

B. I. Gusev · R. I. Rosenson · Zh. N. Abylkassimova

The Semipalatinsk nuclear test site: a first analysis of solid cancer incidence (selected sites) due to test-related radiation

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Abstract Since 1956, cancer incidences have been analysed in several rayons of the Semipalatinsk oblast, with cross-sectional analyses being conducted every 5 years. Data on different tumor localizations were recorded within a heavily contaminated so-called main area of nine villages (estimated average effective equivalent dose about 2000 mSv) and a so-called control area (estimated average effective equivalent dose about 70 mSv), each including approximately 10 000 persons. Up to 1970, the excess cancer incidence in the exposed villages was observed to have increased; after 1970, a decrease was noted, followed by a second increase in the late 1980s. The main sites of excess cancer included the esophagus, stomach, and liver. Up to 1970, the esophagus cancer incidence was predominant, but it decreased thereafter, while the incidence of stomach and liver cancers increased. The second peak of excess cancer rates was mainly due to lung, breast, and thyroid carcinomas.

Introduction

The carcinogenic effect of ionizing radiation has been subject to scientific scrutiny for decades. Information about long-term radiation pathology can be obtained from epidemiological and experimental research analyzing the influence and effects of ionizing radiation. Most of the current knowledge on long-term radiation effects is based on studies of the Japanese atomic bomb survivors. Fifteen years after the atomic bombing, cancer mortality increased for neoplasms at different localizations (see e.g. [1]).

After the airborne singular atomic explosions over Hiroshima and Nagasaki, local population groups were exposed to extremely high gamma and neutron radiation, which resulted in a number of specific early and late post-radiation effects. In contrast, early atmospheric nuclear testings carried out between 1949 and 1963 (and to a minor extent underground testings until 1989) caused chronic radiation exposure at lower dose rates near the test site. The radiological situation that emerged at the Semipalatinsk nuclear test site is unprecedented and has been described recently [2].

During the atmospheric nuclear tests, about 344 000 residents, primarily in some rayons of the Semipalatinsk oblast, were exposed to internal and external irradiation from local radioactive fallout. According to our calculations, the majority of the population, i.e., some 220 000 people, were exposed to doses of between 7 and 350 mSv. About 37 200 residents of these rayons were exposed to radiation doses of between 350 and 990 mSv. In 21 towns, villages, and auls including approximately 28 000 inhabitants, the effective equivalent dose due to external and internal radiation from the passing radioactive cloud exceeded 1000 mSv. Details have been presented by Gusev et al. [2].

In 1957, a secret medical institution specializing in oncology was established, called 'Dispensary No. 4'. In addition to the usual clinical and biomedical activities, data were collected on the health status of the population in the Semipalatinsk oblast. In 1991, as a successor to Dispensary No. 4, the Scientific Research Institute for Radiation Medicine and Ecology was established, which inherited the formerly top secret health archives. The data of these archives are being analyzed to establish the basis for a number of epidemiological studies.

The current study describes the temporal development of solid cancer incidences in two cohorts, referring to average effective equivalent doses of 2000 and 70 mSv, respectively.

B. I. Gusev (✉) · R. I. Rosenson · Zh. N. Abylkassimova
Kazakh Scientific Research Institute
for Radiation Medicine and Ecology,
Semipalatinsk 490050, Post Box 16,
Kazakhstan Republic

R. I. Rosenson
Shimkent Medical University,
Prospect Lenina, 1, Shimkent 486050,
Kazakhstan Republic

Table 1 Assessed doses (mSv) and population groups (as of 1960) in those settlements included in 'main area' and 'control area'

