

Routine Diagnostic X-ray Examinations and Increased Frequency of Chromosome Translocations among U.S. Radiologic Technologists

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Abstract

The U.S. population has nearly one radiographic examination per person per year, and concern about cancer risks associated with medical radiation has increased. Radiologic technologists were surveyed to determine whether their personal cumulative exposure to diagnostic X-rays was associated with increased frequencies of chromosome translocations, an established radiation biomarker and possible intermediary suggesting increased cancer risk. Within a large cohort of U.S. radiologic technologists, 150 provided a blood sample for whole chromosome painting and were interviewed about past X-ray examinations. The number and types of examinations reported were converted to a red bone marrow (RBM) dose score with units that approximated 1 mGy. The relationship between dose score and chromosome translocation frequency was assessed using Poisson regression. The estimated mean cumulative RBM radiation dose score was 49 (range, 0–303). After adjustment for age, translocation frequencies significantly increased with increasing RBM dose score with an estimate of 0.004 translocations per 100 cell equivalents per score unit (95% confidence interval, 0.002–0.007; $P < 0.001$). Removing extreme values or adjustment for gender, cigarette smoking, occupational radiation dose, allowing practice X-rays while training, work with radioisotopes, and radiotherapy for benign conditions did not affect the estimate. Cumulative radiation exposure from routine X-ray examinations was associated independently with increased chromosome damage, suggesting the possibility of elevated long-term health risks, including cancer. The slope estimate was consistent with expectation based on cytogenetic experience and atomic bomb survivor data. [Cancer Res 2008;68(21):8825–31]

Introduction

Routine medical diagnostic X-ray doses to patients per examination have diminished over time; however, there has been a rapid increase in the use of procedures that confer much higher doses, such as helical and other types of computed tomography (CT) scanning, and interventional procedures (1–4).

The U.S. population has nearly one radiographic examination per person per year (2), and new estimates reveal that the average U.S. resident in 2006 was exposed to nearly 6 times the medical radiation of a person of the same age than in 1989.⁷ Much of the increase in medical radiation can be attributed to CT and nuclear medicine procedures. The number of CT scans performed in the United States has increased from 18.3 million in 1993 to 62 million in 2006.⁷ Furthermore, concern about medical radiation and long-term cancer risks has drawn increased attention (3, 5, 6). Excess cancer risks related to diagnostic X-rays were indirectly quantified for 15 countries; the proportions of cancers in the United States and the United Kingdom attributed to diagnostic radiation were estimated to be 0.9% and 0.6%, respectively (7). Direct estimates of cancer risk associated with diagnostic X-ray examinations are problematic due to low doses, absence of radiographic records, long disease latency, and difficulty in individual recall of specific procedures (2).

Cytogenetic damage is caused by radiation exposure and chromosome aberrations have been associated with increased cancer risk (8). Some studies have found increased chromosome abnormalities immediately after radiation exposure from CT scanning (9) or in patients with unusually high numbers of diagnostic procedures (10). To our knowledge, studies to detect chromosome damage from long-term cumulative low radiation doses (under 0.3 Gy or equivalently 300 mGy) from medical radiographic examinations have rarely been attempted because of potential inaccuracies in self-reported X-ray procedures and because the doses were considered to be under the cytogenetic detection limit (~ 300 mGy). However, lowering the detection limit may be achieved (11) with careful subject selection, detailed questionnaire information, large sample size (>100 persons), evaluating huge numbers of cells per person [at least 1,000 cell equivalents (CEs)], and increasing the number of chromosomes analyzed. Error in recalling diagnostic procedures might be mitigated by studying radiologic technologists who probably are more knowledgeable than the general public about past X-ray examinations. Structural chromosome aberrations, specifically translocations enumerated using whole chromosome paints by fluorescence *in situ* hybridization (FISH) in peripheral blood lymphocytes, have been used extensively as biodosimeters of past radiation exposure (12–21). We recently assessed archived translocation data, from over 10 years ago, detected by FISH whole chromosome painting with respect to reported personal diagnostic X-ray examinations, and found a significant positive dose-response

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⁷ <http://www.newswise.com/p/articles/view/529077>

relationship ($P = 0.01$; ref. 22). To determine more definitively whether chromosome damage was associated with self-reports of routine diagnostic X-ray examinations, we expanded our earlier study by nearly doubling the number of subjects from 79 radiologic technologists in the first study to 150 in the current study. We also increased the number of CEs evaluated from 432 to ~1,024 per person in the current study. Here, we report our findings of chromosome translocation frequencies and the association with cumulative lifetime diagnostic red bone marrow (RBM) radiation exposure.

