Occupational Radiation and Hematopoietic Malignancy Mortality in the Retrospective Cohort Study of U.S. Radiologic Technologists, 1983-2012

SUPPLEMENTARY MATERIALS

Dose estimation (expanded)

As described in the Methods section of the main text, the dose estimation exposure assessment component of the USRT study focused on the 110,373 technologists who completed a baseline self-administered questionnaire and often additional questionnaires that supplemented the badge dose measurements. Even though 72% of the 110,373 technologists had at least one badge dose reading (see Table 3 in 28), complete badge dose measurements covered only 35.4% of the occupational radiation exposure (1916-1997). Availability of badge dose data varied by time with limited individual measurements prior to the late 1970s. The historical dose reconstruction of individual technologist annual estimated doses (*i.e.,* dosimetry component) (25,28) was based on an internationally recognized strategy for estimating organ doses from exposure to external photon radiation (33). The dosimetry was corroborated by findings from an analysis of chromosomal translocations in a sample of technologists (29). Due to the multi-decade period of occupational radiation exposures, input data for the dosimetry relied on three types of information: (1) archival individual monitoring badge measurements (N=921,134 covering the period 1960-1997), (2) detailed work history information on radiographic procedures performed, lead apron usage, and type of facility where employed from one or more self-administered questionnaires completed by the technologists (covering the period 1916-1997), and (3) a comprehensive review of the available historical literature on diagnostic radiologic exposures to medical radiation workers (with a major emphasis on the period 1916-1959). These sources of input data were supplemented by assumptions supported by common

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radiologic technology practice based on extensive literature review from peer-reviewed publications, national and international expert radiation protection and measurement committee reports, U.S. and other government historical survey data, phantom measurement data, and historical advertisements for design of lead aprons described in (25,28,36). More detail about the data and methods used to derive estimates for 2.23 million annual badge doses (personal dose equivalent) for the years 1916–1997 for 110,374 technologists can be found in (25,28).

Technologists in this cohort were primarily exposed intermittently to external x-radiation from performing radiologic procedures with peak energies between 70 and 90 kV and mean energies of about 35-50 keV (25). Mean energies varied over time, with a slight increase in later decades, depending on the filtration of the x-ray beam (Table 1 in 25). While patients are exposed to generally small-sized fields on their body during the radiologic procedure, the technologist is exposed primarily to scattered radiation which tends to be relatively uniform over his/her body (at least from the pelvis to the top of head) at locations where they might stand in the examination room (25). The technologist is primarily exposed on the anterior side of the body due to the constraint of having to view the patient. This constraint was the basis of the design of the lead aprons that provide primarily anterior protection (see Fig. 3 in 25). For that reason, dose calculations were made under the assumption of anterior exposure.

The method described in the International Commission for Radiation Protection (ICRP) Report 74 (33) uses as individual input data the personal dose equivalent (mSv) which is reported by badge monitoring services. Typically, badge readings are provided monthly, though in some decades, other practices prevailed. Dose units also varied over time. The term ‘‘badge dose’’ in this work refers to all types of measurements or estimates from personnel radiation monitoring devices over all years during 1916–1997. All estimates of badge dose, regardless of

their original units, were converted to a single, consistent set of units (personal dose equivalent in mSv) for dose calculations.

To estimate the annual dose received by a technologist for a given year, the cumulative (summed) reading of the badge dose measurements over the calendar working year was used. To compute a technologist's bone marrow dose (bone marrow and other organ doses were measured in milligray [mGy]) for a single year, the technologist's annual cumulative badge dose reading was used to estimate the air kerma (dose to air) that would have produced that badge reading. Air kerma was then used to estimate bone marrow dose using coefficients of 'organ dose per unit air kerma' specific for the x-ray energy distributions typical within each decade described in (25). The dose coefficients for this study were derived (25) by weighting published dose coefficients (33) according to the x-ray energy distributions assumed in each decade (Table 1 in 25). The dose coefficients at discrete energies, used in the weighting scheme, had originally been derived from radiation transport calculations on mathematical models of the human body (33). Lifetime occupational dose to bone marrow was estimated as the sum of annual bone marrow doses during each technologist's lifetime working years.

