

Cancer Mortality in the High Background Radiation Areas of Yangjiang, China during the Period between 1979 and 1995

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The objective of the present study was to estimate cancer risk associated with the low-level radiation exposure of an average annual effective dose of 6.4 mSv (including internal exposure) in the high background-radiation areas (HBRA) in Yangjiang, China. The mortality survey consisted of two steps, i.e., the follow-up of cohort members and the ascertainment of causes of death. The cohort members in HBRA were divided into three dose-groups on the basis of environmental dose-rates per year. The mortality experiences of those three dose groups were compared with those in the residents of control areas by means of relative risk (RR). During the period 1987–1995, we observed 926,226 person-years by following up 106,517 subjects in the cohort study, and accumulated 5,161 deaths, among which 557 were from cancers. We did not observe an increase in cancer mortality in HBRA (RR = 0.96, 96% CI, 0.80 to 1.15). The combined data for the period 1979–95 included 125,079 subjects and accumulated 1,698,316 person-years, observed 10,415 total deaths and 1,003 cancer deaths. The relative risk of all cancers for whole HBRA as compared with the control area was estimated to be 0.99 (95% CI, 0.87 to 1.14). The relative risks of cancers of the stomach, colon, liver, lung, bone, female breast and thyroid within whole HBRA were less than one, while the risks for leukemia, cancers of the nasopharynx, esophagus, rectum, pancreas, skin, cervix uteri, brain and central nervous system, and malignant lymphoma were larger than one. None of them were significantly different from RR = 1. Neither homogeneity tests nor trend tests revealed any statistically significant relationship between cancer risk and radiation dose. We did not find any increased cancer risk associated with the high levels of natural radiation in HBRA. On the contrary, the mortality of all cancers in HBRA was generally lower than that in the control area, but not statistically significant.

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INTRODUCTION

Cancer mortality study among the residents in the high-background radiation areas (HBRA) of Yangjiang and its neighboring control areas was started in 1972¹⁾. The control areas (CA) were selected from two counties, Enping and Taishan. Enping County shares its south-western border with Yangjiang City, the political and economic center of Yangjiang area. Taishan is located to the east of Enping and is 300 kilometers from Guangzhou City, capital of Guangdong Province. The average annual effective doses from the natural sources of external and internal exposures in HBRA and CA are estimated to be 6.4 mSv, and 2.4 mSv, respectively²⁾.

Data for 1970–1978 were collected in a retrospective survey and data for 1979–1986 were obtained by means of a prospective survey of a dynamic population, in which newborn babies and immigrants were added to the study population during the investigated period. By the end of 1986, the follow-up study had accumulated person-years (PYRs) of 1,008,769 and 995,070 in HBRA and the control area, respectively, and ascertained 467 and 533 cancer deaths in the respective areas. Cancer mortality in HBRA was slightly lower than that in CA during the period between 1970 and 1986^{1,2)}.

In 1991, a collaborative study involving Chinese and Japanese scientists began³⁾. The major purposes of the study were to accumulate more person-years of observation for improving the statistical precision in cancer risk estimation and to examine the reproducibility of the previous results. Compared with the previous study, there are three distinct features in the cooperative study. First, we established a fixed cohort whose members resided in HBRA and CA as of 31 December 1986. In this follow-up study, we did not add newborns and immigrants to the cohort after 1 January 1987, when follow-up began. Second, we divided the cohort into four groups according to the intensity of dose rate per year: three (high, medium, and low) dose groups from HBRA and a control group from CA. Third, CA was restricted to Enping. The main reason to reject Taishan from the control area was that Taishan was a little too far away from HBRA. It is worth mentioning that the economic development in our study area of Taishan was not much different from that in our investigated area of Enping, although capital of Taishan County is more developed than Enping County.

The results of the mortality study during the period 1987–1990^{3,4)}, which have been reported previously, confirmed the previous findings obtained from the data up to 1986 mentioned above. This paper presents the results obtained from cancer mortality study for the period 1979–1995. Because data for 1970–1978 had not been computerized, we considered only cancer mortality data for 1979–1995 in our present analysis.