	Dose equivalent		Total abs	Men		Women	
	Settlement	(mSv)		Abs	Percentage	Abs	Percentage
'Main area'	Dolon	4 470	1 300	690	53.0	610	47.0
	Mostik	900	600	270	45.0	330	55.0
	Cheremushki	1 000	600	280	46.7	320	53.3
	Kanonerka	1 790	1 500	740	49.3	760	50.7
	Budene	3 500	300	140	46.7	160	53.3
	Sarzhai	2 460	1 500	670	44.7	830	55.3
	Kainar	2 680	1 500	640	42.7	870	57.3
	Znamenka	1 150	700	320	45.7	380	54.3
	Karaul	870	2 000	970	48.5	1 030	51.5
	Total	2 000	9 900	4 720	47.6	5 180	52.4
'Control area'	Kokpekti	70	4 025	1 900	47.2	2 125	52.8
	Ivanovka	70	1 500	710	47.3	790	52.7
	Bolshevik	70	1 600	760	47.5	840	52.5
	Ulguli-Malshi	70	1 700	820	48.2	880	51.8
	Preobrazhenko	70	1 300	610	46.9	690	53.1
	Total		10 125	4 800	47.4	5 325	52.6

Subjects and methods

'Areas'

In order to study cancer effects among the population of the Semipalatinsk oblast exposed to radiation from nuclear explosions at the Semipalatinsk nuclear test site, we established two 'areas' with populations of approximately 10 000 individuals each, with different exposure status based on the dose assessment indicated above. We then conducted periodic cross-sectional surveys.

Population groups

The 'main area' included the residents of nine towns and villages with an established radiation dose (see Tables 1 and 2). These settlements were located in four rayons (Abaysky, Zhana-Semeysky, Beskaragaysky, and Abralinsky) of the Semipalatinsk oblast. Local radiation fallouts were officially registered in each of these settlements, based on calculations of the USSR Department of Defense. Internal doses were calculated according to biokinetic and dosimetric standard modelling procedures. The average effective equivalent radiation dose for the members of the main area was about 2000 mSv (see Table 1).

The 'control area' included the population of the Kokpektinsky rayon in the Semipalatinsk oblast. This population group had also been exposed to radiation throughout the atmospheric nuclear tests, but the effective equivalent radiation dose for the members of the control area was only about 70 mSv.

A crucial factor for the level and structure of cancer incidence is the age spectrum of areas under observation, including the individual ages at the time of exposure. Table 2 gives the data on age and sex characteristics of both areas under study. Throughout our research period, the numbers of men and women in both the main and the control areas were comparable, even concerning individuals of European and Asian descent. The age distribution remained practically unchanged. The main group (0–19 years of age) made up 50% of all included persons, those aged 20–39 years and a third one including individuals who were at least 40 years old made up 25%–28% and 19%–24%, respectively.

The number of inhabitants in the areas under study fluctuated due to natural population movement and migration. To avoid a mixture of the exposed cohort with unexposed persons, immigrants were excluded from examination in the main area, but included in the control area. By 1985, the number of exposed individuals from the

village of Dolon (main area) had for various reasons declined to 100–150 people. We decided to replenish this group by individuals from the village of Korosteli (Borodoulikhinsky rayon) with a recorded estimated radiation dose of 3000 mSv. More detailed information on the establishment of the cohorts will be given in a separate paper.

Cancer cases

Cancer incidences in the main and control areas were analyzed at approximately 5-year intervals, from 1956 through 1994. From 1970 through 1980, we were able to do this on an annual basis, and the incidence for 1956 was assessed statistically, taking into account the entire population of all rayons.

Methods

For both areas, incidence rates were calculated separately and given in rates as of 100 000 persons per year. Due to the fact that the age distribution was comparable between the two areas, we only calculated crude rates. Where error bars are given in the graphs, they refer to the standard error of the rates, which according to Fleiss et al. [3] was calculated as $\sqrt{p \cdot q/n}$.

Comparisons between the main and the control areas are given as rate ratios. The difference between the rates was tested by using the chi-square test. The *P* values given in the text are derived from these tests.

