Cancer Admission and Mortality in Workers Exposed to Ionizing Radiation in Korea

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Objective: *Cancer mortality and morbidity are described for the first time in all Korean workers exposed to ionizing radiation.* ***Methods:*** *Based on hospital admissions, Standardized Rate Ratios (SRR) and Standardized Mortality Ratios (SMR) were modeled with Poisson regression.* ***Results:*** *Cancer admissions during 2000 to 2005 were low compared with autoworkers with the exception of nuclear power workers (SRR = 1.13, 95% CI = 0.94–1.36). Thyroid cancer was statistically significantly elevated in women radiation workers in medical (SRR = 2.90, 95% CI = 1.05–7.94) and research institutions (SRR = 3.91, 95% CI = 1.36–11.0) and industry (SRR = 5.07, 95% CI = 1.56–15.6), and in all nuclear power workers (SRR = 2.59, 95% CI = 1.33–5.13), and there was a significant association with dose (ERR = 20.4 per Sv, 90% CI = −8 to 60, one-tailed P = 0.049). The 935 deaths revealed a healthy worker effect for all causes (SMR = 0.58, 95% CI = 0.54–0.62) and all-cancer (SMR = 0.73, 95% CI = 0.64–0.82). Lung cancer (SMR = 0.77, 95% CI = 0.55–1.05) and leukemia (SMR = 0.59, 95% CI = 0.28–1.06) mortalities were also less than expected. Compared with autoworkers, radiation workers displayed decreased all-cause mortality except for nuclear power workers (statistically not significant).* ***Conclusions:*** *ERRs as high as 300 per Sv appear to be ruled-out in this population with regulated exposure to ionizing radiation while ERRs as high as 100 per Sv are not.* (J Occup Environ Med. *2008;50:791–803*)

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DOI: 10.1097/JOM.0b013e318167751d

Significant excesses of radiogenic leukemia and solid cancers have been found in relatively few studies of populations occupationally exposed to external radiation. Studies that have observed increased cancer risks include the International Agency for Research on Cancer 15-country (lung cancer),[1] the Oak Ridge[2] and Hanford[3] studies (lung cancer), and the Mayak workers study[4] (lung cancer and other sites). The well-known association between radon and lung cancer[5] probably arises from inhalation of dusts with adsorbed radon progeny.

The more common null findings may have resulted from the low doses of occupational exposures, small sample sizes that limit the precision of estimates, and methodological problems unique to individual studies. Therefore, public concern continues on the health effects of workers exposed to relatively low dose radiation.

In Korea, the number of enterprises using radiation and radioisotopes (RIs) has continuously increased since the passing of the Nuclear Energy Act in 1958. In 1974, only 70 institutions were licensed to use radiation sources but by 2005 there were over 1000. These licensed institutions are mainly in the areas of nuclear power, manufacturing industry, and educational, research, public and medical institutes (excluding facilities using only medical x-ray equipment). Currently the number of workers exposed to radiation and RIs is about 27,000 including 10,000 employed in nuclear power plants (Korea Radioisotope Association [KRIA]), 2006, Seoul: *The issue of* *analysis of occupational radiation exposure*).

Radiation is among the most thoroughly regulated occupational hazards in Korea. By the Nuclear Energy Act workers using ionizing radiation have their exposure level checked every 3 months and receive a health examination every 6 months. According to statistics compiled by the KRIA, established in 1985, the mean exposure level of radiation workers was 1.16 milliSieverts (mSv) per year in 2005, which is much lower than the 50 mSv annual occupational dose limit set by the Nuclear Energy Act in Korea and recommended by the International Commission on Radiological Protection (ICRP). The ICRP recommends that levels not exceed 50 mSv per year, and 100 mSv over 5 years, corresponding in practice to less than 20 mSv per year. The highest mean exposure level by type of organization was 3.26 mSv per year for workers of non destructive testing (NDT) firms (KRIA, 2006).

Radiation safety has been aggressively managed since passage of the Nuclear Energy Act. However, policy has focused primarily on prevention of acute radiation over-exposure incidents. There has been less concern about the chronic health effects on workers exposed to low dose radiation except for workers in nuclear power plants. Recently, the Korea Labor Welfare Corporation, Korea's sole worker's compensation provider, compensated six cases of occupational cancer in workers exposed to radiation (four cases of leukemia in a power plant worker, laboratory worker, radiologist, and a technician making dental devices; one thyroid cancer in a nurse, and one cancer of unknown origin in a technician performing NDT). In 2004, the Korean government established within KRIA the Central Registry for Radiation Workers Information. All employer radiation safety management records, including radioactive contamination monitoring and employee medical surveillance, are required to be retained. Records from employers with revoked and/or suspended licenses or those ceasing operations are submitted to KRIA and retained permanently since they may be a valuable archive for identifying effects of occupational radiation exposure in the future.

The present study estimated excess cancer risk in the Korean population under surveillance for ionizing radiation exposure. Using exposure data from the Central Registry for Radiation Workers Information, mortality associations were described as was cancer morbidity based on diagnoses for hospital admissions lasting longer than 3 days.

Materials and Methods

Cohort Definition and Data Collection

The radiation cohort consisted of workers under medical surveillance because of ionizing radiation exposure as required by law. The institutions comprised five sectors: (1) medical treatment and research institutes, (2) other research and education institutes, (3) nuclear power plants, (4) general industry including NDT firms, and (5) others including military, public organizations, etc. The cohort was defined as all Korean workers under radiation surveillance who were first exposed between January 1, 1984 and December 31, 2004, and who were alive on January 1, 1992. Follow-up was from date of first exposure surveillance or January 1, 1992, whichever was later, until the earlier of date of death or December 31, 2004. The KRIA provided the name, Residence Registration Number (RRN, a unique 13-digit number assigned to all Koreans in which the first six digits are the birth date, the seventh digit is gender), year of first exposure and yearly exposure doses, and the type of institution. The KRIA registry has electronic radiation exposure data on workers beginning in 1983. However, we excluded workers whose first recorded surveillance entry was in 1983 because they were likely to have been exposed before 1983 for which there was no electronic record.

