

THYROID CANCER IN THE MARSHALLESE: RELATIVE
RISK OF SHORT-LIVED INTERNAL EMITTERS
AND EXTERNAL RADIATION EXPOSURE

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ABSTRACT

In a study of the comparative effects of internal versus external irradiation of the thyroid in young people, we determined that the dose from internal irradiation of the thyroid with short-lived internal emitters produced several times less thyroid cancer than did the same dose of radiation given externally. We determined this finding for a group of 85 Marshall Islands children, who were less than 10 years of age at the time of exposure and who were accidentally exposed to internal and external thyroid radiation at an average level of 1400 rad. The assumed risk coefficient for children, from external radiation alone, was derived from 1) values in The Effects on Populations of Exposure to Low Levels of Ionizing Radiation: 1980, National Academy Press, 2) values in Report of the Ad Hoc Working Group to Develop Radioepidemiological Tables, National Institutes of Health, and 3) values in Induction of Thyroid Cancer by Ionizing Radiation, National Council on Radiation Protection, Report 80. The risk from internal irradiation was computed from dose, health effect results which were reported in a recent BNL study, and an estimate of the external risk coefficient based on other studies. The external risk coefficient ranged between 2.5 and 4.9 cancers per million person-rad-years at risk, and thus, from our computations, the internal risk coefficient for the Marshallese children was estimated to range between 1.0 and 1.4 cancers per million person-rad-years at risk.

In contrast, for individuals more than 10 years of age at the time of exposure, the dose from internal irradiation of the thyroid with short-lived internal emitters produced several times more thyroid cancer than did the same dose of radiation given externally. The external risk coefficients for the older age groups were reported in the above literature to be in the range of 1.0 to 3.3 cancers per million person-rad-years-at risk. We computed internal risk coefficients of 3.3 to 8.1 cancers per million person-rad-years at risk for adolescent and adult groups. This higher sensitivity to cancer induction in the exposed adolescents and adults, is different from that seen in other exposed groups. The small number of cancers (9) in the exposed population and the influence of increased levels of TSE, nonuniform irradiation of the thyroid, and thyroid cell killing at high dose make it difficult to draw firm conclusions from these studies.

DISCLAIMER

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INTRODUCTION

The long-term health effects of external thyroid irradiation are known to include excess hypothyroidism, thyroid nodules, and thyroid cancer, and in this study we attempt to quantitate the relative risk of internal irradiation of the thyroid, for induction of thyroid cancer. The effects of external irradiation of child thyroids have been summarized in BEIR III (1) and by the NCRP (2). Internal irradiation of the thyroid from a mixture of radionuclides has occurred in children as a result of accidental exposure to fallout from nuclear weapons testing. Larger numbers of persons having received diagnostic and therapeutic doses from ^{131}I used in medical applications. Apart from the Marshallese, studies of internally irradiated human populations have not revealed an increased risk of thyroid malignancy (1,2). For example, studies of a group of children exposed to 90,000 person-rad in Utah have not revealed any excess thyroid cancer. The fallout in Utah contained ^{131}I and was reported to deliver up to several hundred rad of absorbed dose to thyroids of children who were less than 10 years of age (1,2). There are several studies which report no carcinogenic effect from large doses of ^{131}I (2). For example, Holm reported that persons irradiated with ^{131}I , with doses ranging between 6000 and 10,000 rad, exhibited no statistically significant increase in thyroid cancer (2). Studies of the children in the Marshall Islands conducted since 1954, on the other hand, do show a statistically significant increase in thyroid cancer in these irradiated subjects. Since the Marshall Islands' children were exposed simultaneously to external and internal irradiation, we have analyzed the data in an attempt to relate each type of exposure, internal versus external radiation, to the observed thyroid health effects. The mixture of radionuclides, contributing to internal dose in the Marshallese, included mostly short-lived ^{133}I and ^{135}I , and only 10-20% of the thyroid dose came from ^{131}I , thus the radiobiological considerations differ greatly in these various exposure circumstances.

Estimates of thyroid-absorbed dose were recently reassessed for people exposed to fallout in the Marshall Islands (3). The accidental exposure of people on March 1, 1954, occurred as a result of nuclear weapons testing. Over the years, several estimates of thyroid-absorbed dose were made (4,5). The earliest estimate of thyroid dose was reported by Cronkite (4) who indicated a population-averaged thyroid dose. A 1962 study by James (5) listed the most probable thyroid dose to girls who were 3 to 4 years old at the time of exposure. However, the James dose estimate was flawed by the incorrect association of ^{133}I and ^{135}I dose relative to the dose from ^{131}I . The most recent assessment of dose provided detailed information on the type of nuclides in fallout, the mode of intake, and the contributions from internal and external sources. The study of Lessard et al. (3) established greater absorbed dose to people based upon greater intake of the shorter-lived radioiodines. The thyroid dose ranged from several hundred to five thousand rad, and the highest doses were assigned to young people. The revised dose estimates accounted for the radioactivity from all iodine isotopes.

