Medical Radiation Exposure among Atomic Bomb Survivors: Understanding its Impact on Risk Estimates of Atomic Bomb Radiation

Authors: Sadakane, Atsuko, Landes, Reid D., Sakata, Ritsu, Nagano, Jun, Shore, Roy E., et al.

Source: Radiation Research, 191(6) : 507-517

Published By: Radiation Research Society

URL: https://doi.org/10.1667/RR15054.1

RADIATION RESEARCH **191**, 507–517 (2019)
0033-7587/19 $15.00

DOI: 10.1667/RR15054.1

Medical Radiation Exposure among Atomic Bomb Survivors: Understanding its Impact on Risk Estimates of Atomic Bomb Radiation

Atsuko Sadakane,[a,1] Reid D. Landes,[b] Ritsu Sakata,[a] Jun Nagano,[c] Roy E. Shore[d] and Kotaro Ozasa[a]

[a] *Department of Epidemiology, Radiation Effects Research Foundation, Hiroshima, Japan;* [b] *Department of Biostatistics, University of Arkansas for Medical Science, Little Rock, Arkansas;* [c] *Faculty of Arts and Science, Kyushu University, Fukuoka, Japan; and* [d] *New York University School of Medicine, New York, New York*

Sadakane, A., Landes, R. D., Sakata, R., Nagano, J., Shore, R. E. and Ozasa, K. Medical Radiation Exposure among Atomic Bomb Survivors: Understanding its Impact on Risk Estimates of Atomic Bomb Radiation. *Radiat. Res.* 191, 507–517 (2019).

There have been some concerns about the influence of medical X rays in dose-response analysis of atomic bomb radiation on health outcomes. Among atomic bomb survivors in the Life Span Study, the association between atomic bomb radiation dose and exposures to medical X rays was investigated using questionnaire data collected by a mail survey conducted between 2007–2011, soliciting information on the history of computed tomography (CT) scans, gastrointestinal fluoroscopy, angiography and radiotherapy. Among 12,670 participants, 76% received at least one CT scan; 77%, a fluoroscopic examination; 23%, an angiographic examination; and 8%, radiotherapy. Descriptive and multivariable-adjusted analyses showed that medical X rays were administered in greater frequencies among those who were exposed to an atomic bomb radiation dose of 1.0 Gy or higher, compared to those exposed to lower doses. This is possibly explained by a greater frequency in major chronic diseases such as cancer in the ≥1.0 Gy group. The frequency of medical X rays in the groups exposed to 0.005–0.1 Gy or 0.1–1.0 Gy did not differ significantly from those exposed to <0.005 Gy. An analysis of finer dose groups under 1 Gy likewise showed no differences in frequencies of medical X rays. Thus, no evidence of material confounding of atomic bomb effects was found. Among those exposed to atomic bomb doses <1 Gy, doses were not associated with medical radiation exposures. The significant association of doses ≥1 Gy with medical radiation exposures likely produces no substantive bias in radiation effect estimates because diagnostic medical X-ray doses are much lower than the atomic bomb doses. Further information on actual medical X-ray doses and on the validity of self-reports of X-ray procedures would strengthen this conclusion.

Editor's note. The online version of this article (DOI: 10.1667/RR15054.1) contains supplementary information that is available to all authorized users.

[1] Address for correspondence: Department of Epidemiology, Radiation Effects Research Foundation, Hiroshima, Japan, 5-2 Hijiyama Park, Minami-ku, Hiroshima 7320815, Japan; email: sadakane@rerf.or.jp.

INTRODUCTION

The Life Span Study (LSS) of survivors of atomic bombings in Hiroshima and Nagasaki in 1945 has provided valuable information about the health effects of radiation exposures (*1–3*). Individual radiation doses from the bombings, estimated by systematic calculation (*4, 5*), provide reasonably good precision to estimate radiation health risks, because of the wide dose range and evidence that the dose uncertainties are small (*4, 6, 7*). However, there is a potential for biased risk estimates due to lifestyles, socioeconomic status, health consciousness and access to medical care, although it has been shown that a variety of lifestyle and socioeconomic variables have inconsequential effects on the risk estimates for mortality from noncancer diseases (*8*). Another source of potential bias comes from medical X rays that atomic bomb survivors have received (*9*). Survivors had a dose-dependent increase in risk of radiation-associated diseases, so they might also have a dose-dependent increase in cause and opportunity to receive medical care, which may result in more diagnostic and therapeutic medical X-ray procedures. Thus, there is a potential for confounding bias in risk estimates, which is the focus of our study. However, medical X rays administered in the course of diagnosis or treatment of a disease would likely have no causal role in the pathogenesis of that disease and would therefore not affect the dose-response analysis of atomic bomb radiation. In contrast, medical X rays administered apart from the outcome in the analysis, e.g., screening X rays, could possibly distort estimates of risks. Moreover, in the low-dose ranges, adjustment for medical X-ray exposures has the potential to increase the signal-to-noise ratio, thereby increasing the precision of the risk estimates (*9, 10*).

Medical radiation exposures were assessed by the Atomic Bomb Casualty Commission (ABCC) and Radiation Effects Research Foundation (RERF) from the 1960s through the mid-1980s among participants in the Adult Health Study (AHS), a clinical subset of the LSS, as well as among general populations in Hiroshima and Nagasaki (*11–15*). They reported that medical X-ray examinations increased more slowly in Hiroshima and Nagasaki than those for all of Japan from the end of World War II until 1970 (*13, 14*). Moreover, they found no differences in mean diagnostic medical X-ray doses among the ''in-city'' survivors with low, moderate and high atomic bomb radiation doses, but did find higher doses for the survivors than for those who were ''not in city'' (*15*). It is unclear whether these previous findings still hold true in recent periods when modern medical X-ray procedures such as computed tomography (CT) scans are commonly used (*16*) and survivors have reached ages where diseases occur frequently. However, more recent information on medical radiation exposures has not been obtained for the AHS and medical radiation exposures have not been investigated among the general LSS subjects prior to this study.

A self-administered questionnaire survey was conducted among the LSS subjects around the year 2008 (the LSS Mail Survey 2008) to obtain updated information about medical radiation exposures. The objective of the current study was to determine whether atomic bomb radiation dose was associated with medical radiation exposures among the LSS subjects, using the latest data collected from the survey. The findings would help assess whether medical radiation exposures may affect atomic bomb risk estimates. In particular, the issue of possible confounding by medical irradiation is important to the investigation of risks from low-dose atomic bomb radiation.

METHODS

The Life Span Study

The detailed methods of the LSS and the AHS are described elsewhere (*1, 17*). In brief, the LSS is a cohort study of 120,321 subjects, which comprises 93,741 atomic bomb survivors who were exposed within 10 km of the hypocenter in Hiroshima and Nagasaki (in-city subjects) and 26,580 subjects who were not in either city at the time of the bombings (not-in-city subjects). Approximately 22,000 LSS subjects (including 5,000 not-in-city subjects) were selected as members of the AHS. Subjects of the AHS have been invited to the clinics at ABCC/RERF every two years to undergo clinical examinations, in which interviews about medical radiation exposures have been included.