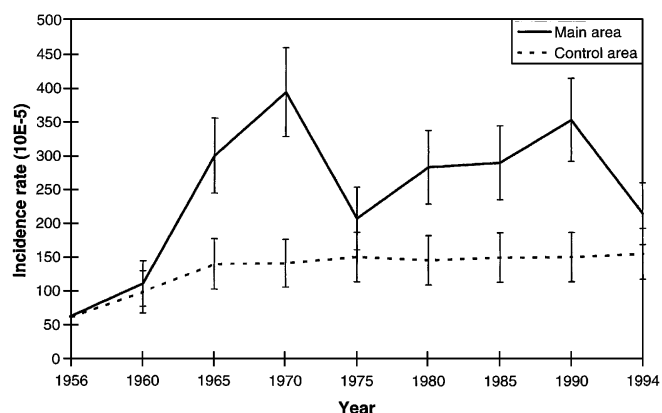
Results

At the beginning of the study period, the official cancer rates for the main and control areas were 63.6 and 61.7 cases per 100 000 persons, respectively. However, these cancer rates at the beginning of the study in 1956 did not reflect the actual situation, but merely characterized the absence of a reliable oncological service in the areas under study.

From 1960 through 1970, the incidences of all malignancies (including leukemias) among the population in the

Table 2 Distribution by age and sex in 'main area' and 'control area'

Age group	Dose equivalent (mSv)	Overall	1960		1965		1970		1975		1980		1985		1990		1994	
			Abs	Percent-age	Abs	Percent-age	Abs	Percent-age	Abs	Percent-age	Abs	Percent-age	Abs	Percent-age	Abs	Percent-age	Abs	Percent-age
'Main area'																		
Total	2 000	39 500	9 900	25.1	9 650	24.4	9 125	23.1	9 620	24.4	9 510	24.1	9 630	24.4	9 320	23.6	10 250	26.2
Men		19 700	4 720	23.9	4 468	22.7	4 517	23.0	4 618	23.4	4 422	22.5	4 719	23.9	4 427	22.5	4 869	24.7
Women		19 800	5 180	26.2	5 182	26.2	4 608	23.3	5 002	25.3	5 088	25.7	4 911	24.8	4 893	24.7	5 381	27.1
0-19			5 000	25.3	5 115	25.7	4 517	22.8	4 954	24.5	4 992	24.1	4 911	24.5	4 567	22.5	5 381	27.1
20-39			2 782	13.9	2 509	12.6	2 327	11.2	2 646	12.7	2 663	12.7	2 504	12.5	2 610	12.7	2 716	13.6
40-59			1 287	6.5	1 158	5.8	1 186	5.9	1 058	5.2	1 094	5.4	1 252	6.2	1 258	6.2	1 435	14.0
60+			831	4.2	868	4.3	1 095	5.4	962	4.7	761	3.6	963	4.7	885	4.3	718	7.0
'Control area'																		
Total	70	23 600	10 125	42.9	10 000	42.4	11 325	48.0	11 265	47.7	10 950	46.4	11 300	47.9	11 270	47.7	10 950	46.4
Men		11 600	4 708	40.6	4 800	41.4	5 210	45.0	5 520	47.6	5 256	45.2	5 453	47.0	5 297	45.9	5 037	43.4
Women		12 000	5 417	45.1	5 200	43.3	6 115	51.0	5 745	47.8	5 694	47.4	5 847	48.6	5 973	49.5	5 913	49.4
0-19			5 113	42.6	5 200	43.3	5 550	49.0	5 745	51.0	5 803	53.0	5 565	50.0	5 748	51.0	5 366	49.0
20-39			2 784	23.2	2 600	21.7	3 171	28.0	3 098	27.5	2 847	26.0	3 005	27.0	3 156	28.0	3 011	27.5
40-59			1 266	10.6	1 300	11.0	1 586	14.0	1 408	12.5	1 423	13.0	1 558	14.0	1 352	12.0	1 369	12.0
60+			962	8.1	900	7.5	1 020	9.0	1 013	9.0	876	8.0	1 002	9.0	1 014	9.0	1 205	11.0

**Fig. 1** Temporal development of cancer incidence, 1956–1994, in 'main area' and 'control area', based on cross-sectional studies (estimation of 1956 rates on the basis of national data)

areas under observation kept increasing (Fig. 1, Table 3). In the control area, the cancer incidence showed only a minor annual variation. By 1960, the initial level was exceeded by a factor of almost 2 in the main area, rising to a rapid fivefold increase by 1965. Five years later, we recorded a peak of cancer incidence that exceeded the initial level by a factor of 5, i.e., $394.5 \cdot 10^{-5}$. In 1970, the rates differed significantly between the main and the control areas (rate ratio, $RR=2.79$, $P<0.001$).

