lymphatic and haematopoietic tissue						
Leukemia (204-208) [3]	14 /16.7	3 /2.4	3 /2.4	3 /1.1	0 /0.5	0.218
Non-Hodgkin's lymphoma (200, 202.0-202.3, 202.5-202.9)	11 /9.6	0 /1.1	1 /1.0	0 /0.3	0 /0.1	0.774
Multiple myeloma (203)	5 /4.0	0 /0.4	0 /0.4	0 /0.1	0 /0.0	0.786
All malignant neoplasms except leukemia (140-203)	325 /327.6	37 /37.4	39 /33.2	8 /9.9	2 /2.9	0.602

1) Expected number of deaths: Number of deaths calculated for each cumulative dose group using the age-specific death rate of the study population
2) Malignant and unspecified nature of the brain neoplasms. No nervous system neoplasms
3) No cases of chronic lymphatic leukemia

under estimation in risk will be excluded. However, a further study may be needed to examine possible bias between the study population and the original population.

The death rates in the cohort due to the following causes of death were found to be significantly lower than in the general population: all causes, non-cancer causes excluding external causes, all neoplasms, malignant neoplasms, malignant neoplasms other than leukemia, and stomach neo-

plasm. In stomach neoplasm, the death rate on a 10-year lag was also significantly lower.

In occupational studies, working populations are often observed to have lower death rates for all causes and for cancer than the general population. This is known colloquially as "the healthy worker effect."[17] The present study indicated healthy worker effect.

In this study, only significant association with dose was noted for malignant neoplasm of the pancreas on a 10-year lag. When an attempt is made to carry out an analysis of many different sites in a population, tests of significance at the 5% level can yield a significant result even by chance in one out of 20. Therefore, prudence must be exercised when interpreting the results of statistical analysis involving malignant neoplasms of many sites such as undertaken in the present study.

When a statistical association is demonstrated between a factor and a disease, various criteria are available for examination of whether a causal relationship exists. In summary, all such criteria require that at least a dose-response relationship be evident, that similar results be available from other credible epidemiological studies, and that reasonable medical and biological explanations for the noted association exist in order for the statistical association to be judged as reflecting a causal relationship.

Although a statistical association of pancreatic cancer to radiation dose was noted in the present study, many previous studies of nuclear industry radiation workers have demonstrated no significant association between radiation dose and cancer of the pancreas.[1,6,10,11,12,18] The exception is the most recent study of Hanford workers (1945-1986) which showed a significant association of cancer of the pancreas with dose on a 2-year lag but not on a 10-year lag. As a result of various considerations, the authors of that study, GILBERT *et al.*[3] felt that no causal relationship could be inferred. International review reports on the results of studies of atomic bomb survivors are useful in interpreting the findings for cancer of the pancreas. BEIR V Report[19] cites the pancreas to be a relatively radioinsensitive organ. Neither have the 1990 recommendations of ICRP[20] assigned any specific tissue weighting factor to the pancreas. After considering these scientific findings, the statistically significant association noted between cancer of the pancreas and dose in the present study can not be immediately judged as indicating a causal relationship with radiation.

IARC has carried out the combined analysis on seven cohorts of nuclear industry workers in the United States of America, United Kingdom and Canada, and estimated the excess relative risk for all cancers excluding leukemia, and leukemia excluding chronic lymphocytic leukemia.[12] In the present study, mean follow-up period was 4.6 years, and the cases of various death causes were relatively small. Under such situation, estimates of risk have larger uncertainty. Therefore, we used score statistic for testing dose-response.

In order to more precisely evaluate the findings, follow-up of workers who were confirmed to be alive in the present study should be continued.

ACKNOWLEDGMENTS: We would like to thank all members of the following committees for collaborating on this study: the Study Evaluation Committee, the Study Operations Committee, the Research Ethics Committee, and the Radiation Dosimetry Committee, which were established under the aegis of the Association's Board Chairman to ensure that the study would be conducted properly. Furthermore, we are grateful to the Radiation Effects Research Foundation (Chairman, Dr. Itsuzo SHIGEMATSU) for critical comments on manuscript. Thanks also to the all staffs of the Institute of Radiation Epidemiology, and Mr. Minoru ARAI, Director of RADREC, who provided the personal dosimetry records.

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