Participants in the Current Study

ABCC and RERF have conducted a series of questionnaire surveys since the 1960s to obtain information such as demographic factors, lifestyles, socioeconomic status and reproductive factors (*18*), which could confound or modify atomic bomb risk estimates. The LSS Mail Survey 2008 was the sixth questionnaire survey. Eligible individuals for the survey were in-city LSS subjects who had responded to the previous mail survey conducted in 1991. In this survey, we identified 24,640 eligible individuals who were alive as of July 1, 2007 and whose current address was available. Eligible individuals included 3,956 AHS subjects selected prior to the current survey. A self-administered questionnaire was mailed to eligible individuals between July 2007 and March 2011. Recipients were asked to complete the questionnaire and return it to RERF by mail. Among the questionnaires sent to the eligible individuals, 18,300 were successfully delivered, but 6,340 questionnaires could not be delivered because of incorrect address (5,564), or the recipients were incapacitated (327) or recently deceased (449). Among those successfully delivered, 3,962 persons gave no response, and 248 persons refused to participate in the survey. We obtained 14,090 eligible responses (77% of the 18,300 persons who received questionnaires), but 272 of them were excluded from the analysis because a pilot questionnaire that did not include questions about medical radiation exposures was used. We also excluded 1,148 subjects whose atomic bomb radiation doses were unknown, because they are excluded from most of the risk estimate analyses in the LSS. This resulted in 12,670 participants for the analysis. Figure 1 summarizes how the participants were selected.

Information about Medical Radiation Exposures, Demographics and Medical Histories

Questions about both diagnostic and therapeutic medical radiation exposures were included in the questionnaire. We focused on medical X-ray procedures that involve relatively high-dose exposures to radiation. For responses to questions about diagnostic X rays, the cumulative number of examinations were categorized (0, 1–2, 3–5 or 6 or more times) for CT scans of the head, chest and abdomen, fluoroscopy examinations of upper and lower gastrointestinal (UGI and LGI) tracts and angiography examinations of cerebral, coronary and hepatic arteries. Questions about radiation therapy consisted of the number of treatments, reason for therapy and age at therapy. The questionnaire also asked about medical histories such as having experienced cancer, stroke, cardiovascular diseases and chronic hepatitis. Information about demographics such as sex, date of birth and city at the time of the bombings (Hiroshima or Nagasaki) was already collected as part of baseline surveys for the LSS.

Atomic Bomb Radiation Doses (DS02R1)

Individual organ doses from atomic bomb radiation were estimated based on the Dosimetry System 2002 Revision 1 (DS02R1) (*5*), in which individual doses were updated from the Dosimetry System 2002 (DS02) (*4*). Individual weighted absorbed doses, which are the sum of doses from gamma ray and ten times those from neutrons, were used in the analysis. We used doses to the colon as a representative dose for all parts of the body. We grouped subjects into four categories according to weighted absorbed colon dose: $<$0.005 Gy; 0.005 to $<$0.1 Gy; 0.1 to $<$1.0 Gy; and $\geq$1.0 Gy.

Statistical Analyses

Statistical summaries. Demographic factors and atomic bomb radiation doses were summarized for three groups: participants in the survey; eligible subjects for the mail survey; and the total in-city members of the LSS cohort. Among the 12,670 participants, differences in demographic factors, medical histories and the number of medical radiation exposures were evaluated among the aforementioned atomic bomb radiation dose categories. To provide overall information about exposures to medical X rays, we showed the numbers of total CT, fluoroscopy and angiography examinations as well as those of individual procedures. Categories for the numbers of individual procedures were 0, 1–2, 3–5 and 6 or more times. When computing total CT procedures, the combination of individual procedure categories resulted in total categories of 0, 1–5 and 6 or more times. The same was true for total fluoroscopy and total angiography procedures. For items with no response (not more than 8.2% and 10.8% of history of exposures and number of exposures, respectively, for any of the nine items), we excluded those data in individual item analyses. When computing totals, missing items were assumed to be 0, except when frequencies of all individual procedures were unknown.

Although we did not have sufficient data to estimate precise doses from medical X rays, we calculated approximations of medical X-ray doses from CT scans and UGI fluoroscopy examinations. We used data on frequency of individual procedures collected by the current

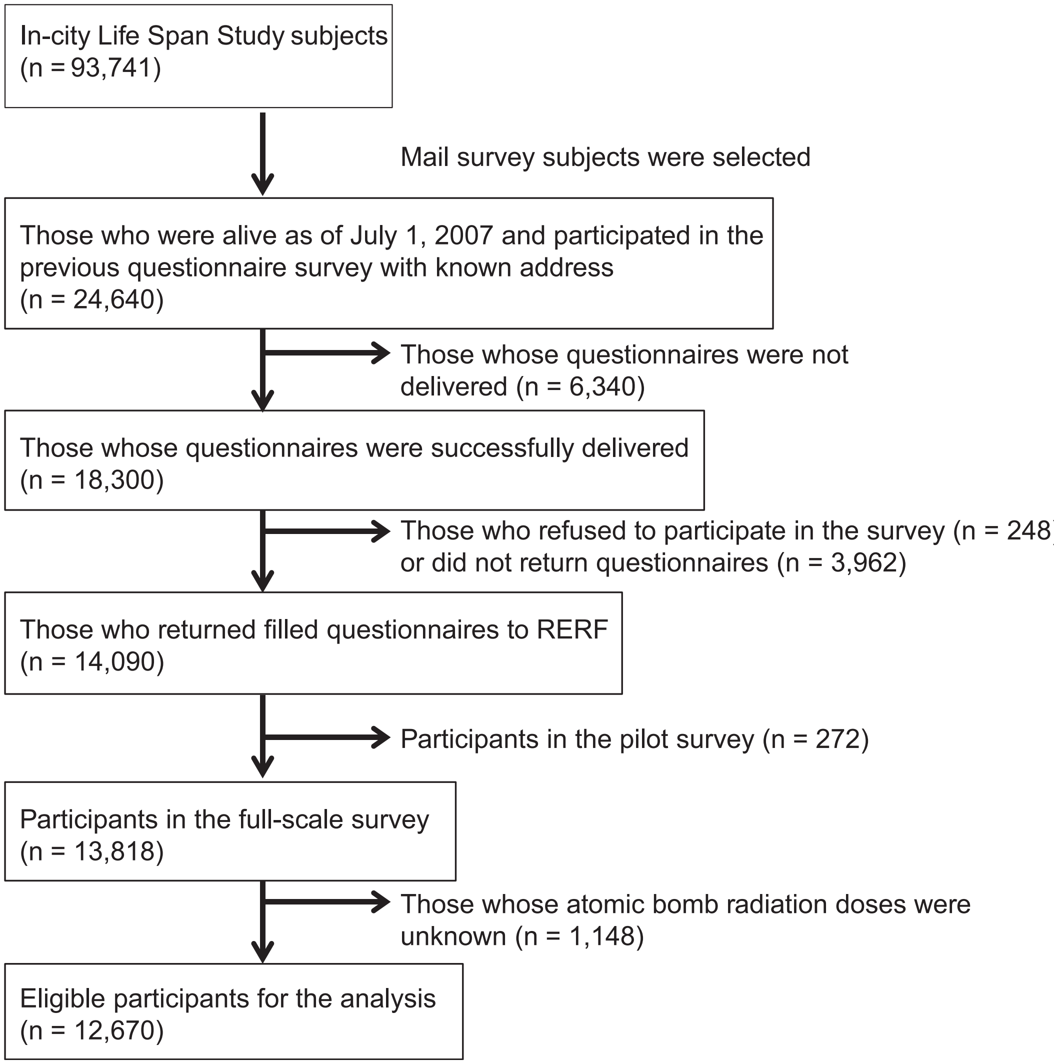

FIG. 1. Schematic of participant selection process.

survey and information about mean bone marrow doses estimated by previously published studies among atomic bomb survivors (*19*). Because the frequency of procedures was categorized, we assigned 1.5 to the category 1–2 times, 4 to 3–5 times and 6 to 6 or more times. Mean bone marrow doses were 4.08 mGy per examination for head CT scan, 7.28 mGy for chest CT scan, 10.32 mGy for whole abdominal CT scan and 1.75 mGy for UGI fluoroscopy (*19*). We did not calculate doses from LGI fluoroscopy and angiography examinations and radiotherapy because no appropriate source of information about mean doses was available.

