Cancer risks in a population with prolonged low dose-rate γ-radiation exposure in radiocontaminated buildings, 1983 - 2002

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Abstract

Purpose: To assess cancer risks in a population who received low dose-rate γ-irradiation for about 10 years as a result of occupying buildings containing ^{60}Co-contaminated steel.

Materials and methods: The cancer risks were compared with those populations with the same temporal and geographic characteristics in Taiwan by standardized incidence ratios (SIRs), adjustment for age and gender. The association of risks with different extents of excess cumulative exposure was further evaluated for their hazard ratios by the Cox regression analyses.

Result: 7,271 people were registered as the exposed population, with 103,225 person-years of follow-up. The average excess cumulative exposure in the exposed cohort was 47.7 mSv (range < 1 to 2,363 mSv). A total of 141 patients with various cancers were observed, while 95 of them who developed solid cancers and leukemia more than 10 and 2 years since beginning of occupancy were included for further analysis. The risks in SIRs for the exposed subjects were lower in all cancers, all cancers excluding leukemia, and all solid cancers combined, while the SIRs were significantly higher for all leukemia combined (n = 6, SIR = 3.4, 95 % confidence interval [CI] 1.2 – 7.4) and acute lymphocytic leukemia (n = 3, SIR = 6.8, 95 % CI 1.4 – 19.8) in men, and marginally significant for thyroid cancers (n = 6, SIR = 2.6, 95 % CI 1.0 – 5.7) in women. All cancers combined, all solid cancers, and a combination of leukemia and thyroid/breast cancers were further shown with exposure-dependent increased hazard ratios in individuals with the initial exposure before 30

years old, but not beyond this age.

Conclusions: Prolonged low dose-rate radiation exposure appeared to increase the risks of developing certain cancers in specific subgroups of this population in Taiwan.

Introduction

Acute radiation exposure has been demonstrated to increase cancer risks in many studies including the Japanese atomic bomb survivors (Preston *et al*. 1994, Thompson *et al*. 1994), persons with medical exposure (Boice *et al*. 1991), and persons exposed in occupational settings (Ivanov *et al*. 1997). It remained uncertain whether chronic low dose-rate radiation exposure would incur increased cancer risks in a general public setting, as addressed in a recent review (Brenner *et al*. 2003). Past studies on carcinogenic effects of low dose-rate ionizing radiation exposure have focused on nuclear workers (Cardis *et al*. 1995, Muirhead *et al*. 1999), and workers in the Mayak nuclear facility in the former Soviet Union were observed to have significant increases in the mortality rates of leukemia (Shilnikova *et al*. 2003). Furthermore, a Swedish study showed an elevated risk of acute lymphocytic leukemia among children and young adults living in uranium-containing alum shale concrete houses with high indoor radon concentrations (Axelson *et al.* 2002). Brenner *et al.* (2003) suggests that a protracted γ-radiation exposure of 50 – 100 mSv can be associated with increased cancer risks in humans. However, there are fewer studies on exposure of the general public, particularly including women and children at different ages of exposure.

In late 1982, several unknown ^{60}Co orphan sources were recycled in the steel scrap industry in northern Taiwan and made into more than 20,000 tons of various steel products employed in over 200 residential, industrial, or school constructions (Chang *et al*. 1993, 1997a). It

was not until August 1992 that some of these contaminated buildings started to be identified. The rates of exposure (0.5 – 270 μSv/hours) in these buildings, measured in 1994, have been estimated to be several to > 1,000 times the background radioactivity (0.08 – 0.1 μSv/hours) in general Taiwanese construction. Cytogenetic analysis in subgroups of the exposed population had shown increased micronucleus frequencies in their peripheral lymphocytes (Chang *et al*. 1997b), increases in acentromeric and single or multiple centromeric cytogenetic damages (Chang *et al*. 1999a), and higher frequencies of chromosomal translocations, rings and dicentrics (Hsieh *et al*. 2002). Persistent depression in peripheral leucocytes and neutrophils (Chang *et al*. 1999b), increased eosinophils, altered distributions in lymphocyte subpopulations (Chang *et al*. 1999c), increased frequencies of lens opacities (Chen *et al*. 2001), delay in physical height in children (Wang *et al*. 2001), increased risk of thyroid abnormalities (Chang *et al*. 2001), as well as late consequences in haematopoietic adaptation in children were also observed (Wang *et al*. 2002). This follow-up study was designed to evaluate risks of developing cancers in this exposed population more than 10 years after their initial exposure.

