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CANCER AND OTHER CAUSES OF MORTALITY AMONG RADIOLOGIC TECHNOLOGISTS IN THE UNITED STATES

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Data are limited on the role of chronic exposure to low-dose ionizing radiation in the etiology of cancer. In a nationwide cohort of 146,022 U.S. radiologic technologists (73% female), we evaluated mortality risks in relation to work characteristics. Standardized mortality ratios (SMRs) were computed to compare mortality in the total cohort *vs.* the general population of the United States. Mortality risks were low for all causes (SMR = 0.76) and for all cancers (SMR = 0.82) among the radiologic technologists. We also calculated relative risks (RR) for the 90,305 technologists who responded to a baseline mailed questionnaire, using Poisson regression models, adjusted for known risk factors. Risks were higher for all cancers (RR = 1.28, 95% confidence interval [CI] = 0.93–1.69) and breast cancer (RR = 2.92, 95% CI = 1.22–7.00) among radiologic technologists first employed prior to 1940 compared to those first employed in 1960 or later, and risks declined with more recent calendar year of first employment (*p*-trend = 0.04 and 0.002, respectively), irrespective of employment duration. Risk for the combined category of acute lymphocytic, acute myeloid and chronic myeloid leukemias was increased among those first employed prior to 1950 (RR = 1.64, 95% CI = 0.42–6.31) compared to those first employed in 1950 or later. Risks rose for breast cancer (*p*-trend = 0.018) and for acute lymphocytic, acute myeloid and chronic myeloid leukemias (*p*-trend = 0.05) with increasing duration of employment as a radiologic technologist prior to 1950. The elevated mortality risks for breast cancer and for the combined group of acute lymphocytic, acute myeloid and chronic myeloid leukemias are consistent with a radiation etiology given greater occupational exposures to ionizing radiation prior to 1950 than in more recent times.
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Medical radiation workers were among the earliest occupational groups exposed to ionizing radiation. Almost half of all workers in the United States (U.S.) exposed to measurable doses of ionizing radiation exposure have been employed in medical fields.[1] While the majority of radiation-exposed U.S. workers, other than those employed in medical or related fields, have been male, about 75% of radiation-exposed U.S. medical workers have been female.

Previous studies on chronic low-dose radiation exposure and cancer in medical workers yielded inconsistent results. U.S. and other radiologists first employed prior to 1940[2–7] experienced elevated risks of leukemia, skin cancer and other malignancies, but cancer risks were not generally increased among radiologists first employed after 1940 (with the possible exception of multiple myeloma among U.S. radiologists).[4,5] Some,[7,8] but not all,[9,10] cohorts of radiologic technologists experienced an elevated leukemia risk. None of the earlier studies reported risks in relation to individual lifetime work histories, and only a few[7,10] included female technologists.

We followed a large, predominantly female cohort of 146,022 U.S. radiologic technologists.[11–13] A subset of 90,305 completed a baseline questionnaire, providing information on job history, work practices and other factors.[11] Using data from the entire cohort and the subset of technologists who completed the questionnaire, we examined total cancer mortality, as well as mortality from specific radiogenic cancers, including leukemia, lung cancer and breast cancer, the latter of which was also the subject of a recent brief communication.[14] Compared to our earlier articles,[12,13] the current report extends follow-up by 7 years, evaluates risks according to individual work history characteristics (*e.g.,* year first worked, number of years worked overall and within specific calendar-year periods, specific procedures performed and protective measures used) and assesses potential confounding.

MATERIAL AND METHODS

Cohort design and follow-up

Details of the study population are provided elsewhere.[12] In brief, the cohort included 146,022 radiologic technologists, who were certified by the American Registry of Radiologic Technologists (ARRT) for 2 years or longer during 1926–1982 and resided in the U.S.

Active members of ARRT were followed through annual certification renewals, while inactive registrants were traced using state (including motor vehicle bureaus and state mortality tapes), national (including U.S. Post Office address correction requests, the Social Security and Health Care Financing Administrations, the National Death Index and the Internal Revenue Service through an interagency agreement with the National Institute of Occupational Safety and Health) and commercial databases (telephone and other directories and credit reports).

At the end of follow-up on December 31, 1997, vital status was available for 99.3% of the technologists; a total of 12,624 deaths

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had occurred. We obtained death certificates and National Death Index reports for decedents, and underlying causes of death were coded according to the International Classification of Diseases, Eighth or Ninth Revisions depending on which coding system was used at the time.[15] Cause of death information was available for 94% of the decedents.

During 1983–89, a detailed self-administered questionnaire was sent to all subjects located alive and for whom a current address was available (n = 132,519, or 91%). Included were questions on work history and practices, selected medical conditions and treatments, smoking history, alcohol consumption and other known or suspected cancer risk factors.[11] There were 90,305 respondents to the questionnaire (68% response rate), including 69,525 women.

Occupational and exposure information

Few prior investigations focusing on medical radiation workers have described dose data.[7,16] Average yearly exposures of U.S. medical radiation workers employed prior to 1950 may have been 30 times higher than exposures during the 1980s.[1,17–20] The decline in estimated radiation exposure levels over time likely resulted from changes in the recommended exposure limit from 70 rem/year before 1934 to 30 rem/year in 1934, 15 rem/year in 1949 and 5 rem/year in 1958.[19–21] Since 1958, the recommended limits have remained unchanged in the U.S. Thus, we assumed that technologists who first worked before 1950 and who worked for many years prior to 1950 were exposed to substantially higher doses of radiation than those who first began working in later decades. We further assumed that a summary measure of the total cumulative years that a technologist worked, without regard to the year first worked or the calendar years of employment, might not be a good surrogate for cumulative exposure. Since comprehensive lifetime individual radiation dose estimates were not available, we used the questionnaire-derived, self-reported information about job history and work practices. We assessed risks associated with the year first worked and the number of years worked as a radiologic technologist in different calendar year periods as surrogate measures of exposure. This strategy enabled us to incorporate the above information about temporal changes in recommended occupational radiation exposure levels and work practices over time.