Inferential analyses. For each medical X-ray procedure, odds ratios (ORs) of medical radiation exposure (never, ever) dependent on categorized atomic bomb radiation dose (<0.005 Gy, 0.005 to <0.1 Gy, 0.1 to <1.0 Gy and ≥1.0 Gy) were estimated using logistic regression, which adjusted for these potential confounding factors: city (Hiroshima or Nagasaki); sex; age at the time of the bombings (<10 years, 10 to <20 years or ≥20 years); and the AHS membership (yes, no). To evaluate trends of medical radiation exposures with atomic bomb radiation doses, we treated atomic bomb radiation dose as a continuous variable. The potential confounding factors in the subsequent models were the same as the above. We report the linear coefficient on atomic bomb radiation dose as the trend statistic. In addition, we modeled categorical numbers of head and chest CT scans and UGI fluoroscopy examinations with multinomial (polytomous) logistic regression models (*20*). Substantial proportions of participants underwent these medical radiation procedures frequently; the increased variability (compared to other medical radiation procedures) among categorized medical radiation exposures warranted examination as multinomial dependent variables. The multinomial logistic regressions accounted for categorized or continuous atomic bomb radiation dose and the aforementioned potentially confounding factors. Although ordinal logistic regression models could also be used for these ordinal outcomes (*21*), testing for the proportional odds assumption did not support the use of ordinal logistic regression models. Some radiologic procedures may have been diagnostic or therapeutic in nature; this is ''reverse causation,'' i.e., the disease ''causes'' the radiologic procedure. Unfortunately, we did not have the dates of reported radiologic procedures. Therefore, we further employed logistic regression models, which were additionally adjusted for medical histories of cancer as well as noncancer diseases such as stroke (in the models for head CT scan and cerebral angiography), cardiovascular diseases (in the models for coronary angiography) or chronic hepatitis (in the models for hepatic angiography) to explore the possibility that these medical histories could explain the relationship of atomic bomb radiation doses with exposures to medical X rays (*22*). We also estimated ORs of medical radiation exposures via logistic regression stratified by absence/presence of medical histories of cancer, stroke, heart diseases or

TABLE 1
Basic Characteristics of Participants in the Survey Compared to Eligible Mail Survey Subjects and to In-City LSS Subjects

	Participants		Mail survey subjects		In-city LSS subjects	
	n	(%)	n	(%)	n	(%)
City						
Hiroshima	8,756	(63.4)	15,422	(62.6)	61,984	(66.1)
Nagasaki	5,062	(36.6)	9,218	(37.4)	31,757	(33.9)
Sex						
Men	5,325	(38.5)	9,027	(36.6)	39,005	(41.6)
Women	8,493	(61.5)	15,613	(63.4)	54,736	(58.4)
Age at the time of the bombings						
<10 years	6,704	(48.5)	11,263	(45.7)	18,699	(20.0)
10 to < 20 years	5,577	(40.4)	9,587	(38.9)	20,024	(21.4)
≥20 years	1,537	(11.1)	3,790	(15.4)	55,018	(58.7)
Mean (SD)	10.4 (7.2)		11.8 (7.9)		28.9 (19.2)	
Age at survey						
<70 years	4,127	(29.9)	8,564[e]	(34.8)	NA	
70 to < 80 years	5,063	(36.6)	9,742[e]	(39.5)	NA	
≥80 years	4,628	(33.5)	6,334[e]	(25.7)	NA	
Mean (SD)	75.5 (7.6)		74.4 (7.9)[e]		NA	
Adult Health Study membership[a]						
Yes	2,709	(19.6)	3,956	(16.1)	17,397	(18.6)
No	11,109	(80.4)	20,684	(83.9)	76,344	(81.4)
DS02R1 weighted absorbed colon dose						
<0.005 Gy	5,762	(41.7)	10,101	(41.0)	39,024	(41.6)
0.005 to <0.1 Gy	4,416	(32.0)	8.204	(33.3)	29,676	(31.7)
0.1 to <1 Gy	2,226	(16.1)	3,872	(15.7)	15,789	(16.8)
≥1 Gy	266	(1.9)	450	(1.8)	2,231	(2.4)
Unknown[b]	1,148	(8.3)	2,013	(8.2)	7,021	(7.5)
Mean (SD)[c]	0.10 (0.28)		0.10 (0.27)		0.11 (0.30)	
Total	13,818[d]	(100)	24,640	(100)	93,741	(100)

[a] The Adult Health Study (AHS) was established in 1958 and was extended in 1977 and 2008. Individuals who were added to the AHS in 2008 were not included in this tally.
[b] Excluded from subsequent analyses.
[c] Among those with known DS02R1 weighted absorbed colon dose.
[d] The number of the participants for analysis was reduced to 12,670 after exclusion of participants with unknown DS02R1 weighted absorbed colon dose.
[e] Age as of September 30, 2008, the time of first round of mailing of the full-scale survey.

chronic hepatitis. Lastly, we investigated the association between atomic bomb radiation doses and medical radiation exposures among subjects restricted to atomic bomb radiation doses less than 1.0 Gy using finer atomic bomb radiation dose categories: <0.005 Gy, 0.005 to <0.1 Gy, 0.1 to <0.2 Gy, 0.2 to <0.5 Gy and 0.5 to <1.0 Gy. Logistic models with adjustment for city, sex, age at the time of the bombings and the AHS membership were used. The models were further adjusted for medical histories of cancer as well as noncancer diseases.

Stata 14 (StataCorp LLC, College Station, TX) was used in the statistical analyses. We present 95% confidence intervals (CIs) for parameters of interest. Two-sided statistical tests were performed, with $P \leq 0.05$ considered as statistically significant.

Power Analyses

For a given medical exposure, coded as ''never/ever,'' valid responses from 12,670 participants would allow detection of ORs of size 1.06 for a 1 Gy increase in atomic radiation dose with 0.90 power on a two-tailed, 0.05 level test. This calculation assumes the overall proportion of an ''ever'' is 0.50 for the entire sample. If the overall proportion of an ''ever'' is as low as 0.10 (or 0.90 by symmetry), the detectable OR would be 1.10 for a 1 Gy increase in atomic bomb radiation dose. These calculations assume atomic bomb radiation dose is not related to the other factors in the model and is normal in distribution. (For our study, other factors were city, sex, age at the time of bombing and AHS membership.)

Ethical Considerations

This research was based on RERF Research Protocols 1-75 and 2-08, which were approved by the Institutional Ethical Review Board of the RERF.

