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JOURNAL CLUB:

Cancer Risks in U.S. Radiologic Technologists Working With Fluoroscopically Guided Interventional Procedures, 1994–2008

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Keywords: brain, breast, cancer, fluoroscopically guided interventional procedures, interventional radiology, radiologic procedures

DOI:10.2214/AJR.15.15265

Received July 1, 2015; accepted after revision November 7, 2015.

Funded by the intramural program of the Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, U. S. Department of Health and Human Services.

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Supplemental Data
Available online at www.ajronline.org.

AJR 2016; 206:1101–1109

0361–803X/16/2065–1101

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OBJECTIVE. The purpose of this study was to examine risks of cancer incidence and mortality among U.S. radiation technologists performing or assisting with fluoroscopically guided interventional procedures.

SUBJECTS AND METHODS. A nationwide prospective cohort of 90,957 radiologic technologists, who responded to a 1994–1998 survey that collected information on whether they had ever worked with fluoroscopically guided interventional procedures, was followed through completion of a subsequent cohort survey during 2003–2005 (for cancer incidence) or December 31, 2008 (for cancer mortality). Sex-adjusted hazard ratios (HRs) and 95% CIs were calculated by use of Cox proportional hazards models for incidence and mortality from all cancers other than nonmelanoma skin cancer and for specific cancer outcomes in participants who reported ever performing fluoroscopically guided interventional procedures compared with technologists who never performed these procedures.

RESULTS. The analysis showed an approximately twofold increased risk of brain cancer mortality (HR, 2.55; 95% CI, 1.48–4.40) and modest elevations in incidence of melanoma (HR, 1.30; 95% CI, 1.05–1.61) and in breast cancer incidence (HR, 1.16; 95% CI, 1.02–1.32) but not mortality (HR, 1.07; 95% CI, 0.69–1.66) among technologists who performed fluoroscopically guided interventional procedures compared with those who never performed these procedures. Although there was a small suggestive increase in incidence of all cancers combined, excluding nonmelanoma skin cancers (HR, 1.08; 95% CI, 1.00–1.17), mortality from all cancers combined, excluding nonmelanoma skin cancers, was not elevated (HR, 1.00; 95% CI, 0.88–1.14). We similarly observed no elevated risk of cancers of the thyroid, skin other than melanoma, prostate, lung, or colon and rectum or of leukemia that was not chronic lymphocytic leukemia among workers who performed fluoroscopically guided interventional procedures.

CONCLUSION. We observed elevated risks of brain cancer, breast cancer, and melanoma among technologists who performed fluoroscopically guided interventional procedures. Although exposure to low-dose radiation is one possible explanation for these increased risks, these results may also be due to chance or unmeasured confounding by nonradiation risk factors. Our results must be confirmed in other studies, preferably with individual radiation dose data.

In the past few decades the capability of performing fluoroscopically guided interventional procedures has allowed major advances in the medical treatment of several common diseases, such as cardiovascular conditions, and continues to provide major benefits for patients. These procedures, however, produce radiation doses that may cause adverse effects in patients and medical workers. Although there is substantial evidence that exposure to ionizing radiation at moderate to high levels (≥ 100 mSv cumulative or acute exposure) is associated with cancer [1], there is only limited information regarding risks at radiation doses less than 100 mSv, such as risks to medical radiation workers performing fluoroscopically guided interventional procedures. In light of these possible risks, a 2014 statement from the American Heart Association [2] highlighted the need for better information regarding disease risks at radiation doses less than 100 mSv.

In 2006 alone, approximately 17 million fluoroscopically guided interventional procedures were performed in the United States, and more than one-fourth of these procedures were cardiac examinations [3]. In addition to patients, a large population of medical workers are occupationally exposed during

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fluoroscopically guided interventional procedures. Although the use of these procedures is growing, published research findings regarding late health effects in patients undergoing them and in medical workers who perform or assist with them are sparse.