Uncertainties with the dose estimates are associated with the amount of radioactivity measured in the urine of the exposed people, the intake of the short-lived radiotellurium and radioiodine isotopes and percent of thyroid uptake as determined from a physiologic model, errors in estimating the exact amount of each radioiodine isotope, the dose rate and pattern of energy distribution from this radioiodine mixture, and the shape and thickness of the thyroid.

Adams et al. (6) reported the medical status of the Marshallese accidentally exposed to fallout. Through March 1985 there were 35 adenomatous nodules, 5 adenomas, 9 papillary carcinomas, 1 atypical adenoma or follicular carcinoma, and 2 occult papillary carcinomas. A comparison group of equal

size exhibited 3 adenomatous nodules, 1 adenoma, 2 carcinomas, and 2 occult papillary carcinomas, one of which may have been a follicular carcinoma. Uncertainty was associated with diagnosis of follicular carcinoma, one in the exposed group and one in the comparison group, because of equally divided opinion among consulting pathologists. However, it was reasoned that both follicular carcinomas could be excluded from a risk coefficient estimate without seriously biasing the results. Diagnoses on five other individuals are pending. All five are from Utirik Atoll; three are in the <10-year old age group, and two are in the 10- to 18-year-old age group.

METHODS

Adams et al. (6) classified thyroid abnormalities following a scheme similar to that used by the World Health Organization and a committee of pathologists who had special expertise in diseases of the thyroid (7). The following nomenclature was used:

Adenomatous nodule: a focal proliferative lesion consisting of changes typical of adenomatous goiter; the lesions do not fulfill criteria of true neoplasms.

Adenoma: an encapsulated proliferative lesion with a uniform internal growth pattern and benign clinical course.

Occult papillary carcinoma: a small nonencapsulated sclerosing carcinoma, considered to be clinically benign even with positive regional lymph nodes.

Papillary carcinoma: larger, infiltrating carcinoma, usually containing both papillary and follicular components. The smallest lesion diagnosed as a papillary carcinoma, by the consultant pathologists, was 0.8 cm in diameter.

The recent computation of thyroid absorbed dose was performed for inhabitants of Rongelap, Utirik, and Ailingnae Atolls who were exposed to fallout on March 1, 1954. The amount of fallout activity taken into the body was estimated from the value of ^{131}I excreted in urine obtained from 64 persons who were at Rongelap. The other components of fallout taken into the body, particularly ^{133}I and ^{135}I , had to be inferred from studies on fallout composition. The authors of the reassessment study made dose estimates on the basis of actual BRAVO fallout composition. The intake pathway and the time post-detonation at which intake was likely to have occurred were obtained from interviews with the exposed people, and historical records and were factored into the new dose estimates. A detailed development of the dose reassessment was reported by Lessard et al. (3).

The radioepidemiological tables assembled by the Working Group (8) represented the best scientific judgment for the assignment of cancer risk from external radiation; thus we obtained one estimate of external exposure risk coefficient from this source. For persons less than 20 years of age, the Working Group adopted an average risk coefficient of 3.3 excess cancers per million person-rad-years at risk, and for persons 20 years or older they chose a value of 1.0 excess cancer per million person-rad-years at risk. A 10-year minimum latent period was chosen for thyroid cancer. The Working Group calculated thyroid cancer risk based on a linear dose-response function and maintained that the estimates of risk applied to external x and gamma irradiation, but not to the intake of radioisotopes of iodine.

The BEIR III (1) risk coefficients were based, in large part, on external

exposure of children less than 10 years of age, and upon data available through 1979. A central value of 4.0 cancers per million person-rad-years at risk was reported, but after review of their report, we modified the estimate to 4.9 cancers per million person-rad-years at risk. Our result, based on this modification, is discussed in the text and is noted in Table 7. The adjustment was based on weighting the risk coefficient from each study according to the number of excess cancers observed; that is, we gave more weight to cancer risk coefficients developed from studies reporting the greatest number of cancers. The BEIR risk coefficient was based on a minimum latent period of 10 years and on studies involving only external irradiation of the thyroid.

Risk coefficients for external and internal radiation were given in NCRP Report 80 (2), and these coefficients were estimated for a five-year latent period. Report 80 indicated the external risk coefficient applied to ^{135}I and ^{131}I intake, but not for ^{131}I exposure. The two short-lived isotopes of iodine were assumed to have the same effectiveness as x rays, because of the fairly uniform distribution of dose, and because of the comparatively higher dose rates (2). In our analyses, we used risk coefficients for external exposure computed for 5- and 10-year latent periods derived from the following reports. We used external risk coefficients from NCRP Report 80 because they were based on a five-year latent period, and these appear in the results section along with the coefficients developed by the Working Group, which were based on a ten-year latent period.

