Paper

PROJECTED LIFETIME CANCER RISKS FROM EXPOSURE TO REGIONAL RADIOACTIVE FALLOUT IN THE MARSHALL ISLANDS

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Abstract—**Radioactive fallout from nuclear test detonations during 1946–1958 at Bikini and Enewetak Atolls in the Marshall Islands (MI) exposed populations living elsewhere in the MI archipelago. A comprehensive analysis, presented in seven companion papers, has produced estimates of tissue-specific radiation absorbed dose to MI residents at all historically inhabited atolls from internal (ingested) and external irradiation resulting from exposure to radioactive fallout, by calendar year, and by age of the population at time of exposure. The present report deals, for the first time, with the implications of these doses for cancer risk among exposed members of the MI population. Radiation doses differed by geographic location and year of birth, and radiation-related cancer risk depends upon age at exposure and age at observation for risk. Using dose-response models based on committee reports published by the National Research Council and the National Institutes of Health, we project that, during the lifetimes of members of the MI population potentially exposed to ionizing radiation from weapons test fallout deposited during the testing period (1948–1958) and from residual radioactive sources during the subsequent 12 y (1959–1970), perhaps 1.6% (with 90% uncertainty range 0.4% to 3.4%) of all cancers might be attributable to fallout-related radiation exposures. By sub-population, the projected proportion of cancers attributable to radiation from fallout from all nuclear tests conducted in the Marshall Islands is 55% (28% to 69%) among 82 persons exposed in 1954 on Rongelap and Ailinginae, 10% (2.4% to 22%) for 157 persons exposed on Utrik, and 2.2% (0.5% to 4.8%) and 0.8% (0.2% to 1.8%), respectively, for the much larger populations exposed in mid-latitude locations including Kwajalein and in southern locations including Majuro. By cancer type, point estimates of attributable risk varied, by location, between 12% and 95% for thyroid cancer, between 2% and 78% for leukemia, and between 0.8% and 55% for all cancers combined. The largest projected risks pertain to the Rongelap Island community and the lowest risks pertain to the populations resident on the southern-most atolls. While the projected cancer risks are smaller than those estimated by the National Cancer Institute in a more simplistic analysis conducted in 2004, these estimates of cancer risk are the best available as they are based on the most detailed dose reconstruction to date and comprehensively include populations at all locations and dose contributions from all nuclear tests.**

Health Phys. 99(2):201–215; 2010

Key words: cancer; fallout; Marshall Islands; nuclear weapons

INTRODUCTION

Previously administered by Japan under a League of Nations mandate, the Marshall Islands (MI) archipelago was occupied by the United States (U.S.) during World War II. The group of atolls and islands was administered by the U.S. as a United Nations Trust Territory until 1986 when the Republic of the Marshall Islands (RMI) was established as a sovereign nation in free association with the U.S.

After World War II, the U.S. established the Pacific Proving Grounds, essentially the atolls of Bikini and Enewetak and the nearby ocean at the northwestern end of the archipelago, for testing nuclear weapons. The populations of Bikini and Enewetak were relocated to other atolls prior to testing. Between 1946 and 1958, 66 nuclear test detonations were carried out on or near to the atolls of the Marshall Islands. As discussed in four of the companion papers (Beck et al. 2010; Bouville et al. 2010; Simon et al. 2010a and b), 20 of these tests resulted in varying levels of radiation exposure from radioactive fallout to residents of the inhabited islands in the archipelago. Significant exposures to radioactive fallout began in 1948, and exposures to residual fallout radioactivity continued after the cessation of testing in 1958, until about 1970. The highest exposures by far were from the thermonuclear test (code name Castle Bravo) detonated on Bikini on 1 March 1954, which unexpectedly resulted in very substantial radiation exposure to 82 members of the Rongelap community who were on Rongelap Island and nearby Sifo Island (Ailinginae Atoll) and substantial

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(*Manuscript accepted* 5 *March* 2010)

0017-9078/10/0

DOI: 10.1097/HP.0b013e3181dc4e84

exposure to 157 members of the Utrik community. Lesser exposures of different degrees affected approximately 13,000 other Marshallese then living elsewhere in the archipelago, including the major population centers of Majuro and Kwajalein.

The purpose of the present paper is to update and replace the cancer risk estimates of an earlier report (DCEG 2004) titled "Estimation of the Baseline Number of Cancers among Marshallese and the Number of Cancers Attributable to Exposure to Fallout from Nuclear Weapons Testing Conducted in the Marshall Islands" and to provide thorough documentation of the methods used to estimate cancer risks. Presented here, for the first time, is a comprehensive assessment of cancer risks from exposure to fallout from all nuclear tests for all Marshallese alive during the years 1948 through 1970.

MATERIALS AND METHODS

Ionizing radiation exposure is a known cancer risk factor and, because it is often possible to estimate tissue-specific radiation doses with reasonable precision, the relationship between dose and subsequent cancer risk is probably better quantified than for any other common environmental carcinogen. In the companion papers, estimates of organ-specific radiation absorbed doses from fallout-related internal (ingested) and external radioactive materials are derived for residents of different atolls affected by different test explosions, by year and age. These values have been summarized to provide yearly radiation doses corresponding to all calendar years from 1948 through 1970, all historically inhabited atolls, and all ages when exposures occurred.

Although small-scale medical studies have been reported describing early and late health effects among residents of Rongelap and Utrik in particular (Conard et al. 1970; Hamilton et al. 1987; Cronkite et al. 1997; Takahashi et al. 1997, 2001), and records are available concerning compensation claims awarded to RMI residents who developed cancers and other health problems subsequent to fallout-related events (NCT 2004), the infrastructure of medical reporting and records in the RMI is not sufficient to support detailed epidemiological studies such as those carried out among survivors of the atomic bombings of Hiroshima and Nagasaki, Japan (Preston et al. 2003, 2007). Fortunately, however, much of the dose-response information provided by studies of the atomic bomb survivors and of other populations exposed to medical, occupational, and other sources of radiation, is summarized in the recent report of the U.S. National Research Council's Committee to Assess Health Risks from Exposure to Low Levels of Ionizing Radiation, otherwise known as BEIR VII (NRC 2006). The goal of the present investigation is to estimate the likely consequences of the nuclear tests in terms of cancer risk to the MI population from fallout-related radiation exposures, and to that end we have used the BEIR VII dose-response models, with a few modifications which are noted in the text. Cancer risk projections are provided for post-1948 lifetime baseline[‡] and radiation-related numbers of leukemias and cancers of the thyroid, stomach, colon, and all remaining solid cancer sites considered as a group. Lifetime risk is further divided into "past" (from 1948 through 2008) and "future" (after 2008) periods.

Population

Table 1 shows total MI population numbers by sex, as determined by censuses carried out in 1935, 1958, 1967, and 1973 (RMI 1987, Tables 1.1 and 1.7). These data indicate that the MI population increased by about 33% over the 1935 value between 1935 and 1958, by 36% of the 1958 value between 1958 and 1967, and by another 28% between 1967 and 1973, and that the male/female ratio decreased from 1.10 in 1935 to 1.06 in 1958 and to a little over 1.04 in 1967 and 1973. Fig. 1 shows estimated sex-specific MI population sizes by year, obtained by interpolation using the standard fitted Bezier cubic spline curve algorithm (Foley et al. 1992) as implemented in the Microsoft Excel[§] spreadsheet command for XY scatter plot with data points connected by smoothed lines.

The census reports of 1958, 1967, and 1973 also gave total population numbers by atoll (RMI 1987, Table 1.2), which we used to apportion the total populations for these and other years by atoll. As a general rule, for yearly apportioning of the interpolated yearly total numbers among the various atolls, we used the 1958 proportional allocation for each of the years 1948–1957, and interpolated linearly between 1958 and 1967 for 1959–1966 and between 1967 and 1973 for 1968–1970. Estimated numbers are plotted by year in Fig. 2 for the combined populations of the northern atolls of Rongelap and Utrik, the mid-latitude population center Kwajalein, a group of six other mid-latitude atolls (Ailuk, Likiep, Mejit, Ujelang, Wotho, and Wotje), the southern population center Majuro, and the remaining 13 southern atolls (Ailinglaplap, Arno, Aur, Ebon, Jaluit, Kili, Lae, Lib, Maloelap, Mili, Namorik, Namu, and Ujae). Fig. 2

[‡] Cancers that presumably would have occurred in the absence of exposure to radioactive fallout.

