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**Incidence of Skin Cancer among Nagasaki Atomic Bomb Survivors
(Preliminary Report)**

NAOKI SADAMORI¹, MARIKO MINE², MAKOTO HORI³, NAOKO FUJIWARA⁴,
OSAMU TAKAHARA⁴, KATSUTARO NISHIMOTO⁵, HIROHISA OTA⁵,
YOSHINORI NODA⁶, KATSUYA NAMBA⁶, MICHIKO SADAMORI⁷, YUTAKA
OKUMURA^{2,8}, HIKOTARO YOSHIDA³ AND MICHITO ICHIMARU¹

¹ Department of Internal Medicine, Atomic Disease Institute, Nagasaki University School of Medicine, 7-1 Sakamoto-machi, Nagasaki 852, Japan

² Scientific Data Center of Atomic Bomb Disaster, Nagasaki University School of Medicine, 12-4 Sakamoto-machi, Nagasaki 852, Japan

³ Department of Dermatology, Nagasaki University School of Medicine, 7-1 Sakamoto-machi, Nagasaki 852, Japan

⁴ Nagasaki Atomic Bomb Hospital, Japan Red Cross Society, 3-15 Mori-machi, Nagasaki 852, Japan

⁵ Nagasaki Citizens Hospital, 6-39 Shinchi-machi, Nagasaki 850, Japan

⁶ Department of Plastic and Reconstructive Surgery, Nagasaki University School of Medicine, 7-1 Sakamoto-machi, Nagasaki 852, Japan

⁷ Showakai Hospital, 6-51 Higashiyamate-machi, Nagasaki 850, Japan

⁸ Department of Radiation Biophysics, Atomic Disease Institute, Nagasaki University School of Medicine, 12-4 Sakamoto-machi, Nagasaki 852, Japan

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Among a total of 65,268 Nagasaki atomic bomb survivors recorded in the Scientific Data Center of Atomic Bomb Disaster, Nagasaki University School of Medicine, 140 cases with skin cancer were collected from 31 hospitals in Nagasaki City from 1961 through 1987. Subsequently, these cases of skin cancer in Nagasaki atomic bomb survivors were statistically analyzed in relation to the estimated distance from the hypocenter by age, sex, histology and latent period. The results were as follows: 1. A high correlation was observed between the incidence of skin cancer and the distance from the hypocenter. 2. The incidence of skin cancer in Nagasaki atomic bomb survivors now appears to be increasing in relation to exposure distance. 3. Among 140 cases, basal cell epithelioma was observed in 67 cases (47.9%) and squamous cell carcinoma in 43 cases (30.7%).

Address for correspondence: Naoki Sadamori, M.D. Department of Internal Medicine, Atomic Disease Institute, Nagasaki University School of Medicine, 7-1 Sakamoto-machi, Nagasaki 852 JAPAN

貞森直樹：長崎大学医学部原研内科，長崎市坂本町7番1号 〒852

INTRODUCTION

More than 40 years have elapsed since the explosion of atomic bombs over Hiroshima and Nagasaki. During this time, the increased incidence of leukemia and certain other radiation-induced malignant tumors has been confirmed in atomic bomb survivors, especially in those proximally exposed. In 1969, Johnson *et al*¹⁾ carried out an extensive study of skin cancer in atomic bomb survivors in Hiroshima and Nagasaki but found no evidence of increased incidence. Reports on skin cancer in the literature, however, indicate that the latent period from therapeutic irradiation to occurrence is long. It is assumed, therefore, that long-term observations are necessary to determine whether or not the occurrence of skin cancer is increased in atomic bomb survivors. In the present study, the authors attempt to clarify the occurrence of skin cancer in Nagasaki atomic bomb survivors and the relationship of the incidence of skin cancer to the exposure distance from the hypocenter.