Risk coefficient estimates, made here, were based on the total external and internal thyroid dose, the total number of cancers, the risk value published for external irradiation of the thyroid, and the partitioning of external and internal dose as follows

$$A + B + C + D = (A + C)E, \quad (1)$$

where

- A = the person-rad to all thyroids from radioisotopes of iodine,
- B = the risk coefficient for internal exposure of the thyroid from radioisotopes of iodine, cancers per person-rad-years at risk,
- C = the person-rad to all thyroids from external gamma radiation,
- D = the risk coefficient from external exposure of the thyroid, for example, 1.0×10^{-6} cancers per person-rad-years at risk for adults, or in the case of children <10 years of age, 4.9×10^{-6} cancers per person-rad-years at risk, and
- E = the risk coefficient determined from the observed health effects, the total thyroid dose, and the spontaneous rates of thyroid disease in the Marshall Islands subjects. The value of E was computed from Eq. (2-1) given in NCRP Report 80 (2).

Computations of B and E were for latent periods of both 5 and 10 years, since the length of latent period affects the years at risk and the risk coefficient. Years at risk are the period from the end of the latent period to the time cancer is observed in a subject. The value for years at risk strongly affected the computation of risk coefficients.

RESULTS

The data in the Appendix are the result of 31 years of medical and

radiological follow-up and, in the case of cancer diagnosis, of consensus opinion of pathologists. The Appendix is provided to allow others to perform different analyses of the data, recognizing that the data base is incomplete. Verifying the data over the last seven years has resulted in changes in age, identification number, assigned dose, and diagnosis. Several independent groups reported age at exposure, and the Adams et al. (6) version was used here. Different ages at exposure influences the age distribution of cancers, which in turn impacts strongly on the risk coefficient for a given age group.

The external thyroid dose was due to gamma exposure from the fallout cloud and fallout on the ground, and was taken as equal to the external whole-body dose reported by Lessard et al. (3), i.e., 190 rad at Rongelap, 110 rad at Ailingnae, and 11 rad at Utirik.

These external doses were estimated for a point which was 1 meter above the ground, thus some variation in external thyroid dose with a person's height may have occurred. To a first approximation external thyroid dose is inversely proportional to height above the ground. We derived this proportionality by neglecting photon attenuation and buildup, and by limiting the height above ground to between 0.5 and 1.5 meters. The impact on the risk coefficient estimates, relative to assuming that external thyroid dose was height dependent, was minimal, since the person-rad from external exposure was much less than the person-rad from internal exposure.

The data for the unexposed comparison groups are indicated in Table 1. In the age- and sex-matched comparison group used for this study, two papillary carcinomas have been observed. The summary is completed through 1983. To apply the data for risk coefficient determination, we modified the matched group results by the ratio of 31/29, which corrects for the difference in the number of reported observation years. The larger, less defined comparison population studied by Conard et al. (7) is shown in the first half of Table 1 to show that spontaneous cancer risk is not a strong function of group age for the Marshallese people. The comparison data indicated a spontaneous rate of 3×10^{-4} cancers per person-rad-years at risk. A lower spontaneous rate has been reported for the U.S. population, 1×10^{-4} per person per year (2). The Marshallese comparison data were used in the risk coefficient computations made here.

A summary of data in the Appendix appears in Tables 2 through 4. Note that out of 9 papillary cancers listed in the Appendix, only 2 were observed in males. This male to female ratio is similar to that reported in other studies (1,2,8). Tables 2 through 4 contain the input data which we used with Eq. (1). The data were grouped in the same manner as in other reports dealing with cancer and radiation exposure of the thyroid. The age groups were the same as that used by Conard et al. (7) and Adams et al. (6). To determine the average years post-exposure to onset of carcinoma, we set onset of carcinoma as the time of clinical observation of a thyroid nodule; thus, a latent period was assumed, but a period of several years could have elapsed before a nodule became large enough for detection by routine palpation by the physician. Therefore, the true latent period could be shorter than that assumed here. Tables 2 through 4 include the expected carcinomas, computed from the age- and sex-matched comparison group, and a summary of the total person-rad from man-made internal and external sources.

Table 1

Summary of Thyroid Abnormalities in the
Marshalllese Unexposed Comparison Groups 1954-1983

<u>Group Age 1954</u>	<u>Number</u>	<u>Total Nodules</u>	<u>Carcinoma</u>	<u>Hypofunction</u>
<10	229	6	2	--
10-18	79	6	1	1
>18	292	25	2	1
Total	600	37	5	2

Age- and Sex-

Matched Group 227

5

2

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Followed

Since 1954

Table 2

Age Group <10 Data Summary

Number of Persons.....	85
Internal Exposure, Person-Rad.....	120,000
External Exposure, Person-Rad.....	5400
Number of Observed Carcinomas.....	3
Average Years Post-Exposure to Onset of Carcinoma.....	22
Assumed Latent Period, Years.....	5 and 10
Number of Expected Spontaneous Carcinomas.....	0.80