In addition to comparisons to the general Korean population (with standardized mortality ratios [SMRs]), an unexposed comparison cohort was selected to reduce the potential for confounding, as in the healthy worker and survivor effects, because of differences between workers and general populations. This group consisted of Korean workers in the manufacture of motor vehicles, trailers and semitrailers who had taken the required annual specialized health examination (SHE) during 2000 to 2004 and who were exposed to noise but not to other occupational agents known to cause leukemia such as benzene, butadiene, formaldehyde, ethylene oxide, or solid cancers such as hexavalent chromium, cadmium asbestos, silica, etc. In Korea, workers exposed to hazards designated by Ministry of Labor (about 200 kinds) have a SHE annually or twice a year. All results including exposure information (the agents exposed to) of this SHE are electronically reported to Korea Occupational Safety and Health Agency (KOSHA) and accumulated in a database. In this study, we used the SHE data of workers manufacturing motor vehicles, trailers and semitrailers from the database of KOSHA. This control group was selected considering socioeconomic status affecting workers' health. In Korea, workers' health largely depends on the size of company.[6,7] Because radiation workers were employed in large companies like nuclear power utilities and in small companies like those affiliated with nuclear power plants and NDT firms, control groups were selected reflecting this proportion. Follow-up for this group was from the date of examination until the earlier of date of death or December 31, 2004.

For cancer morbidity, incidence rates during 2000 to 2005 were estimated using the National Health Insurance Claim Data (NHICD) database and requiring more than 3 days admission in a third degree (tertiary care) hospital. National health insurance claim records include the 13-digit RRN, admission date, and diagnosis of diseases. Diagnoses were classified according to the *Korea Classification of Diseases and Causes of Death*, 4th edition (KCD-4), using three-character codes. The KCD-4 is very similar to the International Classification of Diseases, 10th revision (ICD-10). Thus, Neoplasm in KCD-4 is the same as in ICD-10 (C00-D48); "total cancer" here means malignant neoplasms (C00-C96 of ICD-10), and "lung cancer" means malignant neoplasm of bronchus and lung (C34 of ICD-10). "Non-Hodgkins lymphoma" (NHL) means follicular (C82), diffuse (C83) and other and unspecified types (C85) of NHL in ICD-10, and "Leukemia" means lymphoid (C91), myeloid (C92), monocytic (C93), other leukemias of specified cell types (C94) and unspecified (C95). Thus, leukemia also includes chronic lymphocytic leukemia (CLL) although there were no cases of CLL mortality and morbidity among radiation exposed workers in this study.

Study subjects were matched to the NHICD database using the RRN. The completeness of the NHICD database is more than 99% because all Koreans have been covered by National Health Insurance since 1989 (since 1977 for large employers), including pharmacy. Thus, virtually all cancers are captured by NHICD, however, the validity of NHICD diagnoses is lower than for data from the National Cancer Registry (which, with less complete reporting but higher specificity, was unavailable for this study). The specific morbidity outcomes selected for study included cancers of the lung, colon, breast and thyroid, as well as leukemia and NHL, and were chosen based on numbers of cases available and prior interest in radiogenic cancers. In Korea, NHL is commonly perceived to be radiogenic by the medical community because of the well-known effects of radiation on bone marrow.

Deaths were identified by the Korean National Statistical Office (KNSO), a registry estimated to achieve greater than 95% registration of deaths; cause of death was available beginning in 1992. KNSO records provide the RRN, cause of death (KCD-4) and date of death. Study subjects were matched to the KNSO database using the RRN. Reference mortality rates for the Korean population were derived from KNSO data for 1992 to 2004. The causes of death selected for study included all cancer as well as lung cancer, leukemia and NHL, again based on numbers of cases available and prior knowledge concerning radiogenicity.

Exposure Assessment

Personal radiation monitoring is conducted for all employees entering radiological areas or handling radioactive materials. For personal dosimetry, beginning in 1976, radiation workers used film badges or a thermoluminescence detector device for recording doses. Film-badge monitoring was conducted for all employees potentially exposed to ionizing radiation in their work-areas or, in some cases, just for those employees known to be exposed. Using electronic records of annual whole body equivalent exposure doses (available since 1983 in the Central Registry for Radiation Workers Information) this study calculated the cumulative dose in milliSieverts for each worker during follow-up by summing across time the worker's average annual exposure dose in the prior monitoring periods. For categorical analyses, cumulative dose was classified in four levels: (1) no exposure (0 mSv), (2) 0.01 to 9.99 mSv, (3) 10.00 to 49.99 mSv, and (4) greater than 50 mSv.

Statistical Methods

A classification table for Poisson Regression analysis of mortality was calculated as described previously.[8] About 774,249 person-years of observation (in 10 day units of observation) were jointly classified in 10 age (<20, 20–24, 25–29, 30–34, . . . ,65+), two calendar (1992–1999, 2000–2004), six sector and 50 cumulative exposure (in mSv) levels. For some analyses, the classification was based on a 5-year lag (1 year for lymphohematopoietic or thyroid cancer). These choices for lagging were a compromise to accommodate both incidence and mortality, and the relatively short period of follow-up (mean = 10.2 years). For lagged analyses by sector, follow-up in the initial period corresponding to the lag (eg, first 5 years) was excluded if the sector classification (radiation cohort) or employment status (autoworker cohort) was unknown at that time (before first surveillance record or hire date, respectively). Although classified jointly, the effects of sector or cumulative dose were analyzed separately.