In our previous analysis [4]—the first epidemiologic study, to our knowledge, to assess cancer and other disease risks related to working with fluoroscopically guided interventional procedures—we observed no exposure-associated excess mortality risk from all malignant cancers combined in a prospective cohort follow-up of U.S. radiologic technologists who reported ever working with these procedures. These findings were limited by the short follow-up period at the time (5–9 years) and the small number of cancer deaths, which resulted in reduced power to detect moderate increases in risk, particularly if these risks were restricted to specific cancer outcomes, as would be expected with radiation exposure. The current study included five additional years of follow-up, included risks of specific cancer outcomes, and separately assessed incidence and mortality risks for cancer when data were available. Our specific objective was to examine whether cancer incidence and mortality of selected cancers are elevated among radiologic technologists who perform or assist with fluoroscopically guided interventional procedures in comparison with other radiologic technologists.

Subjects and Methods

Overview and History

The U.S. Radiologic Technologists Study is a long-term collaboration between the U. S. National Cancer Institute, the University of Minnesota, and the American Registry of Radiologic Technologists (ARRT). We briefly describe the overall study population and methods; greater detail is available in a previous publication [5] and at the U.S. Radiologic Technologists Study website. The U.S. Radiologic Technologists Study cohort comprises 146,022 radiologic technologists identified from the records of the ARRT who resided in any U.S. state or territory and were certified for at least 2 years before 1983. The cohort is followed through yearly ARRT recertification records. For those who do not recertify, records are linked with the Social Security Administration database to ascertain vital status. For those who have died or are presumed to have died, records are linked with the National Death Index (NDI Plus, U.S. Centers for Disease Control and Prevention).

Additional cohort follow-up was conducted through a series of mailed questionnaire surveys. The first two questionnaires (administered from 1983 to 1989 and 1994 to 1998) collected detailed information regarding employment as a radiologic technologist, disease risk factors, history of personal diagnostic and therapeutic medical radiation procedures, diagnoses of specific types of cancer, and other health outcomes. Baseline information on fluoroscopically guided interventional procedure work practices was first collected in the second questionnaire. The third questionnaire (administered 2003–2005) collected additional work history and risk factor information and event details for a larger number of neoplastic and other health outcomes.

Study Population and Outcome Assessment

During 1994–1998, 90,957 of 126,628 (72%) living technologists completed the second survey (which collected information on fluoroscopically guided interventional procedure use) and were eligible for the current study. For all second survey responders, vital status was determined through December 31, 2008, and underlying causes of death were obtained from NDI Plus. Because incident outcomes were identified from the third survey (2003–2005), incidence analyses were limited to the subset of 63,482 technologists who completed both the second and third surveys. We attempted to validate all reported cancers with pathology reports and other medical records and obtained records for a subset of reported cancers. Unconfirmed self-reported cancers other than brain cancer were included in incidence analyses because positive predictive values (PPVs) were high (Table S1). (Tables S1–S5, supplemental tables, can be

TABLE 1: Specific Outcomes Examined and Covariates Included for Adjustment in Statistical Models

Outcome and International Classification of Diseases, 10th Revision, Codes	Covariates[a] Considered for Adjustment
All malignant cancers (except nonmelanoma skin cancer), colorectal cancer (C18, C20, D01.0, D01.2)	No. of alcoholic drinks consumed per week (1–6, 7–13, ≥ 14)
	Smoking status (never, former, current)
	Body mass index (< 18.5, 18.5–24.9, 25.0–29.9, 30.0–34.9, ≥ 35)
Thyroid (C73, D09.3) and prostate (C61, D07.5) cancers	Smoking status, body mass index
Lung and bronchial cancer (C34, D02.2)	Smoking status
Breast cancer (C50, D05)	Age at menopause (< 40 y, 40–44, 45–49, ≥ 50, premenopausal)
	Age at first childbirth (< 25 y, 25–29, ≥ 30, nulliparous)
	No. of live births (1–4, ≥ 5, nulliparous)
	Family history of breast cancer (yes, no)
Melanoma (C43, D03), basal cell carcinoma (C44, D04 with histologic findings 8090–8119), squamous cell carcinoma (C44, D04 with histologic findings 8050–8089)	Skin tone (fair, medium, dark)
	Hair color (blond, light brown, dark brown or brunette, red or auburn, black)
	Eye color (blue, brown, green, hazel, gray, black)
Leukemia other than chronic lymphoid leukemia (C91-C95 except C91.1)	Education (grade school, high school, other vocational, radiation technologist program, college)
	Smoking status
Brain and CNS cancer (C71–C72)	Education

[a]Data on alcohol and smoking use, body mass index, age at menopause, age at first childbirth, number of live births, family history of breast cancer, skin tone, hair color, and eye color obtained from responses to the second mail questionnaire. Income and education obtained from the third questionnaire.