In 1975, the cancer incidence in the main area decreased dramatically to $207.3 \cdot 10^{-5}$. The cancer incidence in the control area remained practically unchanged at a level of $150.9 \cdot 10^{-5}$. There was no statistically significant difference between the two areas ($RR=1.37$, $P=0.42$).

In 1980, the cancer incidence of the main area rose again and reached a second peak of $354.1 \cdot 10^{-5}$. In 1990, the rate in the main area decreased to $214.6 \cdot 10^{-5}$. For the control area and during the same period, the cancer incidences were 150.8 and 155.3, respectively. In 1994, the observed number of cases from the 9 different years under study totalled 213 in the main and 130 in the control area, which corresponds to overall rates of $267.5 \cdot 10^{-5}$ and $142.5 \cdot 10^{-5}$, respectively, and which results in a relative risk of 1.88 ($P<0.001$). Figure 1 presents the temporal development of cancer incidences in the main area by steep upward and downward slopes.

Throughout our research period, the relative cancer risk among the exposed populations of the main area had a clearly defined temporal development, as compared with the control area (Table 4). Starting in 1960, the relative risk among the population of the main area increased steadily and reached its peak in 1970 ($RR=1.13$, 2.15, and 2.79, respectively). By 1975, its value declined to 1.37 ($P=0.42$). By 1980, it increased again ($RR=1.94$, $P=0.047$) and kept growing through 1990 ($RR=2.35$, $P=0.005$). In 1994, the relative risk for cancer among the population of the main area remained higher than in the control area, although without statistical significance ($RR=1.38$, $P=0.40$).

The average age of the individuals with oncological diseases of the selected localisations did not differ substan-

Table 3 Cancer incidences in 'main area' and 'control area' by year of investigation

	'Areas'	Year										Sum	Men		Women	
		1956	1960	1965	1970	1975	1980	1985	1990	1994	Abs		Per-centage	Abs	Per-centage	
All sites	Main	7	11	29	36	20	27	28	33	22	213	120	56.3	93	43.7	
	Control	6	10	14	16	17	16	17	17	17	130	70	53.8	60	46.2	
Esophagus	Main	5	7	16	17	10	12	11	10	7	95	56	58.9	39	41.1	
	Control	4	6	6	9	9	7	6	7	6	60	36	60.0	24	40.0	
Stomach/ liver cancer	Main	2	1	5	7	3	4	4	6	3	35	19	54.2	16	45.8	
	Control	2	1	4	4	2	3	3	3	4	26	14	53.8	12	46.2	
Lung cancer	Main	–	1	2	3	1	3	2	4	2	18	12	66.6	6	33.4	
	Control	–	1	1	1	1	1	2	2	1	10	5	50.0	5	50.0	
Other sites incl. leukemia	Main	–	2	6	9	6	8	11	13	10	65	33	50.9	32	49.1	
	Control	–	2	3	2	5	5	6	5	6	34	15	45.0	19	55.0	

Table 4 Cancer incidence rates, rate ratios, and *P* values for selected cancer sites in 'main area' and 'control area' by year of investigation; *P* values are either based on Yates-corrected chi-square test

or on two-tailed exact Fisher test, whichever fits the data situation better (*n.a.* not available or not applicable)