MATERIALS AND METHODS

The mortality data for the period 1979–1986 were collected from a population of around 80,000 inhabitants in HBRA and a similar number of residents in the control area²⁾. In 1979, we established the Health Household Registry (HHR) in every village of our study area in order to

carry out an efficient and complete mortality survey. Our registry consisted of two elements, i.e., a demographic survey and a survey of cause of death. Fundamental Registrars (FRs), who were selected from village doctors by our research group, collected demographic information on subjects in their own villages and filled out an HHR form for each subject. Our task group, consisting of three physicians from the Guangdong Institute for Prevention and Treatment of Occupational Diseases who had trained at Guangdong Province Tumor Hospital, visited each village once a year to check the HHR records. Using a list of deceased subjects' names prepared by the FRs, the task force interviewed family members of the deceased and village doctors to collect information about hospitals deceased patients visited, the diagnostic procedures and treatments they underwent, and possible causes of death. Task group members also reviewed biopsies, X-rays and ultrasonic examination lists as well as case lists of all county hospitals in the study areas and relevant major hospitals in the province. When the task group found the name of a deceased patient from our study areas, they extracted relevant medical information from the records. On the basis of information collected in this way and recorded on a one-page Death Registration Card, we determined causes of death. We determined the underlying causes of death and coded them according to the ninth revision of the International Classification of Diseases and Injuries (ICD-9)⁵⁾.

A similar follow-up method, with some modifications, was used for the cohort study from 1987 to 1995. Major changes were as follows: our research group visited each village once a year to collect demographic information and, with the help of local cadres and doctors, completed a newly developed four-page form, the Questionnaires on Cause of Death, which replaced the former Death Registration Card. Our researcher recorded all information related to causes of death on the new form, such as a brief description of medical history, signs and symptoms, medical diagnoses, pathological findings and so on.

In the mortality risk analysis, the study subjects in HBRA were divided into three dose groups based on the environmental dose-rates per year, which were measured in every hamlet in the investigated areas⁶⁾. Relative risks (RRs) were calculated to compare cancer mortality between each of the three radiation dose groups in HBRA and the control group. RRs and 95% confidence intervals (CI) were obtained from Poisson regression analysis using AMFIT in Epi-cure⁷⁾. All the p values presented are two-sided.

RESULTS

Table 1 shows the number of subjects and person-years of the follow-up, and Table 2, the numbers of all deaths and cancer deaths. There were 446 cancer deaths and 752,577 person-years during the period 1979–1986 and 557 cancer deaths and 926,226 person-years during the period between 1987 and 1995. Cancer deaths in the two periods accounted for 8% and 11% of the total deaths, respectively. During the period 1987–1995, there were 1296 (1.6%) and 792 (2.8%) subjects who were lost to our follow-up in HBRA and its control area, respectively. The main reason of the lost to follow-up was migration of study subjects into an area other than our study areas. We do not have computerized data regarding the migration of study subjects during the period

Table 1. Number of subjects and person-years by sex, age and dose group

	Control		HBRA							
			Low		Medium		High		Subtotal	
	N ^a	PYR ^b	N	PYR	N	PYR	N	PYR	N	PYR
Period 1979–1986										
Sex										
Female	16342	97635	13827	89817	13753	88890	11253	72530	38833	251237
Male	16309	108173	14425	102437	14640	103289	12742	89806	41807	295532
Age group										
0–29	22967	123724	20485	124760	20482	124245	17109	103688	58076	352693
30–	2506	24739	2302	21217	2173	20202	1859	16869	6334	58288
40–	2441	16968	2130	16834	2209	16473	1917	14481	6256	47788
50–	2372	19390	1496	13845	1676	15294	1513	13366	4685	42506
60–	1527	13210	1146	9109	1162	9717	944	8410	3252	27236
70–	724	6571	583	5251	570	5119	535	4365	1688	14735
80+	114	1207	110	1238	121	1129	118	1157	349	3524
Total	32651	205808	28252	192254	28393	192179	23995	162336	80640	546769
Period 1987–1995										
Sex										
Female	13514	117164	13087	113893	13057	113948	10496	91658	36640	319499
Male	14389	124122	14589	126706	14780	128845	12605	109889	41974	365441
Age group										
0–29	16509	125100	17750	141055	17799	141281	14549	115637	50098	397973
30–	3888	40815	3321	33817	3279	34452	2677	28203	9277	96473
40–	2079	24128	2231	22611	2140	21984	1858	18383	6229	62978
50–	2330	18337	2088	18938	2196	18967	1906	16355	6190	54260
60–	1912	19492	1279	14103	1439	15576	1289	13860	4007	43539
70–	967	10383	785	7493	789	8128	619	6915	2193	22537
80+	218	3032	222	2580	195	2405	203	2193	620	7179
Total	27903	241287	27676	240599	27837	242793	23101	201547	78614	684939

