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Cancer and circulatory disease risks in U.S. radiologic technologists associated with performing procedures involving radionuclides

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Abstract

Objectives: The number of nuclear medicine procedures has increased substantially over the past several decades, with uncertain health risks to the medical workers who perform them. We estimated risks of cancer and circulatory disease incidence and mortality associated with performing procedures involving the use of radionuclides.

Methods: From a nationwide cohort of 90,955 U.S. radiologic technologists who completed a mailed questionnaire during 1994–1998, 22,039 reported ever performing diagnostic radionuclide procedures, brachytherapy, radioactive iodine therapy, or other radionuclide therapy. We calculated multivariable-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for incidence (through 2003–2005) and mortality (through 2008) associated with performing these procedures.

Results: Ever (versus never) performing radionuclide procedures was not associated with risks for most endpoints examined. However, we observed increased risks for squamous cell carcinoma of the skin (HR=1.29, 95% CI: 1.01–1.66) with ever performing diagnostic radionuclide procedures, for myocardial infarction incidence (HR=1.37, 95% CI: 1.10–1.70), all-cause mortality (HR=1.10, 95% CI: 1.00–1.20), and all-cancer mortality (HR=1.20, 95% CI: 1.01–1.43) with ever performing brachytherapy, and for mortality from all causes (HR=1.14, 95% CI: 1.01–1.30), breast cancer (HR=2.68, 95% CI: 1.10–6.51), and myocardial infarction (HR=1.76, 95% CI: 1.02–3.04) with ever performing other radionuclide therapy procedures

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(excluding brachytherapy and radioactive iodine); increasing risks were also observed with greater frequency of performing these procedures, particularly before 1980.

Conclusions: The modest health risks among radiologic technologists performing procedures using radionuclides require further examination in studies with individual dose estimates, more detailed information regarding types of procedures performed and radionuclides used, and longer follow-up.

Keywords

nuclear medicine; ionizing radiation; cardiac diseases; cancer; occupational exposure

INTRODUCTION

The field of nuclear medicine, in which radiopharmaceuticals are utilized in the diagnosis and treatment of a wide range of medical conditions, has undergone dramatic changes since its recognition as an official medical specialty in 1971.[1] In the U.S., the number of nuclear medicine procedures performed increased from an estimated 7 million during 1980–1982 to 18 million in 2006.[2] Between the early 1970s and early 2000s, the corresponding effective doses to patients increased 5- to 7-fold, mostly attributable to an increase in relatively high-dose diagnostic cardiac procedures.[3] Such procedures have resulted in enormous medical benefits to patients. However, exposure to radiation, especially from higher-dose or frequently-performed procedures using radionuclides, poses potential health risks to the medical workers who perform them.

In a large prospective cohort of radiologic technologists, we evaluated risks for cancer and circulatory disease incidence and mortality in technologists who ever versus never performed procedures involving the use of radionuclides. To our knowledge, this is the first epidemiologic study to prospectively assess risks for cancer and circulatory disease incidence and mortality in medical radiation workers working with radionuclide procedures.

METHODS

Overview of Study

The U.S. Radiologic Technologists (USRT) Study is an ongoing collaboration between the U. S. National Cancer Institute, the University of Minnesota, and the American Registry of Radiologic Technologists (ARRT). The study population and methods have been described in detail previously.[4,5] Briefly, a search of the ARRT records identified 146,022 radiologic technologists who were certified for at least 2 years during 1926 through 1982 and resided in any U.S. state or territory. The cohort is followed through a combination of annual recertifications with the ARRT and linkage with the Social Security Administration database to determine vital status. Those who are found deceased or presumed deceased are linked to the National Death Index (NDI-*Plus*) to ascertain causes of death. The study was approved by the Institutional Review Boards of the National Cancer Institute and the University of Minnesota, and all subjects provided written informed consent.

Information about cancer and circulatory disease incidence, work history as a radiologic technologists, personal diagnostic and therapeutic radiation, and cancer risk factors was ascertained in mailed questionnaires (sent in 1983–89, 1994–98, and 2003–05). We attempted to validate a subset of reported cancers with pathology reports and other medical records. Self-reported but unconfirmed cancers (other than brain cancer) were included in analyses due to high positive predictive values (70–100%).