Table 3

Age Group 10 to 18 Data Summary

Number of Persons.....	32
Internal Exposure, Person-Rad.....	18,000
External Exposure, Person-Rad.....	2500
Number of Observed Carcinomas.....	3
Average Years Post-Exposure to Onset of Carcinoma.....	28
Assumed Latent Period, Years.....	5 and 10
Number of Expected Spontaneous Carcinomas.....	0.30

Table 4

Age Group >18 Data Summary

Number of Persons.....	120
Internal Exposure, Person-Rad.....	48,000
External Exposure, Person-Rad.....	8,000
Number of Observed Carcinomas.....	3
Average Years Post-Exposure to Onset of Carcinoma.....	16
Assumed Latent Period, Years.....	5 and 10
Number of Expected Spontaneous Carcinomas.....	1.1

Table 5

Risk Coefficients^a for Marshall Islanders, 10-Year Latent Period

Group		Excess		Years	
Age 1954	Number	Thyroid	Total	at	Risk
		Cancers	Person-Rad	Risk	Coefficient
<10	85	2.2	120,000	12.2	1.5×10^{-6}
10-18	32	2.7	21,000	17.7	7.4×10^{-6}
>18	120	1.9	56,000	6.2	5.4×10^{-6}
Total	237	6.8	200,000	11.3	3.0×10^{-6}

^aThyroid cancers per person-rad-years at risk, based on thyroid dose from internal plus external sources.

Table 6

Risk Coefficients^a for Marshall Islanders, 5-Year Latent Period

Group		Excess		Years	
<u>Age 1954</u>	<u>Number</u>	<u>Thyroid</u>	<u>Total</u>	<u>at</u>	<u>Risk</u>
		<u>Cancers</u>	<u>Person-Rad</u>	<u>Risk</u>	<u>Coefficient</u>
<10	85	2.2	120,000	17.2	1.1×10^{-6}
10-18	32	2.7	21,000	22.7	5.8×10^{-6}
>18	120	1.9	56,000	11.2	3.0×10^{-6}
Total	237	6.8	200,000	14.9	2.3×10^{-6}

^aThyroid cancers per person-rad-years at risk, based on thyroid dose from internal plus external sources.

Table 7

Estimated Risk Coefficient^a for Internal and External Exposure

Group		<u>10-Year Latent Period</u>		<u>5-Year Latent Period</u>	
		<u>External</u>	<u>Internal</u>	<u>External</u>	<u>Internal</u>
<u>Age 1954</u>	<u>Number</u>	<u>Risk</u>	<u>Risk</u>	<u>Risk</u>	<u>Risk</u>
		<u>Coefficient</u>	<u>Coefficient</u>	<u>Coefficient</u>	<u>Coefficient</u>
<10	85	3.3×10^{-6}	$1.4 \times 10^{-6(b)}$	2.5×10^{-6}	1.0×10^{-6}
10-18	32	3.3×10^{-6}	8.0×10^{-6}	2.5×10^{-6}	6.3×10^{-6}
>18	120	1.0×10^{-6}	6.1×10^{-6}	1.3×10^{-6}	3.3×10^{-6}
Total	237	2.1×10^{-6}	4.7×10^{-6}	1.9×10^{-6}	2.9×10^{-6}

^aThyroid cancers per person-rad-years at risk.

^bA value of 1.3×10^{-6} results when 4.9×10^{-6} is used for the external risk coefficient.

The risk coefficient, E, for different age groups, computed from total dose resulting from internal plus external exposure for Marshall Islanders, ranged from 1.5×10^{-6} to 7.4×10^{-6} per person-rad-years at risk, assuming a 10-year latent period, and 1.1×10^{-6} to 5.8×10^{-6} , assuming a 5-year latent period. These data are indicated in Tables 5 and 6, respectively. The total risk coefficient, E, was used in Eq. (1) to determine the internal risk coefficient, B. For external risk coefficients and 10-year latent period, we chose 3.3×10^{-6} for age <20 and 1.0×10^{-6} for age >20 based on the Working Group study (8); for 5-year latent period we chose 2.5×10^{-6} for age <18 and 1.3×10^{-6} for age >18, based on NCRP Report 80 (2). The results for internal risk coefficients are in Table 7. Finally, as we explained in the Methods, we chose a special value for the <10-year age group, since it was based on a large group of children exposed to x rays (1). This value was 4.9×10^{-6} cancers per person-rad-years at risk, and the estimate for the internal risk coefficient was 1.3×10^{-6} , virtually the same as the value given in Table 7 for the 10-year latent period.

A tabulation of risk coefficient versus internal thyroid dose is given in Table 8. These internal dose groupings resulted in little variation in external dose as a function of age. These groupings were made to examine the affect of dose on the value for internal risk coefficient.

Table 8

Average Dose Versus Internal and
External Risk Coefficients, 10-Year Latent Period

Group	Average		Average		Total
	Internal Thyroid Dose, rad	Internal Risk Coefficient ^a	External Thyroid Dose, rad	External Risk Coefficient ^b	
<u>Age 1954</u>					<u>Coefficient^a</u>
<10	1400	1.4×10^{-6}	63	3.3×10^{-6}	1.5×10^{-6}
10-18	560	8.0×10^{-6}	78	3.3×10^{-6}	7.4×10^{-6}
>18	400	6.1×10^{-6}	66	1.0×10^{-6}	5.4×10^{-6}

^aThis study.

