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Cancer Mortality Survey in a Spa Area (Misasa, Japan) with a High Radon Background

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The 1952–88 cancer mortality records for inhabitants of the Misasa spa area, Japan, which has a high radon background, and a neighboring control area without any radon spa were analyzed (average outdoor Rn concentration: 26 mBq·liter^{-1} in Misasa vs. 11 mBq·liter^{-1} in the control area). Standardized mortality ratios (SMRs) for cancers of all sites were significantly lower among the inhabitants of both Misasa (male 0.538; female 0.463) and the control area (male 0.850; female 0.770), than in the whole Japanese population. Poisson regression analysis showed that the relative risks among the inhabitants of Misasa were significantly lower than in the control area for deaths from cancers of all sites (0.67) and stomach cancer (0.59). The relative risk of lung cancer death was also lower (0.55 times) in Misasa than in the control area, although the difference was not statistically significant. These results suggest that the linear no-threshold hypothesis for radiation risk may not be valid for exposure to low doses of radon.

Key words: Cancer mortality — Misasa spa area — Radon exposure — Alpha emitter — Threshold for cancer

The Environmental Protection Agency (EPA) of the USA has suggested that as many as 20,000 lung cancers annually could be due to radon in homes and recommended that indoor radon levels be kept below 4 pCi (=0.15 Bq)/liter.[1] This EPA policy is based on a report by the National Research Council; the responsible committee used linear extrapolation from lung cancer deaths in miners exposed to high doses of radon to estimate the risk at the low doses recommended by the EPA.[2] In 1988, the US Congress passed the Indoor Radon Abatement Act setting for the EPA the goal of reducing indoor levels to those of outdoor air; on average the cost to homeowners would be of the order of $10,000 each.[1] Recently, Cohen[3] conducted an epidemiologic test of the linear no-threshold hypothesis by accumulating a data set that covers over 400 counties of the US; the obtained correlation of average radon exposure in various counties and their lung cancer mortality rates is substantially negative, in contrast to the positive correlation assumed by the no-threshold hypothesis.

If the linear no-threshold hypothesis is not valid, as suggested by Cohen's work, regulation of indoor radon concentration would not improve public health, but rather would be a waste of money and might unjustifiably increase public fear of radiation. Before introducing such regulation, we think it is necessary to investigate the relationship between exposure to low doses of radon and cancer mortality, using actual observations in humans. However, this type of investigation is usually very difficult, because it requires a large sample with a sufficiently long observational period.

A good method for investigating the effect of low-dose radon exposure would be to utilize the mortality records of inhabitants of a spa area where a high radon concentration is present. There are such areas in Japan. Masutomi spa used to provide hot springs with the highest radon concentration in Japan (160 kBq·liter^{-1}) but is now closed. Ikeda spa provides cold springs with radon of 24 kBq·liter^{-1}, but the quantity is small. Misasa spa provides a large quantity of hot spring water (3×10^6 liters·day^{-1}) with an average concentration of 437 Bq·liter^{-1} (total radon radioactivity, 1.3 GBq·day^{-1}).[4,5] These radon concentrations are comparable to those in Lacco Ameno spa in Italy (av. 37 kBq·liter^{-1}), Therma spa in Greece (10 kBq·liter^{-1}), Brambach spa in Ger-

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many (30 kBq·liter^{-1}), and Badgastein in Austria (1 kBq·liter^{-1}).[5] We chose Misasa because of its relatively large population exposed to radon.

The town of Misasa (Misasa-cho) is located in Tottori Prefecture on the main island of Japan (Fig. 1). For the purpose of this study, Misasa-cho was divided into Misasa itself, an urban area with radon spas, and a neighboring control area consisting of farming villages (Mitoku, Oshika, Takeda, and Asahi). The age distribution of the populations of Misasa and the control area obtained by the national population survey are shown in Table I. Details of measurement of radioactivity of hot springs and the environment are given elsewhere.[4, 5] Briefly, the town includes 90 hot spring sources, yielding a total volume of spring water of 3×10^6 liters·day^{-1}. The hot water (temperature: 36.5–86.1°C, average 54°C) is of the dilute neutral NaCl-HCO_3 type. The concentration of ^{222}Rn in the spring water ranges from 17.4 to 9361 Bq·liter^{-1}. Average radon concentrations are 26 mBq·liter^{-1} in the open air and 35 mBq·liter^{-1} in indoor air of ordinary homes in the Misasa spa area, and 11 mBq·liter^{-1} in open air in the control area without any spa, and the average radiation dose rates are 12, 14, and 9 μR·h^{-1} in open and indoor sites in Misasa spa, and in open air in the control area, respectively.[4] In Misasa, the radon concentration in indoor air ranges from 0.3 to 5 Bq·liter^{-1} in the patient treatment bathroom of Misasa Branch Hospital of Okayama University[4] and from 0.2 to 8 Bq·liter^{-1} in radon-water bathing rooms of hotels.[6] Hot springs are commonly used by Japanese as part of their regular life-style, mainly for bathing, and have also been used for medical treatment of patients at Misasa Branch Hospital of Okayama University Medical School, where improvement of peripheral blood perfusion by radon water has been observed.[7]