Materials and methods

Study population

On August 1992, the radioactive contamination event was brought to public attention by a local newspaper (Chang *et al.* 1997a). Since the discovery of these radiocontaminated buildings, the nuclear regulatory authority in Taiwan (the AEC), the Department of Health, and a designated research team began to establish a registry for all residents and students who had stayed in these buildings by using household and school registration records. The household registration system in Taiwan has been maintained by the Ministry of Interior (MOI) since the 1950s and has been completely computerized since the 1990s. As the household registration was accessible by National Identification Numbers (NIN), we were able to trace all individuals with official residential occupancy in these contaminated buildings since 1982 when these individuals first moved in. Moreover, individuals identified by house-owner's records or reported by other registrants to have resided in those buildings, but not registered in the MOI residential registration, were further analyzed for details of their occupancy and exposure through extensive contacts and interviews. Those who left before the beginning of the registration in 1992 were also traced by household registration and further analyses.

After these individuals moved out of contaminated buildings or after the contaminated steel was removed, the individuals were designated as not having continuous excess exposure.

Systematic questionnaire interviews were administered to each registered individual, including medical history, occupation, education, and detailed exposure history, including dates moved in and out, and lifestyles in these radiocontaminated buildings. Excess exposure to other radiation sources in these registrants, such as occupational and medical exposure, such as radiotherapy, were evaluated carefully. If registered individuals were deceased, interviews were conducted with their families, as well as teachers at school and employers when necessary. The protocols for conducting the questionnaire survey were reviewed by the Internal Review Boards of the National Yangming University and further approved by the National Health Research Institute, DOH, which had supported the research, to ensure confidentiality and quality. The interviews were conducted only after the contents were fully explained to the individuals and informed consent was acquired. These individuals were further periodically evaluated since they relocated to non-contaminated buildings. Deaths amongst the study cohort were further matched by the National Mortality Registry of Taiwan, which had been maintained by the Bureau of Vital Statistics in Taiwan since early 1950s. To the end of 2002, 7,271 people were registered (including 3,461 men and 3,810 women), while living individuals were followed up closely.

The person-years of follow-up on each cohort member were calculated from their moving into the contaminated buildings to the date of death, the date of cancer diagnosis, or December 31, 2002, whichever came first. The latent periods of 2 years for leukemia and

10 years for other cancers were also considered when cancer risks were evaluated (ICRP. 1990).

Ascertainment of cancer cases

Cancer cases were identified through the National Cancer Registry of Taiwan (NCRT) as well as interviews through a medical care program in designated hospitals. The NCRT was established in 1979 and was based on the International Classification of Disease for Oncology (ICD-O). The NCRT is a population-based cancer registry which collected information on all newly diagnosed cancer patients from all health care sectors in Taiwan and had provided data to many nationwide and international cancer studies (Guo *et al*. 1997, Chien *et al*. 2001).