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Specific predefined outcomes evaluated were cancers consistently associated with radiation exposure at moderate to high doses (leukemia other than chronic lymphocytic leukemia (CLL), basal cell carcinoma of the skin, cancer of the female breast, and cancers of the thyroid, lung, brain, and colon and rectum) [1]; other cancers previously associated with radiation in the U.S. Radiologic Technologists study cohort (melanoma) [6]; cancers of specific concern to workers who perform fluoroscopically guided procedures (brain cancer [7], squamous cell carcinoma of the skin); and a common nonradiogenic cancer of general concern to the public (prostate cancer) to check for the specificity of radiation-related associations. CLL was excluded from leukemia because of the general lack of evidence of radiogenic risk for this endpoint in many other datasets [8, 9]. Specific International Classification of Diseases, 10th revision, codes are listed in Table 1.

For most of the cancer outcomes, both incidence and mortality data were available and assessed in separate incidence and mortality analyses. For basal cell carcinoma, squamous cell carcinoma, and thyroid cancer, only incidence data were used because of their low fatality rates. For brain cancer, only mortality data were evaluated because the validation process for reported cancers indicated a low PPV for the incidence endpoint. Details of exclusions for each outcome are shown Tables S2 (incidence) and S3 (mortality).

To be eligible for follow-up for cancer outcomes other than nonmelanoma skin cancer (NMSC), technologists had to be free of all cancer (other than NMSC) before completing the second questionnaire, and the first primary cancer (other than NMSC) was considered for analysis. For basal cell carcinoma and squamous cell carcinoma, participants had to be completely cancer free at the time of the second questionnaire (i.e., history of NMSC was an additional exclusion criterion at baseline), and the first primary cancer was evaluated in the incidence analysis.

Exposure Assessment

The work history section of the second questionnaire requested information from responders on how often (never or rarely, monthly, weekly, or daily) they worked with fluoroscopically guided interventional procedures in each of three defined time periods (before 1980, during 1980–1989, and during 1990 or later). Technologists were classified as ever worked with fluoroscopically guided interventional procedures if they reported working with the procedures in any of the three time periods; otherwise, they were classified as never worked with the procedures. Further analyses within individual time periods were not conducted because of small numbers of outcomes.

Statistical Analysis

Cancer risks were estimated with Cox proportional hazards models to compute hazard ratios (HRs) with 95% CIs for technologists who ever performed or assisted with fluoroscopically guided interventional procedures compared with technologists who never worked with the procedures. In the models, age was used as the timescale. The models were stratified by birth cohort (before 1930, 1930–1939, 1940–1949, 1950 and beyond) to control for secular trends and included sex as a variable for adjustment (minimally adjusted models). Data were also analyzed with a second set of models adjusted for total number of years worked as a radiologic technologist in different time periods (before

TABLE 2: Distribution of Selected Characteristics of 84,966 Radiologic Technologists Who Completed the Second Survey and Were Eligible for Mortality or Incidence Analyses