In our previous mortality analysis,[12] we assessed year first certified and the number of years certified as a radiologic technologist as the key surrogate measures for radiation exposure. While the correlation between year first worked and year first certified is high (correlation coefficient 0.96), the number of years worked and the number of years certified are less closely related (correlation coefficient 0.52). The lower correlation coefficient characterizing the relationship between the number of years worked and the number of years certified can be explained by the substantial numbers of technologists who worked without recertifying each year or who recertified annually to maintain their licensure even though they did not work. Thus, the year first worked and the number of years worked reflect the individual work history more accurately than the year first certified and the number of years certified as a radiologic technologist.

We examined in detail the effects of year of first use and duration of use of specific procedures, including fluoroscopy and multifilm procedures, which have been shown to have higher exposure potential than general diagnostic procedures such as chest x-rays.[22] We also evaluated the effects of other specific procedures or types of radiation (routine x-rays, portable x-rays, radium and other isotopes, dental x-rays, ultrasound examinations, C-T scans), use of specific radiotherapy equipment (orthovoltage, Cobalt 60, betatron and linear accelerator units) and behavioral practices (the frequency of holding patients who were x-rayed, the frequency of allowing other technologists to take practice x-rays on oneself and the use of protective shields or lead aprons).

Statistical analysis

For the entire cohort, we compiled person-years according to sex, race (white, non-white), age during the follow-up period (*i.e.,* attained age; 0–29, 30–34,. . .75–79, 80+) and calendar period of follow-up (<1930, 1930–1934,. . .1990–1994, 1995–1998) from the date of first certification with the ARRT through the end of 1997, the date of death or the date when lost to follow-up, whichever occurred first. Individuals last found alive before 1979 (prior to the availability of the U.S. National Death Index) were exited at their date last known alive; technologists who were known alive in 1979 or later and for whom a record was not found in the National Death Index were assumed to be alive and were exited at the end of the study. Those workers with an unknown date of death were considered lost to follow-up at the date last known to be alive. For subjects with an unknown cause of death (n = 811), person-year accumulation ceased at the date of death, but these subjects only contributed to the category designated "all causes of death" and not to any specific cause of death category when calculating standardized mortality ratios (SMRs). SMRs were calculated using sex-, race-, age- and calendar year-specific U.S. mortality rates.[23]

For the subset of questionnaire respondents, person-years were compiled in the same way as described above, except that follow-up began at the date of questionnaire completion. Relative risks (RR) for mortality from breast cancer (based on 69,525 female respondents), lung cancer and the combined group of radiogenic leukemias [acute lymphocytic (n = 7), acute myeloid (n = 13), chronic myeloid (n = 8) and acute leukemias of unspecified cell types (n = 9)] were estimated using loglinear Poisson regression models.[23] We evaluated mortality risks from breast cancer, lung cancer and the leukemias in more detail, since these malignancies are frequently increased in persons exposed to radiation. We analyzed radiogenic leukemias as a combined group because there were too few cases of each subtype to provide stable risk estimates and this grouping of leukemias has been used in other investigations of radiation-exposed populations. We did not include chronic lymphocytic leukemia (CLL) in the combined group of radiogenic leukemias because CLL has not been associated with radiation exposure.[24] Histologic type was available for 91% of the leukemia deaths. The background risk was estimated nonparametrically within the cohort using models stratified by sex, race and 5-year categories of calendar year and age.

The year a subject first worked and the total number of years a subject worked were analyzed together in a multivariate model. Analysis of the number of years a subject worked in a specific time period was restricted to subjects 15–65 years of age, thus eligible for employment during that time period, and adjusted for the number of years that subject worked in the other time periods. These radiation exposure surrogates (*e.g.,* the year first worked, the number of years a subject worked during each time period) are correlated with attained age and calendar year. Since cancer rates are known to vary with age and calendar year, the correlation of year first worked, number of years worked during specific calendar year periods, attained age and calendar year can induce intrinsic confounding leading to co-linearity in extreme situations. Therefore, we also conducted analyses using external mortality rates from the general U.S. population. While comparison of the mortality risks among the U.S. radiologic technologists with external mortality rates from the general U.S. population can be useful to disentangle the effects of correlated variables, it is necessary to assume that the background mortality in the cohort is proportional to that in the general population. The results based on external comparisons were generally similar to the internal comparisons, although the risk estimates were smaller (data not shown).

We evaluated potential confounding factors for breast cancer including age at menarche (≤11, 12, 13, ≥14), age at menopause (premenopausal, <45, ≥45), number of live births (nulliparous, 1, 2–3, 4–5, ≥6), age at first birth (nulliparous, <25, 25–29, ≥30) and family history of breast cancer (no family history of breast cancer, breast cancer in first-degree relatives, breast cancer in other relatives). For lung cancer, we examined the amount and duration of cigarette smoking (nonsmoker, smoker for ≤10 years, for 11–20 years, for 21–30 years, for >30 years, smoker of unknown duration). Potential confounders examined for leukemia included use of hair dyes (nonuser, user for <10 years, user for ≥10 years) and the amount and duration of cigarette smoking (as above).

We calculated 95% Wald-based confidence intervals.[23] All tests were 2-sided at the 5% significance level. Trend tests were used to describe whether mortality risks increased or decreased over calendar time for the year first employed and if risks rose or declined with the number of years employed and were based on the slope estimate for continuous values of the respective variables. EPICURE software[25] was used for person-year calculation and risk modeling.