^a Number of subjects.^b Person-years.

1979–1986.

Table 3 shows the distribution of the medical facilities where cancer diagnoses were made. During the period between 1979 and 1986, cancer diagnosis made in the prefecture hospitals or higher level hospitals accounted for 67% and 78% in HBRA and the control areas, respectively. During the period between 1987 and 1995, the figures reached 90% and 91% in the respective areas, and the difference between the two areas observed in the period 1979–1986 disappeared. Table 4 shows the method of cancer diagnosis. The proportion of cancer deaths diagnosed on the basis of pathological findings among all cancer deaths in HBRA rose from 23% in the period 1979–1986 to 29% in the period 1987–1995, whereas the proportion in the control area went down from 32% to 23% during the two periods. Cancer diagnosis made on the basis of clinical findings only or verbal autopsy, where the Task Group made diagnoses on the basis of the information they gathered, accounted for 23% and 11% of all cancer deaths for the period 1979–1986

Table 2. Number of deaths by sex, age and dose group

	Control area		HBRA							
			Low		Medium		High		Subtotal	
	All causes	Cancer	All causes	Cancer	All causes	Cancer	All causes	Cancer	All causes	Cancer
Period 1979–1986										
Sex										
Female	725	57	633	48	594	35	487	35	1714	118
Male	779	72	633	67	727	75	676	57	2036	199
Age group										
0–29	239	12	295	16	279	18	264	10	838	44
30–	56	7	63	11	63	18	42	7	168	36
40–	76	24	67	15	70	14	81	18	218	47
50–	162	39	103	24	129	24	102	23	334	71
60–	297	30	218	33	226	21	188	20	632	74
70–	460	16	332	13	343	12	286	12	961	37
80+	214	1	188	3	211	3	200	2	599	8
Total	1504	129	1266	115	1321	110	1163	92	3750	317
Period 1987–1995										
Sex										
Female	624	47	576	52	580	38	470	31	1626	121
Male	846	117	722	92	709	103	634	77	2065	272
Age group										
0–29	93	13	107	9	104	11	74	7	285	27
30–	49	16	46	10	56	8	51	15	153	33
40–	83	31	85	32	78	25	56	15	219	72
50–	122	28	125	36	119	35	104	25	348	96
60–	303	44	236	36	239	37	217	32	692	105
70–	481	26	369	17	384	22	321	14	1074	53
80+	339	6	330	4	309	3	281	0	920	7
Total	1470	164	1298	144	1289	141	1104	108	3691	393

and the period 1987–1995, respectively, in HBRA. Clinical diagnosis and verbal autopsy accounted for about 10% of cancer deaths in the control area during the two periods.

First, we analyzed the data for the period 1987–1995, which was obtained by the China-Japan collaborative study. As shown in Table 5, the RR of all cancers in entire HBRA during this period was 0.96 (95% CI, 0.80 to 1.15), indicating that the mortality rate of all cancer in HBRA was slightly lower than that in the control area, but without statistical significance. The three most common cancers in the study area were cancers of liver, nasopharyngeal and lung. There was no risk increase statistically in any cancer sites examined in HBRA.