Materials and Methods

Study population. In 1982, the National Cancer Institute, in collaboration with the University of Minnesota and the American Registry of Radiologic Technologists, initiated a study of cancer incidence and mortality among 146,022 U.S. radiologic technologists (USRT) who were certified for at least two years between 1926 and 1982. This study has been approved annually by the human subjects review boards of the National Cancer Institute and the University of Minnesota. In brief, during 1984 to 1989, 1995 to 1998, and 2003 to 2005, postal surveys were conducted that included questions related to several health outcomes, work history, cancer risk factors, and history of diagnostic X-ray procedures (for questionnaires, see the U.S. Radiologic Technologists Study Web site⁸; for study details, see ref. 23). To date, 110,418 technologists have responded to 1 or more surveys that formed the basis for several reports of cancer incidence associated with a history of working as a radiologic technologist (24–26).

Subject selection and recruitment for the USRT biodosimetry study have been described in detail elsewhere (21). Briefly, technologists were selected based on occupational characteristics from among a core group of 3,441 cohort members who began working before 1950, were alive, and had a known address in 2003. A prescreening questionnaire identified and excluded cohort members with a prior cancer diagnosis, a family history of chromosomal instability disorders, or who reported smoking 10 or more cigarettes per day. After these exclusions, 207 eligible technologists were serially recruited and 159 (77%) agreed to participate by providing a venipuncture blood sample and completing a telephone survey about personal history of diagnostic and therapeutic radiologic procedures. In-home blood samples were collected using a nation-wide phlebotomy service and shipped overnight to the cytogenetics laboratory. The final sample size was 150 individuals because two subjects died after blood sampling, but before their interview, 2 samples were unusable due to delays in shipment, and 5 samples did not grow in cell culture.

FISH assay for chromosome aberrations. Laboratory personnel (DP and JDT) determined the frequency of translocations using FISH whole chromosome painting without knowledge of ionizing radiation exposure of the technologists. Cell cultures were initiated on blood collected in heparinized vacutainer tubes within 24 h of phlebotomy and processed according to routine cytogenetic methods (27). The slide preparation, staining, and cell scoring were performed using standardized chromosome painting protocols (27, 28).

Chromosomes 1, 2, and 4 were painted red and 3, 5, and 6 were painted simultaneously in green using probes from Cytocell Technologies, Ltd. The slides were counterstained with 4',6-diamidino-2-phenylindole. This combination of paints detects 56% of all the chromosome exchanges (29, 30). Only well-spread metaphase cells that met established criteria (31) were scored. All chromosome aberrations were classified according to the Protocol for Aberration Identification and Nomenclature Terminology (32). Approximately 1,800 metaphase cells were evaluated per subject, and this was equivalent to $1,800 \times 0.56 = 1,000$ metaphase cells (define as CEs) as if the full genome had been scored. All translocations in cells were enumerated and the frequency of translocations per 100 CEs was used as the dependent variable in the statistical analyses.

Occupational radiation exposure. The USRT dosimetry system provides annual RBM doses for each technologist as log-normally distributed probability densities for each year that they worked (33). We summed the mean values of each annual distribution to derive cumulative mean occupational RBM radiation doses for adjustment in the statistical analysis (for further detail, see ref. 21). A summary of the most current occupational dose distribution is shown in Table 1 and reflects some dosimetry improvements recently implemented.

Personal diagnostic exposure. We used self-reported information about personal diagnostic X-ray procedures to assign weighted RBM dose scores. The doses associated with specific radiographic procedures were assigned midpoint RBM dose values from a comprehensive list of examination types (34). We used the midpoint doses and frequencies to weight the dose scores for the types of radiographic procedures reported by the technologists (see Table 2 and footnotes), multiplied the number of examinations by the corresponding dose, and then summed the doses to estimate the total cumulative personal diagnostic X-ray weighted RBM dose score. Although one unit of the dose score is ~1 mGy, because of uncertainties in recall and dose estimates of the procedures, we prefer the term "cumulative RBM radiation dose score" rather than dose per se. The RBM radiation dose from one chest CT scan would roughly correspond to 10 mGy or 10 units of the cumulative RBM dose score.