Study Population and Follow-up

Eligible for the current study were the 90,955 out of 126,628 living technologists (72%) who completed the second survey during 1994–1998. Incidence and mortality were evaluated separately due to differences in eligibility criteria, sources of data, and length of follow-up. Incidence analyses for cancers other than non-melanoma skin cancer (NMSC) were restricted to the 63,482 technologists who responded to both the second and third surveys and did not have a prior diagnosis of cancer other than NMSC through the second survey. Technologists who reported a diagnosis of NMSC by the second survey (n=5,863) were additionally excluded from analyses of basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) of the skin. Circulatory disease incidence analyses were restricted to the 63,182 technologists who responded to both the second and third surveys and did not report a prior diagnosis of circulatory disease other than hypertension by completion of the second survey. Person-time for incidence analyses was calculated from completion of the second survey to the earliest of date of diagnosis of any first primary cancer other than NMSC (for other cancer incidence analyses), any first primary cancer (for NMSC incidence analyses), any circulatory disease other than hypertension (for circulatory disease incidence analyses), or completion of the third survey (2003–2005).

Cancer mortality analyses were restricted to the 84,952 technologists who responded to the second survey and were cancer-free other than NMSC at that time. Circulatory disease mortality analyses were restricted to the 86,700 technologists who responded to the second survey and had no prior diagnosis of circulatory disease other than hypertension at that time. Person-time for mortality analyses accrued from second survey completion until date of death or December 31, 2008, whichever came first.

Incidence and mortality outcomes were chosen *a priori* according to the following criteria: cancers that have been consistently associated with radiation exposure (non-CLL leukemia, BCC, and cancers of the female breast, thyroid, lung, brain, and colorectum),[6] other cancers associated with radiation in the USRT cohort (melanoma),[7] cancers of specific concern to medical radiation workers (brain cancer, SCC),[8] circulatory diseases that have been associated with radiation (stroke, heart diseases [including ischemic heart disease and, more specifically, myocardial infarction]),[9–11] and a common cancer not consistently associated with radiation exposure (prostate cancer) to check for the specificity of radiation-related associations. For specific ICD-10 codes for the outcomes evaluated,[12] see Supplemental Table 1.

Performing procedures using radionuclides was evaluated in relation to incidence and mortality for all cancers combined, female breast cancer, melanoma, prostate cancer, lung cancer, colorectal cancer, leukemia other than chronic lymphocytic leukaemia (non-CLL), stroke, and myocardial infarction. Because of low fatality from BCC, SCC, and thyroid cancer, only incident outcomes were evaluated. For all causes combined, all circulatory diseases, all heart diseases, ischemic heart disease, and brain cancer, only mortality outcomes were evaluated.

Exposure Assessment

In addition to other work history questions, technologists were asked to report in the second survey whether they ever performed selected medical procedures and, if so, how frequently (never or rarely, monthly, weekly, or daily) they performed these procedures during three defined time periods (before 1980, 1980–1989, and 1990+). Four types of procedures involving radionuclides were queried, including diagnostic radionuclide, brachytherapy, radioactive iodine therapy, and other radionuclide therapy (e.g., for malignant effusion or for palliative treatment of bone metastases).

Statistical Analysis

Cox proportional hazards models were used to compute hazard ratios (HRs) with 95% confidence intervals (CIs) associated with ever, compared with never, performing procedures involving radionuclides. These models used age as the time scale (to control for age), were stratified on birth cohort (<1950, 1950–59, 1960–69, 1970+) to control for secular trends, and were adjusted for sex and ever/never worked with all other radionuclide procedures. Missing values were modeled using a separate indicator variable. We further evaluated risks in relation to the frequency (never, monthly, weekly, daily) with which they performed these procedures before 1980, 1980–1989, and 1990+. Linear trends were assessed by assigning ordinal values to each category level and modeling these values continuously, excluding subjects with missing values and those who did not work in that time period.

Covariates that were considered *a priori* to be risk factors for specific outcomes were evaluated as potential confounders (see Supplemental Table 1 for a list of covariates examined by outcome). Data on alcohol consumption, cigarette smoking, 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 were obtained from the second mailed survey. Education was obtained from the third questionnaire.

Formal tests did not indicate a lack of convergence of the Cox models or departure from the assumption that hazards were proportional over the age timescale.