[§] Provided for information purposes only. Identification of software does not imply any endorsement.

Table 1. Census-based total Marshall Islands population by sex and census year (RMI 1987).

Sex	Census year			
	1935	1958	1967	1973
Males	5,480	7,175	9,658	12,335
Females	4,966	6,753	9,267	11,800

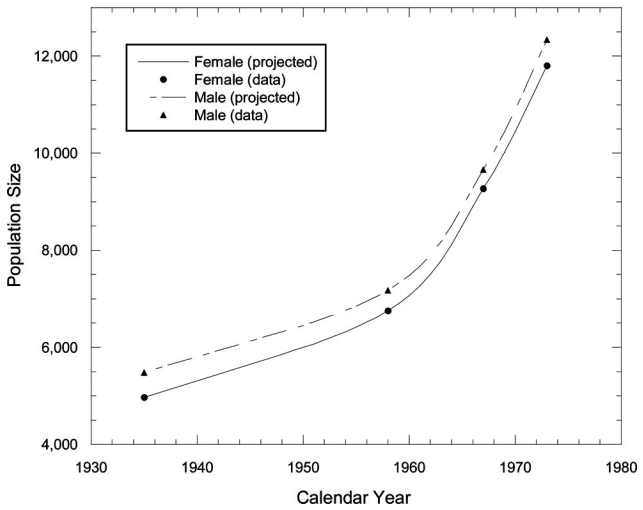

Fig. 1. Fitted Bezier cubic splines expressing yearly interpolated, sex-specific population numbers for the entire Marshall Islands population, based on census results for 1935, 1958, 1967, and 1973.

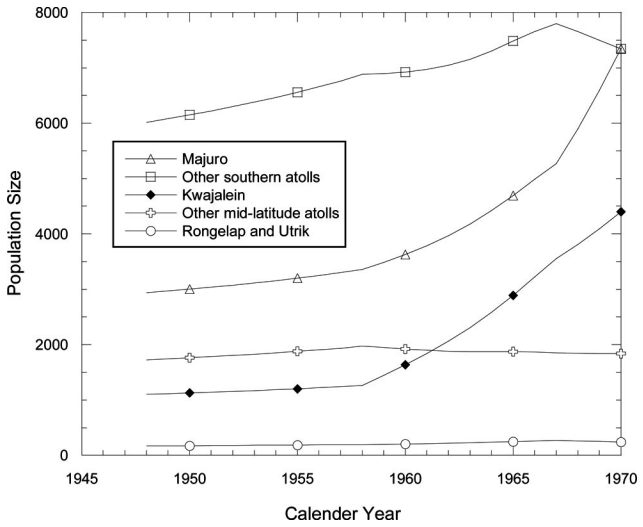

Fig. 2. Estimated population sizes over time for Majuro, 13 other southern atolls, Kwajalein, 6 other mid-latitude atolls, and the Rongelap and Utrik communities including members not present at the time of the Castle Bravo test on 1 March 1954.

clearly indicates a substantial trend over time of migration to the two population centers from nearby as well as remote atolls. The populations of Kwajalein and Majuro increased over 1948–1970 by factors of 4 and 2.5, respectively, compared to 1.2 for southern atolls other than Majuro, 1.07 for mid-latitude atolls other than Kwajalein, and 1.05 for Rongelap and Utrik.

The census reports for 1958 and 1973, but not 1967, gave distributions for the entire MI population by sex and age interval, as shown in Table 2 (RMI 2003, Table 2.7). Using what might be termed a "global enumeration algorithm," we applied the 1958 sex-specific age distributions to all atolls for 1948–1957, and interpolated linearly between the 1958 and 1973 distributions for 1959–1970. Two exceptions were 82 members of the Rongelap community who received very high radiation doses from exposure to fallout from Castle Bravo on 1 March 1954, while on Rongelap (64) or Ailinginae (18), and 157 members of the Utrik community who received 10-fold lower, but still substantial, doses while exposed on Utrik to fallout from the same event. Both groups were enumerated in historical documents (see for example, BNL 1975) by age and sex when they were evacuated several days later. For community members who were not present at the time of Castle Bravo, numbers of people and their distribution by year, age, and sex were estimated using the above-mentioned global enumeration algorithm.

Radiation dose

Estimation of tissue-specific radiation absorbed doses to bone marrow, thyroid gland, stomach, colon, and other organs and tissues from fallout-related internal (ingested) and external radioactive sources is discussed in the companion papers (Bouville et al. 2010; Simon et al. 2010b). External doses were assumed to be essentially

Table 2. Distribution of Marshall Islands population by age and sex in 1958 and 1973: number of persons and percent (%) (RMI 2003).

Age group (y)	1958 male	1958 female	1973 male	1973 female
<1	268 (3.8)	246 (3.7)	485.23[a] (3.9[a])	409.19[a] (3.5[a])
1–4	1,078 (15.2)	1,073 (16.1)	1,951.77[a] (15.9[a])	1,784.81[a] (15.2[a])
5–9	1,162 (16.4)	953 (14.3)	2,023 (16.4)	1,876 (15.9)
10–14	782 (11.1)	703 (10.5)	1,550 (12.6)	1,538 (13.1)
15–19	452 (6.4)	476 (7.1)	1,379 (11.2)	1,385 (11.8)
20–24	411 (5.8)	426 (6.4)	1,070 (8.7)	975 (8.3)
25–29	462 (6.5)	443 (6.6)	741 (6.0)	770 (6.5)
30–34	421 (6.0)	390 (5.8)	489 (4.0)	446 (3.8)
35–39	386 (5.5)	387 (5.8)	429 (3.5)	432 (3.7)
40–44	294 (4.2)	291 (4.4)	427 (3.5)	362 (3.1)
45–49	317 (4.5)	274 (4.1)	358 (2.9)	369 (3.1)
50–54	201 (2.8)	231 (3.5)	357 (2.9)	359 (3.1)
55–59	201 (2.8)	220 (3.3)	328 (2.7)	312 (2.7)
60–64	231 (3.3)	178 (2.7)	263 (2.1)	249 (2.1)
65–69	151 (2.1)	112 (1.7)	159 (1.3)	189 (1.6)
70–74	120 (1.7)	102 (1.5)	113 (0.9)	139 (1.2)
75–79	50 (0.7)	53 (0.8)	63.64[a] (0.5[a])	56.91[a] (0.5[a])
80–84	50 (0.7)	57 (0.9)	63.64[a] (0.5[a])	61.21[a] (0.5[a])
85+	43 (0.6)	66 (1.0)	54.73[a] (0.4[a])	70.88[a] (0.6[a])
Total	7,080 (100)	6,681 (100)	12,305 (100)	11,784 (100)

[a] 1973 age detail apportioned according to 1958 detail.

the same for all organs, but separate internal doses were estimated for bone marrow, thyroid gland, colon, and stomach. Total site-specific radiation dose estimates accumulated over time varied substantially by geographical location (atoll) and year of birth. Fig. 3, drawn from Table 8 in Simon et al. (2010a), illustrates the 10-fold differences in total thyroid absorbed dose between Rongelap and Utrik and between Utrik and Kwajalein (the latter representative of the other mid-latitude islands and atolls), and the two-fold difference between Kwajalein and Majuro (representative of the other southern latitude communities). Fig. 3 also gives some idea of the overwhelming significance of fallout from the 1954 Castle series of tests (see Table 1 of Simon et al. 2010a), with a steep drop of 1–2 orders of magnitude in dose corresponding to birth dates before and after 1954.