To assess the reproducibility of recall of personal diagnostic procedures by cohort members, we compared self-reports from 354 radiologic technologists who completed the same questionnaire twice during a 4-y period. The distributions by age, gender, race, and selected work history characteristics were similar for these technologists when compared with the full study cohort. We evaluated the number of reported procedures and the decade they first occurred for the following common or high-dose examinations: upper gastrointestinal series, angiography, CT scans, mammography (among women age 50 years or older), and chest X-rays.

Personal therapeutic radiation exposure. We included an indicator variable in the statistical model for having therapeutic irradiation (ever/never). Information on personal history of therapeutic irradiation to the head and neck, pelvis, extremities, and chest, for benign conditions, was available from the baseline questionnaire. Because the majority of adult bone marrow is located in the pelvis, torso, and head (35), we categorized those who had therapeutic radiation to the extremities as "never." Those categorized as "ever" reported treatment for the following benign conditions: acne ($n = 6$), shoulder pain ($n = 3$), skin cancer ($n = 2$), boils ($n = 2$), and other varied reasons ($n = 4$).

Statistical analysis. We used the AMFIT module of EPICURE (Hirosoft) to construct linear Poisson regression models for associations between cumulative personal diagnostic X-ray-weighted RBM dose score and translocation frequency. The models were of the following general form:

$$\lambda(a, d) = \lambda_0(a) + \beta d$$

where λ is the expected number of translocations per cell, a represents covariates affecting translocation frequency, and d is the personal diagnostic X-ray RBM dose, $\lambda_0(a)$ is the covariate specific background number of translocations per cell, and β is the increase in translocations per cell per unit dose score. A Pearson scale factor was added to the models to account for overdispersion of the data.

Selected covariates were included in a multivariate model to minimize confounding. Potential confounders were covariates whose inclusion in the model changed the association between weighted RBM dose score and translocation frequency, i.e., variable β , by 10% or more. The final model included the covariate age at blood draw, but not gender, race, cigarette smoking, prior therapeutic radiation, a past history of allowing others to take practice X-rays, or occupational radiation dose. For ordinal variables, tests for trend were performed in univariate linear Poisson regression models using categories as continuous variables.

To determine if the observed dose-response relationship was influenced by outliers, we excluded seven individuals with the highest cumulative medical diagnostic X-ray RBM doses and/or the highest translocation frequencies and evaluated the effect on the slope estimate. We individually

⁸ <http://radtechstudy.nci.nih.gov>

Table 1. Distribution of covariates among biodosimetry study subjects, mean translocation frequencies, and rate ratios by covariate categories, U.S. Radiologic Technologists Study

Characteristic	Subjects (<i>n</i> = 150)*	Mean number of translocations per 100 CEs	Translocation rate ratios [†] (95% CI)
Age at blood draw (y) [‡]			
71–74	17 (11%)	0.9	0.7 (0.5, 1.0)
75–78	59 (39%)	1.4	1.0 (reference)
79–82	31 (21%)	1.3	1.0 (0.8, 1.2)
83–86	31 (21%)	1.5	1.1 (0.9, 1.4)
87–90	12 (8%)	1.9	1.5 (1.1, 2.0)
Gender			
Female	104 (69%)	1.2	1.0 (reference)
Male	46 (31%)	1.7	1.3 (1.1, 1.6)
Race			
Caucasian	147 (98%)	1.4	N/A
African American	1 (<1%)	N/A	N/A
Other	2 (1%)	N/A	N/A
Former cigarette smoking (number of pack-years)			
0	87 (58%)	1.4	1.0 (reference)
>0–20	31 (21%)	1.2	1.1 (0.8, 1.5)
>20–50	17 (11%)	1.5	1.2 (0.9, 1.6)
>50	14 (9%)	1.6	1.7 (0.8, 3.7)
History of X-ray therapy for benign conditions			
Never	133 (89%)	1.4	1.0 (reference)
Ever	17 (11%)	1.6	1.2 (0.9, 1.5)
In the past, allowed others to take practice X-rays			
Never	88 (59%)	1.3	1.0 (reference)
1–24 times	35 (23%)	1.4	1.0 (0.8, 1.3)
≥25 times	15 (10%)	1.8	1.3 (1.0, 1.7)
Estimated occupational radiation dose to the RBM [§]			
≤10 mGy	53 (35%)	1.1	1.0 (reference)
>10–20 mGy	43 (29%)	1.3	1.1 (0.9, 1.5)
>20–30 mGy	27 (18%)	1.7	1.5 (1.2, 2.0)
>30–40 mGy	17 (11%)	1.5	1.4 (1.0, 1.8)
>40 mGy	10 (7%)	1.7	1.4 (1.0, 2.0)
Cumulative personal diagnostic RBM radiation dose score			
0–20	51 (34%)	1.2	1.0 (reference)
>20–50	51 (34%)	1.3	1.1 (0.9, 1.4)
>50–100	28 (17%)	1.3	1.1 (0.9, 1.4)
>100	20 (13%)	2.0	1.6 (1.2, 2.0)

