

Incidence of Skin Cancer among Nagasaki Atomic Bomb Survivors

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Of the 66,276 Nagasaki atomic bomb survivors registered at the Scientific Data Center for the Atomic Bomb Disaster at the Nagasaki University School of Medicine, 140 were identified as having skin cancer from the records of 31 hospitals in Nagasaki City. From the cases of these survivors, a statistical analysis was made of the incidence of skin cancers by age, gender, histology and latency period in Nagasaki atomic bomb survivors. The results showed a high correlation between the incidence of skin cancer and distance from the blast hypocenter, and that the incidence of skin cancer in the Nagasaki survivors appears now to be increasing with exposure distance.

INTRODUCTION

It is now more than 45 years since atomic bombs were dropped on Hiroshima and Nagasaki. In the interim, increased incidences of leukemia and certain other radiation-induced malignant tumors have been confirmed in the atomic bomb survivors, especially in those proximal to the blasts. In 1969, Johnson et al.¹⁾ made an extensive study of skin cancer in the atomic bomb survivors of Hiroshima and Nagasaki but found no evidence of increased incidence. Reports in the literature, however, indicate that the latency period for the development of skin cancer from therapeutic irradiations is a long one. Therefore long-term observations are necessary to determine whether skin cancer is increased in atomic bomb survivors. We undertook to clarify the occurrence of skin cancer in Nagasaki atomic bomb survivors and the relation of the incidence of skin cancer to exposure distance from the blast hypocenter.

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MATERIALS AND METHODS

The subjects were 66,276 Nagasaki atomic bomb survivors registered at the Scientific Data Center for the Atomic Bomb Disaster at the Nagasaki University School of Medicine. We collected records of cases of skin cancer from 31 hospitals (inclusive of most of the major hospitals in Nagasaki City) based on histological reports made from 1961 to 1987. The cases collected were collated with the information on the 66,276 individuals registered at the Scientific Data Center as to the estimated distance of these survivors from the hypocenter of the atomic bomb explosion. In all 140 cases of survivors with skin cancer were collected from 18 of the 31 hospitals. The distribution of these cases based on the survivors estimated distances from the hypocenter is shown in Table 1. These 140 cases of skin cancer were analyzed both in relation to the patient's distance from the blast and the available clinical and histological information. The logistic regression model²⁾ was used to analyze the relation of the incidence of skin cancer to distance. The model equation used was

$$P(x) = \frac{e^{b_0 + b_1x}}{1 + e^{b_0 + b_1x}}$$

where x is distance, b_0 a constant and b_1 the coefficient of distance.

Correlation was used to relate the latency period to age at the time of the bombing (ATB), age at the onset of skin cancer, and distance from the blast. Analysis of variance was used to relate the histological type of cancer with age ATB, age at the onset of the disease and the latency period. The 66,276 survivors including those with skin cancer were classified into distance groups of 500-m intervals, the median value for each category being used. To clarify the relation between the incidence of skin cancer and the survivors distance from the hypocenter, we divided the cases in three groups: those who were less than 2.0 km from the hypocenter; those who were less than 2.5 km away including those less than 2.0 km; and those 3.0 km or more away. These three groups were compared statistically. In general, atomic bomb survivors who were less than 2.5 km from the hypocenter would have been exposed to a significant dose of radiation, but the actual dose received may have been

Table 1. Number of Cases of Skin Cancer in Nagasaki Atomic Bomb Survivors by Sex and Distance

Distance (km)	0-0.9	1.0-1.4	1.5-1.9	2.0-2.4	2.5-2.9	3.0+	Total
Sex							
Male	0	9	9	7	7	31	63
Female	2	6	8	8	8	45	77
Total	2	15	17	15	15	76	140

moderate by shielding conditions. Unfortunately, no information of the exposure dose received by individuals is available at the Scientific Data Center.

The 140 skin cancer patients consisted of 63 men and 77 women, ranging in age from 42 to 95 (median 71) at the onset of the disease. The histologic type distribution was basal cell epithelioma (BCE) in 67 cases (47.9%), squamous cell carcinoma (SCC) in 43 (30.7%), basosquamous cell carcinoma (BSCC) in 3 (2.1%), malignant melanoma (MM) in 11 (7.9%), Paget's disease in 7 (5.0%), tumors of epidermal appendages (such as sweat gland carcinoma) in 6 (4.3%) and dermatofibrosarcoma, etc. in 3 (2.1%) (Table 2). Bowen's disease was not included in this study.