For risk projection purposes, colon dose estimates were used for organs other than bone marrow, thyroid, and stomach. The exposures associated with any one fallout event were considered to be continuous (and, in general, decreasing over time until 1970, after which they were considered to be negligible), as distinguished from the acute (i.e., near-instantaneous), direct external radiation exposures experienced by persons exposed to the Hiroshima and Nagasaki atomic bombings; the Hiroshima-Nagasaki experience forms the primary basis for current dose-response estimates of radiation-related cancer risk (Preston et al. 2007; NRC 2006) on which the risk projections presented later in this report are based. Estimated dose varied by atoll, fallout event, calendar year, and age at exposure. As discussed in the companion papers, the precision of the dose reconstruction data was considered to be better for external as compared to internal radiation sources. Moreover, exposures on Rongelap and Ailinginae were more precisely estimated than for those on Utrik, and both were judged to be more precise than the estimates of exposures on the mid-latitude and southern atolls. Accordingly, the lognormal uncertainty distributions for estimated doses were described by geometric standard deviations (GSD) of 1.2 and 2.0 for external and internal exposures, respectively, on Rongelap and Ailinginae, 1.5 and 2.5 for exposures on Utrik, and 1.8 and 3.0 for exposures on the other atolls.

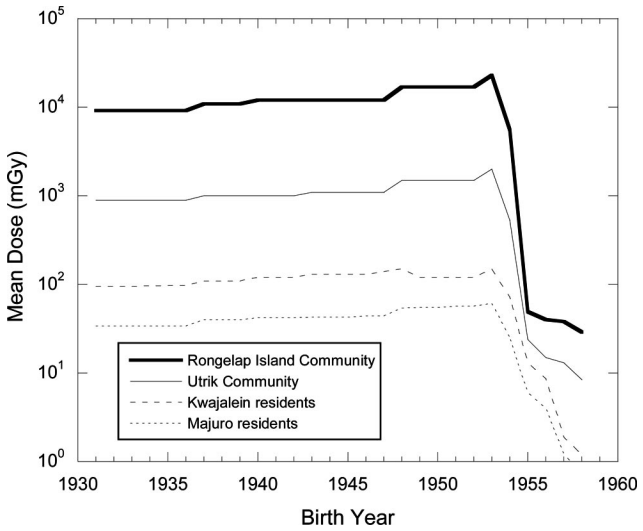

Fig. 3. Estimated cumulative thyroid doses for four different communities, by year of birth, drawn from Table 8 in Simon et al. (2010b). Dose estimates for persons born in 1931 also pertain to persons born earlier.

External and internal dose estimates were assumed to be highly correlated because they both depended strongly on estimated fallout deposition levels. In practice, it made very little difference to the calculation outcomes whether the correlation coefficient was assumed to be about 0.8 or 1.0, so perfect correlation was assumed for computational convenience. Also, each dose estimate was assumed to represent the mean of its lognormal uncertainty distribution, which implies that the median of that uncertainty distribution therefore equals the point estimate divided by $\exp[0.5 \times \ln^2(\mathrm{GSD})]$. For example, an estimated radiation dose to the thyroid gland, in 1954, of 0.01 Gy from external sources and 0.03 Gy from internal sources at a mid-latitude atoll would be treated as the sum of two perfectly correlated lognormal random variables. A Monte Carlo simulation indicates that the uncertainty distribution of this sum is approximately lognormal with mean = 0.0390 Gy, GSD = 2.51, and geometric mean (GM) = 0.02558 Gy.**

Estimation of baseline cancer rates

In the absence of comprehensive cancer incidence data for the Marshall Islands, approximate tissue-specific, baseline cancer rates were calculated by age and sex, using incidence rates reported by the Surveillance, Epidemiology, and End Results (SEER) registry of the U.S. National Cancer Institute (NCI) for all ethnic groups combined (NCI 1997). These rates were adjusted to reflect the ratio of site-specific, age-standardized (world) rates for ethnic Hawaiians from the Hawaii Tumor Registry (which is a part of the SEER registry) to the corresponding age-standardized (world), or ASW, rates for the SEER registry as a whole. ASW rates are weighted averages of age-specific rates, with the weights determined by the estimated sex-specific age distribution of the entire world population, which is somewhat younger than those for most developed countries (Parkin et al. 2002). For example, the 1973–1998 SEER

** Here and elsewhere, results of intermediate calculations are given to greater than two significant digits as needed for subsequent calculations.

baseline rate for thyroid cancer among U.S. females (all races) at age 62 is 12.85 per 100,000 per year (NCI 2008). After multiplying by the Hawaii Tumor Registry ASW rate (11.0) for native Hawaiian females and dividing by the corresponding ASW rate (7.33) for U.S. females, the projected baseline rate per 100,000 per year at age 62 for MI women was calculated as $12.85 \times 11.0 \times (7.55)^{-1} = 19.28$.

The computation of baseline rates in this paper is based upon a number of assumptions, the uncertainties of which are difficult to quantify. However, it can be argued that, when dealing with a past radiation event, the attributable risk, i.e., the proportion of total cancer cases related to exposure, has more practical significance than the total number of radiation-related cancers. Attributable risk, for example, is the primary basis in the U.S. for evaluating compensation claims for possible radiation-related cancer (NIH 1985, 2003; Kocher et al. 2008). Projection of attributable risk is also less sensitive to uncertainties in baseline risk.

Models for estimation of radiation-related cancer risk

BEIR VII linear dose-response models (NRC 2006, Tables 12-1, 12-2, and 12-3) for estimating the excess relative risk (ERR) per unit dose are shown in Table 3 for radiation-related leukemia, for cancers of the thyroid gland, stomach, and colon, and for solid cancers other than thyroid and non-melanoma skin cancer. Age-specific and lifetime risks for a "residual" category of solid cancers, leaving out stomach and colon as well as thyroid and non-melanoma skin cancer, were obtained by subtraction.

The BEIR VII algorithms express cancer-specific ERR as a sex-specific, parametric function linear in radiation dose, with dose coefficients β_M for males and β_F for females. Sex-specific dose response was modified by sex-independent functions of age at exposure, attained age, and/or time since exposure. These estimates pertain to the population of atomic bomb survivors studied by the Radiation Effects Research Foundation (RERF) in Hiroshima and Nagasaki, Japan (Preston et al. 2007) and, for thyroid cancer, a pooled analysis of incidence data from seven different studies (Ron et al. 1995). The general form of the expression for ERR per unit dose (i.e., per Gy) for specified solid cancers, as derived from the BEIR VII report (NRC 2006, Table 12-2), is

$$\text{ERR Gy}^{-1} = \beta \times \exp[\gamma \times e + \eta \times a], \qquad (1)$$

where β, γ, and η are uncertain parameters estimated from epidemiological data. If exposure age (years) ≥ 30, $e = 0$; otherwise:

$$e = (\text{exposure age} - 30) \times 10^{-1}, \qquad (2)$$

while

$$a = \ln(\text{attained age} \times 60^{-1}). \qquad (3)$$

Parameter β is sex-specific (β_M for males and β_F for females), whereas parameters γ and η are sex-neutral.

For leukemia other than chronic lymphocytic leukemia (CLL), the dose response is a quadratic function of dose for acute exposures but is linear in dose for exposures protracted in time such as those from radioactive fallout. From BEIR VII (NRC 2006, Table 12-3), the

Table 3. Values of parameters for BEIR VII dose-response models for excess relative risk:

$$\text{ERR} = \beta \times D \times \exp\{\gamma \times e + \eta \times a + \delta \times t + \varphi \times e \times t\}.$$

Here, β (β_M for males and β_F for females), γ, η, δ, and φ are uncertain parameters; D is radiation dose in Gy; $e = 0$ for exposure age ≥ 30 and $e = (\text{exposure age} - 30) \times 10^{-1}$ otherwise; $a = \ln(\text{attained age} \times 60^{-1})$ and $t = \ln[(\text{attained age} - \text{exposure age}) \times 25^{-1}]$. In the table, point estimates of parameters are given with 95% uncertainty limits in parentheses except where treated in BEIR VII as constants (γ and η for cancers of the thyroid gland, stomach and colon). The sex-specific parameters β_M and β_F are assumed to have lognormal uncertainty distributions for solid cancers and beta distributions for leukemia, while parameters γ, η, δ, and φ, if not constant, are assumed to have normal (Gaussian) uncertainty distributions.