Log-linear relative rate models in Poisson regression were evaluated for the effects of sector, controlling for age, calendar time, and gender: rate = $\exp(\hat{a}_0 + \hat{a}_1X_1 + \hat{a}_2X_2 + \ldots)$, where, $\hat{a}_0$ (intercept), $\hat{a}$, $\hat{a}_1$, $\hat{a}_2, \ldots$ are parameters to be estimated. Linear relative rate models were used for cumulative dose effects of the form: rate = $[\exp(\hat{a}_0)] \times [1 + \hat{a}_1X_1]$, yielding excess relative risk (ERR) = $[\exp(\hat{a}_0)] \times \hat{a}_1X_1$.

Poisson regression models were fit using EPICURE software (Preston DL, Lubin JH, Pierce DA et al. 1993. *Epicure Users Guide*. Seattle, WA: Hirosoft International Corp.). Models with the largest decrease in deviance (ie, decrease in –2log [likelihood]) with addition of exposure terms were considered "best" fitting. In some models, external standardization on age and calendar time was accomplished using the calculated Korean mortality age-, calendar-, and gender-specific rates as a multiplier of person-years (offset) which yields models of SMRs. The intercept in these models is an estimate of the (log) SMR for workers without the specified exposures. This method permits internal comparisons on exposures externally adjusted for age,

TABLE 1
Demographic Characteristics of Radiation Workers and Comparison Group: Automobile Workers

	Radiation Workers													
	Medical Institutes		Nuclear Power		Education and Research		Industry		Others		Total		Automobile	
N	6735		27,322		14,641		30,147		834		79,679		51,195	
P-Yrs	54,152		230,233		86,923		255,163		6689		633,159		141,090	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Gender														
Men	3660	54.3	26,878	98.4	9512	65.0	28,514	94.6	715	85.7	69,279	86.9	43,535	85.0
Women	3075	45.7	444	1.6	5129	35.0	1633	5.4	119	14.3	10,400	13.1	7660	15.0
Yr first exposed*														
1984–89	1433	21.3	6972	25.5	938	6.4	5199	17.2	146	17.5	14,688	18.4	8650	16.9
1990–99	3225	47.9	13,792	50.5	6388	43.6	17,409	57.7	449	53.8	41,263	51.8	18,335	35.8
2000–04	2077	30.8	6558	24.0	7315	50.0	7539	25.0	239	28.7	23,728	29.8	24,210	47.3
Cumulative exposure† (mSv, unlagged)														
0.00	232	3.4	10,620	38.9	1622	11.1	522	1.7	63	7.6	13,059	16.4	—	—
0.01 to 9.99	5680	84.3	12,886	47.2	12,797	87.4	23,455	77.8	712	85.4	55,530	69.7		
10.00 to 49.99	762	11.3	2889	10.6	216	1.5	5311	17.6	58	7.0	9236	11.6		
50.00≥	61	0.9	927	3.4	6	0.0	859	2.8	1	0.1	1854	2.3		
Cumulative exposure† (mSv, 5 yr lag)														
0.00	254	5.0	8583	39.4	1320	14.7	719	3.0	19,396	97.3	30,272	38.0	—	—
0.01 to 9.99	4142	82.2	9597	44.1	7512	83.8	18,165	75.8	498	2.5	39,914	50.1		
10.00 to 49.99	608	12.1	2844	13.1	122	1.4	4155	17.3	42	0.2	7771	9.8		
50.00≥	35	0.7	745	3.4	8	0.1	932	3.9	2	0.0	1722	2.2		
Age at first exposure‡														
Mean ± SD	28.7 ± 6.1		30.4 ± 8.7		28.2 ± 6.4		27.2 ± 6.5		33.4 ± 7.4		28.7 ± 7.4		28.7 ± 8.9	
Median	27.2		27.7		26.4		26.1		32.0		26.8		25.8	
Duration under radiation surveillance														
Mean ± SD	4.1 ± 4.7		4.0 ± 5.5		3.1 ± 3.7		3.5 ± 4.3		3.6 ± 3.9		3.6 ± 4.7		—	
Median	2.00		1.01		2.00		2.00		2.0		2.0			
Cumulative exposure (mSv, unlagged)														
Mean ± SD	4.7 ± 9.7		6.6 ± 20.2		1.5 ± 2.9		8.1 ± 15.4		3.2 ± 5.5		6.1 ± 15.7			
Median	1.4		0.2		0.7		2.9		1.2		1.2		—	

*For reference population (autoworkers): year of hire.
†Cumulative exposure at the end of follow-up; lagged observation time with unknown sector identity (prior to observation) classified as "others."
‡For reference population (autoworkers): age at hire.

etc; however, bias can arise from age-exposure interactions. In other models, direct or internal adjustment was achieved by "stratification," a procedure in EPICURE in which categorical classifying variables such as age, year, and gender (and all interactions) are included in the model but parameter estimates not presented. These directly standardized rate ratios (SRRs) allowed unbiased comparisons across exposure and other descriptive variables. For cancer admissions only directly (internally) SRRs were calculated because appropriate reference rates were not available.

Results

Demographics of Mortality Cohort

Of 82,926 radiation workers identified, 3247 (3.9%) were excluded because they had exposure data from 1983 and were potentially exposed before 1983. About 79,679 radiation workers (69,279 men, 10,400 women) and 51,195 automobile workers (43,535 men, 7660 women) were followed for a total 633,159 and 141,090 person years, respectively (Table 1). Radiation workers employed in manufacturing industry (n = 30,147) contributed the most observation time (255,163 P-yrs) followed by nuclear power plants (n = 27,322; 230,233 P-yrs), education and research institutes (n = 14,641; 86,923 P-yrs), medical institutes (n = 6735; 54,152 P-yrs), and others (n = 834; 6689 P-yrs) (Table 1). The mean age at first exposure was 28.7 years and about two-thirds were first exposed between the ages of 20 and 30. The mean cumulative exposure was 6.06 mSv, which is quite low compared with existing standards (the maximum allowed over mean duration of follow-up was: 633159/79,679 × 20 mSv/yr = 159 mSv).