RESULTS

Description of the cohort

The majority of technologists were born from 1940–1959 (73%), first certified from 1960–1979 (76%) and less than 30 years of age at the time of first certification (89%) (Table I). The average length of follow-up from the date of first certification was 26.7 years. Approximately 82% of the technologists were followed for 20 years or more, and 60% of the original cohort members were still certified as of 1997. The subset of technologists who responded to the questionnaire was similar to the entire cohort with respect to these characteristics, except that higher proportions of men and women completing the questionnaire were still certified in 1997 or later (Table I). The average age at questionnaire

TABLE I – DEMOGRAPHIC CHARACTERISTICS OF RADIOLOGIC TECHNOLOGISTS[1] CERTIFIED BY THE AMERICAN REGISTRY OF RADIOLOGIC TECHNOLOGISTS (ARRT) BY GENDER

Characteristic	Entire cohort certified by ARRT				Subset of questionnaire respondents			
	Females (n = 106,884)		Males (n = 39,031)		Females (n = 69,525)		Males (n = 20,780)	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Birth year								
<1930	11,757	11.0	6,245	16.0	4,864	7.0	2,746	13.2
1930–39	14,019	13.1	6,085	15.6	8,634	12.4	3,196	15.4
1940–49	33,546	31.4	13,081	33.5	22,383	32.2	7,080	34.1
1950–59	46,633	43.6	13,545	34.7	32,959	47.4	7,712	37.1
1960+	929	0.9	75	0.2	685	1.0	46	0.2
Year first certified								
1926–39	1,905	1.8	389	1.0	299	0.4	47	0.2
1940–49	4,178	3.9	1,518	3.9	1,742	2.5	602	2.9
1950–59	13,764	12.9	5,358	13.7	8,098	11.7	2,679	12.9
1960–69	30,738	28.8	10,204	26.1	20,410	29.4	5,470	26.3
1970–79	50,760	47.5	19,658	50.4	35,132	50.5	10,941	52.7
1980+	5,539	5.2	1,904	4.9	3,844	5.5	1,041	5.0
Age at first certification (year)								
<18	43	0.04	10	0.03	18	0.03	2	0.01
18–19	10,470	9.8	1,051	2.7	22,526	32.4	1,949	9.4
20–22	68,058	63.6	13,707	35.2	33,927	48.8	7,377	35.6
23–24	9,619	8.9	6,933	17.8	4,822	6.9	3,560	17.2
25–29	8,806	8.2	10,627	27.2	4,272	6.2	5,136	24.8
30–34	4,301	4.0	3,484	8.9	1,935	2.8	1,533	7.4
35–39	2,745	2.6	1,700	4.4	1,096	1.6	686	3.3
40+	2,842	2.7	1,519	3.9	929	1.3	537	2.4
Year last recertified								
<1970	5,197	4.9	2,217	5.7	964	1.4	410	1.9
1970–79	6,605	6.2	3,288	8.4	2,394	3.4	969	4.6
1980–89	11,825	11.1	5,990	15.4	5,838	8.4	2,474	11.9
1990–96	16,595	15.5	6,522	16.7	11,438	16.5	3,731	12.0
1997+	66,662	62.4	21,014	53.8	48,891	70.4	13,196	63.6
Year first employed[2]								
<1940	—	—	—	—	802	1.2	253	1.2
1940–49	—	—	—	—	2,859	4.1	1,502	7.2
1950–59	—	—	—	—	9,603	13.8	3,120	15.1
1960+	—	—	—	—	55,163	79.4	15,433	74.3
Never worked/unknown	—	—	—	—	1,098	1.6	472	2.3
Age at first employment								
<18	—	—	—	—	26,207	37.7	2,969	14.3
18–19	—	—	—	—	24,043	34.6	5,482	26.4
20–22	—	—	—	—	11,404	16.4	5,887	28.2
23–24	—	—	—	—	2,148	3.1	2,468	11.9
25–29	—	—	—	—	2,421	3.5	2,447	11.8
30–34	—	—	—	—	1,213	1.8	643	3.1
35–39	—	—	—	—	618	0.9	241	1.2
40+	—	—	—	—	373	0.5	171	0.8
Never worked/unknown	—	—	—	—	1,098	1.6	472	2.3
Number of years worked (year)[2]								
<10	—	—	—	—	32,057	46.1	7,000	33.8
10–19	—	—	—	—	28,170	40.6	8,485	40.8
20+	—	—	—	—	8,200	11.8	4,823	23.3
Never worked/unknown	—	—	—	—	1,098	1.6	472	2.3

[1]The questionnaires of 81 respondents contained insufficient information for analysis and were excluded from relative risk analysis; we also excluded 31 subjects who reported first working when they were younger than 10 years old. Eight respondents were also excluded from relative risk analysis of breast cancer due to a reported age of 65 or older at menopause.–[2]This information is available only for technologists who answered the questionnaire.

completion was 39 years, and the average length of follow-up from questionnaire completion to the end of follow-up was 12 years.

Standardized mortality ratios in the entire cohort (external comparisons)

There were 12,624 deaths from all causes *vs.* 16,587 expected among the 146,022 radiologic technologists, corresponding to a significantly low mortality risk of 0.76 (Table II). Significant deficits also occurred for all cancers combined; cancers of the larynx, lung, bone, colon, buccal cavity, skin and uterine cervix; and diseases of the circulatory, respiratory, digestive and genitourinary systems. Mortality risks were generally similar for males and females, except for a significantly reduced risk of dying from infectious and parasitic diseases among women (SMR = 0.62, 95% confidence interval [CI] = 0.50–0.75) compared to a significantly increased risk for men (SMR = 1.21, 95% CI = 1.07–1.38). The excess among men was mainly attributed to deaths from AIDS.

Cancer mortality among questionnaire respondents (internal comparisons)

Nonradiation-related risk factors. Known risk factors for breast cancer demonstrated the expected pattern. Breast cancer risks were higher among women age 45 years or older at menopause compared to women younger than age 45 (RR = 1.28), greater among women age 30 years or older at first birth compared to women younger than age 25 at first birth (RR = 1.40) and elevated among women with breast cancer in a relative compared to women with no family history of breast cancer (RR = 1.31). However, breast cancer risk varied little with age at menarche or number of live births. Subsequent analyses of breast cancer in relation to work history and practices as a radiologic technologist were adjusted for age at menopause, age at first birth and family history of breast cancer. Lung cancer risks were increased 40-fold among technologists who smoked more than 2 packs per day for more than 30 years compared to nonsmokers. Lung cancer analyses were adjusted for amount and duration of cigarette smoking. Since leukemia risks varied little with duration of hair dye use and amount or duration of cigarette smoking, analyses of leukemia were not adjusted for these variables.