NOTE: In cytogenetic studies of radiation-exposed individuals, it is common to express the translocation frequency as per 100 or per 1,000 CEs as this allows a comparison with other laboratories that may have painted a different combination of chromosomes.

Abbreviation: N/A, not applicable.

*Does not always sum to 150 or 100% due to small numbers and percentages in the unknown category: Smoking, *n* = 1; worked with radioisotopes, *n* = 2; in the past allowed others to take practice X-rays, *n* = 12.

[†] Poisson regression adjusted for age; unknowns not included.

[‡] $P_{\text{trend}} = <0.001$ from Poisson regression with ordinal age categories treated as a continuous variable.

[§] $P_{\text{trend}} = 0.006$ from age-adjusted Poisson regression with ordinal estimated occupational RBM dose categories as a continuous variable.

^{||} $P_{\text{trend}} = 0.001$ from age-adjusted Poisson regression with ordinal estimated personal diagnostic RBM dose score categories treated as a continuous variable. One dose score unit is approximately equivalent to 1 mGy.

examined the work histories for those persons with extreme translocation values and found no unusual characteristics, although the technologist with the highest number of translocations reported working almost exclusively with radioisotopes. We found very little effect of the exclusions, so that in the final analyses, we included all subjects.

Results

Descriptive features of the study population are shown in Table 1. Technologists ranged in age from ages 71 to 90 years

(median, 78), were predominately female (69%), Caucasian (98%), and nonsmokers (58%). All began working in the 1940s and worked an average of 22 (range, 1–49) years (data not shown). Eleven percent reported having therapeutic radiation for benign conditions to the pelvis, torso, or head; adult body sites with the most RBM.

Mean translocations by categories of covariates and age-adjusted translocation rate ratios comparing categories of these covariates are also presented in Table 1. The average number of translocations

Table 2. Estimated RBM radiation doses for personal diagnostic X-ray procedures reported by technologists and the corresponding weighted RBM radiation dose score, U.S. Radiologic Technologists Study

Examination type reported by technologists*	Examination type included in Preston-Martin and colleagues, 2003 [†]	RBM dose (mGy) per examination in Preston-Martin and colleagues, 2003 [†]	Proportion of examinations in Preston-Martin and colleagues, 2003 [†] by grouped category	Number of examinations reported by radiologic technologists (total = 5,287)	Proportion of total examinations reported by radiologic technologists	Weighted RBM dose score assigned to examinations reported by technologists [‡]				
Face or neck X-ray	Cervical spine	0.1	0.55	410	0.08	0.2				
	Facial/nasal bones	0.1	0.04							
	Mandible	0.1	0.02							
	Neck soft tissue	0.1	0.02							
	Sinuses	0.1	0.26							
	Skull	0.5	0.11							
Spine or back X-ray	Entire spine	2.4	0.06	711	0.13	1.4				
	Lumbar spine	1.5	0.24							
	Lumbosacral spine	1.1	0.44							
	Myelogram	3.7	0.05							
	Sacrum/coccyx	1.7	0.02							
	Thoracic	0.7	0.14							
	Thoracic/cervical spine	0.4	0.01							
	Thoraco-lumbar spine	2.4	0.03							
	GI or abdomen X-ray	Abdomen	0.4				0.27	641	0.12	3.8
		Barium enema	6.3				0.16			
Cholangiogram		2.3	0.02							
Cholecystogram		1.6	0.03							
Colon		1.3	0							
Endoscopic Retrograde Cholangiopancreatography		4.2	0.01							
Esophagram		4.1	0.01							
GI tract		0.7	0.01							
Lower GI Series		6.3	0.2							
Pancreas		1.0	0							
Small bowel series		3.5	0							
Small bowel		3.5	0							
Upper GI series		3.6	0.23							
Upper GI + esophagram		7.7	0.02							
Upper GI + small bowel		7.1	0.03							
Urinary system X-ray		Cystogram	1.7	0.01	138	0.03	1.6			
		Kidneys/ureters/bladder	0.5	0.32						
	Pyelogram, i.v.	2.1	0.59							
	Pyelogram, retrograde	2.2	0.07							
	Urethrogram	2.6	0.01							
Bony pelvis or hip X-ray	Hip	0.4	0.42	385	0.07	0.4				
	Pelvis	0.4	0.43							
	Pelvis/hips	0.6	0.15							
Chest X-ray	Chest	0.05	0.97	2,463	0.47	0.1				
	Ribs	0.4	0.02							
	Sternum	0.6	0.01							
Chest fluoroscopy	Chest, fluoroscopic	1.4	NA [§]	206	0.04	1.4				
Cerebral arteriogram	Cerebral arteriogram	1.0	NA	23	0.00	1.0				
Carotid arteriogram	Cerebral arteriogram	1.0	NA	15	0.00	1.0				
Pulmonary arteriogram	Pulmonary arteriogram	1.4	NA	4	0.0	1.4				
Renal arteriogram	Renal arteriogram	2.1	NA	5	0.00	2.1				
Coronary angiogram	Coronary angiogram	12.7	NA	91	0.02	12.7				
Head or neck CT	Head/neck	3.0	NA	65	0.01	3.0				
Chest CT	Chest	9.6	NA	43	0.01	9.6				
Abdomen CT	Abdomen	14.6	NA	36	0.01	14.6				
Pelvis CT	Pelvis	9.1	NA	6	0.00	9.1				
Upper back CT	Thoracic spine	2.6	NA	6	0.00	2.6				
Lower back CT	Lumbar spine	5.6	0.56	31	0.01	4.8				