MATERIALS AND METHODS

The subjects were 65,268 Nagasaki atomic bomb survivors recorded in 1965 in the Scientific Data Center of Atomic Bomb Disaster, Nagasaki University School of Medicine (referred to hereafter as the Data Center). "Atomic bomb survivor" is defined in the present study as a person who has been issued the "Atomic Bomb Survivor's Health Handbook" in Nagasaki City since the establishment of the Atomic Bomb Survivors Medical Treatment Law in April 1957. The Data Center preserves computerized data on holders of the survivors health handbook, or in other words, on the atomic bomb survivor population. Information on atomic bomb survivors, including death and changes of address, has been updated monthly with the cooperation of the Department for Atomic Bomb Survivors Affairs at Nagasaki City Hall. Currently, information on 110,000 atomic bomb survivors is available. The registered cases include directly exposed persons, early entrants to the city, those engaged in rescue service and fetuses. Only cases of skin cancer registered since 1965 in directly exposed persons were used as the subjects of this study. Although the Data Center was established in 1972, the sampling of the population goes back to 1965, and deaths before 1974 have not been discarded.

The exposure distance was determined from information on exposure status in the application forms for the Atomic Bomb Survivors Health Handbook at City Hall. All information on exposure distance is recorded in the computer at the Data Center. The exposure distance of the skin cancer cases was recorded before the development of the skin cancer. The number of subjects of the present study by exposure distance is shown in Table 1.

As many skin cancer cases as possible were collected from 31 hospitals, i.e. most of major hospitals in Nagasaki City, using histological reports for the period from 1961 to 1987. The medical records and histological reports of all the 140 patients were reviewed by the first author. The 31 medical institutions include all the major institutions in Nagasaki

Table 1. Atomic Bomb Survivors (Number of Persons and Person Years) by Sex and Exposure Distance Reviewed in the Present Study

Distance (km)	Number of Persons			Person Years		
	Total	Male	Female	Total	Male	Female
0-0.9	879	354	525	13550	5058	8492
1.0-1.4	3471	1708	1763	58524	27389	31135
1.5-1.9	5170	2162	3008	76333	28621	47712
2.0-2.4	5704	2212	3489	84125	28616	55509
2.5-2.9	9703	3783	5920	149106	50926	98180
3.0+	40341	15996	24345	673186	232422	440764

City and vicinity, as well as all 21 institutions from which Radiation Effects Research Foundation (RERF) collects information for its tumor registry. A retrospective review disclosed that all skin cancer cases in the RERF tumor registry are included in the present study. These cases were collated with individuals in the Data Center, where the estimated distance from the hypocenter at atomic bomb exposure is recorded. Finally, 140 cases of skin cancer were collected from 18 of the 31 hospitals investigated. The period of survey, the names of the hospitals and the number of cases in each hospital have been reported in detail elsewhere²⁾. The distribution of these cases by estimated distance from the hypocenter is shown in Table 2. The 140 cases of skin cancer were analyzed in relation to distance as well as to clinical and histological data. The "Mantel-extension method"³⁾ was used to analyze the relationship between incidence of skin cancer and distance. The age adjusted incidence was calculated by the indirect method using the entire population of atomic bomb survivors as the basic population.

The term "Correlation" was used for the relationship between latent period and age at the time of the bomb (ATB), age at onset of skin cancer, and distance, while "analysis of variance" was used for the relationship between histological type and age ATB, age at onset of the disease, and latent period. The 65,268 individuals in 1965, and our cases were classified into distance groups by 500 m intervals and the median value for each category

Table 2. Number of Cases with Skin Cancer of Nagasaki Atomic Bomb Survivors by Sex and Distance

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

Table 3. Number and Percentage of Cases in the Various Kinds 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)

was used. To clarify the relationship between incidence of skin cancer and distance from the hypocenter, cases were divided into three groups, i.e., persons exposed at less than 2.0 km, those exposed at less than 2.5 km (including those in the less than 2.0 km group) and those exposed at 3.0 km or more from the hypocenter. These three groups were compared statistically. In general, atomic bomb survivors who were less than 2.5 km from the hypocenter were exposed to a significant dose of radiation, although the actual exposure dose may be influenced by shielding conditions. Unfortunately, information on exposure dose is not available at the Data Center.

The 140 cases of skin cancer consisted of 63 males and 77 females, ranging in age from 42 to 95 years (median 71 years) at the onset of skin cancer. As shown in Table 3, the distribution of histologic type 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 the epidermal appendages such as sweat gland carcinoma in 6 (4.3%) and dermatofibrosarcoma and others in 3 (2.1%). Bowen's disease was not included in this study.

RESULTS

A review was conducted on the relationship between the incidence of skin cancer and distance from the hypocenter, between the latent period and age ATB, age at onset of skin cancer and distance, and between the histological type and age ATB, distance, age at onset of the disease and latent period. The major findings with statistical significance are as follows.