Mortality by Type of Institution

The overall mortality of radiation workers (935 deaths, SMR = 0.58, 95% CI = 0.54–0.62) and automobile workers (206 deaths, SMR = 0.66, 95% CI = 0.57–0.75) was low compared with the Korean general population (Table 2). Total cancer mortality of radiation workers (256 deaths, SMR = 0.73, 95% CI = 0.64–0.82) and automobile workers (53 deaths, SMR = 0.70, 95% CI = 0.53–0.90) was also lower than that of Korean population, but mortality from non-Hodgkin lymphoma was greater than expected (10 deaths, SMR = 1.26, 95% CI = 0.63–2.22) in radiation workers, concentrated in nuclear utility workers (seven deaths, SMR = 1.98, 95% CI = 0.85–3.82). Overall mortality and cancer mortality were less than expected for radiation workers in all five sectors. Mortality from lung cancer (38 deaths, SMR = 0.77, 95% CI = 0.55–1.05) and leukemia (nine deaths, SMR = 0.59, 95% CI = 0.28–1.06) in radiation workers were also less than expected but nonsignificantly (Table 2), but lung cancer mortality in automobile workers was (nonsignificantly) greater than expected (11 deaths, SMR = 1.12, 95% CI = 0.58–1.92). Compared with automobile workers, radiation workers overall displayed decreased all-cause mortality except for workers at nuclear power plants who had higher (but statistically not significant) all-cause and all-cancer mortality (Table 2).

Mortality by Cumulative Exposure: SMR

Compared with the Korean population, overall mortality in four strata of (lagged) cumulative dose was significantly less than expected (in increasing dose levels: SMR = 0.61, 0.54, 0.68, and 0.46) (Table 3). All-cancer mortality was also less than expected (SMR = 0.75, 0.70, 0.80, and 0.75, respectively). Lung cancer and leukemia exhibited similar patterns and non-Hodgkin lymphoma showed a not significant doubling of mortality at both the unexposed (five cases) and 10.00 to 49.99 mSv (two cases) dose levels (Table 3) compared with the Korean general population.

Based on internal comparisons adjusting for age, calendar time, and gender, regression models of the dependence on lagged dose compared with workers with 0 mSv exposure, suggested elevated mortality at the 10.00 to 49.99 mSv dose level for all-causes (SRR = 1.16, 95% CI = 0.92–1.45), and for all-cancer (SRR = 1.11, 95% CI = 0.69–1.72) (Table 4). At the highest dose level, there was a three-fold excess of leukemia deaths but based on just one

TABLE 2
Standardized Mortality Ratio by the Type of Institution

	Radiation Workers						
P-yrs	Medical Institute 54,152	Nuclear Power Plants 230,233	Education & Research 86,923	Industry 255,163	Others 6689	Total 633,159	Automobile Workers 141,090
Total death							
Death	25	536	58	310	6	935	206
SMR	0.23	0.72	0.31	0.56	0.27	0.58	0.66
95% CI	0.15–0.33	0.66–0.78	0.24–0.40	0.50–0.63	0.11–0.55	0.54–0.62	0.57–0.75
Total cancer							
Death	9	151	24	72	0	256	53
SMR	0.36	0.84	0.58	0.71	0.0	0.73	0.70
95% CI	0.18–0.66	0.72–0.98	0.38–0.85	0.56–0.89	0.0–0.57	0.64–0.82	0.53–0.90
Lung cancer							
Death	0	26	5	7	0	38	11
SMR	0.0	0.93	0.90	0.59	0.0	0.77	1.12
95% CI	0.0–1.02	0.61–1.33	0.32–1.93	0.26–1.15	0.0–4.08	0.55–1.05	0.58–1.92
Leukemia							
Death	1	4	0	4	0	9	0
SMR	0.84	0.65	0.0	0.69	0.0	0.59	0.0
95% CI	0.05–3.69	0.20–1.50	0.0–1.57	0.21–1.59	0.0–16.8	0.28–1.06	0.0–0.95
NHL							
Death	0	7	1	2	0	10	1
SMR	0.0	1.98	1.06	0.73	0.0	1.26	0.56
95% CI	0.0–5.31	0.85–3.82	0.06–4.66	0.12–2.24	0.0–28.6	0.63–2.22	0.03–2.47

Unlagged classification; reference: Korean general population.
NHL indicates non-Hodgkin's lymphoma.

TABLE 3
Standardized Mortality Ratio in Radiation Workers by Cumulative Exposure

mSv P-yr	0 321,381	0.01–9.99 248,149	10–49.99 52,273	≥50 11,257
Total death				
Death	447	383	92	13
SMR	0.61	0.54	0.68	0.46
95% CI	0.55–0.67	0.49–0.59	0.55–0.83	0.25–0.76
Total cancer				
Death	115	114	23	4
SMR	0.75	0.70	0.80	0.75
95% CI	0.62–0.90	0.58–0.83	0.52–1.18	0.23–1.73
Lung cancer				
Death	14	21	3	0
SMR	0.65	0.90	0.78	0.0
95% CI	0.37–1.06	0.57–1.35	0.19–2.02	0.0–5.02
Leukemia				
Death	2	5	1	1
SMR	0.56	0.54	0.51	2.35
95% CI	0.09–1.72	0.19–1.15	0.03–2.26	0.13–10.3
NHL				
Death	5	3	2	0
SMR	2.50	0.63	2.07	0.0
95% CI	0.90–5.37	0.16–1.64	0.34–6.39	0.0–14.3

Lagged; reference: Korean general population.
NHL, non-Hodgkin's lymphoma.