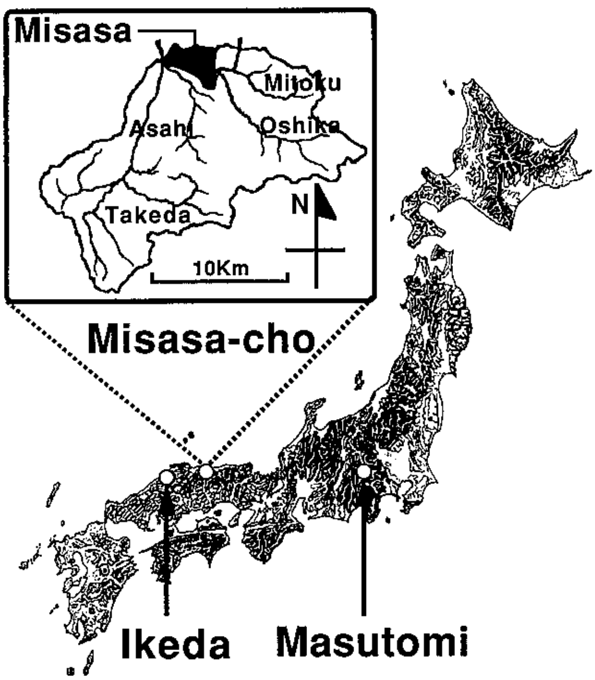

Fig. 1. Map of Japan with enlargement of the Misasa radon spa area and the control area in the town of Misasa (Misasa-cho), also showing two other major radon spas in Japan.

Determination of the standardized mortality ratio (SMR) followed the method described by Brown and Hollander.[8] Mortality records in the Misasa spa and control areas from 1952 to 1988 were those maintained at health centers of Tottori Prefecture. These data were arranged in 10-year age ranks for males and females separately (data not shown). The 10-year ranking analysis was applied in this study, since population figures were available only for the 10-year ranking category each year. Cancer mortality data for all Japan were obtained from Vital Statistics Data of the Ministry of Health and Wel-

Table I. Populations of Misasa Spa Area with a High Background of Radon and the Control Area

Age (years)	Misasa (year) 1955	1965	1975	1985	Control area (year) 1955	1965	1975	1985
0–9	483	408	421	426	1965	1168	573	673
10–19	365	471	403	454	1596	1394	867	539
20–29	460	416	409	326	1456	626	600	570
30–39	403	455	414	520	1122	1063	551	704
40–49	278	413	471	442	913	953	950	562
50–59	226	333	426	506	800	743	829	923
60–69	133	208	308	373	647	674	629	761
70–	76	125	237	334	431	555	697	767
Total	2424	2829	3089	3381	8930	7176	5696	5499

Table IIa. Standardized Mortality Ratios for Male Inhabitants 1952–1988, in Misasa Spa Area and the Control Area

Site of cancer	ICD-9	Misasa				Control area			
		O	E	SMR	Test	O	E	SMR	Test
All sites		53	98.48	0.538	——	228	268.23	0.850	—
Buccal mucosa, Pharynx, Larynx	140–149, 160, 161	0	2.83	0.000		10	7.64	1.309	
Stomach	151	16	40.01	0.400	——	86	108.38	0.794	—
Colon, Rectum	153, 154	2	6.76	0.296		14	18.63	0.752	
Liver	155, 156	13	12.20	1.066		32	32.74	0.978	
Pancreas	157	2	3.71	0.539		4	10.06	0.398	
Peritoneum	158, 159, 197	1	1.05	0.950		3	2.78	1.080	
Lung	162	6	12.64	0.475		33	35.65	0.926	
Unknown primary site	195, 196, 198, 199	2	1.97	1.017		2	5.47	0.365	
Leukemia	204–208	1	2.25	0.445		11	5.48	2.009	+
Others		10	14.15	0.707		33	38.92	0.848	

ICD: International classification of diseases. O: Observed number of cancer deaths.
E: Expected number of cancer deaths. ——, $P<0.01$; —, $P<0.05$; +, $P<0.05$.

Table IIb. Standardized Mortality Ratios for Female Inhabitants 1952–1988, in Misasa Spa Area and the Control Area

Site of cancer	ICD-9	Misasa				Control area			
		O	E	SMR	Test	O	E	SMR	Test
All sites		37	79.88	0.463	——	156	202.64	0.770	——
Buccal mucosa, Pharynx, Larynx	140–149, 160, 161	0	1.40	0.000		2	3.65	0.547	
Stomach	151	12	26.55	0.452	——	58	68.58	0.846	
Colon, Rectum	153, 154	1	7.07	0.142	—	13	18.14	0.717	
Liver	155, 156	2	9.14	0.219	—	19	23.67	0.803	
Pancreas	157	2	3.08	0.649		7	7.77	0.901	
Peritoneum	158, 159, 197	2	1.16	1.721		9	3.00	3.000	++
Lung	162	1	5.34	0.187		5	13.57	0.369	—
Breast	174	1	3.89	0.257		5	8.89	0.563	
Uterus	179–182	4	8.97	0.446		12	22.45	0.535	—
Unknown primary site	195, 196, 198, 199	0	2.16	0.000		2	5.51	0.363	
Leukemia	204–208	1	1.87	0.534		5	4.26	1.174	
Others		11	9.24	1.190		19	23.18	0.820	