	Parameter (associated regression variable)					
Cancer type	β_M	β_F	$\gamma(e)$	$\eta(a)$	$\delta(t)$	$\varphi(e \times t)$
All solid cancers[a]	0.33 (0.24, 0.47)	0.57 (0.44, 0.74)	−0.3 (−0.51, −0.10)	−1.4 (−2.2, −0.7)	0	0
Thyroid	0.53 (0.14, 2.0)	1.05 (0.28, 3.9)	−0.83[b]	0	0	0
Stomach	0.21 (0.11, 0.40)	0.48 (0.31, 0.73)	−0.3[b]	−1.4[b]	0	0
Colon	0.63 (0.37, 1.1)	0.43 (0.19, 0.96)	−0.3[b]	−1.4[b]	0	0
Leukemia[c]	1.1 (0.10, 2.6)	1.2 (0.10, 2.9)	−0.4 (−0.78, 0.0)	0	−0.48 (−1.1, 0.20)	0.42 (0.0, 0.96)

[a] Except thyroid cancer and non-melanoma skin cancer.
[b] Error assumed to be negligible, following BEIR VII (NRC 2006).
[c] Because dose from fallout was considered to have been received at a low dose rate, the parameter for the dose-squared term in the BEIR VII model for leukemia was set equal to zero.

ERR for protracted exposure is assumed to be proportional to radiation dose in Gy, and the ERR per Gy is expressed as:

$$\text{ERR Gy}^{-1} = \beta \times \exp(\gamma \times e + \delta \times t + \varphi \times e \times t). \quad (4)$$

Here, δ and φ are additional uncertain parameters, and

$$t = \ln[(\text{attained age} - \text{exposure age}) \times 25^{-1}]. \quad (5)$$

The parameters in equations (1) and (4) are assumed to be random variables: β_M and β_F are distributed as lognormal for solid cancers and beta for leukemia, and γ, η, δ, and φ are normal or constant. Parameter medians and 95% uncertainty limits are presented in Table 3 for all solid cancers less thyroid and non-melanoma skin cancer, for leukemia, and for cancers of the thyroid gland, stomach, and colon.

While the approach used in the present analysis uses BEIR VII dose-response estimates, it differs from BEIR VII with respect to modification of dose response at low doses and low dose rates (as discussed below under "Adjustment for protracted exposures"), transfer between the Japanese A-bomb survivors and the exposed Marshall Islands population (as discussed above under "Estimation of baseline cancer rates" and below under "Transfer of estimated excess risk to the exposed MI populations"), and to treatment of the latent period between radiation exposure and diagnosis of cancer (as discussed below under "Latent period"). In these matters, we followed an earlier National Institutes of Health approach (NIH 1985, 2003) to evaluate the extent to which a given cancer diagnosis might be attributable to a given prior history of exposure to ionizing radiation.

Example. From Table 3, the estimated ERR per Gy, according to BEIR VII, for radiation-related thyroid cancer in a woman at age 62 y, following exposure at age 12 y, is:

$$\text{ERR Gy}^{-1} = 1.05 \times \exp[-0.83 \times (12 - 30) \times 10^{-1} - 0.0 \times \ln(62 \times 60^{-1})] = 4.678. \quad (6)$$

(Note that the ERR for excess thyroid cancer, unlike that for other cancers, does not depend upon attained age.) We treat this estimate as an uncertain value distributed as approximately lognormal with geometric mean GM = 4.68 and GSD = 1.96 (as indicated by the 95% uncertainty bounds for the parameter β_F in Table 3). The arithmetic mean of this distribution is:

$$\text{mean} = \text{GM} \times \exp[0.5 \times \ln^2(\text{GSD})] = 4.678 \times 1.2533 = 5.862. \quad (7)$$

For an uncertain dose estimate of 0.04 Gy (0.01 Gy from external radiation and 0.03 Gy from internal radiation as discussed above under "Radiation dose"), the estimated ERR must reflect the statistically independent uncertainties of both the estimated ERR per Gy and the estimated dose in Gy. Given a lognormal uncertainty distribution for the estimated dose with GM = 0.02558 Gy and GSD = 2.51 (see "Radiation dose" above), the estimated ERR at mean dose 0.04 Gy, then, is considered to be approximately lognormal with

$$\text{GM} = 0.02558 \text{ Gy} \times 4.678 \text{ Gy}^{-1} = 0.1197, \quad (8)$$

$$\text{GSD} = \exp\{[\ln^2(2.51) + \ln^2(1.96)]^{1/2}\} = 3.127, \quad (9)$$

and

$$\text{mean} = \text{GM} \times \exp[0.5 \times \ln^2(\text{GSD})] = 0.1197 \times \exp[0.5 \times \ln^2(3.127)] = 0.229. \quad (10)$$

Adjustment for protracted exposures

In the BEIR VII report (NRC 2006), as elsewhere, a linear-quadratic dose-response model is used for leukemia ERR associated with an acute radiation dose, but for protracted doses, the coefficient for dose-squared is set equal to zero, giving a linear dose-response model for leukemia. For solid cancer risk following protracted or very low-dose exposures, the ERR is divided by a dose-and-dose-rate effectiveness factor (DDREF). The present calculations involve a different DDREF, shown in Fig. 4 (left panel), which was developed for the "Interactive Radio-Epidemiological Program" (IREP) used to facilitate adjudication of compensation claims against the U.S. government for radiation-related cancers (NIH 2003; Kocher et al. 2008). When applied to the thyroid cancer example introduced under "Models for estimation of radiation-related cancer risk," the uncertainty distribution for the ERR estimate divided by the DDREF, evaluated by Monte Carlo simulation, corresponds closely to a lognormal distribution with GM = 0.0805 and GSD = 3.40 (mean = 0.170) (Fig. 5).

Latent period

As shown in Table 3, the dose-specific ERR may depend upon attained age and/or time following exposure, but experimental studies at the cellular and animal level strongly suggest that the process of radiation carcinogenesis requires time; i.e., there is a minimum latent period of uncertain duration that is superimposed

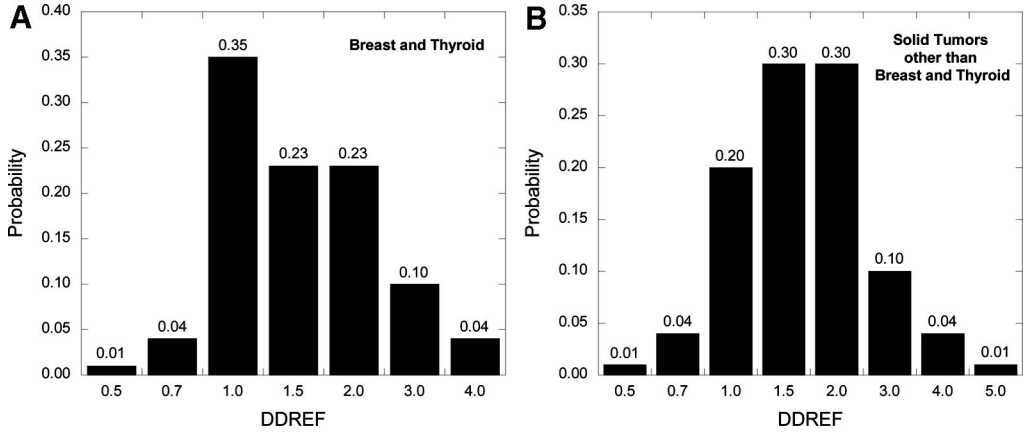

Fig. 4. IREP uncertainty distributions for the dose-and-dose-rate effectiveness factors (DDREF) to be applied at low doses and low dose rates to risk estimates for (a) breast and thyroid cancer (left panel), and (b) solid cancers other than breast and thyroid (right panel).