Tumor sites	'Areas'	Years									
		1956	1960	1965	1970	1975	1980	1985	1990	1994	
All tumor sites	Main area	63.0	111.1	300.5	394.5	207.3	283.9	290.8	354.1	214.6	
	Control area	61.7	98.8	140.0	141.3	150.9	146.1	150.4	150.8	155.3	
	Rate ratio	1.03	1.12	2.15	2.79	1.37	1.94	1.93	2.35	1.38	
	<i>P</i>	<i>n.a.</i>	0.96	0.024	0.0006	0.42	0.047	0.042	0.005	0.40	
Esophagus	Main area	33.0	70.7	165.8	186.3	163.6	126.2	114.2	107.3	68.3	
	Control area	33.0	59.3	60.0	79.5	79.9	63.9	53.1	62.1	54.8	
	Rate ratio	1.0	1.19	2.76	2.34	2.04	1.97	2.15	1.73	1.25	
	<i>P</i>	<i>n.a.</i>	0.97	0.045	0.053	0.73	0.22	0.19	0.38	0.91	
Stomach, liver	Main area	7.0	10.1	51.8	76.7	31.1	42.1	41.5	64.4	29.3	
	Control area	7.0	9.9	40.0	35.3	17.8	27.4	26.5	26.6	36.5	
	Rate ratio	1.0	1.02	1.30	2.17	1.75	1.54	1.57	2.42	0.80	
	<i>P</i>	<i>n.a.</i>	1.0	0.75	0.24	0.67	0.71	0.71	0.32	1.0	
Lung	Main area	<i>n.a.</i>	10.1	20.7	32.9	10.4	31.5	20.8	42.9	19.5	
	Control area	<i>n.a.</i>	9.9	10.0	8.8	8.9	9.1	17.7	17.7	9.1	
	Rate ratio	<i>n.a.</i>	1.02	2.07	3.74	1.17	3.96	1.18	2.42	2.14	
	<i>P</i>	<i>n.a.</i>	1.0	0.62	0.33	1.0	0.34	1.0	0.42	0.61	

Table 5 Average age of individuals with cancer in selected sites

Cancer site	'Main area'		'Control area'	
	Men	Women	Men	Women
Esophagus	62.3±0.7	63.4±0.9	62.5±0.8	64.2±1.2
Stomach, liver, colon	57.5±0.8	58.4±0.7	56.8±0.9	75.8±0.9
Lung	56.3±0.7	57.1±0.6	58.0±0.9	57.4±0.7

tially between men and women in the main and the control areas (Table 5).

Esophagus cancers

The relative proportions of different cancer sites changed during the study period. In the first years, a high proportion (e.g., 72.7% of all cases, in 1960) was observed for cancers

of the esophagus, stomach, and liver, of which esophagus cancers were predominant. According to the Kazakh national statistics, its spontaneous level exceeded the national average by a factor of 3 or 4 (data not given in the tables).

In 1960, there was a small cancer rate increase (RR=1.19, *P*=0.97), and in 1970, the esophagus cancer incidence showed its peak of $186.3 \cdot 10^{-5}$ within the main area, whereas it was $79.5 \cdot 10^{-5}$ in the control area. This difference is of borderline significance. The relative risk for persons in the exposed area was 2.34 (*P*=0.053).

In 1980, the rates in the main area and in the control area were $126.2 \cdot 10^{-5}$ and $63.9 \cdot 10^{-5}$, respectively. This is an insignificant elevation by a factor of 1.97 (*P*=0.22). In 1994, the rate decreased to $68.3 \cdot 10^{-5}$ in the main area. Compared to a rate of $54.8 \cdot 10^{-5}$ in the control area, there was only a marginal difference by a factor of 1.25 (*P*=0.91). The temporal development of the esophagus cancer incidence is given in Fig. 2.