An additional adjustment was made to improve individualization of the bone marrow dose calculation for each cohort member by accounting for his/her individual body mass index (BMI). The ICRP (33) dose coefficients assume an adult phantom of typical size to most western nations. Because of attenuation by the body, variations of the true BMI from the assumed BMI of the phantom model would lead to a larger bone marrow dose estimate for thinner individuals and a smaller bone marrow dose estimate for heavier individuals. The National Council on Radiation Protection and Measurements Report No. 158 (34) summarized coefficients derived from phantoms for other national populations, each with a different body

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mass index (BMI). Those data were used to derive an adjustment to the ICRP dose coefficients (see Fig. 2 in 25) for differences in individual BMI from the assumed value. The dose estimation in the current dose estimation used BMI data from individual cohort members collected in the baseline questionnaire to make the adjustment (28). Using this adjustment, the dose to bone marrow could be adjusted to be as much as 40% higher (for very thin individuals) to 20% lower (for heavy individuals) compared to that from the more generalized ICRP dose coefficient. The baseline survey-reported BMI values were assumed to be representative for the individual technologist's adult working years.

For decades prior to 1960, cohort member badge doses were not available on an individual basis and had to be estimated based on other available data. We determined that the population distribution of badge doses for a given year (for which substantial numbers of badge dose data were available) could be described reasonably well by a lognormal distribution in which the annual geometric mean (median) depended primarily upon facility type where the technologist was employed (hospital, physician office, combination) and whether the workplace was civilian or military. As described in (Table 1 in 28), we used different methods to characterize the population badge dose distributions for different time periods. For annual dose estimates prior to 1940 and during 1940-1949, we relied on literature-based descriptions of the decade-specific population dose distributions using the lognormal model. To estimate annual doses for the period 1950-1955 and for the period 1956-1965, we interpolated between the literature-based estimates for the earliest years and the actual dose distributions of cohort member badge readings for the period 1966-1976. For the late 1970s we estimated population dose distributions using the archival badge dose readings available for a subset of cohort members. In later years, the reported annual badge dose measurements for each individual were

used. Each cohort member badge dose that was estimated, rather than measured, was treated as an uncertain variable and multiple values for each subject were selected by Monte Carlo simulation. Other parameters, as discussed below, were also uncertain and were selected by similar procedures.

Lead aprons are effective at reducing the incident air kerma and, hence, reducing the organ dose for shielded anatomic sites. Based on calculations (25) using published mass-energy attenuation coefficients for x-rays (see https://www.nist.gov/pml/x-ray-mass-attenuation-coefficients), the shielding effectiveness of aprons was estimated to be between 93% and 99% (Table 6 in 25) depending on the x-ray energy and the thickness of the apron, both which varied by time (Table 1 in 25). The attenuation afforded by the apron was used as a multiplicative modifier for the incident air kerma used to make the bone marrow dose calculation. The calculation of a representative total bone marrow dose was derived as the weighted sum of the dose from the lead apron-shielded and unshielded doses, weighted by fraction of the body exposed and not exposed, respectively (25). When a lead apron is worn, the bone marrow dose, which is an average for the entire body, is significantly reduced overall. Based on data provided in (35), when lead aprons were worn, we estimated the fraction of the bone marrow potentially exposed to x-irradiation to be about 20% of the total (Table 10 in 25).

Although we included detailed questions about use of lead aprons in the third questionnaire (administered during 2001-2003), we collected only limited information about apron use in earlier questionnaires. None of the questionnaire-derived information could be validated. Questionnaire-based work history information and probabilistic methods were employed to estimate the fraction of the annual exposure that might have been reduced by a lead apron. For example, aprons are rarely used in nuclear medicine (where radiopharmaceuticals are

employed) but more frequently in diagnostic (x-ray) radiology (36). Work history questionnaire data provided the basis for algorithms that we developed for frequency of apron usage (28).