RESULTS

The relation of the incidence of skin cancer to distance from the hypocenter; the latency period with age ATB; age at the onset of skin cancer and distance; and the histological type of cancer with age ATB, distance, age at onset of the disease and latency period were investigated. Major findings of statistical significance were as described below.

1. Incidence of skin cancer and distance from the hypocenter

The number of cases and the incidence of skin cancer based on distance of the survivors registered at the Scientific Data Center are shown in Table 3. The relation between incidence and distance found by logistic regression is shown in Fig. 1. Calculations made with the equation

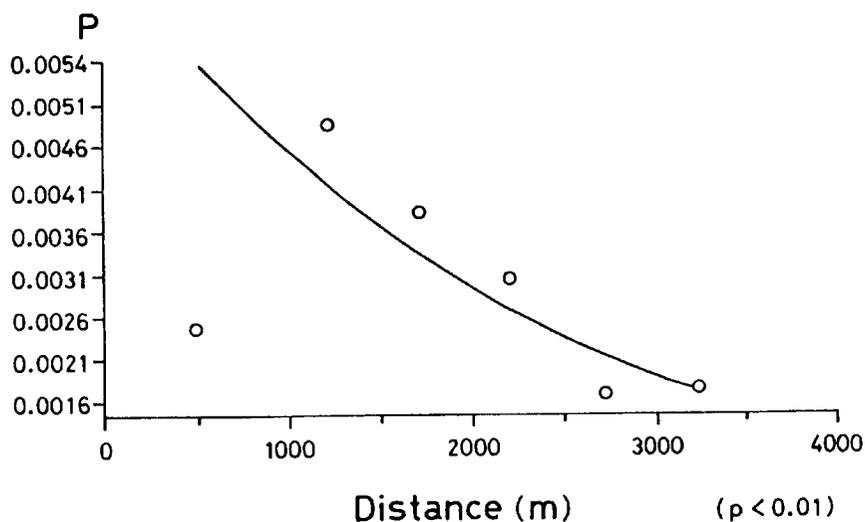
$$P(x) = \frac{\exp(-5.0077 - 0.00042292x)}{1 + \exp(-5.0077 - 0.00042292x)}$$

Table 2. Number and Percentage of Cases of the Various Types of Skin Cancer

Kinds	Number of cases (%)
Basal cell epithelioma	67 (47.9)
Squamous cell carcinoma	43 (30.7)
Basosquamous cell carcinoma	3 (2.1)
Malignant melanoma	11 (7.9)
Paget's disease	7 (5.0)
Tumor of epidermal appendages	6 (4.3)
Others	3 (2.1)
Total	140 (100.0)

Table 3. Incidence of Skin Cancer in Nagasaki Atomic Bomb Survivors by Distance (Sexes combined)

Distance (km)	Survivors in 1975	Number of skin cancer cases	Incidence (%)
0-0.9	852	2	0.2
1.0-1.4	3,215	15	0.5
1.5-1.9	4,611	17	0.4
2.0-2.4	5,199	15	0.3
2.5-2.9	8,922	15	0.2
3.0+	43,504	76	0.2
Total	40,580	77	0.2

**Fig. 1.** Incidence of skin cancer in Nagasaki atomic bomb survivors based on distance (both sexes, $p < 0.01$).

showed that the incidence of skin cancer significantly decreased with distance from the hypocenter ($p < 0.01$). Table 4 shows the number of cases and Table 5 the incidence of skin cancer in men and women. A high correlation was found between distance and the incidence of skin cancer even when cases were divided by sex; males ($p < 0.01$), females ($p < 0.05$) (Figs. 2 and 3).