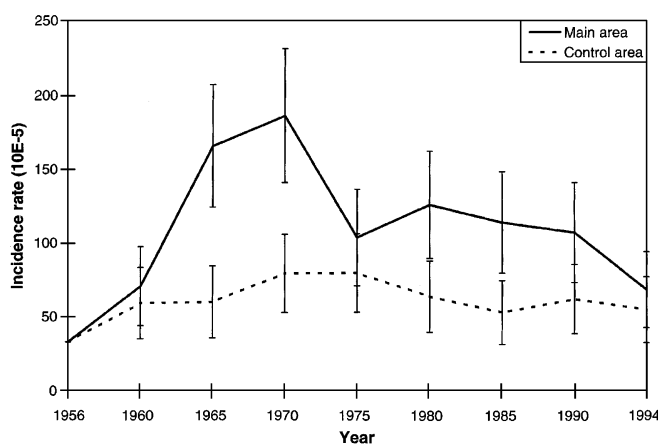


Fig. 2 Temporal development of esophagus cancer incidence, 1956–1994, in ‘main area’ and ‘control area’, based on cross-sectional studies (estimation of 1956 rates on the basis of national data)

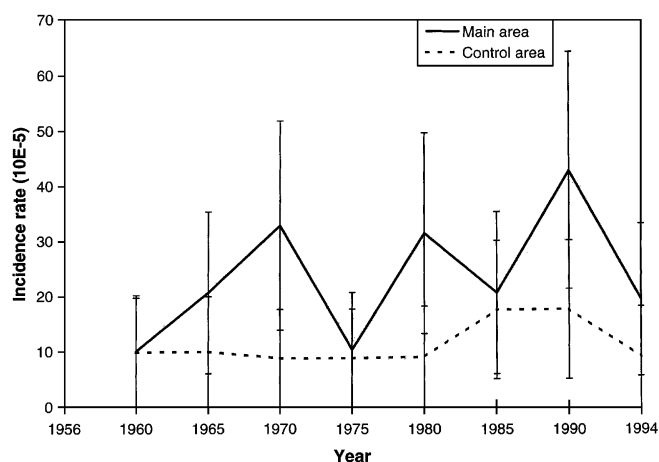


Fig. 4 Temporal development of the lung cancer incidence, 1960–1994, in ‘main area’ and ‘control area’, based on cross-sectional studies

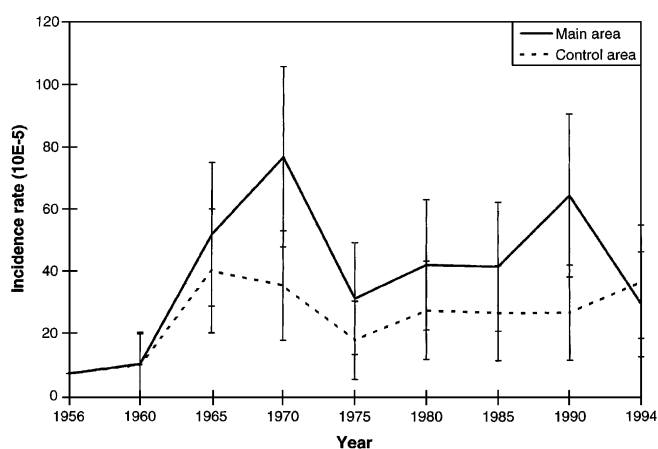


Fig. 3 Temporal development of incidence of stomach and liver cancer, 1956–1994, based on cross-sectional studies (estimation of 1956 rates on the basis of national data)

Stomach and liver cancers

We observed a similar temporal development when analyzing the incidence of carcinomas of the stomach and liver. It was assumed that liver cancer (making up no more than 1.5%–2.0% of all cancers of the gastrointestinal tract) followed the temporal pattern of stomach carcinomas.

In 1965, an abrupt increase in the incidence of stomach and liver carcinomas took place among both groups under study. In 1970, the incidence rate of stomach and liver cancers reached values of $76.7 \cdot 10^{-5}$ in the main area and $35.3 \cdot 10^{-5}$ in the control area, respectively. The relative risk in the main area was 2.17 ($P=0.24$). In 1975, the incidence in the main area decreased to $31.1 \cdot 10^{-5}$ compared with $17.8 \cdot 10^{-5}$ in the control area ($RR=1.75$, $P=0.67$). In 1980, the incidence in the main area rose to $42.1 \cdot 10^{-5}$ and exceeded the control area rate ($27.4 \cdot 10^{-5}$) by a factor of 1.54 ($P=0.71$).