All statistical tests were two-sided and were performed using the SAS Version 9.2 statistical software (Cary, NC).

RESULTS

Table 1 compares selected demographic and work history characteristics for the 90,955 radiologic technologists who were eligible for any of the incidence or mortality analyses by ever/never performed diagnostic radionuclide, brachytherapy, radioactive iodine therapy, or other radionuclide therapy procedures. The majority (77%) of participants were female. A total of 22,039 technologists (24% of the 90,955 respondents) reported ever working with procedures involving radionuclides, including 14,270 (16%) with diagnostic radionuclide, 6,809 (7%) with brachytherapy, 11,153 (12%) with radioactive iodine therapy, and 5,390 (6%) with other radionuclide therapy procedures. The distributions among technologists who ever and never performed any and specific radionuclide procedures were generally similar according to the characteristics in Table 1. Notable exceptions include consistently higher percentages of male and college-educated technologists and technologists who ever performed fluoroscopically-guided procedures among those who ever versus never performed these procedures. Additionally, technologists born in the 1940s, who were generally 50–59 at completion of the second survey, were somewhat more likely to have ever vs. never performed brachytherapy, radioactive iodine, and other radionuclide therapy procedures.

Because additional adjustment for the potential confounders (see Supplemental Table 1 and 2), as well as ever (versus never) performing fluoroscopically-guided interventional procedures, had little influence on the HRs (<10% change in log-transformed HRs for specific radionuclide procedures after inclusion in models), results presented were based on minimally-adjusted models (i.e, adjusted only for sex and work with other nuclear medicine procedures and stratified by birth cohort). We found no associations between ever working with diagnostic radionuclide procedures and all-cancer incidence, total mortality, or mortality from specific causes; however, we observed a 29% increased risk for SCC incidence (HR=1.29, 95% CI: 1.01–1.66) (Table 2). Ever working with brachytherapy procedures was associated higher myocardial infarction incidence (HR=1.37, 95% CI: 1.10–1.70), total mortality (HR=1.10, 95% CI: 1.00–1.20), and mortality from all cancers (HR=1.20, 95% CI: 1.01–1.43), but no associations were observed for the other outcomes examined.

Apart from an inverse association for female breast cancer mortality (HR=0.40, 95% CI: 0.17–0.94), based on 10 deaths, no associations were observed for ever working with radioactive iodine therapy procedures.

While we observed no association between ever working with other radionuclide therapy and cancer or cardiovascular disease incidence, increased mortality risks were observed for all causes (HR=1.14, 95% CI: 1.01–1.30), female breast cancer (HR=2.68, 95% CI: 1.10–6.51), and myocardial infarction (HR=1.76, 95% CI: 1.02–3.04). Ever working with any radionuclide procedure was associated with increased all-cause mortality (HR=1.13, 95% CI: 1.06–1.19) and lung cancer mortality (HR=1.37, 95% CI: 1.10–1.70).

For the outcomes that were significantly associated with ever (versus never) performing radionuclide procedures, we further investigated risks associated with frequency of performing these procedures (never, monthly, weekly, daily) in three time periods (before 1980, 1980–89, 1990+) (Supplemental Table 3). Positive associations were observed for technologists who more frequently performed the procedures before 1980 for SCC incidence with diagnostic radionuclide procedures, for all-cause mortality, all-cancer (except NMSC) mortality, and myocardial infarction incidence with brachytherapy, and for all-cause, female breast cancer, and myocardial infarction mortality with other radionuclide therapy procedures. All-cause and myocardial infarction mortality increased significantly with frequency performed other radionuclide therapy procedures in 1980–1989. No associations were observed with frequency performed radionuclide procedures in 1990+.

DISCUSSION

Based on a relatively short follow-up from completion of the second survey (1994–1998) to completion of the third survey (2003–2005) for incident outcomes (median=9 years) and to the end of 2008 for mortality outcomes (median=13 years), results from this study suggest some potential modest adverse health effects associated with performing radionuclide procedures, particularly for three types of outcomes: SCC in technologists performing diagnostic radionuclide procedures, female breast cancer in technologists performing other radionuclide therapy procedures (this category excludes brachytherapy and radioactive iodine therapy), and myocardial infarction in technologists performing brachytherapy procedures and other radionuclide therapy procedures. All-cause mortality was also associated with ever performing brachytherapy, and mortality from all causes and all cancers (except NMSC) were related to ever performing other radionuclide procedures. Greater frequency with which these procedures were performed, especially before 1980, was positively associated with risks of most of these outcomes.