Exposure evaluation

An exposure assessment system, the Taiwan Cumulative Dose (TCD), had been established in the beginning of the cohort registration and applied to exposure reconstruction for the cohort on an individual basis. The TCD integrated the time-activity analysis recommended by the U.S. National Institute for Occupational Safety and Health advisory committee (Cardarelli *et al*. 1997) and the highly occupied zone (HOZ) model of this study group (Hwang *et al*. 1998), incorporating a detailed history of occupancy duration in each radioactive area of the buildings and area-specific radiation exposure to the whole-body of

each individual. Each cohort member was asked to recall and provide as much detailed information as they could about previous occupancy, including daily regular durations in each HOZ. Environmental radioactivities of representative spots in each room were measured accordingly. Cumulative excessive exposures were corrected for the half-life of radioactive decay, i.e., 5.27 years for Co-60, and integrated with lifestyle patterns while residing in the contaminated buildings.

Due to inadequate information from some registered members, only 6,246 subjects were available for TCD evaluation until this analysis. The average excessive cumulative exposure, i.e., above background radiation exposure, was 47.7 ± 166.4 mSv (ranging from < 1 mSv to 2,363 mSv), with 2,287 (36.6 %) with less than but close to 1 mSv, 3,134 (50.2 %) 1 to 50 mSv, and 825 (13.2 %) more than 50 mSv. When the exact exposure duration for each individual was taken into consideration, the estimated dose-rate of excess exposure was 10.5 ± 50.2 mSv/year on average (< 1 to 1,413 mSv/year), including 63 % with less but close to 1 mSv/year, 16 % with 1 - 5 mSv/year, and 21 % with more than 5 mSv/year. Owing to large variations of occupancy durations in each irradiated area of these buildings and variations in the radioactivity in these areas, from slightly higher than 0.1 μSv/hour up to 500 μSv/hour, there was a wide range of cumulative exposures.

Statistical analysis

The cancer risks in the exposed population were compared with those observed in populations with the same temporal and geographic characteristics in Taiwan, including those in Taipei City and Taipei, Keelong, Taoyuan, and Changhwa counties, where the radiocontaminated buildings were located (Chang *et al*. 1997a). The population sizes of these administrative areas included 2.6 million in Taipei City, 3.4 million in Taipei County, 0.4 million in Keelong County, and 0.3 and 0.2 million in Taoyuan and Changhwa counties, respectively. A standardized incidence ratio (SIR) adjusted for age and gender was calculated with the observed number of cancer cases as the numerator and the expected number of specific cancer cases as the denominator (Breslow *et al*. 1987). This was designed to compare cancer risks with a smaller reference population. Moreover economic factors, which somehow determined residency, were not matched. According to the Life Span Study (Thompson *et al*. 1994, Preston *et al*. 1994), the top three cancers associated with radiation were leukemia (ERR = 4.37), breast cancers (ERR = 1.74) and thyroid cancers (ERR = 1.50). Therefore, we also combined these three cancers as the target cancer group to assess the exposure-response relationship.

Cox proportional hazards regression models were employed to estimate the hazard ratios (HRs = $e^{\beta 1\,(\text{sex}) + \beta 2\,(\text{attained age}) + \beta 3\,(\text{cumulative exposure})}$) after adjustment for covariates including gender and cumulative exposure. The 95 % confidence interval (CI) for each SIR was constructed using the exact limits given by Pearson and Hartley (Pearson *et al*. 1976). All

statistical tests were performed using SAS for Windows at the two-sided significance level of 0.05.

Results

These 7,271 cohort members were followed-up for 15.9 ± 4.0 years on average (3 to 20 years), with the mean initial exposure at 17.2 ± 16.0 years of age (< 1 to 80 years) and a total of 103,225 person-years of follow-up (48,932 for men and 54,293 for women; table 1). 141 of them were identified with various cancers, of which 95 subjects with latent periods longer than the minimum latent periods were included for further analysis (table 2). These 95 cancer cases included 42 men and 53 women and 82 solid cancers, 7 leukemia (all types), 5 malignant lymphoma and 1 multiple myeloma.