I. Incidence of skin cancer and distance from the hypocenter

Table 4 shows the age-adjusted incidence of skin cancer by distance in the sample

Table 4. Incidence (Cases/10⁵ Person/Years) of Skin Cancer in Nagasaki Atomic Bomb Survivors by Distance and Sex Adjusted for Age

Distance (km)	Total	Male	Female
0-0.9	26.3	0.0	29.9
1.0-1.4	33.3	38.6	29.1
1.5-1.9	25.3	37.6	18.5
2.0-2.4	20.3	30.0	15.9
2.5-2.9	11.2	15.9	8.9
3.0+	12.7	12.4	11.2

recorded in the Data Center. The incidence of skin cancer decreased significantly with the increase of distance ($p < 0.01$). A high correlation was also observed between the distance and the incidence of skin cancer even when the cases were divided by sex, i.e., males ($p < 0.01$) and females ($p < 0.05$).

II. Time trend in incidence of skin cancer

No case of skin cancer was collected in 1961. As calculation of the incidence was made for five-year intervals because of the limited number of cases, the time trend in incidence of skin cancer was studied using 133 cases during the period from 1962 to 1986, excluding 7 cases collected in 1987. As shown in Table 5, the number of cases by five-year interval increased steadily from 1962 to 1986. The ordinate in Fig. 1 shows the number of all skin cancer cases per 100,000 persons per year by distance since 1965, because the number of persons by distance was first identified in 1965 at the Scientific Data Center. As far as Fig. 1 is concerned, it is likely that the incidence of skin cancer has continued to increase since 1965, especially in those proximally exposed at less than 2.5 km since 1975. Calculation by Chi-square test showed a significant increase of the incidence in the proximal exposure group after 1975 ($p < 0.01$). Chi-square test of incidence by period in various groups yielded a significant difference between the period of 1970-1974 and that of 1975-1979 in the exposure groups within 2.0 km and also within 2.5 km ($p < 0.01$).

Table 5. Number of Skin Cancer Cases in Nagasaki Atomic Bomb Survivors by Five-Year Intervals

Year	Male	Female	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

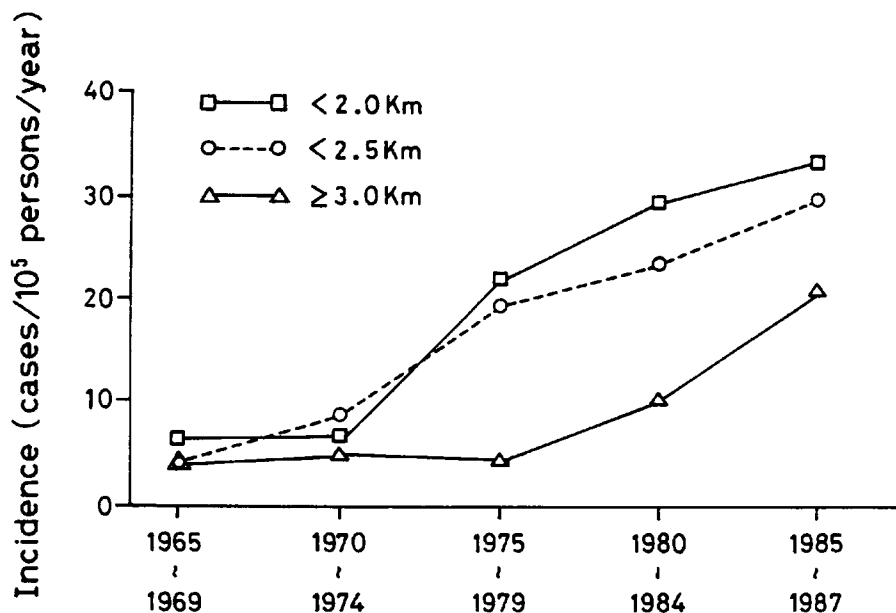


Fig. 1. Incidence of skin cancer in Nagasaki atomic bomb survivors at five-year intervals. Calculation by Chi-square test showed a significant increase of the incidence in the proximal exposure groups within 2.0 km and also within 2.5 km after 1975 ($p < 0.01$).

III. Other analyses

Analyses were made using "correlation" and "analysis of variance" to examine any possible correlation between two or three combined items which have been described, for the purpose of elucidating the relationship between atomic bomb exposure and occurrence of skin cancer. Comparisons between males and females and between histological types were also attempted. Despite the variety of review items, no statistically significant correlations emerged.