^bReference 8.

A sensitivity analysis, of the parameters in Eq. (1), shows that the value for the total risk coefficient, E, impacts greatly on the estimate of the internal risk coefficient, B, in this specific Marshall Islands study. This is because of the wide difference between internal thyroid dose, A, and external thyroid dose, C. Thus, our estimate of internal risk coefficient depends largely on the observed incidence of thyroid cancer because the total risk coefficient, E, is very sensitive to the small number of spontaneous and excess thyroid cancers observed.

DISCUSSION/CONCLUSION

Interest in the relative risk of ^{131}I taken internally and external radiation dose to the thyroid relates to radiation protection and medical care issues. Unfortunately for those interested in obtaining information on this important issue, the complex mixture of radionuclides taken up by the Marshallese precludes such an analysis. The results obtained for these studies are specific to the case where the thyroid dose was due to a mixture of short-lived radioisotopes of iodine, some of which were produced by the decay of tellurium within the body. Current information on animal and human data was summarized recently in NCRP Report 80 (2). The Committee concluded that ^{131}I was less than one third as effective for thyroid cancer induction as external radiation. This can not be compared directly to the results of the present study because of the small amount of ^{131}I in the Marshallese exposures. In most animal studies, which used rodents, high TSH levels were found to be necessary co-factors for thyroid cancer induction. Thus, goitrogen plus ^{131}I exposures were needed to induce thyroid cancer, except in several studies using Long-Evans rats, which behaved differently from all other strains studied. Results of ^{131}I treatment of children for hyperthyroidism were reported in two large studies. In reviewing results of treatment of nine children, Sheline et al. (9) found that all of them subsequently developed thyroid nodules and one was diagnosed as having of thyroid cancer, about which there was disagreement regarding pathology. None of those children received thyroid replacement therapy after ^{131}I treatment, and all presumably developed high endogenous TSH levels. In Los Angeles, at a later date, 73 children were treated with approximately the same ^{131}I dose, all were placed on thyroid replacement, and none developed thyroid nodules (10). Thus the relative risk of thyroid dose from internal emitters compared to external radiation for Marshall Islanders may be influenced by a high TSH co-factor, since thyroid replacement therapy began 11 years after exposure. Replacement therapy was recommended only for the high-dose group which, at that time, was thought to be the people at Rongelap.

Also no increased incidence of thyroid cancer was seen in large numbers of human subjects exposed to similar or higher doses of ^{131}I in the treatment of thyrotoxicosis (11), or in children given ^{131}I in lower diagnostic doses (12).

Hypothyroidism is a nonstochastic effect of ionizing radiation exposure, with estimated threshold for induction of 2000 rad to the thyroid (1). In the Marshallese children, whose thyroids were exposed to doses in the several thousand rad range, hypothyroidism and increased TSH levels certainly existed in the early years following exposure. In later years, uneven acceptance of thyroid supplementation by children may have led to persistent increased TSH levels. The combination of high TSH and high internal and external radiation doses may account for the unusually high incidence of nodules in this population, and in the unusual age distribution of sensitivity.

The numbers of individuals in the study are small, and statistical segregation of the interacting factors is not possible. Thus, it will be difficult to draw precise conclusions from this study with respect to apportionment of risk between internal and external doses. Further, the differences between the radiological characteristics of ^{131}I , ^{133}I , and ^{135}I and the larger doses from ^{133}I and ^{135}I make it difficult to assess the relative risk of ^{131}I and external radiation in this circumstance. A simple statistical model was used (3) to indicate the one sigma confidence interval. This confidence interval is indicated in the following paragraph in parentheses. The standard deviation of the risk estimate, E, was 1.5 times the average value for the risk estimate, and development of this standard deviation was given by Lessard et al. (3).

The results support the notion that external risk coefficients are different from internal risk coefficients following exposure to a mixed radiation field. The total risk coefficients [3.0×10^{-6} ($\pm 4.5 \times 10^{-6}$) cancers per person-rad-year at risk, 10-year latent period, and 2.3×10^{-6} ($\pm 3.5 \times 10^{-6}$) cancers per person-rad-year at risk, 5-year latent period] are similar to the literature values (1,2) for this age distribution and for external exposure. The literature values are 2.1×10^{-6} for a 10-year latent period and 1.9×10^{-6} for a 5-year latent period. However, if the risk is examined as a function of age or as a function of dose, differences are encountered. For example, the ratio of the risk coefficient for external exposure to the risk coefficient for internal exposure, in the <10 year age group, is 2.5 (0.38 to 4.6). In the 10- to 18-year age group, this risk coefficient ratio is 0.40 (0.22 to 2.6).