Similar to the situation for an unknown badge dose or individual apron usage, other parameters of the dose estimation method were also not accurately known on an individual basis, *e.g.*, x-ray energy, beam filtration, etc. To account for these uncertainties, probability density functions (PDFs) to characterize the frequency of each uncertain parameter were developed from based on historical literature. One thousand sets of doses for the entire cohort (each set termed a 'realization') were simulated by Monte Carlo selection of each unknown parameter value from its PDF and use of the dose algorithm. Procedures for selection of unknown parameter values from the specified PDFs are discussed in detail in (28).

The population mean badge doses on an annual basis (derived from Table 4 in 28) decreased substantially over successive decades, from about 1500 mSv in the 1920s, 710 in the 1930s, 270 in the 1940s, 110 in the 1950s, 69 in the 1960s, 36 in the 1970s, and 15 in the 1980s to about 5.5 in the 1990s. Decreases were largely due to improvements in technology, greater awareness of radiation protection needs, and changes in radiological imaging protocols. Annual badge doses for individuals could have been up to 10-fold smaller or greater than the average values listed above. Cumulative bone marrow dose, as a fraction of the badge dose, was overall on average about 8.5 mGy. The distribution and population mean of the estimated bone marrow dose, would have decreased similarly over time as did badge doses

Corroboration of the estimated bone marrow doses was evaluated by chromosome aberration analysis. For that purpose, we assessed chromosome translocation frequencies using fluorescent *in situ* hybridization (FISH) for 229 study participants (37) to examine the chromosome translocation dose-response relationship (29) using the bone marrow doses reported

in (28). About 95% of the bone marrow dose estimates ranged from 0.2–100 mGy. With these dose estimates, we found a statistically significant association (p=0.0188) with a slope of 5.7 (95% CI 0.2, 11.3) translocations per 100 cell equivalents per Gy, after adjusting for personal diagnostic medical radiation exposure (29). Two findings from this analysis were important: (i) a significant excess translocation rate was observed with increasing bone marrow dose estimated from the dose reconstruction, and (ii) our observed dose-response value was closely similar to the dose-response of 5.4 from translocation studies reported in atomic bomb survivors of Hiroshima and Nagasaki (see Table 6 in 29). Both findings confer confidence in the estimated bone marrow doses obtained by the methods described herein.

Linet MS, *et al. Occup Environ Med* 2020; 77:822–831. doi: 10.1136/oemed-2019-106346

Table E1. ICD-9 and ICD-10 codes used in analysis of occupational radiation and mortality from hematopoietic malignancies

Type of hematopoietic malignancy*	ICD-9 codes	ICD-10	Comments
AML	205.0, 206.0, 207.0, 207.2	C92.0, C92.4, C92.5, C93.0, C94.0	For some analyses, we combined myelodysplastic syndromes, (previous nomenclature 'refractory anemia'), with acute myeloid leukemia recognizing myelodysplastic syndromes as a neoplasm and a frequent precursor of acute myeloid leukemia.
MDS	238.7, 285.0	D46.9	
CML	205.1	C92.1, C92.7	
Leukemia excluding CLL			
CLL	204.1, 204.2	204.1, 204.2	
NHL	200.0, 200.8, 202.0, 202.2, 202.8, 202.9	C82.0, C82.1, C82.2, C82.7, C82.9, C83.0, C83.1, C83.2, C83.3, C83.4, C83.5, C83.7, C83.8, C83.9, C84.0, C84.4, C84.5, C85.0, C85.1, C85.7, C85.9	
MM	203.0, 203.2	C90.0, C90.2	
ALL	204.0	C91.0	
HL	201.0-201.9	C81.0, C81.1, C81.2, C81.3, C81.7, C81.9	