Characteristic	Performance of Fluoroscopically Guided Interventional Procedures						
	Ever Worked With		Never Worked With		Unknown		Total
	No.	%	No.	%	No.	%	No.
Sex							
Female	13,925	21	44,175	68	7031	11	65,131
Male	7057	36	10,620	54	2158	11	19,835
Year of birth							
Before 1930	634	12	3195	62	1300	25	5129
1930–1939	1980	18	7355	66	1825	16	11,160
1940–1949	6753	24	18,632	65	3069	11	28,454
1950–1959	11,400	29	25,159	64	2952	7	39,511
1960 and after	215	30	454	64	43	6	712
Age at completion of second survey (y)							
30–39	4089	29	8924	64	912	7	13,925
40–49	11,161	27	26,201	64	3458	8	40,820
50–59	4227	21	12,942	66	2530	13	19,699
≥ 60	1505	14	6728	64	2289	22	10,522
Race							
White	19,706	25	52,085	65	8531	11	80,322
African American	713	27	1521	58	386	15	2620
Other	544	28	1135	59	247	13	1926
Unknown	19	19	54	55	25	26	98
Income (U.S.$)							
< 50 K	2006	19	7384	69	1240	12	10,630
50–74 K	3304	25	8636	66	1101	8	13,041
75–99 K	3077	29	6886	64	813	8	10,776
≥ 100 K	4138	30	8427	62	1084	8	13,649
Unknown	8457	23	23,462	64	4951	13	36,870
Education							
High school or less	74	16	318	70	65	14	457
Other (vocational)	438	23	1232	64	260	13	1930
Radiologic technology program	5671	22	17,331	68	2415	10	25,417
College	7236	28	15,976	63	2318	9	25,530
Unknown	7563	24	19,938	63	4131	13	31,632

(Table 2 continues on next page)

TABLE 2: Distribution of Selected Characteristics of 84,966 Radiologic Technologists Who Completed the Second Survey and Were Eligible for Mortality or Incidence Analyses (continued)

Characteristic	Performance of Fluoroscopically Guided Interventional Procedures						
	Ever Worked With		Never Worked With		Unknown		Total
	No.	%	No.	%	No.	%	No.
Alcohol intake (drinks/wk)							
< 1	10,719	23	30,938	67	4258	9	45,915
1–6	6249	28	14,441	64	1918	8	22,608
≥ 7	2616	28	5757	62	899	10	9272
Unknown	1398	19	3659	51	2114	29	7171
Cigarette smoking							
Never smoked	10,866	24	29,708	66	4645	10	45,219
Former smoker	6761	24	17,705	64	3262	12	27,728
Current smoker	3190	28	7006	62	1118	10	11,314
Unknown	165	23	376	53	164	23	705
Body mass index							
< 25	9999	23	28,441	66	4626	11	43,066
25.0–29.9	6900	26	16,475	63	2814	11	26,189
≥ 30.0	3641	26	8822	64	1400	10	13,863
Unknown	442	24	1057	57	349	19	1848
Year first worked							
Before 1960	2311	16	9663	66	2703	18	14,677
1960 or after	17,872	27	42,941	64	5792	9	66,605
Never worked	86	14	423	69	103	17	612
Unknown	713	23	1768	58	591	19	3072
Age first worked (y)							
< 21	12,269	25	32,791	66	4899	10	49,959
≥ 21	7914	25	19,813	63	3596	11	31,323
Never worked	86	14	423	69	103	17	612
Unknown	713	23	1768	58	591	19	3072
No. of years worked (at second questionnaire)							
< 10	2180	14	11,495	73	2051	13	15,726
10–19	7440	26	18,453	65	2298	8	28,191
≥ 20	9358	30	18,625	61	2766	9	30,749
Never worked	86	14	423	69	103	17	612
Unknown	1918	20	5799	60	1971	20	9688

Note—Percentages may not total 100 owing to rounding.

1950, 1950–1959, 1960–1969, 1970 and beyond) as a proxy for unmeasured total occupational radiation dose and reported work with brachytherapy and other radionuclide procedures. Other covariates were considered for inclusion in the final models for specific outcomes if they were considered a priori to be risk factors and thus potential confounders (Table 1). Finally, we performed analyses stratified by sex.

Tests for interaction were conducted with the likelihood ratio test [10]. All statistical tests were two sided and were conducted with SAS software (version 9.3, SAS Institute). Missing values were included as a separate category for all categoric variables. A Schoenfeld residual test [11] with respect to the main covariates in the model (sex, fluoroscopically guided interventional procedures status) and models with interactions for age and fluoroscopically guided procedure status (and sex) were used to formally test the assumed proportionality of the hazard over the age timescale.