Small group size, in this study, and the uncertainties reported in studies on medical and fallout exposures make it difficult to establish relative risks of thyroid cancer from internal and external radiation doses to the thyroid. The possible synergistic effect of internal and external exposures and the modifying factors such as high TSH levels and nonuniform irradiation of thyroid cells complicate the biological interpretation of the risk. In this study, different age groups correspond to different dose levels, and very high dose to the thyroid may be a significant modifying factor. Because of the high interest in evaluating human sensitivity to ^{131}I , continued efforts are needed to obtain data and to conduct analyses that will establish better estimates of risk coefficients than are now available. It is not likely that data for the Marshallese exposures will contribute to the answer to that important question.

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REFERENCES

1. Committee on the Biological Effects of Ionizing Radiation, The Effects on Populations of Exposure to Low Levels of Ionizing Radiation: 1980, National Research Council Report, National Academy Press, Washington, DC, 1980.
2. Recommendations of the National Council on Radiation Protection and Measurements, Induction of Thyroid Cancer by Ionizing Radiation, NCRP Report No.80, Bethesda, MD, 1985.
3. Lessard, E.T., R.P. Miltenberger, R.A. Conard, S.V. Musolino, J.R. Naidu, A. Moorthy, and C.J. Schopfer, Thyroid Absorbed Dose for People at Rongelap, Utirik and Sifo on March 1, 1954, Brookhaven National Laboratory Report, Upton, NY, BNL 51882, 1985.

4. Cronkite, E.P., V.P. Bond, and C.L. Dunham, A Report on the Marshallese and Americans Accidentally Exposed to Radiation from Fallout and a Discussion of Radiation Injury in the Human Being, in: Some Effects of Ionizing Radiation on Human Beings, U.S. Atomic Energy Commission, Washington, DC, USAEC-TID 5358, 1956.
5. James, R.A., Estimate of Radiation Dose to Thyroids of Rongelap Children Following the BRAVO Event, Lawrence Radiation Laboratory Report, Livermore, CA, UCRL-12273, 1964.
6. Adams, W.H., J.A. Harper, R.S. Rittmaster, P.M. Heotis, and W.A. Scott, Medical Status of the Marshallese Accidentally Exposed to BRAVO Fallout Radiation: January 1980 Through December 1982, Brookhaven National Laboratory Report, Upton, NY, BNL 51761, 1982.
7. Conard, R.A. et al. (9 co-authors), Review of Medical Findings in a Marshallese Population Twenty-Six Years After Accidental Exposure to Radioactive Fallout, Brookhaven National Laboratory Report, Upton, NY, BNL 51261, 1980.
8. Ad Hoc Working Group to Develop Radioepidemiological Tables, Report of the National Institutes of Health, January 4, 1985. Office of the Director, NIH Publication No. 85-2748. U.S. Dept. HHS, PHS, NIH.
9. Sheline, G.E. et al., "Thyroid Nodules Occurring Late After Treatment of Thyrotoxicosis with Radioiodine," J. Clin Endoc. & Metab. 22, 8, 1962.
10. Starr, P., "Later Results of I-131 Treatment of Hypothyroidism in 73 Children and Adolescents: 1967 Follow-up," J. Nucl. Med. 10, 586-590, 1969.
11. Dobyns, B.M. et al., "Malignant and Benign Neoplasms of the Thyroid in Patients Treated for Hypothyroidism: A Report of the Cooperative Thyrotoxicosis Follow-up Study," J. Clin. End. & Metab. 38, 976-998, 1974.
12. Holm, L.E. et al., "Incidence of Malignant Thyroid Tumors in Humans After Exposure to Diagnostic Doses of I-131," J. National Cancer Institute, 64, 1055-1059, 1980.
13. Prentice, R.L. et al., Radiation Exposure and Thyroid Cancer Incidence among Hiroshima and Nagasaki Residents, National Cancer Institute Monograph 62, 207-212, 1982.
14. Ishimaru, T. et al., Incidence of Thyroid Cancer Among Atomic Bomb Survivors and Controls Hiroshima and Nagasaki, 1958-79: Relationship to Radiation Absorbed Dose in the Thyroid, RERF Technical Report 1984.