Radiation-related occupational exposures. Mortality risks for all cancers combined increased modestly, albeit significantly (p-trend = 0.04), with earlier calendar year first employed, but there was no relation with the cumulative number of years worked (Table III). Total cancer mortality risks were 19% higher (95%

TABLE II – OBSERVED AND EXPECTED DEATHS AND STANDARDIZED MORTALITY RATIOS[1] IN THE ENTIRE COHORT OF 146,022 RADIOLOGIC TECHNOLOGISTS BY CAUSE OF DEATH, STRATIFIED ON GENDER

Cause of death (ICD-8th Revision)	Males			Females		
	Observed deaths	SMR	95% CI	Observed deaths	SMR	95% CI
All causes (000–999)[2]	5,057	0.76	0.7–0.8	7,567	0.76	0.7–0.8
Infectious and parasitic diseases (000–136)	245	1.21	1.1–1.4	100	0.62	0.5–0.8
All malignant neoplasms (140–209)	1,137	0.73	0.7–0.8	2,558	0.86	0.8–0.9
Buccal cavity and pharynx (140–149)	23	0.59	0.4–0.9	29	0.89	0.6–1.3
Esophagus (150)	27	0.67	0.4–1.0	20	0.95	0.6–1.5
Stomach (151)	43	0.84	0.6–1.1	52	0.81	0.6–1.1
Colon (153)	98	0.75	0.6–0.9	203	0.80	0.7–0.9
Rectum (154)	25	0.86	0.6–1.3	39	0.85	0.6–1.2
Liver, gallbladder, bile ducts (155–156)	26	0.98	0.6–1.4	45	0.89	0.7–1.2
Pancreas (157)	73	0.99	0.8–1.2	110	0.93	0.8–1.1
Larynx (161)	7	0.37	0.2–0.8	5	0.59	0.2–1.4
Lung, trachea, bronchus (162)	358	0.67	0.6–0.7	423	0.80	0.7–0.9
Bone (170)	2	0.40	0.1–1.5	3	0.36	0.1–1.1
Skin, including melanoma (172–173)	29	0.63	0.4–0.9	42	0.70	0.5–0.9
Breast (174)	2	1.06	0.1–3.8	703	1.01	0.9–1.1
Cervix (180)	—	—	—	36	0.31	0.2–0.4
Uterus (181–182)	—	—	—	36	0.31	0.2–0.4
Other female genital (183–184)	—	—	—	178	0.89	0.8–1.1
Prostate (185)	87	0.89	0.7–1.1	—	—	—
Testis/unspecified male genital (186–187)	5	0.55	0.2–1.3	—	—	—
Bladder (188)	20	0.60	0.4–0.9	25	0.94	0.7–1.3
Kidney/unspecified urinary organs (189)	37	0.89	0.6–1.2	43	0.94	0.7–1.3
Eye (190)	2	1.98	0.2–7.2	1	0.54	0.1–3.0
Brain and other CNS (191–192)	43	0.77	0.6–1.0	83	0.92	0.7–1.1
Thyroid (193)	1	0.36	0.1–2.0	6	0.79	0.3–1.7
Non-Hodgkin's lymphoma (200, 202)	80	1.01	0.7–1.6	133	0.98	0.7–1.1
Hodgkin's disease (201)	9	0.61	0.3–1.2	25	1.06	0.7–1.6
Multiple myeloma (203)	25	1.13	0.7–1.7	33	0.91	0.6–1.3
Leukemia (204–207)	60	0.95	0.7–1.2	98	0.92	0.8–1.1
Benign and unspecified neoplasms (210–239)	18	1.04	0.6–1.6	35	0.85	0.6–1.2
Endocrine, nutritional diseases (240–279)	159	1.08	0.9–1.3	160	0.52	0.4–0.6
Blood/blood-forming organs (280–289)	16	1.09	0.6–1.8	34	1.00	0.7–1.4
Mental disorders (290–315)	36	0.52	0.4–0.7	90	1.10	0.8–1.3
Nervous system/sense organs (320–389)	50	0.57	0.4–0.8	128	0.73	0.6–0.9
Diseases of circulatory system (390–458)	1,918	0.74	0.7–0.8	2,353	0.66	0.6–0.7
Arteriosclerosis and CHD (410–414)	1,316	0.73	0.7–0.8	1,276	0.65	0.6–0.7
Vascular lesions of CNS (430–438)	222	0.80	0.7–0.9	517	0.74	0.7–0.8
Diseases of respiratory system (460–519)	309	0.76	0.7–0.9	447	0.73	0.7–0.8
Diseases of digestive system (520–577)	199	0.63	0.5–0.7	265	0.62	0.6–0.7
Diseases of genitourinary system (580–629)	62	0.87	0.7–1.1	98	0.63	0.5–0.8
Skin and subcutaneous tissue (680–709)	1	0.22	0.1–1.2	14	0.99	0.5–1.7
Diseases of musculoskeletal system (710–738)	12	1.01	0.5–1.8	53	0.99	0.7–1.3
Accidents, poisonings, violence (800–998)	306	0.53	0.5–0.6	343	0.66	0.6–0.7

[1]Number of observed deaths divided by number of expected deaths based on U.S. population rates.–[2]811 technologists with an unknown cause of death contributed to the SMR for "all causes" but did not contribute to any cause-specific category.