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Table 2. Estimated RBM radiation doses for personal diagnostic X-ray procedures reported by technologists and the corresponding weighted RBM radiation dose score, U.S. Radiologic Technologists Study (Cont'd)

Examination type reported by technologists*	Examination type included in Preston-Martin and colleagues, 2003 [†]	RBM dose (mGy) per examination in Preston-Martin and colleagues, 2003 [†]	Proportion of examinations in Preston-Martin and colleagues, 2003 [†] by grouped category	Number of examinations reported by radiologic technologists (total = 5,287)	Proportion of total examinations reported by radiologic technologists	Weighted RBM dose score assigned to examinations reported by technologists [‡]
Whole body CT	Lumbosacral spine	3.9	0.44	8	0.00	3.5
	Whole body	3.5	NA			

Abbreviation: GI, gastrointestinal.

*Ascertained from telephone interview at the time of blood collection.

[†] Reported by Preston-Martin and Pogoda (2003).

[‡] Determined by weighting each Preston-Martin and Pogoda (2003) exam dose by the frequency with which the exam type occurred in their study population and is an approximation of 1 mGy, because of the uncertainties in recall of various procedures we prefer using the term "diagnostic RBM radiation dose score" rather than standard dose units.

§Not applicable.

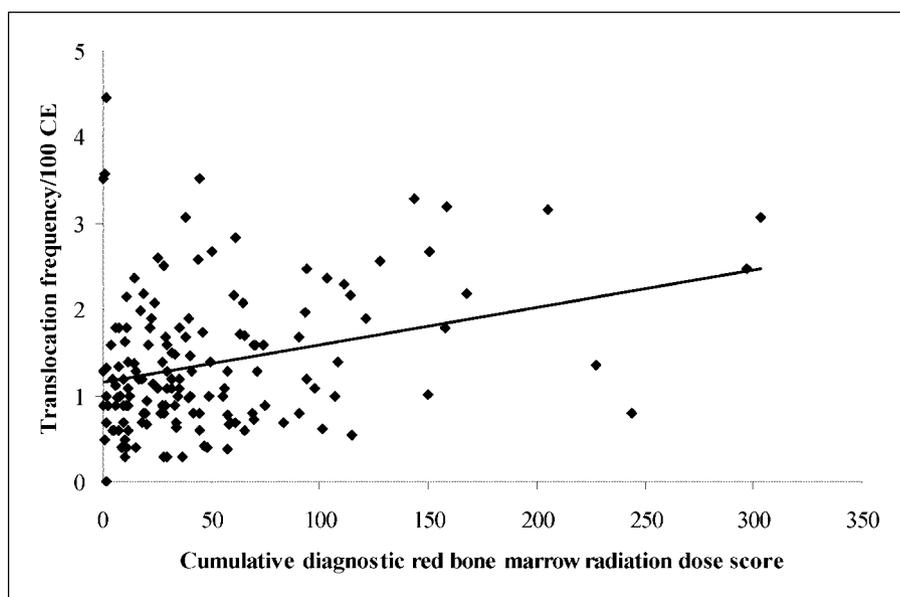
increased with age ($P_{\text{trend}} < 0.001$), male gender [versus female, rate ratio (RR), 1.7; 95% confidence interval (CI) 1.1–1.6], a past history of allowing others to take practice X-rays during technologist training (25 times or more versus never; RR, 1.3; 95% CI 1.0–1.7), occupational RBM dose ($P_{\text{trend}} = 0.006$), and personal diagnostic RBM radiation dose score ($P_{\text{trend}} = 0.001$). Translocation frequencies were not statistically significantly different by pack-years of former cigarette smoking, working with radioisotopes (data not shown), or a history of X-ray therapy for benign conditions.