SIRs were significantly lower in both genders combined for all cancers (SIR = 0.6, 95 % CI 0.5 – 0.7; table 3), all cancers excluding leukemia (SIR = 0.8, 95 %, CI 0.6 –1.0), and all solid cancers combined (SIR = 0.7, 95 % CI 0.6 – 0.9). In men, there were significantly lower SIRs for all cancers combined (SIR = 0.6, 95 % CI 0.4 – 0.8), all cancers combined excluding leukemia (SIR = 0.7, 95 % CI 0.5 – 0.9), and all solid cancers combined (SIR = 0.6, 95 % CI 0.4 – 0.8). In women, there were significantly lower SIRs for all cancers combined (SIR = 0.6, 95 % CI 0.5 – 0.8).

In contrast, for both genders combined there were significantly elevated risks for thyroid cancers (n = 7, SIR = 2.6, 95 % CI 1.1 – 5.4), malignant lymphoma (n = 5, SIR = 3.1, 95 % CI 1.0 – 7.2). There were marginally significantly elevated risks for leukemia excluding

chronic lymphocytic leukemia (n = 7, SIR = 2.2, 95 % CI 0.9 – 4.6), and acute lymphocytic leukemia (n = 3, SIR = 3.6, 95 % CI 0.7 – 10.4) for both genders combined.

In men, there were significantly elevated risks for all leukemia combined (n = 6, SIR = 3.4, 95 % CI 1.2 – 7.4), leukemia excluding chronic lymphocytic leukemia (n = 6, SIR = 3.6, 95 % CI 1.3 – 7.8), and acute lymphocytic leukemia (n = 3, SIR = 6.8, 95 % CI 1.4 – 19.8). For all leukemia, the disease was diagnosed 6 to 18 years (mean 13.3 ± 4.7 years) after initial exposure, while the ages at initial exposure were 5 (two cases), 15, 39, 52 and 70 years old, respectively. A case of papillary thyroid cancer was observed in one subject 47 years old, 10 years after initial exposure. In women, there were marginally significantly elevated risks for thyroid cancers (n = 6, SIR = 2.6, 95 % CI 1.0 – 5.7). The ages at initial exposure were 9, 30, 32, 34, 51 and 67 years old, respectively, and the diagnoses made 10 to 16 years (mean 12.5 ± 2.4 years) after initial exposure. All thyroid cancers were of the papillary cell type.

In order to assess exposure-dependent risks, the cumulative exposure was divided into three categories: less than 1, between 1 to 50 mSv and more than 50 mSv (table 4). Leukemia and thyroid/ breast cancers were combined as the target cancer group to assess the exposure-response relationship. Among those who received the initial exposure before 30 years of age, those who had received cumulative exposures of more than 50 mSv had significantly increased risks for all cancers combined (HR = 5.5, 95 % CI 1.4 – 21.8), all

solid cancers combined (HR = 5.0, 95 % CI 1.0 – 24.7), thyroid, breast and leukemia combined (HR = 5.1, 95 % CI 1.0 – 27.0), as compared with those who had received less than 1 mSv of exposure. There was no significantly higher risk in those receiving initial exposure after 30 years old.

Discussion

Compared to the geographic reference population, the study population had lower incidences of all cancers combined, all cancers combined excluding leukemia, and all solid cancers combined (table 3). Most study cohort members have resided in buildings constructed in the early 1980s while economic developments were at their greatest swing in Taiwan. This observation suggests that the exposed population might have higher socioeconomic status than their geographic reference populations, with healthier lifestyles and consequently lower cancer risks, which have been consistently described in other population studies (Lowry *et al.* 1996, Lantz et al. 1998, Wardle *et al.* 2002). Unfortunately we were not able to match the economic status of these individuals with the reference population in their study. Because the dose reconstruction was made without knowledge of the disease status of residents, it was unlikely to introduce an information bias even though there might be random measurement errors (misclassifications).