APPENDIX

Tabulation of Thyroid Dose
and Thyroid Health Effects

Rongelap and Ailingnae Population

ID Number	Sex	Age in 1954	Comment	Diagnosis	Internal Thyroid Dose, Rad	Years Post Exposure
*1	F	52	Died 1985		290	
2	M	1		Adenomatous Nodule	5000	11
3	M	1		Myxedema	5000	
4	M	36			1000	
5	M	1		Myxedema	5000	
*6	M	1			1300	
7	M	34			1000	
*8	F	5		Adenomatous Nodule	740	18.5
9	M	20			1000	
10	M	22			1000	
11	M	48			1000	
12	F	16			1200	
13	F	59	Died 1966		1100	
14	F	3			3500	
15	F	5	Surgery(2x)	Adenomatous Nodule	2800	22;32
*16	M	37			280	
17	F	1		Adenomatous Nodule	5000	10.5
18	F	19		Papillary Carcinoma	1100	15.5
19	M	3		Adenomatous Nodule	3500	14.5
20	M	5		Adenomatous Nodule	2800	11
21	F	1		Adenomatous Nodule	5000	10.5
22	F	15			1300	
23	M	2		Adenomatous Nodule	4000	14.5
24	F	11			1700	
25	M	44	Died 1956		1000	
26	M	13	Died 1962		1500	
27	M	33			1000	
*28	F	69	Died 1965		290	
*29	M	65	Died 1966		280	
30	F	52	Died 1962		1100	
*31	M	31	Died 1958		280	
32	M	2			4000	
33	F	1		Adenomatous Nodule	5000	12
34	F	43			1100	
35	M	11			1700	
36	M	5		Adenomatous Nodule	2800	15.5
37	M	18			1000	
38	M	75	Died 1957		1000	
39	F	13			1500	
40	M	31			1000	
*41	M	42			280	
42	F	1		Adenomatous Nodule	5000	12
*43	F	67	Died 1964		290	

Tabulation of Thyroid Dose
and Thyroid Health Effects
(Continued)

Rongelap and Ailingnae Population

ID Number	Sex	Age in 1954	Comment	Diagnosis	Internal Thyroid Dose, Rad	Years Post Exposure
*44	M	2				
*45	F	30		Adenomatous Nodule	290	19
46	M	76	Died 1962		1000	
47	M	6			2400	
*48	F	4			820	
49	F	13			1500	
*50	M	34	Died 1971		280	
*51	F	23	Died 1982	Follicular Adenoma	290	20
52	F	46	Died 1963		1100	
*53	F	5		Adenomatous Nodule with Occult Papillary Carcinoma	740	27
54	M	1	Died 1972	Adenomatous Nodule	5000	14.5
55	M	76	Died 1968		1000	
56	F	67	Died 1962		1100	
57	F	98	Died 1963		1100	
58	F	59	Died 1977		1100	
*59	F	44	Died 1968	Adenomatous Nodule	290	12
60	F	56	Died 1972		1100	
61	F	6		Adenomatous Nodule	2400	12
62	F	55	Died 1959		1100	
63	F	34			1100	
64	F	28		Papillary Carcinoma	1100	11
65	F	1		Adenomatous Nodule	5000	12
66	F	29		Adenomatous Nodule	1100	25.5
67	F	12		Papillary Carcinoma	1600	31
68	M	44	Died 1974		1000	
69	F	2		Adenomatous Nodule	4000	10.5
*70	F	5			740	
71	F	26			1100	
72	M	5		Papillary Carcinoma	2800	15.5
73	M	16			1200	
74	F	14		Papillary Carcinoma	1400	22
75	F	10		Adenomatous Nodule with Follicular Adenoma	1800	18.5
76	M	9			2000	
77	M	24			1000	
78	F	35			1100	
79	M	37			1000	
80	M	44	Died 1983		1000	
*81	F	6			640	
82	M	49	Died 1980		1000	
83	M	In Utero		Adenomatous Nodule		20
*64	M	In Utero				

Tabulation of Thyroid Dose
and Thyroid Health Effects
(Continued)

Rongelap and Ailingnae Population

ID Number	Sex	Age in 1954	Comment	Diagnosis	Internal Thyroid Dose, Rad	Years Post Exposure
85	M	In Utero		Adenomatous Nodule		25.5
86	F	In Utero				

*Ailingnae Exposed

Utirik Population

2101	M	48	Died 1968		150	
2102	M	3			480	
2103	M	43			150	
2104	F	22			160	
2105	M	45			150	
2106	M	4			430	
2107	F	25			160	
2108	M	11			250	
2109	F	45	Died 1978		160	
2110	M	47			150	
2111	F	6			340	
2112	M	53	Died 1968		150	
2113	F	3			480	
2114	M	40			150	
2115	M	1			670	
2116	F	21	Died 1960		160	
2117	F	24			160	
2119	F	18			160	
2120	M	4	Died 1982		430	
2121	M	57	Died 1965		150	
2122	M	82	Died 1959		150	
2123	M	15			200	
2124	M	2			550	
2125	M	37			150	
2126	F	5			390	
2127	M	68	Died 1959		150	
2128	F	8	Died 1985		310	
2129	F	17			160	
2130	F	3			480	
2131	F	29	Died		160	
2132	F	1		Adenomatous Nodule	670	27
2134	F	1			670	
2135	M	31	Died 1977		150	

Tabulation of Thyroid Dose
and Thyroid Health Effects
(Continued)