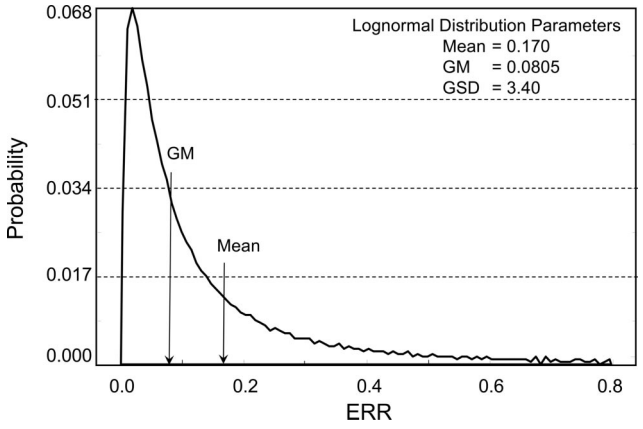

Fig. 5. Results of a Monte Carlo simulation to evaluate the effects of adjusting an uncertain thyroid cancer excess relative risk (ERR) projection distributed as lognormal with geometric mean (GM) = 0.1197 and geometric standard deviation (GSD) = 3.127, by the DDREF with uncertainty distribution shown in Fig. 4, left panel. The simulated uncertainty distribution is approximately lognormal with GM = 0.0688 and GSD = 3.40.

upon the age/time dependence of the ERR. This is an important consideration for compensation claims adjudication in cases where the claim involves a cancer diagnosed within a few years after exposure, but it has relatively little importance for estimates of lifetime risk. In the present analysis, we follow IREP (NIH 2003; Kocher et al. 2008), using a sigmoid function multiplier like that used in the report of the NIH Ad Hoc Working Group to Develop Radioepidemiological Tables (NIH 1985), which is discussed in the Appendix. For thyroid cancer, the latent period is somewhat shorter than that for other solid cancers, increasing from zero at age 1 to its full value at 8 years and older (NIH 2003).

Transfer of estimated excess relative risk to the exposed MI populations

The tissue-specific BEIR VII parametric models for ERR (Table 3) apply mainly to the Japanese A-bomb survivor Life Span Study (LSS) cohort studied by the RERF (Preston et al. 2007), which we will denote as ERR_{LSS}. Two simple approaches can be used to transfer estimated ERR_{LSS} from the population of Hiroshima and Nagasaki A-bomb survivors to the MI population. One, called multiplicative transfer, involves assuming that dose-specific ERR values for the MI population (ERR_{MI}) are the same as those for the LSS population even though the two populations may have different baseline cancer rates, i.e.,

$$ERR_{MI}(\text{mult}) = ERR_{LSS}. \quad (11)$$

The other, called additive transfer, involves the assumption that the product, ERR times the age-specific baseline rate (B), does not vary by population:

$$ERR_{LSS} \times B_{LSS} = ERR_{MI}(\text{add}) \times B_{MI}; \quad (12)$$

i.e.,

$$ERR_{MI}(\text{add}) = ERR_{LSS} \times B_{LSS} \times B_{MI}^{-1}. \quad (13)$$

The BEIR VII approach uses multiplicative transfer for thyroid cancer, additive transfer for breast cancer, and a weighted average, on the logarithmic scale, with weights of 0.7 on multiplicative transfer and 0.3 on additive transfer, for leukemia, stomach cancer, colon cancer, and for solid cancers other than thyroid, lung, and female breast. For lung cancer, the corresponding weights are 0.3 for multiplicative and 0.7 for additive transfer. The approach used in the present analysis is the same, except that the Monte Carlo weighted averages are on the arithmetic, rather than the logarithmic, scale. We

separately estimated risks for leukemia, thyroid cancer, stomach cancer, and colon cancer. For the residual group of all solid cancers except thyroid, stomach, and colon, we subtracted the estimates for stomach and colon cancer from the estimate for the combination of all solid cancers excepting thyroid cancer and non-melanoma skin cancer (obtained using weights 0.7 and 0.3 for multiplicative and additive transfer, respectively).

For thyroid cancer, the estimated ERR (ERR_{LSS}) obtained above for thyroid cancer is directly applicable to the MI population (i.e., $ERR_{MI} = ERR_{LSS}$). Thus, ERR_{MI} has a lognormal uncertainty distribution with GM = 0.0805 and GSD = 3.40 (mean = 0.170) (Fig. 5).

Life tables

Until this point, the narrative has concerned only estimates of ERR at specific ages. Projected lifetime risk, however, is calculated as a differentially-weighted sum of age-specific absolute risks in which the weights reflect the inverse relationship between the likelihood of reaching a given age and the numerical value of that age. For this purpose, we used a 1989–1991 life table for the U.S. (NCHS 1997) (Fig. 6) to adjust for competing, age-specific mortality in estimating cumulative baseline and radiation-related excess risk for exposure to a given radiation dose at a given age. This life table, based on sex- and age-specific mortality rates for the U.S. in 1989–1991, provides one-year survival data for persons alive at any given age during that period, i.e., the proportion of persons of a given age that survived until the next year of life. However, it is often used, as in Fig. 6, to show the average likelihood that a newborn person would survive until one, two, three, etc. years of age

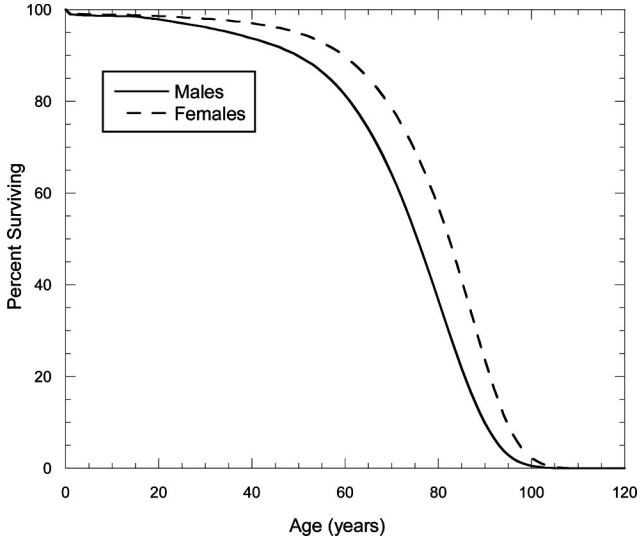

Fig. 6. U.S. male and female life tables used in the preparation of this report. Drawn from data in NCHS (1997).

provided that the age-specific mortality rates observed in 1989–1991 also were to hold for every other calendar year (which, of course, may not be the case). If we multiply age-specific baseline rates by the life table survival probability for that age, and sum over the different ages, the "life-table-weighted sum" is an estimate of lifetime cancer risk, here also assuming that age-specific baseline cancer rates, as well as survival probabilities, do not change over time. With the same assumptions, we can calculate the lifetime excess cancer risk for each year following exposure to a given dose at a given age, as the life-table-weighted sum of estimated age-specific excess risks. Of course, in order to be exposed at a given age one must have survived until that age, so a modified life table is required, conditional on survival to the specified exposure age.

As noted in the previous paragraph, life tables are not perfect, but they do provide a standard way of accounting for competing mortality risks when estimating future and lifetime risk associated with a particular exposure of interest. For computational convenience, we used a simple life table for projecting lifetime radiation-related excess risk rather than a doubly-decremented life table which takes account of additional mortality due to radiation-related cancer. This likely resulted in a slight overestimation of excess cancer risks for most of the communities, and probably more so for risks associated with the higher-dose exposures experienced on Rongelap, Ailinginae, and Utrik in 1954. Similarly, in the absence of any MI life tables, the use of standard U.S. life tables may have led to overestimation of both baseline and radiation-related cancer; however, the effect on relative risk and attributable risk is unlikely to be great considering the greater influences of uncertainty in radiation dose and year-to-year variation in population sizes by atoll.

Calculation of projected lifetime baseline and excess risks

In the present analysis, lifetime baseline risk is calculated from birth or from 1948, whichever occurred first. Thus, for someone born in 1950, the sex-specific life table survival probabilities in Fig. 6 would be used, but for someone born in 1942, and known (or assumed) to have been alive in 1948, an adjusted life table would be used, with probabilities of survival to ages one, two, …, six, each set equal to one and probabilities of survival until ages seven, eight, etc. (from Fig. 6), each divided by the Fig. 6 probability of survival to age six (i.e., survival until 1948). Denoting the adjusted life table probability to age a by $L(a)$ and the age-specific baseline cancer rate by $B_{MI}(a)$, the lifetime baseline rate from age six is calculated as the life table-weighted sum over ages a

from seven through 120 of $B_{MI}(a)$, i.e., $\sum_{a=7}^{120}[L(a) \times B_{MI}(a)]$. In the case of thyroid cancer, that sum is 1.177% (the value for the U.S. SEER population) times the ratio of the ASW rate per 100,000 for native Hawaiians to that for the U.S. SEER population:

$$1.177\% \times 11.0 \times 7.5^{-1} = 1.726\%.$$

Supposing an exposure at age 12 y and, therefore, survival until that age, the appropriate U.S. life table for calculating lifetime excess risk is obtained from Fig. 6 by setting to one the probabilities of survival to ages 1 through 12 y and dividing each of the Fig. 6 life table probabilities of survival to ages 13, 14, etc., by the Fig. 6 probability of survival to age 12 y. Then, using the revised life table survival probabilities for subsequent ages, L(13), L(14), etc., the lifetime excess rate associated with exposure at age 12 y is calculated as the sum over $a = 13$ through 110,

$$\sum_{a=13}^{110}[L(a) \times B_{MI}(a) \times ERR_{MI}(12, a)]. \qquad (14)$$

Here, the notation $ERR_{MI}(12, a)$ is required because of the time-dependent, uncertain latent period discussed above under "Latent period." In fact, the notation above is somewhat overly simplified because radiation dose varied by calendar year in each location; the above formulation should be understood as corresponding to a given calendar year as well.