TABLE III – RELATIVE RISKS[1] FOR ALL CANCERS AND SELECTED CANCERS AMONG 90,216 RADIOLOGIC TECHNOLOGIST QUESTIONNAIRE RESPONDENTS ACCORDING TO YEAR FIRST WORKED AND NUMBER OF YEARS WORKED AS A RADIOLOGIC TECHNOLOGIST

Year first worked	No. of years worked			*p*-trend[2]	All years worked[3]
	<10	10–19	20+		
All cancers relative risks (no. of deaths)[4]					
1960+	1.0[5] (152)	1.01 (198)	1.12 (64)		1.0[6] (414)
1950–59	1.27 (114)	1.31 (106)	1.18 (205)		1.18 (425)
1940–49	1.21 (70)	1.01 (46)	1.29 (201)		1.17 (317)
<1940	1.15 (18)	1.38 (29)	1.37 (80)		1.28 (127)
p-trend					(0.04)
All time periods[3]	1.0[6] (354)	1.00 (379)	1.03 (550)	>0.5	(1,283)
Breast cancer relative risks (no. of deaths)[4,7]					
1960+	1.0[5] (42)	1.15 (57)	1.48 (17)		1.0[6] (116)
1950–59	1.71 (30)	1.29 (18)	1.26 (27)		1.24 (75)
1940–49	3.15[8] (16)	3.49[8] (13)	2.02 (16)		2.44[8] (45)
<1940	0.77 (1)	5.55[8] (9)	2.98[8] (9)		2.92[8] (19)
p-trend					(0.002)
All time periods[3]	1.0[6] (89)	1.08 (97)	0.91 (69)	(0.38)	(255)
Lung cancer relative risks (no. of deaths)[4]					
1960+	1.0[5] (22)	1.09 (35)	0.57 (9)		1.0[6] (66)
1950–59	0.79 (22)	0.88 (24)	0.91 (57)		0.96 (103)
1940–49	0.79 (16)	0.64 (11)	0.80 (52)		0.83 (79)
<1940	0.97 (5)	0.88 (7)	0.84 (19)		0.93 (31)
p-trend					>0.5
All time periods[3]	1.0[6] (65)	1.04 (77)	0.98 (137)	(>0.5)	(279)
Acute lymphocytic, acute myeloid and chronic myeloid leukemias relative risks (no. of deaths)[4]					
≥1950	1.0[5] (8)	1.34 (12)	1.15 (7)		1.0[6] (27)
<1950	0.83 (1)	1.82 (2)	2.38 (7)		1.64 (10)
p-trend					0.13
All time periods[3]	1.0[6] (9)	1.44 (14)	1.50 (14)	0.45	(37)

[1]All relative risks were stratified for attained age, calendar year of follow-up, race, and gender. Breast cancer analysis adjusted for age at menopause, age at first birth and family history of breast cancer, and lung cancer and all cancers combined analyses for duration of smoking and amount smoked.–[2]*p*-trend was based on the slope of the corresponding continuous variable; parentheses indicate negative slope estimate.–[3]Relative risks for all years worked adjusted for total duration of employment; relative risks for all time periods adjusted for year of first employment.–[4]Subjects who never worked as a radiologic technologist (1,057 females and 455 males) were included in this analysis and coded as separate categories (estimates not shown in the table).–[5]Referent group for the joint analyses of the number of years worked and year first worked.–[6]Referent group for the separate analyses of number of years worked and year first worked.–[7]Only female subjects included for the breast cancer analysis; all subjects included for all other analyses.–[8]$p < 0.05$.

CI = 0.93–1.52) for those who first worked prior to 1950 than for those who first worked in 1960 or later (data not shown). Similarly, risks of dying from breast cancer were significantly increased among women first employed prior to 1940 (RR = 2.92; 95% CI = 1.22–7.00) and from 1940–1949 (RR = 2.44; 95% CI = 1.26–4.75) (Table III), for an overall 50% significantly elevated risk (95% CI = 1.29–4.82) among those first employed prior to 1950 (data not shown) compared to women first employed in 1960 or later. Breast cancer mortality risks did not vary, however, with the cumulative number of years worked (Table III). The majority (54%) of the women in our study began working as a radiologic technologist when they were between the ages of 18 and 24 years, and about 38% began working as a technologist prior to age 18. There were no significant differences in breast cancer mortality risks among women according to age at first employment when the analysis was adjusted for year first worked (data not shown).

Mortality risks for lung cancer were not associated with the year of first employment nor with the cumulative duration of employment (Table III). Risks of death from lung cancer were not elevated (RR = 0.85; 95% CI = 0.54–1.35) among technologists first employed prior to 1950 compared to women first working in 1960 or later (data not shown). Even after combining acute lymphocytic, acute myeloid and chronic myeloid leukemias, the small number of deaths among those who first worked prior to 1950 precluded calculation of stable risk estimates for the periods prior to 1940 and for 1940–49, during which the recommended exposure limits steeply declined. Subjects first employed prior to 1950 had a nonsignificant 64% increased mortality risk compared to those first employed in 1950 or later. In contrast to the pattern for the other cancer categories examined, mortality risks for the combined group of leukemias increased nonsignificantly with the total number of years worked (Table III).

When we examined mortality risks according to the number of years worked in different time intervals, risks did not increase for all cancers combined with an increasing number of years worked prior to 1950, although risks did increase slightly with increasing number of years worked in the 1960s and decreased slightly in the 1970s (Table IV). For lung cancer, mortality risks did not vary substantially with years worked in any decade. With regard to breast cancer, however, mortality risks rose with an increasing number of years worked prior to 1950 (*p*-trend = 0.018), but not in more recent time intervals. Mortality risks for the combined group of radiogenic leukemias also increased significantly with the number of years worked before 1950 (*p*-trend = 0.05, based on 15 cases), but not in other calendar time periods (Table IV). The small number of deaths from chronic lymphocytic leukemia ($n = 13$) precluded detailed analyses.

Mortality risk for female breast cancer was elevated among technologists who first worked with fluoroscopy (Table V) before 1950 compared to those who first worked with these procedures later. Based on small numbers of cases, increased risks were also seen for the combined group of leukemias. In contrast, mortality risks were not increased for all cancers combined or for lung cancer among those first working with fluoroscopy before 1950 or during any other time periods (Table V). Duration of performing fluoroscopy was not linked with mortality risks for all cancers combined, female breast cancer, lung cancer or the group of combined leukemias (Table V).