Results

The number of events and person-years at risk for the various cancer outcomes are summarized in Table S4. Selected demographic characteristics stratified by ever or never worked with fluoroscopically guided interventional procedures are shown in Table 2 for the 90,957 radiologic technologists who completed the second questionnaire and were eligible for any mortality or incidence analysis. Although differences were small, technologists who worked with fluoroscopically guided interventional procedures were more likely to be male, younger, better educated, users of alcohol and tobacco, have a higher income, and have worked more years than technologists who never worked with fluoroscopically guided interventional procedures.

The results were similar for minimally adjusted and fully adjusted Cox proportional hazards models (Table 3). In fully adjusted models, the incidence of basal cell carcinoma, squamous cell carcinoma, cancers of the thyroid, prostate, lung, colon and rectum, and non-CLL leukemia were not associated with working with fluoroscopically guided interventional procedures. Although there was a small suggestive increase in incidence of all cancers combined other than NMSC (HR, 1.08; 95% CI, 1.00–1.17), mortality from all cancers combined including NMSC was not elevated. We observed elevated risks for incidence of female breast cancer (HR, 1.16; 95% CI, 1.02–1.32) and melanoma (HR, 1.30; 95% CI, 1.05–1.61) among technologists who worked with fluoroscopically guided interventional procedures.

No significant increase in mortality was observed from all malignant disease combined among technologists who worked with fluoroscopically guided interventional procedures (HR, 1.00; 95% CI, 0.88–1.14). Similarly, mortality risks from female breast cancer, cancer of the prostate, lung, or colon and rectum, or non-CLL leukemia were not elevated in association with performing or assisting with fluoroscopically guided interventional procedures. However, on the basis of 26 exposed cases, we observed approximately twofold significantly increased risk of brain cancer among technologists who worked with fluoroscopically guided interventional procedures (HR, 2.55; 95% CI, 1.48–4.40).

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TABLE 3: Hazard Ratios and 95% CIs for Mortality and Incidence From Malignant Cancers and Specific Cancer Outcomes Associated With Working With Fluoroscopically Guided Interventional Procedures Among U.S. Radiologic Technologists Who Completed the Second Survey (1995–1998)

	Incidence[a]				Mortality[b]			
	No. of Cases		Hazard Ratio[c]		No. of Cases		Hazard Ratio[c]	
Cancer Type	Ever Worked With	Never Worked With	Minimally Adjusted	Fully Adjusted	Ever Worked With	Never Worked With	Minimally Adjusted	Fully Adjusted
All cancers excluding nonmelanoma skin cancer	900	2431	1.07 (0.99–1.16)	1.08 (1.00–1.17)	341	1043	1.03 (0.91–1.17)	1.00 (0.88–1.14)
Brain cancer					26	34	2.16 (1.28–3.66)	2.55 (1.48–4.40)
Female breast cancer	324	962	1.18 (1.04–1.34)	1.16 (1.02–1.32)	28	97	1.10 (0.72–1.68)	1.07 (0.69–1.66)
Melanoma	141	288	1.32 (1.07–1.62)	1.30 (1.05–1.61)	6	25	0.66 (0.27–1.65)	0.63 (0.25–1.61)
Basal cell carcinoma	501	1427	0.98 (0.89–1.09)	0.98 (0.88–1.09)	—	—		
Squamous cell carcinoma	144	418	1.01 (0.83–1.22)	0.98 (0.80–1.19)	—	—		
Thyroid cancer	32	96	0.90 (0.60–1.35)	0.91 (0.61–1.38)	—	—		
Prostate cancer	114	211	0.98 (0.78–1.23)	1.01 (0.80–1.28)	8	15	1.25 (0.53–2.97)	1.54 (0.62–3.83)
Lung cancer	19	70	0.91 (0.54–1.53)	0.89 (0.52–1.53)	94	288	1.11 (0.87–1.41)	0.99 (0.77–1.27)
Colorectal cancer	48	159	0.85 (0.61–1.18)	0.88 (0.62–1.23)	20	79	0.80 (0.48–1.31)	0.79 (0.47–1.32)
Leukemia other than chronic lymphocytic leukemia	6	19	0.84 (0.33–2.14)	0.85 (0.32–2.25)	16	31	1.46 (0.78–2.71)	1.53 (0.80–2.90)

Note—Dash (—) indicates not analyzed. Values in parentheses are 95% CI.