In contrast to the BEIR VII dose-response models for leukemia, stomach cancer, colon cancer, and the group of solid cancers other than thyroid and nonmelanoma skin cancer, ERR for thyroid cancer does not depend upon attained age (Table 3). It does, however, depend upon latent period, increasing from zero within the first 2 y after exposure to its full value 8 y after exposure. A reasonable rough calculation, used here for illustration purposes, of lifetime risk (excess absolute risk, or EAR) associated with a 0.04 Gy thyroid dose at age 12 y is obtained by multiplying $ERR_{MI}(12, 20)$, which is distributed as lognormal with GM = 0.0805 and GSD = 3.40 (mean = 0.170), by the lifetime baseline risk at age 16 y, which is 1.172%. The product is lognormal with GM = 0.00094, GSD = 3.40, and mean = 0.0020.

Computational approach

Each factor used in the calculation of the excess number of cancers has an associated uncertainty, including radiation doses, parameter values of dose-response models, DDREF values and other adjustments of dose-related risk. The uncertainty of each component was described using probability distribution functions (e.g., in Table 3), and Monte Carlo methods were used to propagate these uncertainties.

Monte Carlo methods use pseudo-random numbers to generate realizations from each of the assumed uncertainty distributions describing particular uncertain components. The randomly sampled values are introduced in the excess risk equations, and realizations of the excess number of cancers are produced. The collection of values for the excess number of cancers, obtained by repeating the process for many iterations, is analyzed to estimate the mean, median, and uncertainty interval for the excess number of cancers. The uncertainty distributions of several input parameters used in the present analysis (e.g., DDREF) are based partly on expert judgment regarding the appropriateness of the available data about that parameter for the radiation exposures in the Marshall Islands, rather than strictly on statistical analysis of those data, and therefore the term "uncertainty interval" is used instead of "confidence interval" which involves only statistical uncertainty. Given a sufficient number of iterations, Monte Carlo methods are accurate and, compared to first-order analytical methods like those used by the BEIR VII committee, have definite practical advantages for handling any magnitude of uncertainty, distributions of any shape, and for dealing with large numbers of correlated, uncertain parameters.

For this report, 200 estimates of radiation doses from external sources and 200 from internal sources were generated for each of 25 population groups of Marshallese [including a Rongelap control group, see BNL (1958) for a discussion of control subjects], 24 atolls and islands where exposure took place, 23 calendar years of exposure, 100 possible exposure ages (treating anyone exposed at ages 100 y or older as having been exposed at age 99 y), and 5 target organs or groups of organs. The details of the populations, atolls and islands, and exposure years are given in Simon et al. 2010a; it should be noted that cancer risks are only estimated for the Marshallese population, and, therefore, exclude the U.S. military weather observers who were exposed at Rongerik. External and internal doses were assumed to be perfectly correlated within each combination of place and year of exposure and were assumed to be uncorrelated between years and between atolls. Similarly, 200 realizations were generated for the risk per unit dose for each possible combination of sex, exposure age and subsequent attained age, and cancer type. The Monte Carlo estimated doses and risks per unit dose were combined together with the number of individuals in each exposure age group, each sex, and each atoll to obtain two hundred estimates of the predicted number of cancers, from which means, medians, and 90% uncertainty intervals were generated for each cancer type and selected population. The estimated numbers of cancers were then summed to obtain totals for desired groups of

atolls and for the entire Marshallese population. The realizations used for each of the risk calculations were obtained by Median Latin Hypercube sampling (Iman and Shortencarier 1984). For a given sample size, this method provides more precise estimates of the mean, median, and 90% uncertainty limits than are obtainable through simple random sampling.

RESULTS

Cancer risk estimates are based on 12,175 MI residents projected to have been born before 1948 and another 12,608 projected to have been born in the years 1948 through 1970, giving a total exposed population of 24,783. Projected lifetime numbers of baseline and radiation-related cancers are shown in Table 4 by organ site, population, and calendar time period. Reflecting the general decreasing trend in exposure levels from the northern atolls of Ailinginae, Rongelap, and Utrik to more southern latitudes, the atolls of Ailuk, Kwajalein, Likiep, Mejit, Wotho, Wotje, and Ujelang (the relocated Enewetak population) were grouped together in Table 4 as the "mid-latitude" group, while the atolls of Ailinglaplap, Arno, Aur, Ebon, Jaluit, Kili (the relocated Bikini population), Lae, Lib, Majuro, Maloelap, Mili, Namorik, Namu, and Ujae constitute the "southern latitude" group.

The lifetime projection for baseline cancers of all sites, excepting non-melanoma skin cancer which is not covered by the SEER registries, totals 10,600 or a little over 40% of the exposed population. The projected number of radiation-related cancers is 170, or 1.6% of the projected baseline with 90% uncertainty range 0.4% to

Table 4. Projected numbers of baseline cancers and excess (radiation-related) cancers by population group, cancer type, and time period (uncertainty distributions for excess cancers represented by their means and their 5th and 95th percentiles).

Population group and cancer type	Projected lifetime cancers from 1948				Projected cancers 1948–2008				Projected cancers from 2009			
		Excess				Excess				Excess		
	Baseline	Mean	5%	95%	Baseline	Mean	5%	95%	Baseline	Mean	5%	95%
Rongelap Island and Ailinginae exposed community												
Leukemia	0.44	1.6	0.3	4.3	0.27	1.3	0.20	3.7	0.17	0.30	0.072	0.59
Thyroid	0.60	12	4.2	21	0.48	9.5	2.8	18	0.12	2.3	1.2	3.6
Stomach	1.8	1.7	0.23	4.9	1.0	0.79	0.10	2.5	0.80	0.87	0.12	2.7
Colon	3.1	5.4	1.7	11	1.7	2.5	0.77	5.1	1.4	2.9	0.90	5.9
Other solid	28	21	7.0	33	18	16	5.2	27	10	4.9	2.2	7.9
Rounded total	34	41	13	74	21	30	9.0	57	13	11	4.5	21
Utrik community												
Leukemia	1.4	0.34	0.062	1.2	0.77	0.28	0.044	1.0	0.63	0.062	0.016	0.13
Thyroid	1.8	4.4	0.85	11	1.3	3.0	0.56	8.2	0.50	1.4	0.27	3.3
Stomach	5.8	0.30	0.038	0.99	2.8	0.14	0.018	0.39	3.0	0.16	0.020	0.61
Colon	9.7	1.0	0.32	2.3	4.6	0.42	0.13	0.93	5.1	0.58	0.16	1.3
Other solid	91	6.5	1.4	14	49	3.6	0.89	8.7	42	2.9	0.46	6.8
Rounded total	110	12	2.6	30	58	7.4	1.6	19	51	5.1	0.93	12
Kwajalein and other mid-latitude atolls[a]												
Leukemia	35	3.1	0.59	8.8	14	2.5	0.41	7.8	21	0.62	0.15	1.2
Thyroid	46	15	3.0	38	27	10	2.0	26	19	5.0	1.0	12
Stomach	140	2.8	0.36	8.5	44	1.3	0.16	4.1	96	1.5	0.20	4.3
Colon	229	5.3	1.7	12	69	2.3	0.77	4.8	160	3.0	0.9	6.3
Other solid	2,190	31	7.4	66	790	18	4.7	38	1,400	13	2.8	28
Rounded total	2,600	57	13	130	940	35	8.1	80	1,700	23	5.1	52
Majuro and other southern latitude atolls,[b] including Rongelap control population												
Leukemia	103	2.3	0.43	6.5	44	1.9	0.30	5.8	59	0.45	0.13	0.85
Thyroid	138	20	3.5	52	84	13	2.3	34	54	6.7	1.2	18
Stomach	420	2.0	0.29	5.7	140	0.89	0.13	2.6	280	1.1	0.16	3.2
Colon	680	4.8	1.6	9.8	220	2.0	0.68	4.5	460	2.8	0.92	5.7
Other solid	6,500	31	6.9	68	2,500	17	4.6	35	4,000	15	2.8	33
Rounded total	7,800	61	13	140	3,000	34	8.0	82	4,800	26	5.2	60
Entire Marshall Islands population exposed between 1948 and 1970												
Leukemia	140	7.4	1.3	20	59	6.0	0.94	17	81	1.4	0.37	2.6
Thyroid	190	50	12	120	113	35	7.9	85	74	15	3.9	36
Stomach	570	6.7	0.94	20	190	3.1	0.43	9.4	380	3.6	0.51	11
Colon	930	16	5.3	34	300	7.2	2.4	15	630	9.3	2.9	19
Other solid	8,800	90	24	181	3,400	54	16	110	5,400	36	8.6	71
Rounded total	10,600	170	44	380	4,000	105	28	236	6,600	65	14	140