2. Time trend in the incidence of skin cancer

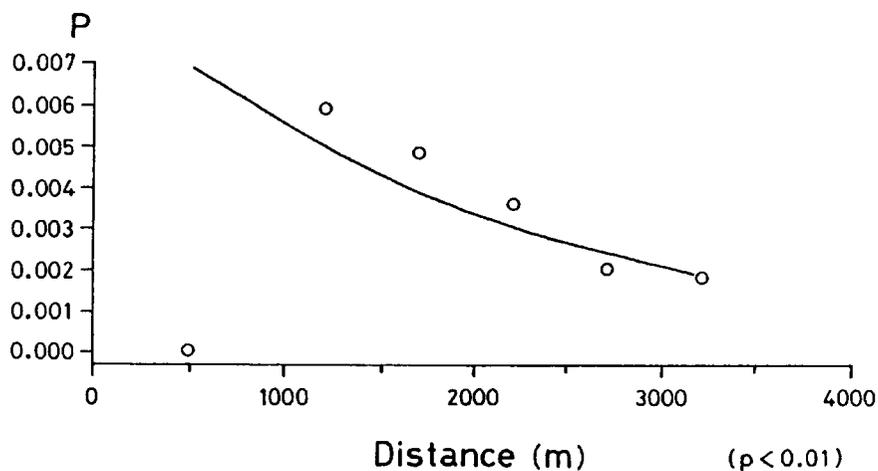
The incidence of skin cancer by year was calculated based on 133 cases reported between 1961 and 1986. Calculations were made for period of five years because of the

SKIN CANCER IN NAGASAKI A-BOMB SURVIVORS

221

Table 4. Incidence of Skin Cancer in Male Nagasaki Atomic Bomb Survivors by Distance

Distance (km)	Survivors in 1975	Number of skin cancer cases	Incidence (%)
0-0.9	319	0	0.0
1.0-1.4	1,517	9	0.6
1.5-1.9	1,846	9	0.5
2.0-2.4	1,970	7	0.4
2.5-2.9	3,382	7	0.2
3.0+	16,662	31	0.2
Total	25,696	63	0.2

**Fig. 2.** Incidence of skin cancer cases in male Nagasaki atomic bomb survivors based on distance ($p < 0.01$).

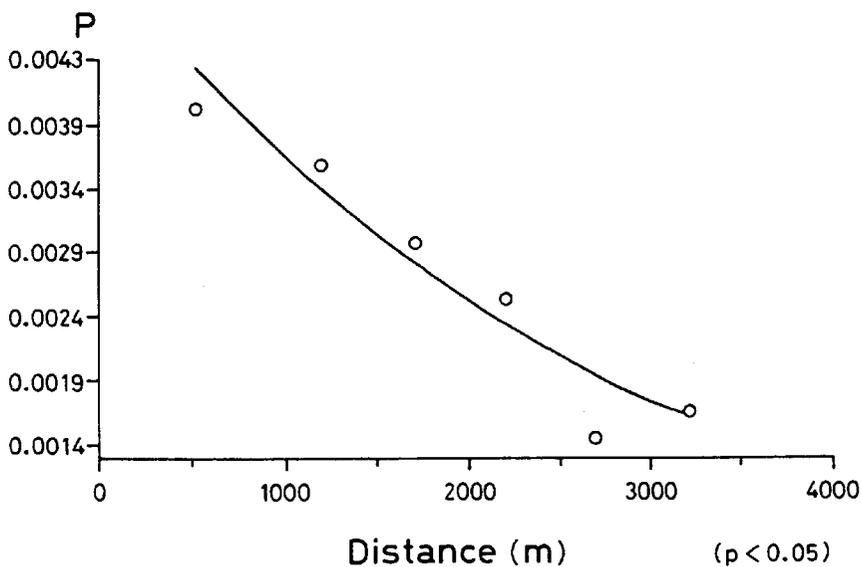
limited number of cases. Table 6 shows that number of cases based on these five-year periods steadily increased from 1962 to 1986. The ordinate in Fig. 4 gives the ratio of skin cancer cases per 100,000 persons per year based on distance from the blast hypocenter. It is likely that the incidence of skin cancer continued to increase after 1965 and especially since 1975 in those proximally exposed who were less than 2.5 km from the hypocenter. Calculations using the χ^2 test showed a significant increase in the incidence of skin cancer in the proximal exposure group after 1975 ($p < 0.01$).

3. Other analyses

Correlation and analysis of variance were used to show all possible correlations between two or three of the various combinations of items described previously in order to

Table 5. Incidence of Skin Cancer in Female Nagasaki Atomic Bomb Survivors by Distance

Distance (km)	Survivors in 1975	Number of skin cancer cases	Incidence (%)
0-0.9	506	2	0.4
1.0-1.4	1,698	6	0.4
1.5-1.9	2,765	8	0.3
2.0-2.4	3,229	8	0.2
2.5-2.9	5,540	8	0.1
3.0+	26,842	45	0.2
Total	40,580	77	0.2

**Fig. 3.** Incidence of skin cancer cases in female Nagasaki atomic bomb survivors based on distance ($p < 0.05$).

determine the relation between atomic bomb exposure and the occurrence of skin cancer. Comparisons between men and women and between histological cancer types also were made. Despite the variety of items, no statistical correlation was found.