Few studies have evaluated health risks associated with repeated, chronic exposure to low doses of radiation, as experienced by radiologic technologists and other medical workers exposed to radiation. Although studies of nuclear medicine workers indicate that annual equivalent doses are well below the maximum recommended levels for individuals occupationally exposed to ionizing radiation,[13–16] risks associated with regular exposure to radiation at these lower levels over a prolonged period of time remain unclear. Prospective studies of occupational exposure to radiation among medical workers, including radiologists and radiologic technologists, have shown elevated incidence or mortality risks for leukemia,[17–22] lymphoma,[19] cancers of the skin,[19,20] pancreas,[20] lung,[19,20] breast,[18,23,24] and thyroid,[25] plus ischemic heart disease and cerebrovascular disease,[18] particularly for those who worked in the earliest decades when doses to medical radiation workers were generally highest. Results from studies of general radiologists and radiologic technologists may not be generalizable to technologists who are certified in nuclear medicine technology and may receive higher cumulative radiation exposure owing to the wide range in photon energies of the radioisotopes used in nuclear medicine procedures and the limited effectiveness of lead aprons in protecting against radiation from procedures involving higher-energy photons, such as positron-emission tomography.[26] Nonetheless, our results, particularly for breast cancer and certain circulatory diseases, are largely consistent with studies of other medical workers, as well as studies of Japanese atomic bomb survivors that are based on a single acute exposure.[11,27] The increased risk of circulatory diseases in this study was similarly observed in the National Registry for Radiation Workers but not the 15-Country Study of nuclear workers.[28,29]

While data on the radiation-related risks of specific types of NMSC are limited, studies of Japanese atomic bomb survivors and patients treated for tinea capitis have shown associations with BCC but not SCC of the skin.[27,30,31] Our finding of an increased risk for SCC, but not BCC, related to ever performing diagnostic radionuclide procedures was supported by an observed increasing risk with increasing frequency with which these procedures were performed, especially before 1980. While similar excesses were not found in technologists who performed brachytherapy, radioiodine therapy, and other radionuclide therapy procedures, which may confer larger per-procedure radiation doses to technologists, diagnostic procedures are generally performed with greater frequency and may have yielded higher cumulative doses. The lack of associations in the current study for leukemia and cancers occurring in other radiosensitive sites, including the brain, thyroid, and colon, may reflect the relatively small numbers of cases or measurement error resulting from the relatively non-specific information available on the specific types of procedures performed.

This was the first study of radiologic technologists to evaluate the relationship between performing procedures involving radionuclides and risks for major health outcomes. A key strength of the study was the prospective design, which minimized the potential for recall and selection biases. Compared with other studies of medical radiation workers, the large number of female participants provided a unique opportunity to assess breast cancer risks. Finally, the detailed covariate data allowed for control of potential confounders.

The major limitation of this study was the lack of estimated doses from the specific procedures examined. We also had limited information on the specific types of procedures performed and other factors related to the cumulative radiation exposure from these procedures during the years in which the participants trained and worked as radiologic technologists. While adjustment for some of the major outcome-specific risk factors did not appreciably alter the radiation-related results, it is possible that residual confounding by these or other unmeasured factors could explain some of the increased risks observed. Also, in view of the total number of associations examined, some of the findings could be due to chance alone.

In this study of U.S. radiologic technologists certified before 1980, ever versus never performing procedures involving radionuclides was not associated with the majority of the cancer and circulatory disease outcomes that we examined. However, we found some evidence that performing these procedures was associated with modest elevations in mortality from all causes, all cancers other than NMSC, female breast cancer, lung cancer, and myocardial infarction, and incidence of SCC of the skin and myocardial infarction. Because per-procedure radiation doses and demand for many of these procedures continue to increase, the preliminary findings from the current study should motivate additional studies on the health risks to nuclear medicine technologists and other medical radiation workers who perform procedures involving radionuclides. Ideally, such studies will have longer follow-up and include more detailed information on factors that predict exposure, such as the specific types of procedures and tasks performed, radioisotopes and protection practices used, and length of contact with and proximity to patients.[26,32]