Study technologists had an average of 1.4 translocations/100 CEs (median, 1.2; range, 0–4.5), a mean occupational RBM dose of 17 mGy (median, 14; range, 0.6–56), and a mean cumulative personal diagnostic RBM radiation dose score of 49 (median, 33; range, 0–303). Personal diagnostic X-ray RBM dose score was uncorrelated with occupational RBM dose ($r^2 = 0.02$). The distribution of the collective (all subjects) diagnostic RBM

radiation dose score was 9.4% before 1950 (collective score, 681), 18.8% between 1950 and 1969 (collective score, 1,365), and 71.9% after 1969 (collective score, 5,228). Translocation frequencies plotted against diagnostic RBM radiation dose score are shown in Fig. 1. In the unadjusted analysis, a one-unit increase in personal radiographic radiation dose score was associated with an increase of 0.004 excess translocations/100 CEs (95% CI, 0.002–0.007; $P = 0.001$). In the analysis adjusted for age at blood collection, the estimate remained unchanged at 0.004 excess translocations/100 CEs ($P < 0.001$). Subsequently adding radiation exposure from therapeutic procedures to the model or dropping extreme values did not alter the point estimate.

Consistency in reporting the numbers of personal diagnostic procedures ranged from agreement of 51% for chest X-rays (within two procedures) to 100% for angiography. If the criteria for chest X-ray agreement was relaxed (within 5), the agreement

Figure 1. Translocation frequency versus the cumulative diagnostic RBM radiation dose score among 150 USRTs [The trend line is from univariate Poisson regression analysis (0.004 translocations/100 CEs/RBM dose score, $P < 0.001$)].



reached 92%. Agreement for the number of mammograms was 68%. Agreement for decade in which the reported procedure first occurred ranged from 79% for upper gastrointestinal series to 86% for angiography. Agreement percentages for decade of first chest X-ray and first mammogram were 84% and 81%, respectively.

Discussion

We observed a statistically significant increase in translocation frequency ($P = 0.001$) with increasing cumulative diagnostic RBM radiation dose score after adjusting for age. The estimate for the slope was unchanged and independent of radiation dose from occupational exposures, as evidenced by multivariate analysis that included several potential confounding variables. We are among the first to show that accumulated radiation doses from a lifetime of routine X-ray examinations was statistically significantly associated with increased cytogenetic damage in the form of chromosome translocations. Extreme values do not explain our finding because the association remained robust after excluding outliers.

Our ability to detect a low-dose relationship, despite the older ages of the radiologic technologists, their relatively low cumulative personal diagnostic RBM radiation dose scores, and the substantial interindividual variability in translocation frequencies, was enhanced by study features designed to overcome these limitations (11, 36). The features were the very large sample size, the scoring of 1,828 cells on average (1,024 cell equivalents) per person (274,234 cells in the whole study), and the ability to select participants who were homogeneous for age. Additionally, we tried to reduce the effect of cigarette smoking on translocation frequencies by restricting the selected sample to nonsmokers or ex-smokers. Although previous studies examining the influence of cigarette smoking on translocation frequency have not been consistent (13, 16, 19, 27, 37–39), a recent pooled study showed a significant increased frequency of chromosome translocations associated with ever smoking (40).