Leukemia was the first cancer type to be observed at higher than normal incidence among the survivors of the atomic bombings of Hiroshima and Nagasaki (Folley *et al*. 1952). This study was able to show that there were significantly elevated risks of leukemia (excluding CLL) in men and for both genders combined. On the other hand, this study did not clearly show the association between non-Hodgkin's lymphoma (NHL) and external low-LET radiation, as addressed in the UNSCEAR report (UNSCEAR 2000). In the present study,

we observed a significantly elevated risk for malignant lymphoma, particularly non-Hodgkin's lymphoma (table 3). Owing to numbers of rare cases, it was inconclusive to address the risk of non-Hodgkin's lymphoma in this population.

A previous study on these residents indicated a significant exposure-dependent increase in thyroid abnormalities (Chang *et al*. 2001). External exposure of the thyroid gland to ionizing radiation, even under 0.05 Gy, was shown to increase the risk of thyroid cancers for children and adolescents (Jacob *et al*. 1999). In the Israeli tinea capitis study, women had an approximately 5 times higher risk of thyroid cancers than men (Ron *et al*. 1989). A pooled analysis of seven studies also showed that the ERR/Gy of thyroid cancers was nearly twice as high for women than men (Ron *et al*. 1995). Our observation in this study was consistent with these observations.

Breast cancer has been linked with radiation exposure in many studies (Preston *et al.* 2002). The present study did not observe an elevated risk for breast cancer (n = 12; SIR = 1.0; 95 % CI 0.5 – 1.7). This may have been due to the small sample size and the relatively shorter follow-up duration in this study (average duration since the initial exposure 16.0 years). A case-control study has shown that early age at first full-term pregnancy, multiple births, and lengthy total lactation history were protective against breast cancer among A-bomb survivors, and found that these factors were also protective against radiation-related breast cancers,

especially among women under 20 years of age ATB (Land *et al*. 1994). Therefore, a further nested case-control study may be helpful to clarify the association between exposure and breast cancer in this cohort population.

The level of the radiation-induced risks is dependent not solely on the dose but also on the factors such as age at exposure and time since exposure. Data on the survivors of the atomic bombings showed that the excess relative risk decreased with increased age at exposure for combined gastrointestinal, stomach, non-melanoma skin, breast and thyroid cancers and leukemia (Preston *et al*. 1994, Thompson *et al*. 1994). This study showed that age at initial exposure less than 30 years old was associated with a higher risk of cancer than those more than 30 years. Owing to relatively younger ages in this exposed population, the total number of cancer cases was small. Chen *et al.* (2004) reported a primitive analysis on a similar, but not exactly the same, cohort population in Taiwan, while suggesting reduced cancer mortality. However, Chen *et al.* (2004) used group analysis for their exposure, and included only a portion of the cohort population mentioned in this study. Their population was based only on initial preliminary community registration by the AEC, but not detailed registration as in this study. Moreover, they did not analyze the age and gender distributions of these exposed persons as we have undertaken.

A particular advantage of incidence data over mortality data was the information they

provided for cancers that are often non-fatal. For some cancers susceptible to induction by radiation, i.e., thyroid and breast cancers, incidence analysis were relatively more sensitive than the mortality analysis. Incidence analysis was also better in the evaluation of association with cancer risks and radiation exposure as the period between exposure and mortality could be affected by health services and cancer treatment.

Although this study cohort was large enough to detect statistically significant increased risks for certain types of cancer, the average follow-up period since initial exposure was still too short to observe the development of the whole spectrum of cancers. Further follow-up of the study cohort is necessary to corroborate our findings and identify other types of cancer that may also be related to the protracted and low dose-rate ionizing radiation.