DISCUSSION

A relation between atomic bomb radiation and malignant neoplasms in Hiroshima and

SKIN CANCER IN NAGASAKI A-BOMB SURVIVORS

223

Table 6. Number of Skin Cancer Cases in Nagasaki Atomic Bomb Survivors based on Five-year Periods

Years	Males	Females	Total
1962-1966	3	5	8
1967-1971	5	10	15
1972-1976	9	10	19
1977-1981	18	19	37
1982-1986	26	28	54
Total	61	72	133

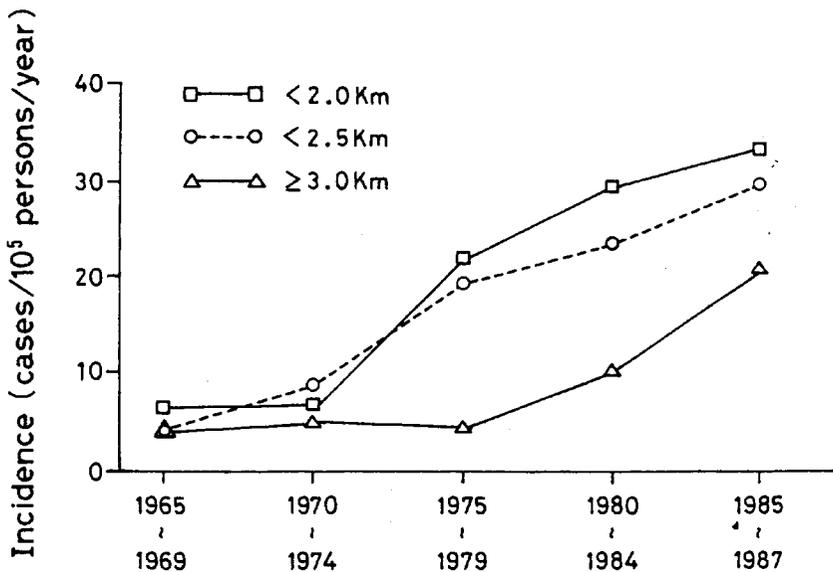


Fig. 4. Incidences of skin cancer in Nagasaki atomic bomb survivors (both sexes) for five-year periods. Calculation made with the χ^2 test showed a shorter exposure distance after 1975 ($p < 0.01$).

Nagasaki survivors has been confirmed for leukemia³⁾ and for thyroid⁴⁾, lung⁵⁾, breast⁶⁾, gastric⁷⁾ and colon cancers as well as salivary gland neoplasms⁸⁾. Many reports have been made on skin cancers induced by medical irradiation, including a squamous cell carcinoma (SCC) case reported by Frieben⁹⁾ in 1902. General remarks also were made by Hood and Young¹⁰⁾; but, Johnson et al.¹⁾ in 1969 reported that no increase in the incidence of skin cancer could be found in atomic bomb survivors in Hiroshima and Nagasaki. No specific studies on skin cancer have been conducted since then.

In this preliminary study, we investigated the incidence of skin cancer from 1961 to

1987 using information from the Scientific Data Center for the Atomic Bomb Disaster at Nagasaki University School of Medicine, 140 skin cancer cases being confirmed among 66,276 subjects who are registered there. The relation between the incidence of skin cancer and distance from the hypocenter was analyzed for the 140 cases by means of logistic regression, which showed that the incidence increased significantly as distance decreased ($p < 0.01$). The same results were found for men ($p < 0.01$) and women ($p < 0.05$). This is a most important conclusion because it is the first evidence of a high correlation between the atomic bomb exposure distance and the incidence of skin cancer. In Figs. 1 and 2, the lower incidence of skin cancer seen for those less than 1.0 km from the hypocenter may indicate that shielding at the time of the blast is a factor that has a major effect on the occurrence of skin cancer.