RESULTS

Basic characteristics of the participants compared to those who were eligible for the mail survey and with the in-city subjects of the LSS cohort are shown in Table 1. Note that those with unknown atomic bomb radiation doses were included in Table 1 to allow for comparison of distribution of radiation doses and that they were excluded from the subsequent analyses. Reflecting the fact that the participants were selected among those who were alive as of 2007, the participants were younger at the time of the bombings compared to the full LSS cohort. Approximately 20% of the participants were AHS cohort members, which was

TABLE 2
Demographic Factors and Self-Reported Medical History by Atomic Bomb Radiation Dose for Survey Participants

	DS02R1 weighted absorbed colon dose (Gy)							
	<0.005		0.005 to <0.1		0.1 to <1.0		≥1.0	
	n	%	n	%	n	%	n	%
City								
Hiroshima	3,029	52.6	3,355	76.0	1,652	74.2	171	64.3
Nagasaki	2,733	47.4	1,061	24.0	574	25.8	95	35.7
Sex								
Men	2,243	38.9	1,796	40.7	830	37.3	108	40.6
Women	3,519	61.1	2,620	59.3	1,396	62.7	158	59.4
Age at the time of the bombings								
<10 years	2,873	49.9	2,316	52.4	1,098	49.3	129	48.5
10 to <20 years	2,286	39.7	1,604	36.3	870	39.1	114	42.9
≥20 years	603	10.5	496	11.2	258	11.6	23	8.6
Mean (SD)	10.2	(0.1)	9.9	(0.1)	10.3	(0.2)	10.4	(0.4)
Age at survey								
<70 years	1,650	28.6	1,570	35.6	715	32.1	64	24.1
70 to <80 years	2,325	40.4	1,543	34.9	733	32.9	111	41.7
≥80 years	1,787	31.0	1,303	29.5	778	35.0	91	34.2
Mean (SD)	75.4	(0.1)	74.7	(0.1)	75.4	(0.2)	76.0	(0.4)
Adult Health Study membership								
Yes	1,031	17.9	243	5.5	794	35.7	242	91.0
No	4,731	82.1	4,173	94.5	1,432	64.3	24	9.0
Medical history								
Cancer	865	15.0	677	15.3	411	18.5	75	28.2
Stroke	481	8.3	402	9.1	196	8.8	38	14.3
Heart diseases	1,380	24.0	976	22.1	520	23.4	64	24.1
Chronic hepatitis	434	7.5	287	6.5	156	7.0	22	8.3
Total	5,762	100	4,416	100	2,226	100	266	100

comparable with the proportions in the potential mail survey subjects and the total in-city LSS cohort members. The distribution of atomic bomb radiation doses was similar among the three groups.

Table 2 shows demographic factors and self-reported medical histories by atomic bomb radiation dose category in the participants. Mean ages both at the time of the atomic bombings and the survey were similar among dose categories. Those exposed to higher atomic bomb radiation doses were more likely to be AHS cohort members; this is not due to self-selection, but because survivors with higher atomic bomb radiation doses were oversampled in the AHS to allow for detection of radiation effects (*17*). This dose-related increase in the proportion of the AHS also exists in the full in-city LSS cohort. The proportions of those who reported a medical history of cancer, stroke or chronic hepatitis were highest among those exposed to ≥1.0 Gy atomic bomb radiation.

Overall, 92% of the participants received at least one CT, fluoroscopy or angiography examination. By procedure, 76%, 77% and 23% of the subjects received at least one CT scan, fluoroscopy, and angiography examination, respectively and 8% of the subjects underwent radiotherapy (data not shown). CT scans were one of the major sources of medical radiation in this population. Supplementary Table S1 (http://dx.doi.org/10.1667/RR15054.1.S1) shows prevalence of self-reported medical histories among those who received medical X rays. Note that these histories were not necessarily underlying conditions of medical X-ray procedures. Overall, prevalence of chronic diseases was higher among those who received angiography examinations and radiotherapy. Heart diseases were the most common medical conditions among those who received CT scans, fluoroscopy examinations, and cerebral and coronary angiography examinations. Chronic hepatitis was the most common among those who received hepatic angiography, and cancer was the most common among those who received radiotherapy.

Associations of the number of medical radiation exposures with demographics and medical history are shown in Supplementary Tables S2 and S3 (http://dx.doi.org/10.1667/RR15054.1.S1). Men were more likely to undergo any medical X-ray procedures. Those who were older at the time of the bombings were more likely to receive some type of medical X rays, except for UGI fluoroscopy. The medical history of cancer was strongly associated with all of the medical X-ray procedures. Histories of stroke, cardiovascular diseases and chronic hepatitis were also associated with specific medical X-ray procedures (data not shown), which were frequently used to diagnose or follow up on these conditions.

The associations between atomic bomb radiation dose and the number of medical radiation exposures are shown in Table 3. The proportions with various X-ray procedures were greater in the group receiving ≥1.0 Gy for several types of medical exposures, but there were no considerable

TABLE 3
Percentages with Frequencies of Medical Radiation Exposures by Atomic Bomb Radiation Dose

	DS02R1 weighted absorbed colon dose			
	<0.005 Gy (n = 5,762)	0.005 to <0.1 Gy (n = 4,416)	0.1 to <1.0 Gy (n = 2,226)	≥1.0 Gy (n = 266)
Total CT scans (%)[a]				
0	21.4	23.0	23.1	15.8
1–5	54.4	53.0	52.1	51.5
6+	18.0	18.2	18.9	24.1
Unknown	6.2	5.8	6.0	8.7
Head CT scans (%)				
0	40.4	40.4	41.2	33.5
1–2	35.7	34.7	34.8	36.1
3–5	13.1	13.7	12.7	15.8
≥6	4.1	4.5	4.2	5.3
Unknown	6.7	6.7	7.1	9.4
Chest CT scans (%)				
0	45.6	47.9	46.8	39.1
1–2	24.9	24.1	23.6	21.1
3–5	11.4	10.4	11.7	15.4
≥6	7.0	7.7	7.4	10.2
Unknown	11.1	10.0	10.6	14.3
Abdominal CT scans (%)				
0	54.1	55.1	53.7	43.6
1–2	21.5	21.1	20.6	25.2
3–5	8.7	8.8	8.9	11.7
≥6	4.8	4.9	5.3	6.4
Unknown	11.0	10.1	11.6	13.2
Total fluoroscopy examinations (%)[b]				
0	20.3	18.3	21.4	27.1
1–5	50.9	50.7	49.2	45.5
≥6	22.6	25.4	22.5	19.6
Unknown	6.2	5.6	6.9	7.9
Upper GI fluoroscopy (%)				
0	24.0	21.5	24.8	32.0
1–2	27.7	28.1	27.5	23.7
3–5	21.4	20.7	19.9	18.1
≥6	19.0	22.5	19.7	16.5
Unknown	7.9	7.1	8.2	9.8
Lower GI fluoroscopy (%)				
0	59.4	60.0	59.7	54.9
1–2	25.9	26.0	25.6	29.7
3–5	6.8	6.2	5.4	6.8
≥6	1.8	1.9	1.6	1.9
Unknown	6.1	5.9	7.8	6.8
Total angiography examinations (%)[c]				
0	73.0	74.2	72.5	62.4
1–5	17.4	16.9	17.8	24.8
≥6	2.3	1.8	2.1	2.3
Unknown	7.3	7.1	7.6	10.5
Cerebral angiography (%)				
Never	84.4	85.1	84.1	75.2
Ever[d]	8.0	8.0	8.0	11.3
Unknown	7.6	6.9	8.0	13.5
Coronary angiography (%)				
Never	80.1	81.8	80.0	72.9
Ever [d]	13.5	12.1	13.3	16.5
Unknown	6.5	6.1	6.7	10.5
Hepatic angiography (%)				
Never	89.0	89.7	87.7	84.2
Ever[d]	3.6	3.1	3.6	5.3
Unknown	7.4	7.2	8.7	10.5

Continued on next page

TABLE 3
Continued.