TABLE 4
Mortality Standardized Rate Ratios Comparing SRRs by Categorical and Continuous Cumulative Exposure

mSv P-yr	0.01–9.99 394,240	10–49.99 82,286	≥50 18,409	Continuous ERR*	 P*
Total death					
Death	383	92	13		
SRR	0.92	1.16	0.84	1.7	0.28
95% CI	0.80–1.06	0.92–1.45	0.46–1.40	−4–7	
Total cancer					
Death	114	23	4		
SRR	0.96	1.11	1.06	7.2	0.11
95% CI	0.74–1.25	0.69–1.72	0.32–2.54	−5–21	
Lung cancer					
Death	21	3	0		
SRR	1.42	1.15	0.0	1.2	0.47
95% CI	0.72–2.88	0.26–3.56	0.0–4.31†	−5–52	
Leukemia					
Death	5	1	1		
SRR	0.95	0.77	3.46	16.8	0.28
95% CI	0.20–6.70	0.04–8.15	0.16–37.1	−34–149	
NHL					
Death	3	2	0		
SRR	0.27	0.821	0.0	17.6	0.27
95% CI	0.06–1.17	0.11–4.05	0.0–5.78	−32–135	

Lagged; reference: radiation workers with cumulative exposure = 0.0 mSv.
*ERR evaluated as excess risk per Sv (same as ERR percent per 10 mSv); 90% CI = displayed for ERR but lower bound not reliably estimated; one-tailed P-value.
†95% CI = calculated using estimate of expected Poisson variate based on expected = death/SRR in 0.01–9.99 column and multiplied by ratio of person-yrs:18409/394240.
NHL, non-Hodgkin's lymphoma.

case. Analyses of trends (using cumulative exposure as a term in linear relative rate model) found all to be positive but small and not statistically significant (Table 4). For all lymphohematopoietic cancer mortality, ERR was 15 per Sv (15% per 10 mSv; 90% CI = −21 to 81) (data not shown).

Cancer Admission by Type of Institution and Cumulative Dose

Overall cancer admission rates in radiation workers, compared with automobile workers, exhibited deficits except possibly for power plant workers (SRR = 1.13, 95% CI = 0.94–1.36), and all radiation groups had lung cancer incidence rates lower than autoworkers' (Table 5). Colon cancer and leukemia rates were nonsignificantly higher in all radiation groups versus autoworkers, as was female breast cancer in four out of five radiation groups. There were no cases of chronic lymphocytic leukemia. Thyroid cancer rates were generally higher than for other outcomes across the types of institutions (SRR = 1.35–2.59) and were statistically significant in the case of nuclear plant workers (SRR = 2.59, 95% CI = 1.33–5.13). Among women, there was a statistically significant excess in all three categories of institution where there were substantial numbers of women workers: medical institutes (SRR = 2.90, 95% CI = 1.05–7.94), education and research institute (SRR = 3.91, 95% CI = 1.36–11.0 and manufacturing industry SRR = 5.07, 95% CI = 1.53–15.6) (Table 5). Other major cancer sites in radiation workers included stomach (51 cases) and liver/gallbladder related cases (74 cases), which are among the leading sites of cancer in Korea, as well as smaller numbers of cases of pancreas (13), kidney (9), oral/lip (4), and other/unspecified (8) cancer.

Comparing the two lowest strata of cumulative radiation dose (0.01–9.99 versus 10.0–49.9), SRRs increased with increasing dose except for cancer of the breast and lung

TABLE 5
Cancer Morbidity (SRR) as Hospital Admissions (Adms) by the Type of Organization

P-yr*	Medical Institute 35,215	Power Plant 143,953	Education and Research 70,551	Industry 161,267	Others 4312	Automobile Workers (Reference) 190,816
Total cancer						
Adms	50	283	60	165	6	254
SRR	0.90	1.13	0.73	0.96	0.70	1.0
95% CI	0.65–1.22	0.94–1.36	0.54–0.97	0.78–1.18	0.28–1.45	—
Lung cancer						
Adms	2	28	3	13	0†	27
SRR	0.46	0.68	0.34	0.63	0.0	1.0
95% CI	0.07–1.55	0.39–1.19	0.08–0.97	0.31–1.21	0.00–5.45	—
Colon cancer						
Adms	2	15	3	9	1	9
SRR	1.33	1.51	1.23	1.53	3.37	1.0
95% CI	0.20–5.39	0.64–3.81	0.27–4.28	0.58–4.15	0.18–18.57	—
Breast cancer in women						
Adms	7	1	7	2	1	14
SRR	1.21	1.22	1.28	0.75	3.94	1.0
95% CI	0.41–3.30	0.07–6.28	0.40–3.78	0.11–3.15	0.21–21.21	—
Thyroid cancer						
Adms	13	24	10	14	0	21
SRR	2.05	2.59	1.51	1.35	0.0	1.0
95% CI	0.95–4.27	1.33–5.13	0.65–3.30	0.64–2.82	0.0–10.8	—
Thyroid cancer in women						
Adms	9	0	9	6	0	10
SRR	2.90	0.0	3.91	5.07	0.0	1.0
95% CI	1.05–7.94	0.0–2.84	1.36–11.00	1.53–15.60	0.0–94.8	—
Leukemia						
Adms	2	5	2	5	0	5
SRR	1.95	1.03	1.14	1.14	0.0	1.0
95% CI	0.26–9.65	0.28–3.86	0.16–5.44	0.31–4.17	0.0–25.6	—
NHL						
Adms	0	6	0	5	0	5
SRR	0.0	1.22	0.0	1.04	0.0	1.0
95% CI	0.0–2.86	0.37–4.25	0.0–1.43	0.29–3.73	0.0–23.4	—

Unlagged; reference: automobile workers.
*Person-yr free of prior cancer admission (since 1989).
†95% CI = calculated using estimate of expected Poisson variate based on expected = death/SRR in industry column and multiplied by ratio of person-yrs: 4312/161267.
NHL, non-Hodgkin's lymphoma.