[a] Ailuk, Kwajalein, Likiep, Meijit, Ujelang (population relocated from Enewetak), Wotho, and Wotje.
[b] Ailinglaplap, Arno, Aur, Ebon, Jaluit, Kili (population relocated from Bikini), Lae, Lib, Majuro, Maleolap, Mili, Namorik, Namu, and Ujae.

3.6%. By population group, the projected number of radiation-related cancers is 41, or about 120% of projected baseline, for the heavily exposed Rongelap Island community (those exposed in 1954 on Rongelap Island and on Ailinginae), 11% of baseline for the Utrik community, 2.2% for the exposed mid-latitude group, and about 0.8% for the southern latitude group, which is estimated to have received the lowest radiation doses.

Except for thyroid cancer, which tends to be diagnosed at younger ages than the majority of cancers, most of the baseline (i.e., non-radiation related) cancers are projected to occur after 2008. An exception to this finding is for the Rongelap Island and Ailinginae exposed community which does not include anyone born after 1954. For that cohort, the projected number of lifetime, radiation-related thyroid cancers (Table 4) is 12, or 20 times the 0.6 baseline cases projected in the absence of exposure to radioactive fallout. The projected lifetime number of excess leukemia cases is 1.6, nearly 4 times the projected baseline of 0.45. About 80% of both the excess and baseline thyroid cancers and leukemias are projected to have been diagnosed by the end of 2008. For stomach, colon, and remaining solid cancers, respectively, the excess cancers are estimated to equal 95%, 180%, and 75% of projected baseline values.

In the results for Utrik, the projected numbers of excess cancers for the relatively small percentage of community members who were not present on the atoll at the time of the Bravo test have been included in the total. In contrast to the Rongelap Island and Ailinginae exposed community, and to a lesser extent the Utrik exposed community, we estimate that among the members of the mid-latitude and southern latitude populations alive at some time during 1948–1970, about 20% were born after 1954. This difference in age distribution is reflected in the fact that proportionally fewer baseline cancers and, except for leukemia, proportionally fewer radiation-related cancers among the mid-latitude and southern latitude populations are projected to have been diagnosed in 2008 or earlier (Table 4).

In Table 5, the values in Table 4 have been converted to estimates of attributable risk, i.e., the projected proportion of cancers attributable to fallout-related radiation dose, calculated as excess risk divided by the sum of baseline and excess risk, and expressed in percent. The values for attributable risk are considered to be the main result of our analysis.

DISCUSSION

The dose-response relationship between ionizing radiation and subsequent cancer risk is among the best quantified for any common environmental carcinogen, and we feel reasonably confident about our risk projections, with a few caveats. First, there is some evidence that Micronesians, including Marshallese, may share similar cancer patterns, including high thyroid cancer rates, with native Hawaiians (Henderson et al. 1985). However, an extensive review of published reports of cancer surveillance studies and epidemiological and clinical cancer studies in the native Hawaiian and Pacific Islander populations (Hughes et al. 2000) found a lack of systematic data collection on cancer incidence and mortality in Pacific Islanders, with wide variations in the status of cancer research among ethnic groups. Thus, baseline cancer rates used in our analysis, which were constructed to be representative of the native population of Hawaii, are not necessarily perfectly representative of the MI population. The second caveat is that any static or time-specific life table, like the U.S. Decennial Life Tables for 1989–1991 used here (NCHS 1997), corresponds to a snapshot in time and reflects current mortality rates when the life table was constructed, which may differ from those 30 y before or 30 y later. However, uncertainties in baseline cancer rates and age-specific, all-cause mortality apply similarly to estimates of excess and baseline risk. Therefore, the estimated proportion of cancers attributable to fallout-related radiation dose as presented in Table 5 should be relatively unaffected. These considerations aside, our calculations project a substantial burden of radiation-related cancer in the more heavily-exposed Marshallese population groups, and a correspondingly lighter burden in the more populous but less exposed atolls in the mid-latitude and southern latitude regions of the MI. We project that over half (55%, with 90% uncertainty limits 28% to 69%) of the cancers (since 1948) that have already been diagnosed or may be diagnosed in the future among members of the Rongelap exposed cohort are attributable to their fallout exposure, whereas radiation exposure accounts for less than 2% (1.6% with limits 0.4% to 3.4%) of past and future cancer diagnoses among the exposed MI population as a whole.

In the exposed MI population, and in all population subsets represented in Table 4, the residual category, "other solid cancers," which makes up about 80% of baseline risk, is projected to account for the largest number of lifetime radiation-related cancers. However, in terms of "attributable risk," or the fraction attributable to radiation exposure, the thyroid gland is the single organ projected to develop the largest attributable fraction of cancers. In the exposed population as a whole, 21% (6% to 39%) of thyroid cancers are projected to be radiation-related compared to 95% (87% to 97%) among members of the Rongelap and Ailinginae exposed cohort,

Table 5. Projected proportion (in %) of total cancer risk attributable to radioactive fallout, by population, cancer site, and time period. Uncertainty distributions represented by their means and their 5th and 95th percentiles.

	Lifetime attributable risk			Attributable risk, 1948–2008			Attributable risk from 2009		
Population group and cancer type	Mean	5%	95%	Mean	5%	95%	Mean	5%	95%
Rongelap Island and Ailinginae exposed community									
Leukemia	78	39	91	83	43	93	63	29	77
Thyroid	95	87	97	95	85	97	95	91	97
Stomach	48	11	73	44	9.2	71	52	13	77
Colon	64	36	78	60	32	75	68	40	81
Other solid	43	20	54	48	23	61	32	17	43
Total	55	28	69	59	30	73	47	26	62
Utrik community									
Leukemia	19	4.3	45	26	5.4	57	9.0	2.5	17
Thyroid	71	32	86	69	29	86	74	35	87
Stomach	4.8	0.64	14	4.5	0.63	12	5.0	0.67	17
Colon	9.4	3.2	19	8.4	2.8	17	10	3.1	21
Other solid	6.7	1.5	14	6.8	1.8	15	6.5	1.1	14
Total	10	2.4	22	11	2.7	25	9.0	1.8	19
Kwajalein and other mid-latitude atolls									
Leukemia	8.4	1.7	20	15	2.9	36	2.9	0.75	5.5
Thyroid	25	6.1	45	28	7.0	49	21	5.1	39
Stomach	1.9	0.26	5.7	2.8	0.37	8.5	1.5	0.20	4.3
Colon	2.3	0.73	4.8	3.3	1.1	6.6	1.8	0.57	3.8
Other solid	1.4	0.34	2.9	2.3	0.60	4.6	0.96	0.20	2.0
Total	2.2	0.50	4.8	3.5	0.86	7.9	1.4	0.30	3.0
Majuro and other southern latitude atolls, plus the Rongelap control population									
Leukemia	2.2	0.41	6.0	4.2	0.67	12	0.76	0.22	1.4
Thyroid	12	2.5	27	13	2.7	29	11	2.2	25
Stomach	0.47	0.069	1.3	0.63	0.089	1.8	0.39	0.058	1.2
Colon	0.69	0.23	1.4	0.90	0.31	2.0	0.59	0.20	1.2
Other solid	0.48	0.11	1.0	0.65	0.18	1.4	0.37	0.071	0.81
Total	0.76	0.16	1.8	1.1	0.27	2.7	0.53	0.11	1.2
Entire Marshall Islands population exposed at any time between 1948 and 1970									
Leukemia	5.1	0.96	12	9.3	1.6	23	1.7	0.46	3.1
Thyroid	21	6.0	39	24	6.5	43	17	5.0	33
Stomach	1.2	0.17	3.4	1.6	0.23	4.7	0.94	0.14	2.8
Colon	1.7	0.59	3.5	2.4	0.80	4.9	1.5	0.46	2.9
Other solid	1.0	0.27	2.0	1.6	0.46	3.2	0.66	0.16	1.3
Total	1.6	0.41	3.4	2.6	0.67	5.6	0.99	0.22	1.9