[a]To be eligible for incidence analyses, technologists had to complete both the second and third surveys. Follow-up began at completion of the second survey and ended at the earliest of date of diagnosis of the outcome of interest, date of diagnosis of other events, or completion of the third survey.

[b]To be eligible for mortality analyses, technologists had to complete the second survey. Follow-up began at completion of the second survey and ended at the earliest of date of death or December 31, 2008 (end of study).

[c]Minimally adjusted models used age as the timescale, were stratified by birth cohort (before 1930, 1930–1939, 1940–1949, 1950 and beyond) to control for secular trends, and included sex as a variable for adjustment. Fully adjusted models additionally included covariates listed in Table 1.

The direction and magnitude of risk were consistent for incidence and mortality estimates for breast cancer but not for melanoma (although numbers were small for melanoma mortality) (Table 3). Risks were similar for men (HR, 2.79; 95% CI, 1.15–6.78; number exposed, 13) and women (HR, 1.91; 95% CI, 0.97–3.75; number exposed, 13) for brain cancer mortality. They were also similar for men (HR, 1.25; 95% CI, 0.86–1.83; number exposed, 49) and women (HR, 1.33; 95% CI, 1.04–1.70; number exposed, 92) for melanoma incidence.

Schoenfeld residuals with respect to the main covariates in the model (sex, fluoroscopically guided interventional procedure status) and in models with interactions for age and fluoroscopically guided interventional procedure status (and sex) did not suggest any lack of proportionality of the hazard over the age timescale ($p > 0.05$ in all cases). There were no indications of lack of convergence.

Discussion

Previous epidemiologic studies of radiologists and radiologic technologists have shown excess risks of leukemia, skin, and female breast cancer in those employed before 1950, but there has been little consistent evidence of cancer risk increases in subsequent years [12, 13]. Cancer risk data for physicians and technologists performing fluoroscopically guided procedures are even more limited. In a large cohort study of registered radiologic technologists, we evaluated incidence and mortality risks of all cancers combined and for specific cancer outcomes associated with working with fluoroscopically guided interventional procedures. Although there was a small suggestive increase in incidence of all cancers combined other than NMSC, mortality from all cancers combined including NMSC was not elevated. We similarly observed no elevated risks of cancers of the thyroid, prostate, lung, or colon and rectum; non-CLL leukemia; or NMSC in workers who reported performing fluoroscopically guided interventional procedures. However, we observed an approximately twofold increased risk of brain cancer mortality (based on 26 exposed cases) and modest elevations in breast cancer incidence and melanoma incidence among technologists who reported working with fluoroscopically guided interventional procedures.

Previous epidemiologic studies have not specifically addressed brain cancers in individuals performing fluoroscopically guided interventional procedures. However, given the potential for radiation exposure, investigators have expressed concern regarding possible elevated risk of brain cancer among physicians performing these procedures [14, 15]. In addition, a small cluster of brain cancer cases was observed among Ontario cardiologists, which the authors attributed to either chance or radiation exposure during fluoroscopically guided interventional cardiac procedures [16]. Because the brain is unprotected by thyroid shields, lead goggles, or lead aprons, doses to the head are likely to be higher than those to other anatomic sites on radiologic technologists.

Elevated risk of glioma and other types of brain tumors has been observed among individuals irradiated in childhood for benign medical conditions [17–19] and receiving radiotherapy for first primary tumors [20, 21].

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The risks of brain cancer at lower radiation doses are less clear [22]. Increased risks of schwannoma (largely benign nervous system tumors), but not glioma, have been observed among atomic bomb survivors [23]. A case-control study based on interview-derived information showed an approximately twofold risk of glioma among adults who reported undergoing three or more CT examinations of the head and neck (odds ratio, 1.97; 95% CI, 0.92–4.23) but only for individuals with a family history of cancer [24]. A more recent medical record–based cohort study of individuals in the United Kingdom undergoing CT as children or young adults [25] showed a statistically significant positive association between radiation dose from CT and brain tumors. It is important to recognize, however, that the radiation sensitivity of brain tissue is likely to be much higher for children than for adults [8, 26].