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Table 1. Characteristics of the exposed Taiwan cohort by gender, 1983-2002

	Men	Women	Total
Number of members	3,461	3,810	7,271
Number of person-years	48,932	54,293	103,225
Average follow-up time (years)	15.8 ± 4.0	16.0 ± 3.9	15.9 ± 4.0
	(3, 20)*	(3, 20)	(3, 20)
Age at initial exposure (years)	16.4 ± 16.1	18.0 ± 15.8	17.2 ± 16.0
	(<1, 77)	(<1, 80)	(<1, 80)
Number of cancers†	42	53	95
Cumulative exposure (TCD‡; mSv)	48.6 ± 163.4	46.9 ± 168.9	47.7 ± 166.3
	(<1, 2,206)	(<1, 2,363)	(<1, 2,363)
Dose rate (mSv year $^{-1}$)	11.2 ± 57.0	9.8 ± 43.1	10.5 ± 50.2
	(<1, 1,413)	(<1, 797)	(<1, 1,413)

* Mean ± 1 SD (min, max)

† Latent period considered

‡ Taiwan Cumulative Dose

Table 2. Cancer cases excluded from analysis*

Cancer site		Latent periods (years)		Cumulative exposure (TCD; mSv)		Age at initial exposure (years)	
	Cases	Mean	(min, max)	Mean	(min, max)	Mean	(min, max)
Solid cancers	45	7.0	(1.1, 10.0)	116.1	(< 1, 1,464.0)	45.2	(5.0, 71.0)
Nasopharynx	1	4.3		9.0		36.0	
Stomach	3	5.9	(1.7, 8.2)	445.0	(378.8, 571.0)	52.7	(48.0, 61.0)
Colon	5	8.4	(5.1, 9.7)	53.8	(5.6, 225.4)	64.4	(54.0, 71.0)
Rectum	4	5.7	(3.8, 9.6)	1.1	(< 1, 3.7)	39.0	(19.0, 56.0)
Liver	3	5.0	(4.2, 6.5)	54.1	(21.7, 105.1)	32.3	(28.0, 39.0)
Lung	3	8.4	(6.2, 9.6)	560.1	(4.0, 1,464.0)	62.0	(48.0, 71.0)
Breast	7	6.2	(1.1, 10.0)	97.9	(< 1, 447.1)	40.0	(26.0, 59.0)
Cervix Uteri	8	6.9	(2.5, 9.9)	81.8	(2.1, 293.4)	41.2	(27.0, 64.0)
Corpus Uteri	2	9.0	(8.9, 9.1)	36.5	(10.3, 62.8)	54.5	(45.0, 64.0)
Ovary	2	9.6	(9.3, 9.8)	113.7	(2.1, 225.4)	28.5	(24.0, 33.0)
Urinary	2	7.5	(6.5, 8.4)	< 1	(< 1, < 1)	61.5	(57.0, 66.0)
Kidney	1	2.3		34.7		70.0	
Thyroid glands	4	8.6	(7.9, 9.8)	8.9	(0.3, 22.1)	27.5	(5.0, 41.0)
Multiple myeloma	1	1.3		256.5		61.0	