71% (32% to 86%) of those in the Utrik population, 25% (6% to 45%) in the mid-latitude atoll populations, and 12% (2.5% to 27%) of those in the southern atoll populations (Table 5). These numbers reflect the large effect of exposure to radioactive iodine in fallout, primarily due to the active uptake of ingested iodine which is used by the thyroid gland for the production of thyroid hormone. From another perspective, the projected 50 lifetime excess of thyroid cancers in the exposed MI population is 30% of the total projected excess of 170 total lifetime cancers, while the corresponding proportion of projected baseline cancers, 190 thyroid cancers out of 11,000 baseline cancers of all types, is less than 2% of the total (Table 4). Roughly the same percentages (thyroid cancer is ~30% of the total cancer excess and ~2% of the total cancer baseline) hold for each of the population subsets represented in Table 4.

If not for the large contribution to total cancers due to exposure to radioiodines in fallout, the fraction of leukemia risk (excluding chronic lymphocytic leukemia, or CLL, which is not included in the BEIR VII model) attributable to radiation exposure might be expected to dominate as it does, for example, in the LSS cohort of atomic bomb survivors (Preston et al. 2003) for whom radioactive fallout was at most a very minor contributor to total radiation dose (Young and Kerr 2005). Overall, non-CLL leukemia accounts for about 4% of total projected radiation-related risk with some variation by sub-population, compared to 1.3% of projected baseline risk. Attributable risk for leukemia is high for the

Rongelap exposed cohort (78% with 90% uncertainty limits 39% to 91%), but 19% (4% to 45%) for Utrik, 8.4% (1.7% to 20%) for Kwajalein and the mid-latitude atolls, and 2.2% (0.4% to 6.0%) for Majuro and the southern atolls.

In conclusion, the reader is reminded that the present analysis is not an epidemiological study but, instead, an application of existing information, gained in recent years from epidemiological studies of other exposed populations, about the relationship between radiation dose and subsequent cancer risk. This information has been combined with new, refined estimates of radiation doses to the populations of different atolls in the Marshall Islands, as discussed in the companion papers. Our conclusions are as follows: (1) a substantial number of cancers have already occurred or are projected to occur in the future (about 170 but perhaps as many as 380 or as few as 44) that would not have occurred in the absence of fallout exposure from nuclear testing in the Marshall Islands; (2) over half of projected past and future cancers among members of the exposed Rongelap Island community (i.e., those exposed to Bravo fallout on Rongelap Island and Ailinginae in 1954) are radiation-related; and (3) with the exception of thyroid cancer, the overwhelming majority of cancers that have occurred or will occur among persons exposed only on atolls and islands in the mid- and southern latitudes are likely to be baseline cancers unrelated to radiation exposure.

Acknowledgments—This work was supported by the Intra-Agency Agreement between the National Institute of Allergy and Infectious Diseases and the National Cancer Institute, NIAID agreement #Y2-A1-5077 and NCI agreement #Y3-CO-5117.

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APPENDIX

Minimum latent period of specific cancer types

The models developed by the BEIR VII committee to estimate ERR and EAR for solid cancers and leukemia do not explicitly account for effects of the time delay between exposure to ionizing radiation and the earliest diagnosis of a radiation-induced cancer. Thus, for calculations of lifetime risk, the risk models need to be modified by a function that is assumed to represent the effect of a minimum latent period on reducing risk at early times since exposure.

In their calculations of lifetime risk, the BEIR VII committee assumed that the risk is equal to zero at times since exposure less than 5 y for solid cancers and less than 2 y for leukemia. No uncertainty was associated with this threshold function.

In this study, to avoid an abrupt increase in risk from zero at times since exposure less than a minimum latency period to their maximum values at times when the minimum latent period has been exceeded, the effect of latency was represented by a sigmoid ("S-shaped") function

$$F_{\text{latency}}(T) = \frac{1}{1 + e^{-\frac{(T-\mu)}{S}}}, \qquad \text{(A1)}$$

where T is the time since exposure in years, μ is the value of T corresponding to the inflection point where $F_{\text{latency}} = 0.5$, and S is a shape parameter that defines the steepness of the function as it increases from values near zero to values near the maximum of 1.0.

For stomach, colon, and all solid cancers as a group, μ is assumed to be 7.5 y and the shape parameter S is set so that the latent period adjustment in equation (A1) attains values of approximately 0.01 and 0.99 at $T = 4$ and 11 y, respectively. Thus, risk is assumed to be very small (close to zero) at $T < 4$ y and to attain its full value at $T > 11$ y. This adjustment, to represent the effect of the minimum latent period on reducing ERR for most solid cancers, is given by the solid curve in Fig. A1.

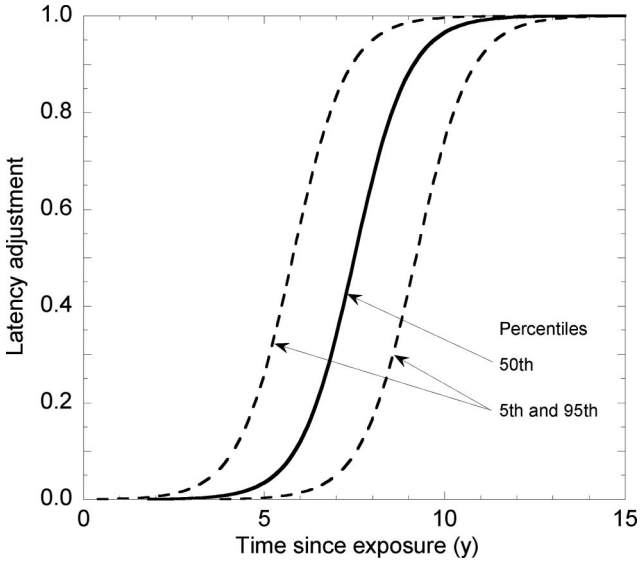

Fig. A1. Sigmoid (S-shaped) function representing the multiplicative adjustment factor (and its uncertainty) applied to the risk of stomach cancer, colon cancer and all solid cancers (less thyroid and non-melanoma) as a group, due to the effect of minimum latency period at early times since exposure.

Thyroid cancer is assumed to have a shorter minimum latent period than all other solid cancers, with a nominal value of μ equal to 5 y. In this case, the latent period adjustment attains values of approximately 0.01 and 0.99 at $T = 2.5$ and 7.6 y, respectively.

Leukemia is assumed to have the shortest minimum latent period with a nominal value of μ set to 2.25 y. The latent period adjustment for leukemia attains values of approximately 0.01 and 0.99 at $t = 0.4$ and 4.1 y, respectively.

To represent uncertainty in the effects of latency on risk estimates, the midpoint, μ, is described by the following triangular probability distributions: stomach, colon and all solid cancers as a group, T(5, 7.5, 10); thyroid, T(3, 5, 7); and leukemia, T(2, 2.25, 2.5). The effect of uncertainty in μ on the adjustment for minimum latency for all solid cancers except thyroid cancer is indicated by the various percentiles of the latency adjustment shown in Fig. A1.

■ ■