	DS02R1 weighted absorbed colon dose			
	<0.005 Gy	0.005 to <0.1 Gy	0.1 to <1.0 Gy	≥1.0 Gy
	(n = 5,762)	(n = 4,416)	(n = 2,226)	(n = 266)
Radiotherapy (%)				
Never	84.6	84.7	83.7	74.8
Ever	7.3	7.5	7.5	12.0
Unknown	8.1	7.8	8.8	13.2
Total (%)	100	100	100	100

[a] Head, chest and abdominal CT scans.
[b] Upper and lower gastrointestinal (GI) fluoroscopy examinations.
[c] Cerebral, coronary and hepatic angiography examinations.
[d] Three responses (1–2, 3–5 and ≥6 times) were combined because the proportions of responses, 3–5 and ≥6, were small.

differences among the dose groups <0.005, 0.005 to <0.1 and 0.1 to <1.0 Gy. This was the case for head, chest, abdominal CT, LGI fluoroscopy, cerebral, coronary and hepatic angiography. In contrast to other procedures, the proportion of those who ever received UGI fluoroscopy was smallest in the highest atomic bomb dose category (≥1.0 Gy). The proportion of those who ever underwent radiotherapy was highest in the highest atomic bomb dose category.

The associations between atomic bomb radiation dose and medical radiation exposures presented as ORs adjusted for potential confounding factors (Table 4-1) were consistent with the above-mentioned findings. Compared to the control radiation group (<0.005 Gy), each of the two radiation groups <1.0 Gy had ORs near unity. In contrast, among those exposed to ≥1.0 Gy atomic bomb radiation, the ORs of all procedures were greater than that for the control group. Particularly, ORs of head and abdominal CT scans, LGI fluoroscopy, cerebral and coronary angiography examinations, and radiotherapy were significantly higher for the ≥1.0 Gy group. There were several significant trends in the probability of medical X-ray procedures when treating atomic bomb radiation dose as continuous; the largest effect observed was an OR of 1.43 (95% CI: 1.15 to 1.77) for cerebral angiography.

For head and chest CT scans and UGI fluoroscopy examination, ORs of the categorical number of examinations rather than ever/never were also calculated (Supplementary Table S4; http://dx.doi.org/10.1667/RR15054.1.S1). Exposures to ≥1.0 Gy atomic bomb radiation were significantly associated with larger numbers of head and chest CT examinations. There was no significant association between atomic bomb radiation doses and the number of UGI fluoroscopy examinations.

The ORs estimated by logistic models additionally adjusted for medical histories are presented in Table 4-2. ORs for atomic bomb radiation dose categories less than 1.0 Gy changed little from ORs when we did not adjust for medical histories. However, after adjusting for medical histories, the ORs for the ≥1.0 Gy group decreased notably in all of the procedures; only the OR of abdominal CT scan remained significant (compare Tables 4-1 and 4-2). These results suggested that more frequent medical radiation exposures among those who were exposed to ≥1.0 atomic

TABLE 4-1
Associations between Atomic Bomb Radiation Dose and Medical Radiation Exposures

		DS02 weighted absorbed colon dose								
		<0.005 Gy	0.005 to <0.1 Gy		0.1 to <1.0 Gy		≥1.0 Gy		Linear trend	
		Reference	OR[a]	95% CI	OR[a]	95% CI	OR[a]	95% CI	OR[a]	95% CI
Total CT	(ever)	1	0.93	(0.84 to 1.02)	0.95	(0.84 to 1.07)	1.57	(1.10 to 2.23)	1.18	(0.99 to 1.40)
Head CT	(ever)	1	1.00	(0.92 to 1.09)	0.96	(0.86 to 1.07)	1.35	(1.02 to 1.78)	1.08	(0.93 to 1.24)
Chest CT	(ever)	1	0.94	(0.86 to 1.02)	0.98	(0.88 to 1.09)	1.30	(0.99 to 1.72)	1.14	(0.98 to 1.31)
Abdominal CT	(ever)	1	1.02	(0.94 to 1.12)	1.05	(0.95 to 1.18)	1.59	(1.21 to 2.09)	1.27	(1.10 to 1.47)
Total fluoroscopy	(ever)	1	0.97	(0.88 to 1.08)	1.03	(0.90 to 1.17)	1.06	(0.79 to 1.43)	1.08	(0.92 to 1.27)
UGI fluoroscopy	(ever)	1	0.99	(0.89 to 1.09)	1.06	(0.94 to 1.19)	1.05	(0.79 to 1.39)	1.09	(0.93 to 1.27)
LGI fluoroscopy	(ever)	1	0.99	(0.90 to 1.08)	1.04	(0.93 to 1.16)	1.52	(1.16 to 2.00)	1.22	(1.06 to 1.41)
Total angiography	(ever)	1	0.93	(0.84 to 1.04)	1.05	(0.92 to 1.19)	1.70	(1.26 to 2.28)	1.36	(1.15 to 1.61)
Cerebral angiography	(ever)	1	0.96	(0.83 to 1.12)	1.01	(0.84 to 1.21)	1.77	(1.18 to 2.65)	1.43	(1.15 to 1.77)
Coronary angiography	(ever)	1	0.89	(0.79 to 1.01)	1.03	(0.89 to 1.20)	1.47	(1.03 to 2.09)	1.28	(1.06 to 1.55)
Hepatic angiography	(ever)	1	0.83	(0.67 to 1.04)	1.02	(0.78 to 1.32)	1.45	(0.80 to 2.63)	1.23	(0.89 to 1.71)
Radiotherapy	(ever)	1	1.03	(0.88 to 1.20)	1.04	(0.86 to 1.26)	1.90	(1.26 to 2.87)	1.41	(1.13 to 1.76)

[a] Adjusted for city, sex, age at the time of the bombings and AHS membership.
OR = odds ratio; CI = confidence interval.

TABLE 4-2
Associations between Atomic Bomb Radiation Dose and Medical Radiation Exposures, Adjusting for Self-Reported History of Cancer and other Chronic Diseases