* Latent periods less than 2 years and 10 years for leukemia and others

Table 3. Standardized incidence ratios for the exposed population, 1983 – 2002*

Cancer site	Men			Women			All		
	Cases			Cases			Cases		
	Observed	Expected	SIR (95 % CI)	Observed	Expected	SIR (95 % CI)	Observed	Expected	SIR (95 % CI)
All cancers	42	74.0	0.6‡ (0.4, 0.8)	53	86.0	0.6‡ (0.5, 0.8)	95	160.3	0.6‡ (0.5, 0.7)
All cancers excluding Leukemia	36	51.9	0.7‡ (0.5, 0.9)	52	59.5	0.9 (0.7, 1.1)	88	111.6	0.8‡ (0.6, 1.0)
All solid cancers	32	50.9	0.6‡ (0.4, 0.8)	50	58.5	0.9 (0.6, 1.1)	82	109.5	0.7‡ (0.6, 0.9)
Tongue	0	1.1	— —	1	0.3	3.7 (0.1, 20.7)	1	1.5	0.7 (0.02, 3.7)
Oral	1	1.4	0.7 (0.02, 4.0)	0	0.2	— —	1	1.7	0.6 (0.02, 3.3)
Nasopharynx	1	2.0	0.5 (0.01, 2.7)	0	1.0	— —	1	3.1	0.3 (0.01, 1.8)
Esophagus	1	1.8	0.6 (0.01, 3.2)	1	0.3	3.6 (0.1, 20.3)	2	2.2	0.9 (0.1, 3.3)
Stomach	5	4.9	1.0 (0.33, 2.4)	2	3.1	0.6 (0.1, 2.3)	7	8.2	0.8 (0.3, 1.8)
Colon	2	4.0	0.5 (0.1, 1.8)	3	3.8	0.8 (0.2, 2.3)	5	7.9	0.6 (0.2, 1.5)
Rectum	3	3.1	1.0 (0.2, 2.8)	2	2.7	0.7 (0.1, 2.7)	5	5.9	0.8 (0.3, 2.0)
Liver	5	8.9	0.6 (0.2, 1.3)	3	3.7	0.8 (0.2, 2.3)	8	13.1	0.6 (0.3, 1.2)
Lung	7	7.6	0.9 (0.4, 1.9)	3	4.5	0.7 (0.1, 2.0)	10	12.5	0.8 (0.4, 1.5)
Connective	1	0.5	2.1 (0.1, 11.9)	1	0.4	2.3 (0.1, 12.6)	2	0.9	2.2 (0.3, 7.9)
Skin	2	1.5	1.4 (0.2, 4.9)	1	1.5	0.7 (0.02, 3.6)	3	3.0	1.0 (0.2, 2.9)
Melanoma skin	0	0.2	— —	1	0.2	5.4 (0.1, 30.1)	1	0.4	2.8 (0.1, 15.7)
Non melanoma skin	2	1.4	1.5 (0.2, 5.3)	0	1.4	— —	2	2.8	0.7 (0.1, 2.6)
Breast	0	0.0	— —	12	12.1	1.0 (0.5, 1.7)	12	11.2	1.1 (0.6, 1.9)
Cervix Uteri	0	0.0	— —	12	12.9	0.9 (0.5, 1.6)	12	11.9	1.0 (0.5, 1.8)
Corpus Uteri	0	0.0	— —	3	1.5	2.0 (0.4, 6.0)	3	1.4	2.2 (0.5, 6.4)
Prostate gland	1	3.4	0.3 (0.01, 1.7)	0	0.0	— —	1	3.8	0.3 (0.01, 1.5)
Kidney	2	1.3	1.5 (0.2, 5.5)	0	1.1	— —	2	2.4	0.8 (0.1, 3.0)
Thyroid glands	1	0.5	2.0 (0.1, 11.1)	6	2.3	2.6† (1.0, 5.7)	7	2.7	2.6‡ (1.1, 5.4)
Leukemia (all types)	6	1.8	3.4‡ (1.2, 7.4)	1	1.5	0.7 (0.02, 3.7)	7	3.3	2.1† (0.8, 4.3)
Leukemia excluding CLL	6	1.7	3.6‡ (1.3, 7.8)	1	1.5	0.7 (0.02, 3.8)	7	3.2	2.2† (0.9, 4.6)
Acute lymphocytic leukemia (ALL)	3	0.4	6.8‡ (1.4, 19.8)	0	0.4	— —	3	0.8	3.6† (0.7, 10.4)
Acute myelocytic leukemia (AML)	2	0.6	3.3 (0.4, 11.8)	1	0.5	1.8 (0.05, 10.1)	3	1.2	2.5 (0.5, 7.4)
Chronic myelocytic leukemia (CML)	1	0.3	3.9 (0.1, 21.9)	0	0.2	— —	1	0.5	2.2 (0.1, 12.1)
Multiple myeloma	1	0.3	3.9 (0.1, 21.5)	0	0.2	— —	1	0.5	2.2 (0.1, 12.3)
Malignant Lymphoma	3	0.9	3.3 (0.7, 9.7)	2	0.7	2.9 (0.4, 10.5)	5	1.6	3.1‡ (1.0, 7.2)
Non-Hodgkin's lymphoma	3	0.5	6.4‡ (1.3, 18.6)	2	0.4	4.7 (0.6, 16.8)	5	0.9	5.5‡ (1.8, 12.8)