DISCUSSION

The relationship between A-bomb radiation and malignant neoplasms occurring in Hiroshima and Nagasaki has been confirmed for leukemia⁴), cancers of the thyroid⁵), lung⁶), breast⁷), stomach⁸), colon and for salivary gland neoplasms⁹). There have been many reports on skin cancer induced by medical irradiation including an SCC case reported by Frieben¹⁰) in 1902. General remarks were published by Hood and Young¹¹). However, Johnson *et al*¹) reported in 1969 no increase in incidence of skin cancer among A-bomb survivors in Hiroshima and Nagasaki, and no specific studies on this matter were conducted thereafter.

In this preliminary study, the occurrence of skin cancer during the period from 1961 to

1987 was examined using data in the Scientific Data Center of Atomic Bomb Disaster, Nagasaki University School of Medicine: 140 skin cancer cases were confirmed among 65,268 subjects. The relationship between the incidence of skin cancer and distance from the hypocenter in the 140 cases was analyzed, and it was noted that the incidence of skin cancer increased significantly with the decrease of distance ($p < 0.01$). This is the most important conclusion of this study, because it is the first indication that a high correlation exists between A-bomb exposure distance and the incidence of skin cancer. The distance-incidence relationship was also true for males ($p < 0.01$) and females ($p < 0.05$) considered separately. The lower incidence of skin cancer in persons exposed less than 1.0 km may be due to the fact that shielding at the time of A-bomb exposure greatly affects the occurrence of skin cancer, because 93.7% of A-bomb survivors exposed at a distance of less than 1.0 km had some shielding according to our data. Table 6 shows the frequency of skin cancer cases by exposure distance among female atomic bomb survivors who were unshielded at the time of exposure. As far as unshielded cases are concerned, the shorter the exposure distance (including exposure at less than 1.0 km), the higher was the frequency of skin cancer cases.

One of the issues of interest and importance is the latent period between exposure to radiation and the development of skin cancer. There have been many reports describing the latent period of skin cancer caused by radiation therapy, and the median latent period varied from 25 to 30 years¹¹⁾. This variation is ascribed to various factors such as sex, age, race, number of cases, irradiated site, dose, type of skin cancer, and follow-up period. In this sense, the study of skin cancer in Nagasaki A-bomb survivors is vitally important, because the incidence and latent period of radiation-induced skin cancer in a single race residing in the same area can be apprehended accurately.

Johnson *et al*¹⁾ reported the incidence of skin cancer in A-bomb survivors in Hiroshima and Nagasaki in 1969. As shown in Fig. 1, this was a period when the number of skin cancer

Table 6. Frequency of Skin Cancer Cases by Exposure Distance in Atomic Bomb Survivors Who Were Unshielded at the Time of Exposure (Females)

Distance (km)	Population in 1975	Skin Cancer Cases	Frequency (%)
0-0.9	506	1	0.20
1.0-1.4	1,698	3	0.18
1.5-1.9	2,765	2	0.07
2.0-2.4	3,229	2	0.06
2.5-2.9	5,540	2	0.04
3.0+	26,842	10	0.04
Total	40,580	20	0.05

($p < 0.01$)

cases in A-bomb survivors was only beginning to increase. This may indicate that the year 1969 was too early to review the incidence of skin cancer in A-bomb survivors. According to our data as shown in Fig. 1, the incidence of skin cancer in persons exposed at a distance of less than 2.5 km is much larger than that in persons exposed more than 3.0 km after 1975 ($p < 0.01$), although the latter also increased after 1980. Recently, Tada and Miki¹²⁾ reported that the incidence of skin cancer in the general population of Japan is also increasing gradually. They state that this increase of skin cancer may be due to prolonged life expectancy, i.e., to the increase in the elderly age population, to more frequent histological verification of the tumors, or to an increase in environmental carcinogenic factors.

Finally, it should be emphasized that there is a need for continuing surveillance of individual A-bomb survivors, especially those proximally exposed, and investigation concerning skin cancer and other malignant tumors, and that further studies using the estimated A-bomb exposure dose of the Radiation Effects Research Foundation (RERF) in Hiroshima and Nagasaki will be necessary before any final conclusion can be reached.

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