Similar risk patterns for mortality from female breast cancer and the combined leukemias were seen with first working with multifilm procedures before 1950 (Table VI). Risk was not substantially elevated for all cancers combined or for lung cancer among those first working with multifilm procedures before 1950. As with

TABLE IV – RELATIVE RISKS[1] FOR ALL CANCERS AND SELECTED CANCERS AMONG 90,216 RADIOLOGIC TECHNOLOGIST QUESTIONNAIRE RESPONDENTS ACCORDING TO NUMBER OF YEARS WORKED IN DIFFERENT CALENDAR YEAR PERIODS

Calendar year period of employment	No. of years worked in the different calendar year periods			*p*-trend[2]
	0	1–4	5+	
All cancers (no. of deaths)[3]				
<1950	1.0[4] (319)	1.00 (212)	1.06 (232)	0.46
1950–59	1.0[4] (270)	1.05 (311)	1.07 (504)	>0.5
1960–69	1.0[4] (306)	1.00 (259)	1.21[5] (712)	0.05
1970–79	1.0[4] (375)	0.88 (174)	0.78[5] (742)	(0.01)
Breast cancer (no. of deaths)[3]				
<1950	1.0[4] (37)	2.17[5] (35)	2.08[5] (29)	0.018
1950–59	1.0[4] (57)	1.18 (67)	1.08 (63)	(>0.5)
1960–69	1.0[4] (63)	1.06 (79)	0.97 (106)	(>0.5)
1970–79	1.0[4] (81)	0.75 (34)	0.76 (143)	(0.17)
Lung cancer (no. of deaths)[3]				
<1950	1.0[4] (95)	0.86 (57)	0.72 (53)	(0.16)
1950–59	1.0[4] (64)	0.97 (73)	1.04 (130)	>0.5
1960–69	1.0[4] (70)	0.79 (43)	0.92 (173)	>0.5
1970–79	1.0[4] (90)	1.14 (42)	0.86 (156)	(>0.5)
Acute lymphocytic, acute myeloid and chronic myeloid leukemias (no. of deaths)[3]				
<1950	1.0[4] (5)	1.46 (3)	4.95 (7)	0.05
1950–59	1.0[4] (14)	0.27 (3)	0.54 (10)	(>0.5)
1960–69	1.0[4] (10)	1.47 (9)	1.03 (17)	(0.5)
1970–79	1.0[4] (4)	1.76 (3)	3.20 (29)	0.32

[1]All relative risks were stratified for attained age, calendar year of follow-up, race and gender, and adjusted for employment in other time periods. Breast cancer analysis also adjusted for age at menopause, age at first birth, and family history of breast cancer, and lung cancer and all cancers combined analyses for duration of smoking and amount smoked.–[2]*p*-trend was based on the slope of the corresponding continuous variable; parentheses indicate negative slope estimate.–[3]The total number of cases may differ for different time periods since analyses were restricted to technologists who were 15–65 years of age and therefore eligible for employment in the respective calendar time periods. The total number of cases may also exceed the numbers in Table III since technologists who never worked were included in this table under the "0" category of number of years worked in the different calendar years periods, while in Table III they were coded as a separate category that is not shown in the table. Only female subjects included for the breast cancer analysis; all subjects included for all the other analyses.–[4]Referent group for number of years worked in respective calendar year period.–[5]$p < 0.05$.

fluoroscopy, there was no association between any cancer mortality and duration of performing multifilm procedures.

Mortality risks for all cancers combined, breast cancer, lung cancer and the group of acute lymphocytic, acute myeloid and chronic myeloid leukemias did not differ according to calendar period of first performing or duration of performing routine x-rays, dental x-rays, ultrasound examinations, C-T scans or teletherapy procedures (*e.g.,* those involving orthovoltage, Cobalt 60, betatron or linear accelerator units) or using radium or other isotopes (data not shown). Further, other work practices (*e.g.,* the frequency of holding patients for x-rays or the frequency of allowing other technologists to take practice x-rays on oneself) or protective measures (use of lead aprons) were not associated with risks for total cancer or specific cancer mortality.

DISCUSSION

In the comparison of radiologic technologists with the general U.S. population, mortality risks were lower for all causes of death and for all cancers combined. However, based on analyses of questionnaire respondents, we found increased risks for mortality from breast cancer and for the combined group of leukemias among subjects who first worked as a radiologic technologist prior to 1950 compared to subjects who first worked later. Risks rose with increasing number of years worked before 1950, but not for number of years worked in later calendar periods. Mortality risks were not associated with the cumulative number of years worked. These findings are consistent with an increased risk of mortality from these malignancies in relation to the substantially higher doses of radiation exposure likely experienced prior to 1950 than in later decades.[1,17–20] Lung cancer mortality was not associated with any of the work history or practices evaluated.

Our results for breast cancer mortality among radiologic technologists compared to the U.S. population were consistent with findings from an earlier follow-up of this cohort.[12] In our current analysis, an additional 7 years of follow-up are included. The analysis of the subcohort of questionnaire respondents permitted evaluation of more specific employment history information and statistical adjustment by known risk factors. A prior analysis of the same cohort, based on a nested case-control design in which prevalent breast cancer cases were identified from responses to the questionnaire,[13] showed a similar lack of relationship with cumulative years worked. However, that study did not find breast cancer risk to be related to any of the various indicators of occupational radiation exposure analyzed, though time-dependent work history effects were not examined in the same level of detail as in our present analysis.