O: Observed number of cancer deaths. E: Expected number of cancer deaths.
——, $P<0.01$; —, $P<0.05$; ++, $P<0.01$.

fare of Japan.[9] Cancer mortalities in Misasa and the control area were respectively compared with those of all Japan on the basis of the SMRs.[10]

SMR values in Misasa and the control area for men and those for women are shown in Tables IIa and IIb, respectively. It is apparent that the mortality due to stomach cancer was the highest in both Misasa and the control area, as in other areas of Japan. Misasa inhabitants had significantly lower total cancer mortality rates than the whole Japanese population (SMRs: 0.538 for men and 0.463 for women). Specifically, in Misasa the mortality due to stomach cancer was lower in both sexes than in the whole Japanese population. Colo-rectal cancer and lung cancer mortalities were also lower in Misasa women. Lung cancer (SMRs: 0.475 for men and 0.187 for women in Misasa) was the point of interest in this study in relation to radon inhalation. In the control area, the total cancer mortality was again significantly lower than in the whole of Japan (SMRs: 0.850 for men and 0.770 for women), although higher cancer mortality was seen in leukemia in men and peritoneal cancer in women.

In order to compare cancer mortalities in Misasa and the control area directly, Poisson regression analysis was

Table III. Relative Risks of Dying of Various Cancers for Inhabitants in Misasa versus the Control Area Estimated by Poisson Regression Analysis[a]

Site of cancer	Relative risk[b]	95% Confidence interval
All sites	0.67	0.53–0.85
Stomach	0.59	0.39–0.88
Lung	0.55	0.25–1.24
Colon, Rectum	0.32	0.10–1.06

a) Variables for sex, age and period were also included.
b) Relative risk for inhabitants in Misasa when mortality in the control area was taken as the reference.

conducted.[10] Study subjects were limited to those who were 40 years old or more, since the number of cancer deaths in persons less than 40 years old was very small. Variables included in the model were sex, age (40–49, 50–59, 60–69, and 70+), period of study (1952–71 and 1972–88) and area (Misasa and control area). For the variable of age, three dummy variables were introduced, so that all variables were treated as dichotomous. Deaths from cancers of all sites, stomach cancer, lung cancer and colo-rectal cancer were analyzed.

Table III shows the relative risks of dying of the above cancers for inhabitants in Misasa versus the control area estimated by Poisson regression analysis. Relative risks of dying of cancers for all sites and stomach cancer were significantly lower than unity among the inhabitants in Misasa. Relative risks of dying of lung cancer and colo-rectal cancer for those in Misasa tended to be lower than unity, although the differences were not statistically significant. Therefore it appears that the increase in radon concentration in Misasa over that in the control area probably has a negative correlation with lung cancer incidence. This conclusion is in accord with the report of Cohen.[3]

It is interesting that mortality rates for stomach cancer in Misasa are significantly lower than those in the control area (Table III). Since negligibly low levels of radon and its radioactive decay products would reach the stomach, a direct correlation of radon with the incidence of stomach and colo-rectal cancers seems very unlikely. There is, however, a possibility that when people bathed in radon-containing warm water, many of them also drank the radon-containing water as they believed in the medical efficacy of the radon-containing water. Another possibility is that radon dissolved in the bath water penetrates through the skin into capillary blood vessels to be circulated throughout the body. The blood circulation of radon was experimentally shown to stimulate tissue perfusion in rabbits when given in combination with carbon dioxide.[7] Of course, hot water bathing itself may have a healing and health-stimulating effect. All in all, the multiple health-stimulating effects of bathing in a radon bath may, at least partly, explain the fact that SMRs for almost all the types of cancer surveyed are lower in Misasa than in the control area (Tables II and III). Whether radon-water bathing is really beneficial to human health may be determined by a comparative epidemiologic study of the effects of bathing in non-radon spas.

There are some methodological problems with the present study. First, individual life-style factors, such as smoking, were not considered as potential confounding elements. However, considering the facts that the smoking rate tends to be higher in an urban area than a rural area, and that the Misasa area is more urbanized than the control area, a difference in smoking habit is unlikely to explain the reduced risk of lung cancer in Misasa. Second, the study populations were not fixed at the beginning of the observation, but rather were migratory. Actually, in the 1960s and the 1970s, the population decreased by about 30% in the control area whereas the population of Misasa continued to increase at a low rate from 1960, reaching about a 10% increase in 1985 (Table I). However, these migrations occurred mainly in the younger age groups, while the older age groups were rather stable (Table I). Although these limitations should be taken into account in interpreting the findings, the results provide encouragement for a further detailed evaluation of the effect of low-dose radiation exposure on humans.

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