		DS02 weighted absorbed colon dose								
		<0.005 Gy	0.005 to <0.1 Gy		0.1 to <1.0 Gy		≥1.0 Gy		Linear trend	
		Reference	OR[a]	95% CI	OR[a]	95% CI	OR[a]	95% CI	OR[a]	95% CI
Total CT	(ever)	1	0.93	(0.84 to 1.03)	0.89	(0.79 to 1.01)	1.27	(0.88 to 1.83)	1.03	(0.86 to 1.23)
Head CT	(ever)	1	0.98[b]	(0.89 to 1.07)	0.92[b]	(0.82 to 1.02)	1.12[b]	(0.83 to 1.52)	0.95[b]	(0.81 to 1.12)
Chest CT	(ever)	1	0.93	(0.85 to 1.01)	0.93	(0.83 to 1.04)	1.12	(0.83 to 1.50)	1.03	(0.89 to 1.21)
Abdominal CT	(ever)	1	1.04	(0.95 to 1.14)	1.01	(0.90 to 1.13)	1.39	(1.04 to 1.87)	1.15	(0.98 to 1.34)
Total fluoroscopy	(ever)	1	0.96	(0.86 to 1.07)	0.99	(0.87 to 1.13)	0.97	(0.71 to 1.32)	1.03	(0.87 to 1.22)
UGI fluoroscopy	(ever)	1	0.98	(0.88 to 1.08)	1.02	(0.90 to 1.15)	0.97	(0.72 to 1.30)	1.04	(0.88 to 1.21)
LGI fluoroscopy	(ever)	1	0.98	(0.89 to 1.07)	1.02	(0.91 to 1.14)	1.32	(0.99 to 1.75)	1.13	(0.97 to 1.31)
Total angiography	(ever)	1	0.92	(0.83 to 1.03)	1.04	(0.91 to 1.19)	1.61	(1.17 to 2.22)	1.30	(1.09 to 1.54)
Cerebral angiography	(ever)	1	0.94[b]	(0.80 to 1.10)	1.06[b]	(0.87 to 1.29)	1.54[b]	(0.98 to 2.40)	1.28[b]	(1.01 to 1.62)
Coronary angiography	(ever)	1	0.95[c]	(0.82 to 1.11)	1.05[c]	(0.87 to 1.26)	1.23[c]	(0.78 to 1.95)	1.16[c]	(0.91 to 1.48)
Hepatic angiography	(ever)	1	0.89[d]	(0.69 to 1.13)	1.03[d]	(0.76 to 1.39)	1.15[d]	(0.55 to 2.41)	1.15[d]	(0.78 to 1.69)
Radiotherapy	(ever)	1	1.07	(0.90 to 1.27)	0.91	(0.74 to 1.13)	1.41	(0.89 to 2.24)	1.14	(0.89 to 1.47)

[a] Adjusted for city, sex, age at the time of the bombings, AHS membership and history of cancer.
[b] Additionally adjusted for history of stroke.
[c] Additionally adjusted for history of heart diseases.
[d] Additionally adjusted for history of chronic hepatitis.
OR = odds ratio; CI = confidence interval.

bomb radiation were possibly mediated by receiving the procedures to diagnose or monitor radiation-associated diseases. Results of stratified analyses by those with and without medical histories of cancer, stroke, heart diseases or chronic hepatitis are shown in Supplementary Table S5 (http://dx.doi.org/10.1667/RR15054.1.S1). ORs for 0.005 to <0.1 Gy and 0.1 to <1.0 Gy groups were near unity in both strata with and without medical histories. Among those without medical histories, ORs of those receiving head and abdominal CT scans, LGI fluoroscopy, and cerebral, coronary and hepatic angiography were increased for the group receiving ≥1.0 Gy doses. Among those with medical histories, ORs of those receiving chest and abdominal CT scans, LGI fluoroscopy, cerebral angiography and radiotherapy were increased for the group with ≥1.0 Gy atomic bomb radiation doses. Doses from atomic bomb were not associated with exposures to UGI fluoroscopy, regardless of medical history.

The associations of low atomic bomb radiation dose with medical radiation exposures using finer dose groups were also assessed (Supplementary Table S6-1; http://dx.doi.org/10.1667/RR15054.1.S1). There were no statistically significant increases in ORs of any medical X-ray procedures for any radiation dose categories compared to the reference group (<0.005 Gy). Again, no significant dose response in probabilities of receiving any medical X-ray procedures with atomic bomb radiation doses was found, except for coronary angiography (OR 1.40; 95% CI: 1.00 to 1.96). These associations were unchanged after adjustment for histories of cancer and other chronic diseases (Supplementary Table S6-2).

We compared calculated mean bone marrow doses from CT scans and UGI fluoroscopy examinations between categories with <1.0 Gy and ≥1.0 Gy of atomic bomb radiation doses. Mean dose from CT scans among those with ≥1.0 Gy atomic bomb radiation dose was significantly higher by 5.6 mGy (95% CI for mean difference: 2.1–9.1) from the mean of 24.4 mGy for those with <1.0 Gy atomic bomb radiation dose; whereas the mean dose from UGI fluoroscopy among the ≥1.0 Gy group was significantly lower by 0.7 mGy (95% CI for mean difference: 0.2–1.2) from the mean of 4.3 mGy in the <1.0 Gy group.

DISCUSSION

This study demonstrated that exposures to medical X rays were more frequent among those who were exposed to ≥1 Gy atomic bomb radiation. Although these participants received medical X rays more frequently than those exposed to lower atomic bomb radiation doses, there is little possibility that medical X rays could affect risk estimate analysis, because diagnostic medical X-ray doses were much lower than those from atomic bomb radiation among those exposed to high atomic bomb doses. For example, according to a nationwide survey of CT practice in Japan in 2000 (*23*), the effective doses per examination were 2.4 mSv, 9.1 mSv and 12.9 mSv for head, chest and abdomen CT scans, respectively. Doses from radiotherapy are quite high to the target tissue: 50–60 Gy for solid tumors (*16*), but radiotherapy is primarily used to treat malignant diseases, which are usually the outcomes of interest in atomic bomb radiation studies, so radiotherapy is also less likely to affect the risk estimates of malignant diseases. Nevertheless, we should note the possibility that radiotherapy could impact risk estimates of noncancer diseases. History of radiotherapy should be taken into consideration when assessing risks for noncancer diseases associated with atomic bomb radiation. On the other hand, the probability of receiving medical X rays was not associated with atomic bomb radiation doses among those who were exposed to <1.0 Gy. Therefore, we have no evidence that medical X-ray exposures have caused appreciable bias in the atomic bomb risk estimates.

In contrast to our findings that frequency of medical X-ray procedures were higher among those with higher atomic bomb radiation doses, in an early study of AHS participants, there was no significant difference in mean cumulative bone marrow doses from diagnostic medical X rays received from 1964 through 1982 by atomic bomb radiation dose: the mean dose was 11.7 mGy, 12.6 mGy and 11.8 mGy in atomic bomb dose categories of <100 mGy, 100–999 mGy and >1,000mGy, respectively (*15*) . Medical radiation exposures have possibly increased over the past several decades, particularly among those who were exposed to high atomic bomb radiation doses, due to an increase in the type and the number of medical X-ray procedures (*16*) and to an increase in morbidity as the cohort ages. According to the latest cancer incidence study in the LSS, approximately one half of the incident solid cancer cases that were ascertained between 1958 and 2009 occurred after the late 1980s (*3*). It was also reported that absolute risks (i.e., excess rates) of solid cancers associated with atomic bomb radiation increased with increasing attained age, although relative risks decreased.

Most of the ORs significantly greater than 1 for medical radiation exposures among those with ≥1.0 Gy atomic bomb radiation were attenuated by adjustment for medical histories, suggesting that those with high doses were likely to develop more diseases associated with atomic bomb radiation and therefore had more opportunities to receive medical X rays. Although self-reported medical history data in the current study were subject to misclassification, results from analyses stratified by medical histories (Supplementary Table S5; http://dx.doi.org/10.1667/RR15054.1.S1) provided additional insight into the associations between atomic bomb radiation dose and medical radiation exposures. We found that exposures to head and abdominal CT scans, LGI fluoroscopy and any angiography were associated with ≥1.0 Gy atomic bomb radiation among those without medical histories. These procedures might be related to radiation-associated diseases that were not considered in the current study. It was also possible that exposures to ≥1.0 Gy atomic bomb radiation were directly associated with these procedures. We can generally assume that those with medical histories receive medical X-ray procedures independently of doses from atomic bomb radiation, and this assumption was supported by the finding that the doses were not associated with exposures to most of the procedures among those with medical histories. However, among those having medical histories, participants with ≥1.0 Gy atomic bomb radiation were significantly more likely to receive abdominal CT scan and radiotherapy. For reasons that remain unclear, these procedures were more intensively administered to those with higher doses.