*Latent period considered; † $0.05 < p < 0.1$; ‡ $p \leq 0.05$; SIR: standardized incidence ratio; CI: confidence interval; —: not applicable

Table 4. Hazard ratio (HR) of cancer by different categories of Taiwan Cumulative Dose (TCD) and age at initial exposure*

	Cohort members	All cancers		All solid cancers		Leukemia excluding CLL		Thyroid cancers		Breast cancers		Thyroid, Breast, Leukemia	
		N§	HR (95 % CI)	N	HR (95 % CI)	N	HR (95 % CI)	N	HR (95 % CI)	N	HR (95 % CI)	N	HR (95 % CI)
Age at initial exposure													
≤ 30 years													
Gender													
Men	2,408	6	1	3	1	3	1	0	1	0		3	1
Women	2,633	19	2.7‡(1.1, 6.8)	17	4.7‡(1.4, 16.2)	0	—	2	—	6		8	2.4 (0.6, 9.3)
TCD (mSv)													
＜1	1,962	3	1	2	1	1	1	1	1	0	1	2	1
1~50	2,489	15	2.8(0.8, 10.0)	12	2.5(0.6, 11.3)	1	1.0(0.06, 15.5)	0	—	3	—	4	1.0(0.2, 5.7)
＞50	590	7	5.5‡(1.4, 21.8)	6	5.0‡(1.0, 24.7)	1	3.9(0.2, 63.6)	1	—	3	—	5	5.1‡(1.0, 27.0)
Total	5,041	25		20		3		2		6		11	
＞30 years													
Gender													
Men	568	31	1	26	1	2	1	1	1	0		3	1
Women	637	31	0.9(0.5, 1.5)	30	1.1(0.6, 1.8)	1	0.5(0.04, 5.3)	4	5.2(0.4, 64.0)	6		11	3.5†(1.0, 12.4)
TCD (mSv)													
＜1	325	18	1	16	1	0	1	1	1	2	1	3	1
1~50	645	34	1.0(0.6, 1.9)	31	1.1(0.6, 2.1)	2	—	3	0.8(0.07, 9.6)	2	0.5(0.07, 3.4)	7	1.2(0.3, 4.7)
＞50	235	10	0.8(0.4, 1.8)	9	0.8(0.4, 2.0)	1	—	1	1.8(0.1, 30.8)	2	1.3(0.2, 9.5)	4	1.9(0.4, 8.5)
Total	1,205	62		56		3		5		6		14	
All age													
Gender													
Men	2,976	37	1	29	1	5	1	1	1	0		6	1
Women	3,270	50	1.2(0.8, 1.9)	47	1.5†(0.9,2.4)	1	0.2(0.02, 1.6)	6	16.1‡(1.3, 196.4)	12		19	2.9‡(1.2, 7.3)
TCD (mSv)													
＜1	2,287	21	1	18	1	1	1	2	1	2	1	5	1
1~50	3,134	49	1.4(0.8, 2.4)	43	1.3(0.7, 2.3)	3	1.6(0.2, 15.9)	3	0.3(0.03, 2.4)	5	1.1(0.2, 5.6)	11	1.1(0.4, 3.3)
＞50	825	17	1.4(0.7, 2.7)	15	1.3(0.7, 2.7)	2	3.5(0.3, 39.7)	2	2.1(0.3, 17.9)	5	3.6(0.7, 18.6)	9	3.0‡(1.0, 9.0)
Total	6,246	87		76		6		7		12		25	

*Attained age was adjusted; † $0.05 < p < 0.1$; ‡ $p \leq 0.05$; § Numbers of cancer cases; —: not applicable