Then we analyzed cancer mortality data for 1979–1995 (Table 6). The RR of all cancers in whole HBRA was 0.99 (95% CI, 0.87 to 1.14). The RRs for cancers of the stomach, colon, liver, lung, bone, female breast and thyroid within whole HBRA were less than one, while the RRs for leukemia and for cancers of the nasopharynx, esophagus, rectum, pancreas, skin, cervix uterus, brain and central nervous system, and malignant lymphoma were larger than one. None were

Table 3. Distribution of medical facilities where cancer diagnosis was made

Period	Medical facility	Control area		HBRA							
				Low		Medium		High		Subtotal	
		No.	%	No.	%	No.	%	No.	%	No.	%
1979–1986	Unknown	.	.	1	0.9	1	0.9	.	.	2	0.6
	Task group	20	15.5	16	13.9	13	11.8	13	14.1	42	13.2
	Village clinic or Town health center	9	7.0	20	17.4	20	18.1	25	27.2	65	20.5
	County or prefecture hospital	69	53.5	59	51.3	51	46.3	36	39.1	146	46.0
	Provincial hospital	31	24.0	19	16.5	25	22.7	18	19.6	62	19.6
	Total	129	100.0	115	100.0	110	100.0	92	100.0	317	100.0
1987–1995	Task group	4	2.4	4	2.8	5	3.5	6	5.6	15	3.8
	Village clinic or Town health center	11	6.7	4	2.8	11	7.8	11	10.2	26	6.6
	County or prefecture hospital	122	74.4	116	80.6	103	73.1	79	73.2	298	75.8
	Provincial hospital	27	16.5	20	13.9	22	15.6	12	11.1	54	13.7
	Total	164	100.0	144	100.0	141	100.0	108	100.0	393	100.0

Table 4. Methods of cancer diagnosis

Period	Medical facility	Control area		HBRA							
				Low		Medium		High		Subtotal	
		N	%	N	%	N	%	N	%	N	%
1979–1986	Pathology	41	31.8	23	20.0	33	30.0	16	17.4	72	22.7
	X-ray/Ultrasonic ^a	73	56.6	60	52.2	53	48.2	52	56.5	165	52.1
	Clinical diagnosis	14	10.9	28	24.3	20	18.2	22	23.9	70	22.1
	Verbal autopsy	.	.	2	1.7	1	0.9	1	1.1	4	1.3
	Unknown	1	0.8	2	1.7	3	2.7	1	1.1	6	1.9
	Total	129	100.0	115	100.0	110	100.0	92	100.0	317	100.0
1987–1995	Pathology	38	23.2	46	31.9	36	25.5	31	28.7	113	28.8
	X-ray/Ultrasonic ^a	110	67.1	85	59.0	88	62.4	63	58.3	236	60.1
	Clinical diagnosis	14	8.5	9	6.3	14	9.9	10	9.3	33	8.4
	Verbal autopsy	2	1.2	4	2.8	2	1.4	4	3.7	10	2.5
	Unknown	.	.	.	.	1	0.7	.	.	1	0.3
	Total	164	100.0	144	100.0	141	100.0	108	100.0	393	100.0

^a Including endoscopic examinations.

significantly different from $RR = 1$, the expected value in the absence of radiation effects. Neither homogeneity tests nor trend tests revealed any statistically significant relationship between RRs and radiation dose levels.

Table 5. RRs (95%CI) of cancer mortality (1987–95)