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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What this paper adds

- Although the number of nuclear medicine procedures has increased substantially over the past several decades, there is little information about the risks of radiation-related cancers and circulatory diseases to the medical workers who perform them.
- Performing procedures involving radionuclides was associated with some modest adverse health effects, including squamous cell carcinoma of the skin in technologists performing diagnostic radionuclide procedures, female breast cancer in technologists performing other radionuclide therapy procedures (this category excludes brachytherapy and radioactive iodine therapy), and myocardial infarction and in technologists performing brachytherapy and other radionuclide therapy procedures.
- Greater frequency with which these procedures were performed, especially before 1980, was positively associated with risks of most of these outcomes.
- These findings provide preliminary evidence that exposure to radiation from procedures involving radionuclides, especially before 1980, may be linked with an increased risk of certain cancers and circulatory diseases.

Table 1.

Distribution of selected characteristics in U.S. radiologic technologists who ever and never performed nuclear medicine procedures

Characteristic	Diagnostic radionuclide		Brachytherapy		Radioactive iodine therapy		Other radionuclide therapy		Any radionuclide procedure	
	Ever	Never	Ever	Never	Ever	Never	Ever	Never	Ever	Never
Number of participants	14,270	68,264	6,809	74,928	11,153	70,383	5,390	76,820	22,039	57,018
Male, %	33	21	21	23	29	22	31	22	28	22
Year of birth, %										
<1930	4	6	7	6	5	6	4	6	5	6
1930–1939	10	14	17	12	15	12	14	13	13	12
1940–1949	36	33	39	33	41	32	41	33	37	32
1950–1959	50	46	36	48	38	49	40	47	44	49
≥1960	1	1	1	1	1	1	1	1	1	1
Age at completion of second survey, %										
30–39	16	17	11	17	10	18	11	17	14	18
40–49	55	47	44	49	48	48	51	48	50	48
50–59	21	24	30	22	29	22	27	23	25	21
≥ 60	8	13	16	12	12	12	11	12	11	12
Race, %										
White	95	95	96	95	95	95	93	95	95	93
Black	2	3	3	3	3	3	4	3	2	4
Other	3	2	2	2	3	2	3	2	2	2
Unknown	0	0	0	0	0	0	0	0	0	0
Education, %										
High school or less	0	1	0	1	0	1	0	1	0	1
Other (vocational)	3	2	3	2	3	2	3	2	3	2
Rad tech program	23	32	26	31	24	31	21	31	25	32
College	37	29	35	30	35	30	37	30	35	29
Unknown	36	37	36	37	37	37	38	37	37	37
Alcohol intake, %										
<1 per week	53	56	53	55	51	56	50	55	53	56
1–6 per week	29	27	27	27	28	27	28	27	27	27

Characteristic	Diagnostic radionuclide		Brachytherapy		Radioactive iodine therapy		Other radionuclide therapy		Any radionuclide procedure	
	Ever	Never	Ever	Never	Ever	Never	Ever	Never	Ever	Never
≥7 per week	12	11	12	11	13	11	14	11	12	11
Unknown	7	7	8	7	8	7	8	7	8	7
Cigarette smoking, %										
Never smoked	53	53	50	53	51	53	50	53	52	54
Former smoker	32	33	34	33	33	33	34	33	33	33
Current smoker	15	13	15	13	15	13	16	13	15	13
Unknown	1	1	1	1	1	1	1	1	1	1
Body mass index , %										
<25	48	51	49	51	48	51	47	51	48	52
25.0–29.9	33	30	31	31	33	30	34	30	32	30
≥30.0	17	16	18	16	17	16	17	16	17	16
Unknown	2	2	2	2	2	2	2	2	2	2
Year first worked , %										
<1960	11	19	23	16	18	17	16	17	16	17
≥1960	85	78	73	80	77	79	80	79	79	80
Never worked	1	1	1	1	1	1	1	1	1	1
Unknown	4	3	3	3	4	3	4	3	4	3
Age first worked, %										
<21	54	60	62	59	57	59	57	59	58	60
≥21	41	36	34	37	38	37	38	37	38	37
Never worked	1	1	1	1	1	1	1	1	1	1
Unknown	4	3	3	3	4	3	4	3	4	3
No. years worked, %										
<10	15	19	15	18	18	17	17	18	17	18
10–19	34	34	30	34	31	34	32	34	32	35
≥20	41	37	43	37	37	38	38	37	39	37
Never worked	1	1	1	1	1	1	1	1	1	1
Unknown	10	10	12	10	13	10	12	10	12	10
Worked with fluoroscopically-guided interventional procedures , %										
Never	54	73	56	70	59	70	53	70	58	73