(Table 6). For thyroid cancer, the upward trend continued across all three levels and was marginally statistically significant ($P = 0.086$, one-tailed test); the ERR was 14.7 per Sv (90% CI = −7 to 50). Analyses using unexposed workers in the radiation cohort as the reference produced unstable baseline rate estimates because there was relatively little observation time available for this group, arising largely as the result of lagging. Including the autoworker cohort in the unexposed stratum substantially increased the numbers of cases there: from 10 to 31 for thyroid cancer, and from 1 to 15 for breast cancer (Table 6). A somewhat stronger increasing trend was then observed for thyroid cancer (ERR = 20.4/Sv, 90% CI = −8 to 60; one-tailed $P = 0.049$), and the deficit for breast cancer was diminished. For all lymphopoietic cancer, the trend on lagged dose was positive corresponding to an ERR of 32.0 per Sv dose (90% CI = −32 to 107), and this trend was marginally significant (one-tailed $P = 0.08$) (data not shown).

Discussion

Strength and Limitations

Quite complete mortality ascertainment was made possible by the low rate of migration of Koreans to other countries. Foreign workers, usually with specialized skills, do not have RRNs and were excluded from this study. However, in this study, cancer morbidity may have been overestimated because cancer cases came from NHICD rather than from the National Cancer Registry (NCR). The NCR has greater than 95% ascertainment of cancer morbidity but also very high validity. The NHICD has high ascertainment (99%) but much lower validity (77%) (Park BJ. *Report on accuracy of disease coding in NHICD*. Seoul National University, School of Medicine, Seoul,

TABLE 6
Cancer Morbidity (SRR) as Hospital Admissions by Categorical and Continuous Cumulative Exposure

mSv	0.01–9.99	10–49.99	≥50	Continuous	
P-yr	192,384	34,515	7048	ERR*	P*
Total cancer					
Admissions	294	49	7		
SRR	1.00	1.13	0.85	2.6	0.23
95% CI	0.84–1.20	0.82–1.54	0.36–1.68	−4–10	
Lung cancer					
Admissions	30	4	0†		
SRR	1.87	1.61	0.0	−2.5	0.42
95% CI	0.98–3.81	0.45–4.64	0.0–5.10	−6–38	
Colon cancer					
Admissions	12	4	0		
SRR	0.64	1.41	0.0	4.7	0.42
95% CI	0.29–1.40	0.40–3.99	0.0–4.36	−3–56	
Breast cancer in women					
Admissions	9	0	0		
SRR	0.66	0.0	0.0	−12.2	0.27
95% CI	0.25–1.77	0.0–1.22	0.0–6.00	−12–79	
(Ref: auto wkrs)					
SRR‡	0.84	0.0	0.0	−12.2	0.29
95% CI	0.35–1.88	0.0–1.56	0.0–7.64	−13–89	
Thyroid cancer					
Admissions	42	7	2		
SRR	1.22	1.39	2.72	14.7	0.09
95% CI	0.63–2.60	0.50–3.66	0.41–10.5	−7–50	
(Ref: auto wkrs)					
SRR‡	1.60	1.74	3.24	20.4	0.049
95% CI	0.98–2.65	0.69–3.85	0.52–11.1	−8–60	
Leukemia					
Admissions	7	3	0		
SRR	0.62	1.39	0.0	15.8	0.27
95% CI	0.18–2.42	0.27–6.54	0.0–7.25	−31–108	
NHL					
Admissions	4	4	0		
SRR	0.48	2.17	0.0	49.5	0.10
95% CI	0.10–2.44	0.47–11.16	0.0–9.82	−35–235	

Lagged; reference: radiation workers with cumulative exposure = 0.0 mSv.
*ERR evaluated as excess risk per Sv (same as ERR percent per 10 mSv); 90% CI = displayed for ERR but lower bound not reliably estimated; one-tailed P-value.
†95% CI = calculated using estimate of expected Poisson variate based on expected = death/SRR in 0.01–9.99 column and multiplied by ratio of person-yrs: 7048/192384.
‡Reference: radiation workers with cumulative exposure = 0.0 mSv together with auto workers.
NHL, non-Hodgkin's lymphoma.

2002) and thus a higher false-positive rate. For this reason, we used cancer cases diagnosed only by tertiary care hospitals (university hospitals) and with more than 3 days admission. This would increase validity of diagnosis. Furthermore, the validity of NHICD diagnoses has improved since 2000, owing to considerable effort by the Korean Health Insurance Review and Assessment Service to improve diagnoses, such that the validity in tertiary hospitals is now believed to be close to that of the NCR registry. Differential detection bias of cancer at admission is not expected to be large when comparing radiation and automobile workers who all have universal health care.

The small numbers of deaths reflected the young age of the cohort and small number of years of follow-up. Excluding workers with 1983 exposure because radiation exposure records before 1983 were not available should not bias exposure associations but did further reduce statistical power particularly among long duration radiation workers, and may have obscured some excess cancer mortality. Furthermore, workers with important radiation exposure that ended before 1983 could have been included in this study misclassified as unexposed or more recently exposed only.

In occupational cohort mortality studies, the healthy worker effect

(HWE) arising largely from employment selection factors is widely acknowledged.[9–17] Although previous study[10–13] has shown that cancer has a smaller healthy worker effect than some other diseases such as respiratory or cardiovascular disease, the healthy worker effect for cancer is not absent.[10,11,14,17] This cohort with short follow-up periods and a high proportion of active workers exhibits a large healthy worker effect for cancer. About 88% of the workers in this cohort were still actively employed at the start of their follow-up that lasted at most 13 years, and thus were highly selected for good health. The strong HWE observed in all-cause mortality (SMR = 0.58, 95% CI = 0.54–0.62) and in all-cancer mortality (SMR = 0.73, 95% CI = 0.64–0.82) for this radiation cohort supports this conjecture and may well have caused excess mortality related to radiation exposure to be underestimated, based on external comparisons.