An alternative explanation for why we detected a low-dose relationship may be that we did not lower the limits of detection, but rather the radiation doses were in fact higher because the radiologic technologists underreported X-ray examinations (41, 42) or repeated X-rays were performed when images were of low quality. Our analysis of the reproducibility of self-reporting among 354 technologists who completed the same questionnaire twice within a 4-year period showed an overall 80% agreement, suggesting radiologic technologists are consistent in their recall of the number of past diagnostic procedures (78% agreement) and the time period they first occurred (83% agreement).

The cytogenetic damage we detected seemed to be associated with more recent routine X-ray examinations because 72% of the collective cumulative medical RBM radiation dose scores occurred after 1969. This is of concern because of the large increase in medical radiation exposure since 1989⁷ and because increased frequencies of chromosome aberrations have been associated with elevated cancer risk (reviewed in ref. 8). Although the link between radiation exposure from personal diagnostic procedures, chromosome aberrations, and cancer risk is indirect, ionizing radiation is a well-known carcinogen.

In studies of high-energy γ rays, the expected frequency of excess translocations per 100 CEs per 1 mGy is 0.0015 (43). The distribution of applicable photon energies in the present study were X-rays of ~ 100 keV or less. For dicentrics, the unstable counterpart of translocations, the linear term for X-rays of 50 to

100 keV is about twice to thrice higher than that for high-energy γ -rays (44). So, for the relevant energies here, an estimated frequency of 0.005 excess translocations/100 CE/mGy is reasonable. If one exposure score unit approximates 1 mGy, the observed association of 0.004 excess translocations/100 CEs/unit diagnostic RBM radiation dose score (95% CI, 0.002–0.007) was consistent with this estimate and generally similar to the occupational RBM estimate of 0.009 excess translocations/100 CE/mGy (95% CI, –0.001–0.02; $P = 0.07$) in the same group of technologists (21). Among the 79 technologists for whom FISH analysis was done over a decade earlier, we estimated 0.007 translocations per 100 CEs per score unit (95% CI, 0.002–0.013; $P = 0.01$, ref. 22). Lending further support to our findings are estimates from Hiroshima and Nagasaki atomic bomb survivors in which the proportion of cells with at least one stable aberration, a similar measure considering the generally low frequencies of translocations, increased by $\sim 0.007/100$ CE/mGy and 0.004/100 CE/mGy RBM absorbed dose, respectively (17). Acknowledging the dosimetric uncertainties in both studies, similar estimates might be expected because the effect of exposure to higher energy γ rays in the atomic bomb survivors (45) could be counterbalanced by the protracted radiation exposure in the radiologic technologists.

Recall error of past diagnostic X-ray procedures has been a legitimate obstacle for conducting large population-based health outcome studies relying on self-report (2). However, because the technologists did not know their translocation frequencies, any recall error would be nondifferential with respect to the outcome measure and would probably attenuate relationships observed, not create them. We lacked information on environmental toxins that could be related to increased chromosome translocations; however, these unmeasured variables would also need to be related to medical X-ray examinations to confound the relationship we observed. Given the absence of confounding for several candidate variables we measured and analyzed, the masking of a true association with an unmeasured covariate is unlikely.

This is one of the first studies to report a significant association between chromosome translocations and estimated cumulative diagnostic RBM radiation exposure. We found that radiation from routine X-ray examinations among radiologic technologists was associated with increased chromosome damage, which has been related to elevated cancer risk. Furthermore, the magnitude of the relationship was consistent with expectation based on knowledge of radiation quality and cytogenetic experience. In an earlier study, we found similar results based on 79 radiologic technologists from the same cohort for whom 432 whole genome equivalents per person were analyzed (22). The present work, which was done in a different laboratory, improves on the first study by increasing the sample size and the number of cells examined per person. Although disease diagnosis and patient treatment have been markedly improved by medical uses of radiation, the dose to the individual from diagnostic tests should be monitored and reduced when possible. Our data indicate the need for careful evaluation before recommending diagnostic radiologic examinations, especially in light of the recent and substantial proliferation in the United States of high-dose examinations, including CT and nuclear medicine procedures. For example, incidental findings of uncertain clinical significance on CTs are followed by additional scans that may not result in patient benefit. Dose reduction can be achieved without lowering diagnostic accuracy⁷, making judicious choices by understanding effective doses from each of the various procedures (4), oversight of cumulative patient doses, and the

avoidance of repeats of poor initial quality diagnostic X-ray examinations.

Disclosure of Potential Conflicts of Interest

The authors declare they have no competing financial interests.

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