Utirik Population						
ID Number	Sex	Age in 1954	Comment	Diagnosis	Internal Thyroid Dose, Rad	Years Post Exposure
2136	M	3			480	
2137	M	14			220	
2138	F	4			430	
2139	F	44			160	
2140	F	45			160	
2141	F	53	Died 1968		160	
2142	M	5			390	
2143	M	3			480	
2144	M	7			330	
2145	M	34			150	
2146	F	36	Died 1980		160	
2147	F	5		Adenomatous Nodule	390	25.5
2148	M	44			150	
2149	F	9		Diagnosis Pending	300	30
2150	M	10			270	
2150	M	12		Follicular Adenoma	240	22
2151	F	4			430	
2152	M	17		Papillary Carcinoma	150	30
2153	M	1			670	
2154	F	40	Died 1965		160	
2155	M	1			670	
2156	M	8			310	
2157	M	26	Died 1984		150	
2158	F	28			160	
2159	F	3			480	
2160	F	4		Papillary Carcinoma	430	21
2161	F	29	Died 1981		160	
2162	F	32			160	
2163	M	65	Died 1964-65?		150	
2164	F	7	Died 1984		330	
2165	M	11			250	
2166	M	38			150	
2167	M	14			220	
2168	M	18	Died 1984	Diagnosis Pending	150	30
2169	M	62	Died 1978		150	
2170	M	41	Died 1959		150	
2171	F	2		Papillary Carcinoma	550	30
2172	F	12		Diagnosis Pending	240	30
2174	M	1			670	
2175	M	57	Died 1970		150	
2176	M	10			270	
2177	M	5	Died 1961		390	
2178	M	19	Died 1972		150	
2179	M	2			550	
2180	M	70	Died 1960		150	

Tabulation of Thyroid Dose
and Thyroid Health Effects
(Continued)

Utirik Population						
ID Number	Sex	Age in 1954	Comment	Diagnosis	Internal Thyroid Dose, Rad	Years Post Exposure
2181	M	65	Died 1967		150	
2182	F	52			160	
2183	M	56	Died 1965		150	
2184	M	60	Died 1961		150	
2185	M	32	Died 1984		150	
2187	F	56	Died 1959		160	
2188	M	3			480	
2189	F	26			160	
2190	F	75	Died 1964-65?		160	
2191	F	75	Died 1969		160	
2192	F	74	Died 1964-65?		160	
2193	F	31		Adenomatous Nodule	160	25
2194	F	35	Died 1984	Papillary Carcinoma	160	22
2195	F	24		Adenomatous Nodule	160	25
2196	F	38		Adenomatous Nodule	160	26.5
2197	F	3		Diagnosis Pending	480	31
2198	F	58	Died 1979		160	
2199	F	42	Died 1961		160	
2200	F	43			160	
2201	F	50	Died 1974		160	
2202	F	59	Died 1967		160	
2203	F	62	Died 1963		160	
2204	F	60	Died 1965		160	
2205	M	29			150	
2206	M	32			150	
2207	M	5			390	
2208	F	37		Adenomatous Nodule	160	19
2209	F	5			390	
2210	F	1			670	
2212	F	34		Adenomatous Nodules	160	19
2213	F	1			670	
2214	M	65	Died 1969		150	
2215	M	1		Adenomatous Nodule with Occult Papillary Carcinoma	670	25.5
2216	F	33			160	
2217	F	22			160	
2218	F	1			670	
2219	F	54	Died 1957		160	
2220	F	25			160	
2221	F	52		Adenomatous Nodules	160	19
2222	F	60	Died 1957		160	
2223	F	66	Died 1967		160	
2224	F	31			160	
2225	F	6		Diagnosis Pending	340	30

Tabulation of Thyroid Dose
and Thyroid Health Effects
(Continued)

Utirik Population						
ID Number	Sex	Age in 1954	Comment	Diagnosis	Internal Thyroid Dose, Rad	Years Post Exposure
2226	F	1			670	
2227	F	4			430	
2228	F	8			310	
2229	F	18		Follicular Carcinoma Possible Atypical Adenoma	160	15.5
2230	F	13			230	
2231	F	1			670	
2232	M	1			670	
2234	M	12			240	
2235	M	7			330	
2236	M	11		Follicular Adenoma	260	24
2237	M	7			330	
2238	F	54	Died 1965		160	
2239	F	3		Adenomatous Nodule	480	27
2240	M	33	Died 1977		150	
2241	F	28	Died 1981		150	
2242	M	1			670	
2243	M	46	Died 1958		150	
2245	M	1			670	
2246	F	5	Died 1971		160	
2247	F	8			310	
2248	F	15		Occult Papillary Carcinoma	200	29
2249	F	15			200	
2250	M	10			270	
2251	F	4			430	
2252	M	39	Died 1972		150	
2253	M	45	Died 1965		150	
2254	F	5			390	
2255	F	1			670	
2256	F	5			390	
2257	M	7			330	
2258	M	47	Died 1971		150	
2259	F	21	Died 1968		160	
2260	F	1			670	
2261	M	26			150	
2268	M	In Utero				
2269	M	In Utero				
2271	M	In Utero				
2273	M	In Utero				
2274	M	In Utero				
2276	M	In Utero				
2277	F	In Utero				
2548	M	In Utero				