The workers of large-scale enterprises, medical institutes, and education and research institutes have relatively high social class status and good health. So, in this cohort, HWE is greater than in most cohorts. To minimize the HWE and other confounding factors, this study used control groups selected among manufacturers of motor vehicles, trailers and semitrailers. Because workers' health depends on company size, reflect socioeconomic status, control groups were selected considering company size. Automobile workers were employed in both large- and small-scale (affiliated company manufacturing automobile accessory) enterprises as was this radiation cohort (large-scale nuclear power plant and mainly small-scale industry like NDT firms). Also, the control groups were nominally exposed just to noise, so that occupational exposure effects on cancer mortality are not expected. Nevertheless, some differential HWE may have been present comparing radiation and autoworkers, as suggested by SMR (Table 2) mortality findings where radiation workers often exhibited lower mortality than autoworkers.

The proportion of total observation time (person years) allocated to workers with greater than 10 mSv cumulative exposure (lagged) was just 10.1%, and the small number of cancer deaths with more than 10 mSv (27 cases) limited the statistical power of this study.

Concordance with Previous Studies

Ionizing radiation has been the subject of intense epidemiological investigation. Studies have demonstrated that exposure to moderate-to-high levels can cause most forms of cancer. Among radiation-induced cancers, leukemia and cancers of the breast, lung, and thyroid have been shown to be particularly sensitive to induction by radiation in previous studies. Predominant among these studies is the Life Span Study of the cohort of survivors of the atomic bombings of Japan in 1945.[18] However, in reference to occupationally exposed populations, a significant excess of external radiation-induced leukemia and solid cancers have been found in very few studies except where separate analyses have been performed of subcohorts with high dose radiation exposures in the early years of their employment. Also, the study subjects were limited to radiologists and radiologic technologists,[19–30] workers exposed to mainly cosmic rays such as aircrew and pilot,[31–34] and workers in nuclear power plants and in nuclear material processing for nuclear weapon manufacturing and experimentation, etc.[2,35–44] Among these groups, radiologists and radiologic technologists employed before 1940[24–26,28,30] and workers in nuclear weapons programs[45,46] received relatively high doses of radiation. The studies based on these workers frequently found a significant excess of radiogenic cancers.

Among radiogenic cancers, leukemia, thyroid, lung, and breast cancer are well known. The risks of these radiation-induced cancers have been dramatically reduced as a result of modern radiation protection standards such as the ICRP recommendations. This situation is the same in Korea. The Radiation Heath Research Institute of the Korea Hydro & Nuclear Power Co Ltd. has performed research on the probability of causation for (PC) to ascertain the likelihood that a particular cancer may be attributed to a particular prior exposure to radiation in Korean workers. A computing program is being developed to calculate PC based on the National Institute for Occupational Safety and Health-Interactive Radio Epidemiological Program (NIOSH-IREP) model and Korean baseline cancer incidence rates NIOSH, Office of Compensation and Support, 2002: NIOSH-IREP technical documentation: Final report; Korea Hydro & Nuclear Power Co Ltd., Radiation Heath Research Institute, Seoul. 2004: Report on model development for causation probability of radiation-induced cancer in Korea.). The PC for four cancers (leukemia, thyroid, lung, and breast) estimated by this computing program were comparable to those calculated by the NIOSH-IREP model. The present study was primarily intended to estimate mortality from these four cancers. However, there was just one breast cancer death among 10,400 woman workers (13.1% of radiation workers) and no thyroid cancer deaths among these radiation workers. Therefore, this study estimated the mortality only of all-cancer, lung cancer and lymphohematopoietic cancer including leukemia and non-Hodgkin lymphoma.

Health effect studies of radiation workers have been rare in Korea. Until now just four studies[1,42,47] (Jeong MS, Jin YW, Lim YK, Kim SG, Lee BY, Jang YK, Sung SH, Lee YJ, Park IK, Kim CS. 2006. Proceedings of Spring Conference for Korea Association for Radiation Protection: *Epidemiologic study on workers of nuclear power plant in Korea. Suanbo-city, Korea*) have been conducted including a 15-country study of nuclear workers in which 7892 Korean workers individually monitored for external radiation were followed for 36,227 person years. A total of 58 deaths and 21 cancer deaths excluding leukemia were observed. The authors were not able to detect excess cancer risk including leukemia in the Korean data. The other Korean radiation study involved workers at four nuclear utilities and followed workers employed for up to 10 years between 1993 and 2002. A total of 58 incident cases of cancer were observed. The standardized incidence ratio (SIR) associated with all-cancer was 0.94 (95% CI = 0.72 to 1.22) compared with the Korean general population. Also, using an internal referent group, risk was not increased with cumulative exposure ($P = 0.25$). Our present investigation included the workers in nuclear power plants from the two study populations mentioned above, but also included all workers employed in enterprises affiliated with the nuclear power industry and those in medical institutes, research and education institutes, and NDT firms, etc. Few other studies have covered all radiation workers employed in many sectors in their country.

In this study, the SMR associated with all-cause mortality was just 0.58 (95% CI = 0.54–0.62) in radiation workers and 0.66 (95% CI = 0.57–0.75) in automobile workers. This result was very similar to those from the French National Electricity workers' study[44] and a nuclear power plant study in United States,[40] which observed a very substantial healthy worker effect with short follow-up periods, averaging 11.7 and 18 years, respectively. A Canadian mortality study of radiation workers was very similar to this study in design, classification of occupation categories and proportion of workers with low cumulative exposure doses (9.6% workers with greater than 10 mSv exposure versus 14.7% in present study).[48] This Canadian study also showed a similar HWE for all causes of death (SMR = 0.59, 90% CI = 0.57–0.60) and all cancer deaths (SMR = 0.68, 90% CI = 0.64–0.71) in men. A cohort mortality study of UK radiation workers also showed a smaller HWE for all cause mortality (SMR = 0.82).[49]