Nevertheless, other mechanisms that produce spurious association between atomic bomb radiation and medical X rays might exist. Confounding of the association by health consciousness among those who were exposed to higher doses of atomic bomb radiation may partly explain them. Although survivors know where they were at the time of the bombings, they generally do not know their estimated doses because ABCC/RERF has never informed study participants of individual doses. In addition, a difference in recall of medical radiation exposures by atomic bomb radiation dose could bias the association. Since atomic bomb doses were positively associated with the probability of being selected for the AHS, in which interviews about medical radiation exposures have been conducted, those who participated in the AHS might have recalled medical radiation exposures more accurately. However, AHS membership was adjusted for in the multivariate analyses to remove that potential bias. No obvious source of other confounding factors was identified in the current study.

Use of medical X rays is not limited to clinical practice. Screening examinations with the use of X rays are common today. Screening X rays have the potential to affect risk estimates of atomic bomb radiation, because screening is usually aimed at healthy individuals and therefore is possibly performed apart from the occurrence of atomic bomb radiation-associated diseases. Although we did not specifically ask questions about medical radiation exposures received for screening purposes, the findings of the current study suggested that substantial proportions of UGI fluoroscopy examinations might have been for screening purposes: approximately 20% of the subjects reported six or more UGI fluoroscopy examinations. Men and those who were younger at the time of the bombings, in more recent birth cohorts, were more likely to undergo the examinations, but atomic bomb doses were not associated with the number of the examinations among those with and without medical histories of major chronic diseases.

To further delineate the use of UGI fluoroscopy for screening, we investigated the medical histories of those who received UGI fluoroscopy examination as well as other diagnostic medical X-ray procedures (Table S1; http://dx.doi.org/10.1667/RR15054.1.S1). We assumed that the reported medical radiation exposures were for screening purposes if there was no medical history of major chronic diseases (cancer, heart diseases, stroke and chronic hepatitis). History of a major chronic disease was more frequent among those who underwent angiography (77.7%) and radiotherapy (73.1%), reflecting the fact that angiography is used to make a definite diagnosis and radiotherapy is used to treat malignant diseases. In contrast, the chronic disease occurrence was lower among those who received CT (50.1%) and UGI fluoroscopy (45.1%), likely due to their possible uses in screening. In Japan, where stomach cancer was the most common cancer site until recently (*24*), one of the most common screening X-ray examinations has been the UGI fluoroscopy (*25*). UGI fluoroscopy has been included in the cancer screening program for the certified atomic bomb survivors. In addition, municipal governments and employers have provided screening opportunities for stomach cancer. Effective doses from UGI fluoroscopy averaged over countries with high healthcare level were reported as 8.9, 7.2 and 3.6 mSv per examination for the periods 1970–1979, 1980–1990 and 1991–1996, respectively (*26*). The findings from the current study indicated that characteristics of exposures to screening X rays were different from those of other medical X-ray procedures used in clinical settings. Although there was no significant dose-response relationship (OR 1.22; 95% CI: 0.93 to 1.61) between atomic bomb radiation doses and the probability of UGI fluoroscopy examinations in the low-dose ranges <1.0 Gy, given their high frequency and higher estimated doses from UGI fluoroscopy compared to those exposed to ≥1.0 Gy atomic bomb radiation, more detailed study of UGI and other screening X-ray procedures may be warranted.

There were some limitations in this study. First, we did not collect information about time at and reasons for examinations for diagnostic X rays. The current study suggested that those who were exposed to high atomic bomb radiation were more likely to receive medical X rays perhaps due to medical practice for diseases associated with atomic bomb radiation, but it is difficult to determine the temporal sequence of the disease and exposure to diagnostic X rays. In addition, medical X-ray doses changed over time, but we could not incorporate that into our analyses.

Next, subjects of the current study did not necessarily represent the full LSS cohort. Although basic characteristics such as atomic bomb radiation doses in the participants were similar to those in the in-city LSS cohort, only approximately 15% of the in-city LSS cohort subjects participated in the current survey and not-in-city subjects, who would serve as a source of information about general populations, were not included. Since the study participants belong to the later birth cohorts within the LSS (earlier cohorts are deceased) and they had greatly benefited from modern medical X-ray procedures as well as from the welfare program for atomic bomb survivors, this study best serves as a source of information on relatively recent medical radiation exposures.

The third limitation is that we could not validate the self-reported data on medical radiation exposures due to the unavailability of medical records. Several studies have assessed the validity of self-reported medical X-ray histories and found over-reporting among those who received fewer medical X-ray examinations, but under-reporting among those who received frequent medical X-ray examinations (*27–29*). In a general Japanese population, over-reporting of screening history was demonstrated, particularly among those who had medical history and family history associated with the target disease of the screening (*30*). However, most studies assessing the validity of self-reported medical X-ray history found non-differential misclassification (*27–29*), which generally alters the exposure-outcome association toward the null.

Another limitation is that the questionnaire did not cover several types of medical X-ray procedures: plain radiographs, nuclear medicine and interventional radiology. Doses from these procedures could affect the risk estimate analysis of exposures to low-dose atomic bomb radiation if they were administered apart from atomic bomb radiation-associated conditions. However, plain radiographs usually deliver much lower doses than CT, fluoroscopy or angiography, and nuclear medicine and interventional radiology are less common than the procedures targeted here.

To obtain full and accurate information about medical radiation exposures depending only on a single source of information is difficult, especially about procedures administered in early periods. Combining the current questionnaire data with the data collected in earlier periods would give a better picture of the full effect of medical X rays. An attempt is underway to assemble and link those data to our questionnaire information.

In conclusion, this questionnaire survey, conducted more than 60 years after the atomic bombings, showed that there were relatively more medical radiation exposures among those who were exposed to atomic bomb radiation of ≥1.0 Gy, perhaps due to high frequency of radiation-associated diseases, but for that group, medical X-ray doses were much lower than atomic bomb doses. Therefore, medical radiation exposure is not thought to appreciably affect the risk estimates of atomic bomb radiation at high-dose ranges. On the other hand, no positive association of atomic bomb radiation dose with medical radiation exposure was seen in the ranges below 1.0 Gy, notably in the low-dose range of 0.005 to <0.1 Gy, compared to the reference group of <0.005 Gy. Although further information on the actual medical X-ray doses would more definitively clarify the extent to which medical radiation exposures affect the accuracy of the risk estimate analysis, the current study provides a reasonable preliminary indication that medical X rays have had little or no effect on risk estimates of atomic bomb radiation among those exposed to atomic bomb doses of approximately <1 Gy.

SUPPLEMENTARY INFORMATION

Table S1. Presence of self-reported medical conditions among those who received diagnostic or therapeutic medical X rays and among total study participants.

Table S2. Associations of the number of medical radiation exposures with demographic factors and history of cancer.

Table S3. Associations of the number of medical radiation exposures with demographic factors and past medical histories.

Table S4. Associations between atomic bomb radiation dose and the number of medical radiation exposures.

Table S5. Associations between atomic bomb radiation dose and medical radiation exposures among those with or without self-reported history of cancer and other chronic diseases.