Site of cancer	Control		HBRA							
	area		Low dose group		Medium dose group		High dose group		Subtotal	
	No.	^a RR ^b	No.	RR(95%CI)	No.	RR(95%CI)	No.	RR(95%CI)	No.	RR(95%CI)
All cancers	164	1	144	1.03 (0.83–1.29)	141	0.97 (0.78–1.22)	108	0.86 (0.67–1.10)	393	0.96 (0.80–1.15)
Leukemia	5	1	4	0.88 (0.23–3.29)	4	0.85 (0.23–3.20)	5	1.31 (0.38–4.55)	13	1.00 (0.35–2.81)
All cancers except leukemia	159	1	140	1.04 (0.83–1.31)	137	0.98 (0.78–1.23)	103	0.85 (0.66–1.09)	380	0.96 (0.80–1.15)
Nasopharynx	28	1	27	1.12 (0.66–1.90)	29	1.16 (0.69–1.95)	19	0.87 (0.48–1.56)	75	1.06 (0.68–1.63)
Esophagus	2	1	4	2.53 (0.46–13.87)	6	3.52 (0.71–17.46)	4	2.72 (0.50–14.89)	14	2.95 (0.67–12.98)
Stomach	20	1	19	1.10 (0.59–2.07)	10	0.56 (0.26–1.20)	9	0.58 (0.27–1.29)	38	0.75 (0.44–1.30)
Colon	2	1	1	0.58 (0.05–6.41)	3	1.68 (0.28–10.08)	2	1.27 (0.18–9.03)	6	1.18 (0.24–5.87)
Rectum	2	1	2	1.13 (0.16–8.02)	2	1.17 (0.16–8.29)	1	0.69 (0.06–7.62)	5	1.01 (0.20–5.23)
Liver	55	1	42	0.90 (0.60–1.34)	38	0.78 (0.52–1.18)	24	0.57 (0.35–0.92)	104	0.75 (0.54–1.05)
Pancreas	1	1	2	2.19 (0.20–24.23)	4	4.27 (0.48–38.37)	3	3.66 (0.38–35.30)	9	3.37 (0.43–26.73)
Lungs	20	1	13	0.79 (0.39–1.59)	14	0.80 (0.40–1.59)	16	1.05 (0.54–2.02)	43	0.87 (0.51–1.49)
Bone	1	1	2	2.61 (0.24–28.99)	0	–	1	1.45 (0.09–23.15)	3	1.33 (0.14–12.81)
Skin	4	1	3	0.95 (0.21–4.27)	6	1.79 (0.50–6.36)	2	0.67 (0.12–3.66)	11	1.16 (0.37–3.65)
Female breast	3	1	3	1.34 (0.27–6.67)	2	0.87 (0.14–5.19)	1	0.51 (0.05–4.86)	6	0.92 (0.23–3.68)
Cervix uterus	0	1	1	–	2	–	0	–	3	–
CNS ^c	2	1	3	1.75 (0.29–10.50)	5	2.87 (0.56–14.79)	1	0.70 (0.06–7.68)	9	1.84 (0.40–8.52)
Thyroid	2	1	1	0.57 (0.05–6.35)	0	–	2	1.45 (0.20–10.31)	3	0.62 (0.10–3.72)
Lymphoma	3	1	1	0.36 (0.04–3.46)	4	1.37 (0.30–6.15)	3	1.21 (0.24–6.04)	8	0.98 (0.26–3.71)

^a Number of deaths.^b The referent category in relative risk calculation.^c Brain and central nervous system.Note: homogeneity test $p > 0.05$ for all.

Further analyses were conducted to identify the factors modifying the magnitude of the relative risks comparing cancer mortality in HBRA and the control area (Table 7). First, we divided the subjects according to the study period, i.e., 1979–86 and 1987–95, and estimated relative risks of cancer mortality in each of the study periods. The relative risks for high-background radiation were not different between two study periods (p for homogeneity test = 0.784). Second, we divided the subjects according to sex. The relative risks showed no difference between two sexes (p for homogeneity test = 0.299). Lastly, we divided the subjects into two groups according to attained age. Those subjects aged sixty and over, who received a cumulative dose of about 200 mSv or larger in HBRA, cancer risk was about ten percent higher than in younger subjects. However, the difference between the two age groups was not significant (p for homogeneity test = 0.707). We also conducted trend tests using the mean dose for each dose group, and found no significance among the risks in the four dose-groups.

DISCUSSION

The present study, which compared cancer mortality in HBRA of Yangjiang and its control area, confirmed the absence of excess of cancer death in HBRA. Actually, cancer mortality of all sites in HBRA was slightly lower than that in the control area but without statistical significance. A significant increase of esophageal cancer risk in HBRA was suggested when compared with that in the control area (RR = 2.85, 95% CI, 1.00 to 8.16; $p = 0.051$). However, the mortality of esophageal cancer did not show a monotonic increasing trend when HBRA was divided into three dose groups.