Characteristic	Diagnostic radionuclide		Brachytherapy		Radioactive iodine therapy		Other radionuclide therapy		Any radionuclide procedure	
	Ever	Never	Ever	Never	Ever	Never	Ever	Never	Ever	Never
Ever	37	22	33	25	30	25	36	24	32	23
Unknown	9	4	11	5	11	5	10	6	11	4

Table 2.

HRs and 95% CIs for all-cause, cancer, and circulatory disease outcomes associated with ever vs. never worked with nuclear medicine procedures

Outcome	Diagnostic radionuclide		Brachytherapy		Radioactive iodine therapy		Other radionuclide therapy		Any radionuclide procedure	
	Events*	HR (95% CI)†	Events*	HR (95% CI)†	Events*	HR (95% CI)†	Events*	HR (95% CI)†	Events*	HR (95% CI)†
Incidence										
All cancer (exc. NMSC)	544/2,865	0.91 (0.82–1.02)	330/3,002	1.09 (0.96–1.23)	494/2,810	1.05 (0.93–1.20)	240/3,125	1.06 (0.90–1.25)	909/2,333	0.98 (0.91–1.06)
Female breast	191/1,121	0.93 (0.77–1.11)	140/1,138	1.19 (0.99–1.43)	187/1,085	1.03 (0.83–1.26)	95/1,197	1.20 (0.92–1.55)	343/904	1.03 (0.91–1.16)
Melanoma	92/343	1.07 (0.81–1.42)	43/384	1.05 (0.76–1.47)	79/340	1.35 (0.96–1.90)	39/391	1.06 (0.70–1.60)	135/280	1.21 (0.99–1.49)
BCC	325/1,622	0.98 (0.85–1.13)	192/1,753	1.16 (0.99–1.35)	270/1,676	0.95 (0.80–1.13)	136/1,827	1.07 (0.86–1.34)	266/523	0.96 (0.84–1.09)
SCC	101/466	**1.29 (1.01–1.66)**	53/509	1.08 (0.81–1.45)	68/487	0.73 (0.53–1.02)	30/531	0.84 (0.54–1.31)	155/387	0.99 (0.82–1.19)
Thyroid	21/107	0.95 (0.55–1.66)	11/120	1.07 (0.56–2.03)	18/112	1.39 (0.73–2.64)	5/124	0.48 (0.17–1.32)	37/86	1.16 (0.78–1.70)
Prostate	69/260	1.12 (0.81–1.54)	23/296	0.81 (0.52–1.26)	44/274	0.72 (0.46–1.13)	22/297	1.04 (0.60–1.83)	88/228	0.83 (0.65–1.06)
Lung	10/81	0.56 (0.26–1.22)	13/78	1.42 (0.75–2.66)	15/74	1.27 (0.61–2.63)	7/83	1.20 (0.45–3.15)	26/62	1.02 (0.64–1.61)
Colorectal	33/184	0.88 (0.57–1.38)	19/196	0.90 (0.55–1.47)	31/176	1.16 (0.71–1.92)	12/199	0.81 (0.40–1.62)	60/140	1.04 (0.77–1.40)
Non-CLL leukemia	1/23	0.29 (0.04–2.37)	1/21	0.72 (0.10–5.46)	1/20	0.88 (0.11–7.22)	0/24	n/a	2/19	0.25 (0.06–1.09)
Stroke	82/445	0.96 (0.72–1.27)	60/451	1.27 (0.95–1.68)	79/447	0.89 (0.65–1.24)	35/479	1.03 (0.67–1.58)	150/351	1.06 (0.88–1.29)
MI	176/729	1.05 (0.86–1.28)	104/771	**1.37 (1.10–1.70)**	139/742	0.82 (0.63–1.06)	78/814	1.24 (0.91–1.67)	267/588	1.06 (0.92–1.23)
Mortality										
All-cause	852/4,821	0.99 (0.91–1.08)	612/4,966	**1.10 (1.00–1.20)**	892/4,767	1.05 (0.95–1.15)	418/5,234	**1.14 (1.01–1.30)**	1,586/3,794	**1.13 (1.06–1.19)**