Table S6-1. Associations between atomic bomb radiation dose and medical radiation exposures for those having atomic bomb radiation dose between 0–1 Gy.

Table S6-2. Associations between atomic bomb radiation dose and medical radiation exposures adjusting for self-reported history of cancer and other chronic diseases for those having atomic bomb radiation dose between 0–1 Gy.

ACKNOWLEDGMENTS

The Radiation Effects Research Foundation (RERF), Hiroshima and Nagasaki, Japan is a public interest foundation funded by the Japanese Ministry of Health, Labour and Welfare (MHLW) and the U.S. Department of Energy (DOE). This publication was supported by RERF Research Protocols 1-75 and 2-08, and in part by the National Center for Advancing Translational Sciences of the National Institutes of Health (NIH; grant no. UL1TR000039) and the National Institute of General Medical Sciences of the NIH (grant no. P20 GM109005). The views of the authors do not necessarily reflect those of the two governments or NIH. We also acknowledge Dr. Paula K. Roberson (University of Arkansas for Medical Sciences) for her cooperation.

Received: January 31, 2018; accepted: March 1, 2019; published online: March 29, 2019

REFERENCES

1. Ozasa K, Shimizu Y, Suyama A, Kasagi F, Soda M, Grant EJ, et al. Studies of the mortality of atomic bomb survivors, Report 14, 1950–2003: an overview of cancer and noncancer diseases. Radiat Res 2012; 177:229–43.
2. Preston DL, Ron E, Tokuoka S, Funamoto S, Nishi N, Soda M, et al. Solid cancer incidence in atomic bomb survivors: 1958–1998. Radiat Res 2007; 168:1–64.
3. Grant EJ, Brenner A, Sugiyama H, Sakata R, Sadakane A, Utada M, et al. Solid cancer incidence among the Life Span Study of atomic bomb survivors: 1958–2009. Radiat Res 2017; 187:513–37.
4. Cullings HM, Fujita S, Funamoto S, Grant EJ, Kerr GD, Preston DL. Dose estimation for atomic bomb survivor studies: It's evolution and present status. Radiat Res 2006; 166:219–54.
5. Cullings HM, Grant EJ, Egbert SD, Watanabe T, Oda T, Nakamura F, et al. DS02R1: Improvements to atomic bomb survivors' input data and implementation of Dosimetry System 2002 (DS02) and resulting changes in estimated doses. Health Phys 2017; 112:56–97.
6. Gilbert ES. Some effects of random dose measurement errors on analyses of atomic bomb survivor data. Radiat Res 1984; 98, 591–605.
7. Pierce DA, Stram DO, Vaeth M. Allowing for random errors in radiation dose estimates for the atomic bomb survivor data. Radiat Res 1990; 123:275–84.
8. Shimizu Y, Pierce DA, Preston DL, Mabuchi K. Studies of the mortality of atomic bomb survivors. Report 12, part II. Noncancer mortality: 1950–1990. Radiat Res 1999; 152:374–89.
9. Uncertainties in the estimation of radiation risks and probability of disease causation. NCRP Report No. 171. Bethesda: National Council on Radiation Protection and Measurements; 2012.
10. Brenner DJ, Doll R, Goodhead DT, Hall EJ, Land CE, Little JB, et al. Cancer risks attributable to low doses of ionizing radiation: assessing what we really know. Proc Natl Acad Sci U S A 2003; 100:13761–6.
11. Antoku S, Russell WJ, Milton RC, Yoshinaga H, Takeshita K, Sawada S. Dose to patients from roentgenography. Health Phys 1972; 23:291–9.
12. Russell WJ. Medical x-ray exposure among Hiroshima and Nagasaki atomic bomb survivors. Nippon Acta Radiol 1971; 30:12–54.
13. Sawada S, Wakabayashi T, Takeshita K, Yoshinaga H, Russell WJ. Radiologic practice since the atomic bombs Hiroshima and Nagasaki. Am J Public Health 1971; 61:2455–68.
14. Sawada S, Fujita S, Russell WJ, Takeshita K. Radiological practice in Hiroshima and Nagasaki: trents from 1964 to 1970. Am J Public Health 1975; 65:622–33.
15. Yamamoto O, Antoku S, Russell WJ, Fujita S, Sawada S. Medical x-ray exposure doses as contaminants of atomic bomb doses. Health Phys 1988; 54:257–69.
16. Effects of ionizing radiation: United Nations Scientific Committee on the Effects of Atomic Radiation: UNSCEAR 2006 Report to the General Assembly, with scientific annexes. New York: United Nations; 2008.
17. Yamada M, Wong FL, Fujiwara S, Akahoshi M, Suzuki G. Noncancer disease incidence in atomic bomb survivors, 1958–1998. Radiat Res 2004; 161:622–32.
18. Sakata R, McGale P, Grant EJ, Ozasa K, Peto R, Darby SC. Impact of smoking on mortality and life expectancy in Japanese smokers: a prospective cohort study. BMJ 2012; 345:e7093.
19. Kato K, Antoku S, Sawada S, Wada T, Russell WJ. Organ doses to atomic bomb survivors during photofluorography, fluoroscopy and computed tomography. Br J Radiol 1991; 64:728–33.
20. Hosmer DW, Lemeshow S. The multinominal logistic regression model. Applied logistic regression. 2nd ed. New York: John Wiley & Sons, Inc.; 2000. p. 260–87.
21. Hosmer DW, Lemeshow S. Ordinal logistic regression models. Applied logistic regression. 2nd ed. New York: John Wiley & Sons, Inc.; 2000. p. 288–308.
22. Szklo M, Nieto FJ. Identifying noncausal associations: confounding. Epidemiology: Beyond the basics, 3rd ed. Burlington: Jones & Bartlett Learning; 2014. p.159–62.
23. Nishizawa K, Matsumoto M, Iwai K, Maruyama T. [Survey of CT practice in Japan and collective effective dose estimation]. Nihon Igaku Hoshasen Gakkai Zasshi 2004; 64:151–8.
24. Katanoda K, Hori M, Matsuda T, Shibata A, Nishino Y, Hattori M, et al. An updated report on the trends in cancer incidence and mortality in Japan, 1958–2013. Jpn J Clin Oncol 2015; 45:390–401.
25. Hisamichi S. Community screening programs of cancer and cardiovascular diseases in Japan. J Epidemiol 1996; 6:S159–63.
26. Sources and effects of ionizing radiation. Volume I: Sources. United Nations Scientific Committee on the Effects of Atomic Radiation, 2000 report to the General Assembly, with scientific annexes. New York: United Nations; 2000.
27. Berrington de Gonzalez A, Ekbom A, Glass AG, Galanti MR, Grimelius L, Allison MJ, et al. Comparison of documented and recalled histories of exposure to diagnostic x-rays in case-control studies of thyroid cancer. Am J Epidemiol 2003; 157:652–63.
28. Pogoda JM, Preston-Martin S. Radiation exposure from diagnostic imaging: agreement between self-report and medical records. Health Phys 2002; 83:907–17.
29. Preston-Martin S, Pogoda JM. Estimation of radiographic doses in a case-control study of acute myelogenous leukemia. Health Phys 2003; 84:245–59.
30. Tsubono Y, Fukao A, Hisamichi S, Hosokawa T, Sugawara N. Accuracy of self-report for stomach cancer screening. J Clin Epidemiol 1994; 47:977–81.