Breast tissue is one of the most sensitive to the carcinogenic action of radiation, particularly at young ages, and previous epidemiologic studies have consistently shown elevated risks of breast cancer with exposure to ionizing radiation. A pooled analysis of data from eight cohorts showed that excess risk of breast cancer depended linearly on dose [27]. Earlier evaluations of the U.S. Radiologic Technologists study cohort identified increased risks of breast cancer incidence [28] and mortality [29] among individuals who began working as radiologic technologists in earlier periods, when radiation doses were likely higher. If well fitted, completely covering the breast, and worn at all times during occupational radiation exposure, lead aprons essentially block the scattered radiation reducing exposure to the breast to negligible levels. The modest increase in risk of breast cancer incidence we observed among women performing fluoroscopically guided interventional procedures, if due to radiation, could have been due to incomplete coverage of the female breast by poorly fitting lead aprons [30].

Although there has been consistent evidence linking NMSC with exposure to moderate to high levels of ionizing radiation, the evidence has been less convincing for melanoma [31–33]. Studies of atomic bomb survivors and individuals treated for ringworm with radiotherapy have shown no association between the well-characterized dose of ionizing radiation and risk of melanoma. In a previous analysis of the U.S. Radiologic Technologists Study cohort, we reported a nonstatistically significant elevated incidence of melanoma among technologists who began working before 1950 (HR, 1.8; 95% CI, 0.6–5.5), when radiation exposures were likely higher, compared with those who began working in 1970 or later. Our finding of increased risk of melanoma among radiologic technologists working with fluoroscopically guided interventional procedures may be due to chance, given the small numbers of incident cases and deaths, but requires further investigation. The lack of association with basal cell carcinoma, a usually radiogenic site, is less surprising given the strong radioepidemiologic [33, 34] and radiobiologic [35–37] evidence that basal cell carcinoma has a highly upwardly curved dose response, consistent with the presence of a threshold of at least 1 Gy, taken together with the fact that there are hardly any individuals with a cumulative dose greater than 1 Gy [38].

Two comprehensive reviews [39, 40] of occupational radiation exposure from fluoroscopically guided interventional procedures indicated considerable variability in the typical radiation dose to physician operators in the past. A physician who performs fluoroscopically guided interventional procedures on a regular basis and uses appropriate protective measures could be expected to receive an annual occupational radiation dose of 2–4 mSv [41–44]. Unfortunately, there is a paucity of literature on radiation exposure to radiologic technologists from fluoroscopically guided interventional procedures. In the United States, radiologic technologists typically wear the same protective garments (lead apron, thyroid collar) used by physician operators. The use of radiation-protective eyewear is not universal and was less common in earlier decades. The risk of cataract was analyzed in U.S. radiologic technologists [45] with an older version of the occupational dosimetry used in the U.S. Radiologic Technologists Study [46], which did not explicitly account for dose from fluoroscopically guided interventional procedures. There was weak evidence ($p = 0.15$) of an increasing trend of cataract prevalence with occupational dose, although a much stronger increasing trend was found with numbers of personal diagnostic radiographs ($p < 0.001$). We plan to repeat this analysis with a group of workers who report use of fluoroscopically guided interventional procedures when individual radiation doses are available from ongoing efforts to refine our recent dosimetry system [38].

The cohort design of our study was a major strength because it allowed assessment of fluoroscopically guided interventional procedure exposure before the ascertainment of cancer, thus eliminating the potential for recall bias. In addition, the large cohort size and the length of follow-up allowed adequate power to detect modest to large associations for occurrence of some solid tumors. The ability to examine radiation-related risk among women is an additional strength, given that previous populations of medical radiation workers studied have been largely male. Finally, we were able to adjust for several nonradiation risk factors because of the availability of covariate information on all study members.