All cancer (exc. NMSC)	212/1,222	0.92 (0.77–1.10)	164/1,242	**1.20 (1.01–1.43)**	214/1,196	0.96 (0.79–1.16)	102/1,311	1.13 (0.88–1.46)	394/960	1.04 (0.92–1.17)
Brain	6/55	0.50 (0.19–1.31)	5/56	0.93 (0.36–2.44)	8/53	1.24 (0.49–3.19)	2/57	0.60 (0.12–2.95)	14/43	0.79 (0.43–1.45)
Female breast	13/112	0.87 (0.45–1.68)	9/117	0.75 (0.37–1.52)	10/115	**0.40 (0.17–0.94)**	9/119	**2.68 (1.10–6.51)**	25/95	0.72 (0.47–1.12)
Melanoma	6/28	0.67 (0.23–1.99)	6/26	1.92 (0.73–5.05)	7/25	1.24 (0.38–4.00)	3/27	1.26 (0.28–5.73)	10/19	1.25 (0.58–2.69)
Prostate	2/24	0.49 (0.09–2.58)	3/22	1.66 (0.46–1.52)	2/21	0.82 (0.14–4.87)	1/25	0.80 (0.08–8.49)	6/17	0.92 (0.36–2.33)
Lung	66/326	1.01 (0.73–1.39)	53/325	1.30 (0.95–1.78)	74/306	1.24 (0.88–1.75)	32/350	0.99 (0.63–1.56)	127/234	**1.37 (1.10–1.70)**
Colorectal	13/92	0.77 (0.39–1.54)	11/92	1.14 (0.59–2.21)	14/91	0.87 (0.41–1.85)	7/98	1.26 (0.48–3.33)	26/78	0.86 (0.55–1.34)
Non-CLL leukemia	7/42	0.75 (0.28–1.99)	6/44	1.21 (0.48–3.05)	8/42	1.08 (0.38–3.07)	3/44	1.05 (0.25–4.45)	14/34	1.04 (0.55–1.94)
All circulatory diseases	102/606	1.07 (0.83–1.38)	73/635	1.08 (0.83–1.40)	102/619	0.90 (0.68–1.19)	48/675	1.30 (0.89–1.89)	191/488	1.14 (0.96–1.35)
Stroke	30/173	1.37 (0.87–2.17)	18/182	0.87 (0.52–1.44)	28/172	1.14 (0.69–1.87)	7/192	0.50 (0.21–1.17)	52/135	1.12 (0.81–1.55)
All heart diseases	80/491	1.03 (0.77–1.37)	56/519	1.01 (0.75–1.35)	80/502	0.86 (0.62–1.19)	39/543	1.41 (0.93–2.14)	152/394	1.11 (0.92–1.34)
Ischemic heart disease	42/317	0.79 (0.54–1.16)	33/331	0.93 (0.63–1.37)	49/320	0.90 (0.60–1.34)	22/341	1.45 (0.84–2.49)	93/252	1.05 (0.83–1.33)

Outcome	Diagnostic radionuclide		Brachytherapy		Radioactive iodine therapy		Other radionuclide therapy		Any radionuclide procedure	
	Events*	HR (95% CI)†	Events*	HR (95% CI)†	Events*	HR (95% CI)†	Events*	HR (95% CI)†	Events*	HR (95% CI)†
MI	36/226	0.91 (0.59–1.41)	34/233	1.28 (0.87–1.90)	39/229	0.84 (0.52–1.35)	26/252	**1.76 (1.02–3.04)**	77/171	1.23 (0.94–1.61)

Abbreviations: BCC, basal cell carcinoma of the skin; CI, confidence interval; CLL, chronic lymphocytic leukemia, HR, hazard ratio; MI, myocardial infarction; NMSC, non-melanoma skin cancer; SCC, squamous cell carcinoma of the skin

Bolded= P-value <0.05

*Number of events is among technologists who ever vs. never worked with procedure.

†Models used age as the time metric, were stratified by birth year, and were adjusted for sex and other nuclear medicine procedures (except for models of “any radionuclide procedure”)