The major difficulty in radiation-induced cancer risk estimation arises from the fact that we cannot distinguish radiation-induced cancer from spontaneously occurring cancers. Radiation epidemiologists confront the enormous task of estimating radiation-related cancer risk by comparing exposed and control populations, which may differ in terms of genetic backgrounds and environmental factors, including life styles. It should be noted here that the confounding effects of covariates in low-dose ranges are even greater than those in high-dose ranges. For example, the RR of lung cancer associated with cigarette smoking in average Chinese men ranges from 5 to 10^8 , which is much greater than the RR one might expect to be associated with low-level radiation exposure. In many radiation epidemiological studies, researchers assumed that the distributions of lifestyle-related factors were not highly dependent on radiation levels, and, therefore, their confounding effects on radiation-related risk estimates could be ignored. Since most of the residents in HBRA and the control area in this study were farmers, we also assumed that the socioeconomic status and lifestyles in the two areas did not differ greatly. To date, surveys have revealed no distinct differences in lifestyles in HBRA and the control area⁹. In one of such survey conducted in our study area, we selected 30 households from each of the three dose groups in the study area using multistage random sampling method⁹, and obtained information from 385 persons (101, 101, 100 and 83 in high, medium, low dose and control groups, respectively) during the period between October and December in 1993. We examined the daily intake of rice and wheat flour, sweet potatoes, and various vegetables, and found no significant differences in the four dose groups. Life style, including cigarette smoking and alcohol intake, showed no significant difference in the four dose groups, either.

One of the major concerns in the present study is the effects of medical X-ray exposure. Three surveys were conducted in 1977, 1982 and 1984 to investigate the frequency of diagnostic X-ray examination in the inhabitants¹⁰⁻¹². The mean frequencies of X-ray examinations in HBRA and the control area from the three surveys combined were 46.78 and 47.93 per 1000 person-years, respectively. According to a dosimetric survey conducted in 1986, the effective doses equivalent to inhabitants resulted from exposure to diagnostic X-rays in HBRA and the control area were estimated to be 4.30 and 4.10×10^{-5} Sv/person-year, respectively. It was reported that the residents in HBRA and the control area showed no significant differences in the frequency of diagnostic X-ray examinations or the average doses received by inhabitants. However, based on a survey conducted in 1984, where we interviewed 918 subjects randomly selected from both areas, 20% and 26% of the interviewees in HBRA and the control area turned out to have re-

ceived various X-ray examinations during their lifetime. This observation is consistent with our general impression that the inhabitants in the control area enjoyed a little higher level medical service¹³⁾.

Another concern was the accuracy of diagnosis. Of the 959 solid cancer cases, 222 cases were diagnosed pathologically, 582 by X-ray/ultrasonic examinations, 131 clinical diagnosis, and 24 by verbal autopsy based on the information obtained from the task group. It should be pointed out that the proportion of cancer pathologically diagnosed varied according to cancer site. Only 51 percent (96/189) of nasopharyngeal carcinomas and 2 percent (6/258) of liver cancers were diagnosed pathologically. These two cancers accounted for 45 percent of all cancer deaths in our mortality data. In addition, the accuracy of diagnosis for certain cancers may not be high enough for site-specific cancer risk analysis. Estimating risk on the basis of diagnosis methods revealed that cancer diagnosis may bias our risk estimates to some extent. When we restricted solid cancer deaths to those diagnosed pathologically, the RR of solid cancer was estimated to be 0.71 (95% CI, 0.51 to 0.99). Using all solid cancer deaths but excluding unreliable diagnosis, (that is clinical diagnosis and verbal autopsy), we calculated the risk as 0.92 (95% CI, 0.79 to 1.08).

In conclusion, the increased cancer risk associated with the high levels of natural radiation in HBRA was not found. On the contrary, the mortality of all cancers in HBRA was generally lower than that in the control area, but was not significant. Further follow-up of the cohort members is necessary to accumulate more person-years so that more cancer risk estimates have narrower confidence intervals.

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