It is well established from the study of female Japanese atomic bomb survivors that instantaneous low-to-moderate doses of radiation can cause a 2–3-fold increase in breast cancer risk.[26–28] In addition, studies among women undergoing repeated diagnostic fluoroscopic examinations for tuberculosis provide evidence that fractionated moderate-to-high doses of radiation delivered at high-dose rates can cause breast cancer.[29,30] However, only 2 other studies of medical radiation workers included sufficient numbers of females to enable an evaluation of the effects of chronic low-to-moderate doses of radiation on breast cancer. A study of Chinese medical radiation workers (n = 27,011 total, including 5,443 females) found a significantly increased incidence risk of breast cancer among females overall (RR = 1.34),[7] while a small Danish study (n = 4,151 total, 82% female) observed no evidence of elevated risk of breast cancer.[10]

Our results for the radiogenic leukemias are generally consistent with the body of evidence for radiation effects associated with this

TABLE V – RELATIVE RISKS[1,2] FOR ALL CANCERS AND SELECTED CANCERS AMONG 90,216 RADIOLOGIC TECHNOLOGIST QUESTIONNAIRE RESPONDENTS ACCORDING TO YEAR FIRST WORKED AND NUMBER OF YEARS WORKED WITH FLUOROSCOPY IN DIFFERENT CALENDAR YEAR PERIODS

Year first worked with fluoroscopy	No. of years worked with fluoroscopy			p-trend[3]	All years worked[4]
	<10	10–19	20+		
All cancers (no. of deaths)[5]					
1960+	1.0[6] (208)	1.05 (135)	1.05 (39)		1.0[7] (382)
1950–59	1.21 (159)	1.26 (107)	1.10 (119)		1.15 (385)
<1950	1.09 (107)	1.08 (67)	1.21 (146)		1.10 (320)
p-trend					(0.20)
All time periods[4]	1.0[7] (474)	1.05 (309)	1.03 (304)	0.41	(1,087)
Breast cancer (no. of deaths)[5]					
1960+	1.0[6] (61)	1.12 (38)	1.13 (9)		1.0[7] (108)
1950–59	1.45 (40)	1.42 (21)	0.82 (11)		1.23 (72)
<1950	1.76 (20)	1.65 (11)	1.59 (14)		1.69 (45)
p-trend					(0.07)
All time periods[4]	1.0[7] (121)	1.07 (70)	0.83 (34)	(0.31)	(225)
Lung cancer (no. of deaths)[5]					
1960+	1.0[6] (28)	1.12 (23)	0.90 (8)		1.0[7] (59)
1950–59	0.91 (30)	1.15 (27)	1.07 (35)		0.96 (92)
<1950	1.02 (27)	0.71 (13)	1.17 (44)		0.95 (84)
p-trend					>0.5
All time periods[4]	1.0[7] (85)	1.04 (63)	1.14 (87)	0.42	(235)
Acute lymphocytic, acute myeloid and chronic myeloid leukemias (no. of deaths)[5]					
≥1950	1.0[6] (5)	2.65 (7)	0.93 (1)		1.0[7] (13)
<1950	3.23 (2)	5.53 (2)	2.13 (1)		2.41 (5)
p-trend					(>0.5)
All time periods[4]	1.0[7] (7)	2.38 (9)	0.84 (2)	>0.5	

[1]861 people with unreasonable values for variables relating to working with specific procedures were excluded from this analysis.–[2]All relative risks were stratified for attained age, calendar year of follow-up, race and gender. Breast cancer analysis adjusted for age at menopause, age at first birth and family history of breast cancer, and all cancers combined and lung cancer analyses for duration of smoking and amount smoked. The analyses for all years worked were adjusted for the duration of employment using fluoroscopy and the analyses for all time periods was adjusted for the year first worked with fluoroscopy.–[3]*p*-trend was based on the slope of the corresponding continuous variable; parentheses indicate negative slope estimate.–[4]Relative risks for all years worked adjusted for total duration of employment with fluoroscopy; relative risk for all time periods adjusted for year of first employment with fluoroscopy.–[5]Subjects who never worked with fluoroscopy or who had unknown values for the variables in the table were included in this analysis and were coded as separate categories (estimates not shown). Only female subjects were included for the breast cancer analysis; all subjects were included for all the other analyses.–[6]Referent group for the joint analyses of the number of years worked and year first worked.–[7]Referent group for the separate analyses of number of years worked and year first worked.–[8]$p < 0.05$.

group of malignancies. Cohort studies of male radiologists in the U.S.[4–6] and U.K.[2,3] have demonstrated 3–6-fold increases of leukemia mortality among those who first worked before 1940 (or before 1921 in the U.K. study) compared to physicians in other specialties (U.S.) or men of high social class (U.K.). Excess risks of leukemia have been reported among male Japanese technologists employed during 1918–1971[8] and among Chinese medical radiation workers exposed during 1950–1985.[7] Elevated risks of leukemia were also observed among nuclear workers who were similarly exposed to chronic doses.[31] Unlike our study, cancer risk estimates for nuclear workers have been linked with individual dose measurements.[31,32] Radiogenic leukemias were not elevated among the small cohorts of Danish medical workers employed during 1954–82[10] or of U.S. Army technologists exposed before 1946.[9] We also found no significant excess leukemia risk associated with year first certified or number of years certified in the prior mortality analysis of this cohort,[12] but our earlier reported results did not incorporate the more detailed work history variables used in the present analysis. Consistent with the increasing risk of radiogenic leukemias with increasing total duration of employment seen among Chinese medical radiation workers, we found a significant association with the number of years worked before 1950 (*p*-trend = 0.05), when radiation exposures were likely high.

Increased lung cancer risk has been found among atomic bomb survivors[27] and patients treated with radiotherapy for breast cancer[33] or Hodgkin's disease.[34] However, similar to results in our present study, lung cancer was not increased in tuberculosis patients who received fractionated doses of radiation from repeated diagnostic fluoroscopic x-rays.[35] Consistent with our results, other studies of medical radiation workers have shown no evidence of increased lung cancer risk.[3,4,7–10]

Although we found no overall increase in cancer mortality risk with cumulative years worked (Table III), we did find a small increase in risk with increasing years worked in the 1960s and a small decrease associated with years worked in the 1970s (Table IV). The explanation for these trends is not obvious, particularly since these trends characterize a combination of many cancer sites.

Our cohort is one of the few occupational cohorts that includes female workers and is unique in the size of the population of female medical radiation workers exposed to chronic low-dose ionizing radiation. Other strengths of our study include the nationwide representation of the cohort, nearly complete mortality follow-up and the availability of data on smoking, other lifestyle, reproductive, and other cancer risk factors to adjust for possible confounding effects. Our study also included a long follow-up period, a wide range of work practices and sufficiently large numbers of technologists to enable us to make internal comparisons and, thus, minimize potential biases due to the healthy worker effect observed when the general population was used as the comparison.