An issue of interest and importance is the latency period from the time of exposure to radiation to the development of skin cancer. Although many reports have described latency periods for skin cancers caused by radiation therapy, the median latency period reported varies from 25 to 30 years¹⁰). This difference can be ascribed to such sample factors as sex, age, race, number of cases, irradiated site, dose, type of skin cancer, and the follow-up period. The study of skin cancer in the Nagasaki atomic bomb survivors is important because the incidence and latency of radiation-induced skin cancer in a single race residing in the same area can be accurately assessed.

The year 1969 when Johnson et al.¹⁾ reported on the incidence of skin cancer in atomic bomb survivors in Hiroshima and Nagasaki was a time when the number of skin cancer cases was not great but there has been a gradual increase since then. This increase suggests that 1969 was too early to detect the incidence of skin cancer in the survivors. According to our information (Fig. 4), after 1975 the incidence of skin cancer in those exposed at distances of less than 2.5 km is much greater than in those who were more than 3.0 km away ($p < 0.01$); but, the incidence for those more than 3.0 km away also showed an increase after 1980. Recently, Tada and Miki¹¹⁾ reported that the incidence of skin cancer in the general Japanese population is gradually increasing. They think that this increase may be due to prolonged life expectancy (the increase in the elderly in the general population), to more frequent histological verification of such tumors, to an increase in environmental carcinogenic factors, or a combination of these factors.

In conclusion, we emphasize that adequate surveillance of individual atomic bomb survivors is needed particularly of those proximally exposed, in relation to skin cancers as well as other malignant tumors. Moreover, further studies that use the estimated atomic bomb exposure dose reported by the Radiation Effects Research Foundation (RERF) for Hiroshima and Nagasaki are necessary before any final conclusion can be reached.

REFERENCES

1. Johnson, M-L.T., Land, C.E., Gregory, P.B., Taura, T. and Milton, R.C. (1969) Effects of ionizing radiation on the skin, Hiroshima and Nagasaki. Atomic Bomb Casualty Commission Technical Report

- No. 20.
2. Dixon, W.J., Brown, M.B., Engelman, L., Frane, J.W., Hill, M.A., Jennrich, R.I. and Toporek, J.D. (1983) BMDP statistical software. University of California Press, Berkeley pp 105–344.
 3. Liu P.I., Ishimaru, T., McGregor, D.H., Yamamoto, T and Steer, A. (1973) Autopsy study of leukemia in atomic bomb survivors, Hiroshima and Nagasaki, 1949–1969. *Cancer* **31**: 1315–1327.
 4. Parker, L.N., Belsky, J.L., Yamamoto, T., Kawamoto, S. and Keehn, R.J. (1974) Thyroid carcinoma after exposure to atomic radiation: A continuing survey of a fixed population, Hiroshima and Nagasaki, 1958–1971. *Ann. Intern. Med.* **80**: 600–604.
 5. Cihak, R.W., Ishimaru, T., Steer, A. and Yamada, A. (1974) Lung cancer at autopsy in A-bomb survivors and controls, Hiroshima and Nagasaki, 1961–1970. 1. Autopsy findings and relation to radiation. *Cancer* **33**: 1580–1588.
 6. Wanebo, C.K., Johnson, K.G., Sato, K. and Thorslund, T.W. (1968) Breast cancer after exposure to the atomic bombings of Hiroshima and Nagasaki. *N. Engl. J. Med.* **279**: 667–671.
 7. Yamamoto, T. and Kato, H. (1971) Two major histological types of gastric carcinoma among the fixed populations of Hiroshima and Nagasaki. *Gann* **62**: 381–387.
 8. Belsky, J.L., Takeichi, N., Yamamoto, T., Cihak, R.W., Hirose, F., Ezaki, H., Inoue, S. and Blot, W.J. (1975) Salivary gland neoplasms following atomic radiation: Additional cases and reanalysis of combined data in a fixed population, 1957–1970. *Cancer* **35**: 555–559.
 9. Frieben, E.A. (1902) Demonstration eines Cancroids des rechten Handrückens das sich nach langdauernder Einwirkung von Röntgenstrahlen entwickelt hatte. *Forschr. Geb. Röntgenstr.* **6**: 106–111.
 10. Hood, I.C. and Young, J.E.M. (1984) Late sequelae of superficial irradiation. *Head Neck Surg.* **7**: 65–72.
 11. Tada M. and Miki, Y. (1984) Malignant skin tumors among dermatology patients in university hospitals of Japan. A statistical survey 1971–1975. *J. Dermatol.* **11**: 313–321.