In the present study, there was no significant excess mortality of all cancer or of individual cancers (lung, leukemia, non-Hodgkin lymphoma and all lymphohematopoietic cancer) although a marginally significant doubling of non-Hodgkin lymphoma mortality was observed among nuclear utility workers. Associations between radiation and non-Hodgkin lymphoma have been reported in a few studies, but results were inconsistent.[50–52]

According to the previous study results, exposure to moderate to high-dose ionizing radiation is an established risk factor for lung cancer, but the relationship between lung cancer and chronic low dose radiation remains uncertain. For example, in 2004 Silver et al[53] found significantly elevated SMRs for death from lung cancer using an expanded cohort of all workers at Portsmouth Naval Shipyard. However, this positive association was no longer present after adjusting for socioeconomic status (smoking surrogate) and welding fume and asbestos exposures.[54] Another study was reported in 2006 using a U.S. cohort of 3864 workers at the Oak Ridge, Tennessee Y-12 nuclear materials fabrication plant. In this study, cumulative external radiation dose under a 5-year lag assumption was positively associated with lung cancer mortality (0.54% increase in lung cancer mortality per 10 mSv, SE = 0.16, likelihood ratio test = 5.84), but cumulative internal radiation dose exhibited a highly imprecise negative association with lung cancer mortality.[2] Recently, the 15-country collaborative study including Korea on cancer risk among radiation workers in the nuclear industry showed a significant excess of lung cancer mortality (ERR/Sv = 1.86, 90% CI = 0.49–3.63) with low-dose protracted exposures to ionizing radiation.[1]

In the present study, lung cancer mortality and hospital admission in the radiation workers was observed to be lower than that of automobile workers. Autoworkers, however, may be generally exposed to lung carcinogens. In a large study of U.S. autoworkers, elevated lung cancer was observed[55] in metalworking (SMR = 1.21, 95% CI = 1.12–1.30) and assembly operations (SMR = 1.11, 95% CI = 1.05–1.17), possibly related to ambient exposures arising from painting processes in the case of assembly workers.[56] However, workers with specific exposures to painting, foundry, forging, and heat treat processes were excluded from the comparison group in this study. Thus the association between lung cancer incidence and low dose radiation remains unclear because of possible confounding variables like smoking and other workplace carcinogens and the limited statistical power of the study.

Recent studies have shown excess leukemia[2] and lung cancer[46] mortality at 10 mSv cumulative exposure but other, larger, studies have not found leukemia elevation at low exposure levels. When Schubauer-Berigan et al[57] conducted a nested case-control study among workers exposed to ionizing radiation at five U.S. nuclear facilities, the relative risk of leukemia for workers receiving more than 10 mSv was higher compared with those receiving lower or no dose. However, the increase in risk was attenuated in the highest exposure group. Also a recent 15-country collaborative study showed that the risk estimate of leukemia excluding CLL was not significantly different from risk in the unexposed.[1] The apparent negative association for breast cancer morbidity and radiation exposure seems to reflect residual uncontrolled confounding, such as by birth parity.

Thyroid cancer morbidity, as manifest in admissions diagnoses, shows significant associations with ionizing radiation exposure in women and nuclear power plant operations generally. The significant excesses in thyroid cancer morbidity among women across institutions suggests that the excess in nuclear power plants is not a chance finding or the result of detection bias arising from aggressive ultrasonography screening or health examination for goiter (common in Korea). Given the prior plausibility of this association,[58–63] and the known high sensitivity of thyroid cancer morbidity to external radiation this finding deserves considerable weight. The ERR for thyroid cancer incidence was about 20 per Sv, which is lower than the estimate from a large pooled analysis of thyroid cancer incidence from seven studies: ERR = 77 per Gy.[61] The Canadian cancer morbidity study of radiation workers with 20 years follow-up found highly significant SIR for thyroid cancer SIR = 1.32, 90% CI = 0.97–1.75 in men; SIR = 1.42, 90% CI = 1.19–1.69 in women), but excess relative risk per unit dose could not be estimated from the available dose information. In the Canadian study, the high SIR was mainly because of medical workers with the low doses compared with those for industrial and nuclear power workers, who do not show a significantly high SIR. However, the present Korean study showed significant excesses in thyroid cancer morbidity among women across institutions including medical. The Canadian study attributed the high thyroid cancer SIR for medical workers to external whole body doses, internal doses from RIs, and risk factors not related to radiation. Internal exposure to radioactive isotopes is another possible explanation for the elevated SIR for thyroid cancer in the present study, especially exposure to compounds containing thyroid-seeking iodine, used in medical procedures in hospitals.[64] The exposure could occur through inhalation of volatile compounds of ^{131}I exhaled by patients who have received therapeutic doses containing this isotope. However, the Canadian and Korean studies did not have radioiodine exposure information available. Further study is needed to elucidate possible risk factors other than external radiation.[64]

Conclusion

This study with short follow-up periods displayed a strong HWE. The all-cause mortality was around half and all cancer mortality was significantly low comparing to Korean general population. Several radiogenic cancers show limited evidence of elevated incidence or mortality but causal interpretation is constrained by limited statistical power due to small numbers of cases. Thyroid cancer morbidity was most clearly elevated, particularly among women in medical/research institutions and among nuclear power plant employees. ERRs as high as 300 per Sv (300% or 3.0 per 10 mSv) seem to be ruled out for the cancers studied in this population with regulated exposure to ionizing radiation but ERRs as high as 100 per Sv are not excluded. More detailed investigation of confounding and future follow-up of this cohort will better define health risks in radiation workers.

Acknowledgment

The authors acknowledge helpful critical comments from Drs. Jay Lubin, Mary Schubauer-Berigan and Megu Ohtaki, and from Randall Smith, as well as from anonymous journal reviewers.

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the U.S. National Institute for Occupational Safety and Health.

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