The most important limitation of our study was the lack of detailed information on radiation doses associated with performing fluoroscopically guided interventional procedures. Our second questionnaire did not capture detailed information on exposure modifiers that could have led to potential variation of dose over time, such as frequency, intensity, and type of occupational exposure from fluoroscopically guided interventional procedures by time period. In addition, not all incident outcomes were validated, which may have led to some misclassification. However, the high PPVs (81–100%) for cancers other than brain cancer (PPV = 19%) and melanoma (PPV = 72%) lend credence to their accuracy (Table S1). With a 98% PPV for breast cancer incidence, the results are unlikely to have been greatly affected by misclassification. Moreover, the observed magnitude of risk of breast cancer was consistent for incidence (self-reported) and mortality (death records). Because of the small number of incident brain tumors reported and the low PPV for brain cancer incidence, we did not evaluate risk for this outcome. The elevated risk we observed for brain cancer mortality was based on death certificates rather than self-reported data, and the validity of brain cancer reported on death certificates has been found to be very high in the United States (93.4%) [47]. Because we lacked validation rates for all endpoints, we did not use more formal methods for adjusting rates and counts based on PPV [48].

Although we controlled for other potential exposures, including a proxy measure for total occupational radiation exposure and outcome-specific risk factors, it is possible that residual confounding by these or other unmeasured factors was responsible for the observed risks. In addition, our power to detect small increases in risk was limited for most outcomes. Incidence of several cancers, including breast cancers and melanoma, appeared higher in this

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population than in the U.S. general population (Table S5). This is partially due to the inclusion of in situ cancers in the U.S. Radiologic Technologists Study data but could also represent some misclassification in self-report or higher levels of screening in this population of medical radiation workers who have greater access to medical care. Finally, the short follow-up time in relation to radiation-induced cancer latency for solid tumors and the small number of outcomes (particularly for brain cancers) preclude the drawing of strong conclusions from these data.

The immense patient benefit provided by fluoroscopically guided interventional procedures is indisputable, and the risks that we observed for brain cancer, breast cancer, and melanoma among technologists who reported working with these procedures should be interpreted in that context. Although our initial findings could be due to exposure to low-dose radiation, we cannot rule out the possibility of confounding by nonradiation factors or chance. Our findings must be confirmed in future epidemiologic studies of technologists and physicians performing fluoroscopically guided interventional procedures, ideally incorporating detailed individual radiation dose to clarify the risks of a broad range of cancers, benign tumors, selected cancer precursor conditions, circulatory diseases, and other radiation-associated diseases in these occupations. Patients should continue to undergo medically necessary imaging examinations [49], but health care providers should keep radiation exposure as low as reasonably achievable without compromising essential diagnostic information.

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Study Guide

Cancer Risks in U.S. Radiologic Technologists Working With Fluoroscopically Guided Interventional Procedures, 1994–2008

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Introduction

1. Does this study address a clinical question?
2. Is an appropriate rationale provided for performing the study? What population is being studied?

Methods

3. What were the inclusion criteria for the study? What were the exclusion criteria?
4. What type of study is described? What limitations exist in this type of study?
5. What statistical measurements are generated and compared in this study? How are these statistics generated? How are the cohorts evaluated in the study stratified?

Results

6. What conclusions are reached in the study? Which malignancies have a higher frequency or mortality rate in technologists involved in fluoroscopically guided interventional procedures?
7. Which malignancies are not associated with performance of fluoroscopically guided interventional procedures? Of those that are associated with fluoroscopically guided interventional procedures, which have increased mortality risks?

Physics

8. What limits are set by the International Commission on Radiological Protection for annual and lifetime whole-body doses? How do these compare with background dose for the general population?

Discussion

9. How might the data described in this study affect the clinical practice of technologists involved in fluoroscopically guided interventional procedures?
10. The data presented in this study lack correlation with any personnel dosimetry measurements. How does this affect the importance of this study?
11. The study uses data from a registry of U.S.-registered technologists. What other studies related to occupation radiation dose could be obtained from surveying this population?

Background Reading

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*Please note that the authors of the Study Guide are distinct from those of the companion article.