The main limitation of our study is the absence of individual lifetime dosimetry data. Our analysis focused on surrogate measures for individual work characteristics based on the information obtained from questionnaires. The subset of questionnaire respondents may not be representative of all radiologic technologists in the cohort since respondents had to survive until the mid-1980s and complete the questionnaire. To assess this possibility, we extended the analysis to the entire cohort, including nonrespondents to the questionnaire and subjects who died before the baseline questionnaire was administered. Since questionnaire information was not available for the entire cohort, the extended analysis relied on data from the ARRT registry, including the year each

TABLE VI – RELATIVE RISKS[1,2] FOR ALL CANCERS AND SELECTED CANCERS AMONG 90,216 RADIOLOGIC TECHNOLOGIST QUESTIONNAIRE RESPONDENTS ACCORDING TO YEAR FIRST WORKED AND NUMBER OF YEARS WORKED WITH MULTIFILM PROCEDURES IN DIFFERENT CALENDAR YEAR PERIODS

Year first worked with multifilm procedures	Number of years worked with multifilm procedures			*p*-trend[3]	All years worked[4]
	<10	10–19	20+		
All cancers (no. of deaths)[5]					
1960+	1.0[6] (190)	1.01 (134)	1.20 (47)		1.0[7] (371)
1950–59	1.26 (135)	1.26 (95)	1.10 (124)		1.16 (354)
<1950	1.19 (74)	1.54 (68)	1.27 (135)		1.26 (277)
p-trend					(0.10)
All time periods[4]	1.0[7] (399)	1.07 (297)	1.00 (306)	(>0.5)	(1,002)
Breast cancer (no. of deaths)[5]					
1960+	1.0[6] (54)	1.15 (39)	1.47 (12)		1.0[7] (105)
1950–59	1.63 (35)	1.58 (20)	1.17 (16)		1.38 (71)
<1950	2.10[8] (16)	2.53[8] (13)	1.00 (8)		1.87[8] (37)
p-trend					(0.01)
All time periods[4]	1.0[7] (105)	1.15 (72)	0.79 (36)	(0.15)	(213)
Lung cancer (no. of deaths)[5]					
1960+	1.0[6] (25)	1.02 (21)	0.68 (6)		1.0[7] (52)
1950–59	1.01 (25)	1.57 (30)	1.08 (34)		1.21 (89)
<1950	1.27 (20)	1.04 (12)	1.26 (38)		1.22 (70)
p-trend					(>0.5)
All time periods[4]	1.0[7] (70)	1.16 (63)	1.01 (78)	>0.5	(211)
Acute lymphocytic, acute myeloid and chronic myeloid leukemias (no. of deaths)[5]					
≥1950	1.0[6] (5)	2.03 (6)	1.65 (2)		1.0[7] (13)
<1950	3.34 (1)	19.56[8] (4)	3.13 (1)		4.93 (6)
p-trend					(0.34)
All time periods[4]	1.0[7] (6)	2.71 (10)	1.11 (3)	0.41	(18)

[1]861 people with unreasonable values for variable on work relating to specific procedures were excluded from this analysis.–[2]All relative risks were stratified for attained age, calendar year of follow-up, race and gender. Breast cancer analysis adjusted for age at menopause, age at first birth and family history of breast cancer, and all cancers combined and lung cancer analyses for duration of smoking and amount smoked. The analyses for all years worked were adjusted for the duration of employment using multifilm procedures and the analyses for all time periods were adjusted for the year first worked with multifilm procedures.–[3]*p*-trend was based on the slope of the corresponding continuous variable; parentheses indicate negative slope estimate.–[4]Relative risks for all years worked adjusted for total duration of employment with multifilm procedures; relative risk for all time periods adjusted for year of first employment with multifilm procedures.–[5]Subjects who never worked with multifilm or who had unknown values for the variables in the table were included in this analysis and were coded as separate categories (estimates not shown). Only female subjects included for the breast cancer analysis; all subjects included for all the other analyses.–[6]Referent group for the joint analyses of the number of years worked and year first worked.–[7]Referent group for the separate analyses of number of years worked and year first worked.–[8]$p < 0.05$.

subject was first certified as a radiologic technologist and the total number of years a subject was certified (information about the year a subject first worked was not available in the ARRT registry). In addition, the analysis could not be adjusted for known risk factors, since information about these factors was not available in the ARRT registry. Because little confounding was found in this cohort, this was not an important limitation. Despite these restrictions, we found similar risk patterns in the analysis of the entire cohort (data not shown), which supports the generalizability of the results from the questionnaire respondents to the entire cohort of radiologic technologists.

In this report, we emphasize the findings from the internal comparisons, instead of using U.S. population mortality rates to model the background risk. This is because we observed no indication of colinearity, *i.e.,* parameter estimates were stable and had small standard deviations, and because general U.S. population mortality data may not be an appropriate comparison for a working population.

In contrast to results from our present study, breast cancer risks among female Japanese atomic bomb survivors[25] and among women undergoing repeated diagnostic x-rays[28,29] have shown remarkable age-dependence, with highest risks occurring among women who were younger than 20 years of age at the time of exposure. The potential independent radiogenic effect of age at first exposure (approximated by a subject's age at initial employment) is difficult to investigate in a study in which the year a subject first worked is strongly linked with the disease outcome. This is because the age at which a subject first worked is a linear function of both the year a subject first worked and the year of the subject's birth, which are both indirectly incorporated into the analysis as the main exposure surrogate and as the birth cohort stratification variable, respectively. Statistically, our finding of an association between mortality risks and the year a subject first worked could also be attributed to age first worked. Epidemiologically, however, there is convincing rationale for an independent effect of year first worked, namely the steep decline in radiation exposure over time.

In summary, we found increased risks for breast cancer and for the combined group of leukemias among technologists with earlier year first worked and with increasing number of years worked prior to 1950. These findings support the potentially important effect of chronic low-to-moderate doses of radiation on risk of developing radiogenic cancers.

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