*Abbreviations: AML=acute myeloid leukemia; MDS=myelodysplastic syndromes; CML=chronic myeloid leukemia; CLL=chronic lymphocytic leukemia; NHL=non-Hodgkin lymphoma; MM=multiple myeloma; ALL=acute lymphocytic leukemia; HL=Hodgkin lymphoma; ICD-9 = International Classification of Diseases, 9th revision; ICD-10 = International Classification of Diseases, 10th revision

Table E2. Descriptive characteristics of U.S. Radiologic Technologists cohort followed up for hematopoietic malignancies, 1983-2012

Characteristics	AML		Leukemia excluding CLL		CLL		NHL		MM		Person-years		Persons (Technologists)	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Total	85	100	155	100	32	100	201	100	112	100	2,638,783	100	110,297	100
Sex														
Male	34	40	62	40	17	53	72	36	43	38	599,887	23	26,642	24
Female	51	60	93	60	15	47	129	64	69	62	2,038,896	77	83,655	76
Race														
White	81	95	144	93	32	100	193	96	98	88	2,495,379	95	103,860	94
Black	1	1	5	3	0	0	0	0	9	8	77,064	3	3,541	3
Other/unknown	3	4	6	4	0	0	8	4	5	4	66,340	3	2,896	3
Year of birth														
<1930	20	24	38	25	16	50	67	33	36	32	158,407	6	9,197	8
1930-1939	26	31	46	30	7	22	63	31	43	38	337,569	13	14,914	14
1940-1949	23	27	43	28	9	28	51	25	25	22	886,716	34	36,237	33
≥1950	16	19	28	18	0	0	20	10	8	7	1,256,091	48	49,949	45
Age at baseline														
<30	5	6	6	4	0	0	9	4	4	4	454,156	17	16,435	15
30-49	41	48	75	48	9	28	77	38	37	33	1,798,129	68	72,445	66
≥50	39	46	74	48	23	72	115	57	71	63	386,498	15	21,417	19
Year first worked														
1916-1949	16	19	30	19	11	34	37	18	21	19	108,364	4	6,325	6
1950-1959	22	26	43	28	8	25	87	43	44	39	359,542	14	16,244	15
1960-1969	21	25	37	24	12	38	42	21	33	29	800,969	30	32,746	30
1970-1980	26	31	45	29	1	3	35	17	14	13	1,369,908	52	543,982	50
Ever worked with fluoroscopically guided procedures														
No	39	46	73	47	14	44	102	51	60	54	1,503,963	57	61,969	56
Yes	21	25	26	17	3	9	21	10	18	16	542,120	21	22,207	20
Unknown	25	29	56	36	15	47	78	39	34	30	592,700	22	26,121	24
Ever worked with nuclear medicine procedures														
No	40	47	69	45	14	44	83	41	66	59	1,500,682	57	61,720	56
Yes	22	26	34	22	4	13	45	22	16	14	613,147	23	25,310	23
Unknown	23	27	52	34	14	44	73	36	30	27	524,953	20	23,267	21
Smoking status														
Never smoker	31	36	59	38	13	41	87	43	48	43	1,262,987	48	51,909	47
Past smoker	33	39	65	42	13	41	80	40	45	40	1,058,970	40	40,264	37
Current smoker	20	24	30	19	5	16	34	17	19	17	312,521	12	17,846	16
Unknown	1	1	1	1	1	3	0	0	0	0	4,304	0.2	278	0.3
Body mass index														
<25	37	44	73	47	22	69	97	48	64	57	1,768,998	67	71,681	65
25-29	39	46	62	40	6	19	69	34	30	27	611,587	23	26,720	24
≥30	7	8	16	10	4	13	31	15	17	15	232,883	9	10,555	10
Unknown	2	2	4	3	0	0	4	2	1	1	25,315	1	1,341	1