By 1994, there was a substantial decrease of the incidences in the main area ($29.3 \cdot 10^{-5}$), at that time lower than in the control area ($36.5 \cdot 10^{-5}$), but this difference was statistically insignificant ($RR=0.80$, $P=1.00$).

The relative risk of esophagus, stomach, and liver carcinomas among the residents in the main area was reflected by a series of changes characterized by its significant increase from 9 to 14 years after the beginning of the study period, by its decrease to almost the level of the control area in 1975, and by its second increase in years 24–34 of the study. Finally, in 1994, it levelled off at the rate in the control group (Table 4, Fig. 3).

Lung cancers

From 1956 to 1994, the incidence of tumors localized in the respiratory system underwent significant changes among the participants of both cohorts. It should be noted that lung cancer was predominant among all cancer sites of the respiratory system, and it was lung cancer that produced an excess incidence among the participants in the main area.

Nine years after the starting point of the study, i.e., in 1965, the incidence rate had grown to $20.7 \cdot 10^{-5}$ in the main area. Although the rate increased even in the control area, it stayed lower than in the main area ($10.0 \cdot 10^{-5}$). In 1970, the incidence of lung cancer reached its first peak in the main area ($32.9 \cdot 10^{-5}$), while the rate in the control area remained lower ($8.8 \cdot 10^{-5}$). In 1975, a substantial decrease was observed concerning lung cancer incidence in the main area ($10.4 \cdot 10^{-5}$). Thereafter, the incidence increased again until 1990, when it reached its highest value ($42.9 \cdot 10^{-5}$). The lung cancer incidence in the control area did not change much and remained lower than in the main area. From 1990 through 1994, it decreased by a factor of 2 in both areas (Table 4, Fig. 4).

Discussion

The first studies on cancer incidence in the early 1960s made the exposed population subject to extensive research of early and late radiation effects. Due to the official denial of any possible irradiation effects from doses lower than 1 Sv, serious epidemiological and clinical research for the population groups with low irradiation doses was omitted. Throughout the entire period of nuclear testing, i.e., from 1949 to 1989, only the military experts – and again only in a limited way – were allowed to carry out radiation monitoring and to take the individual and collective dosimetry. We used documented and recorded exposure doses for the sake of any epidemiological and clinical research in order to assess the consequences of radiation exposure for the population.

Within nine cross-sectional studies, we recorded 213 cases of cancer among the exposed population, and 130 cases in the control group. The temporal development of cancer incidence in the main area passed through a series of dramatic changes, reflected by a verifiable increase 5 years after the last important direct exposure from nuclear tests in 1956, which was the starting point of the study. Fourteen years later, i.e., in 1970, a peak of cancer incidence was observed. During the next 5 years, the cancer incidence decreased gradually, and in 1975 (19 years after the starting point of the study), it reached the level of the control area. A rise of cancer incidence was recorded after 1975, and a second peak was observed in 1990.

No such changes have been seen in the control area. Following an initial but still moderate increase from 61.7 to 170.0 cases per 100 000 people within the first 19 years, no further alteration in cancer incidence was observable.

The proportions of the different cancer sites among all diagnosed cases changed over the years. The percentage of tumors localized in the gastrointestinal tract (such as cancers of the intestine, stomach, and liver) gradually decreased throughout the study period.

The overall increase within the first years of observation may partly be due to a screening effect and to the fact that the medical examination schemes improved, i.e., there may have been an underreporting of cases in the first years. However, this would not explain the difference in the temporal development of the rates within the two areas under study. Though the results are preliminary and represent merely a first analysis of the underlying data, and though they are based on a limited group of persons, the material on the temporal development of cancer incidences for some areas of the Semipalatinsk oblast exposed to irradiation

from atmospheric nuclear tests characterizes postradiation cancer effects. The bi-peaked temporal development of cancer incidence in the exposed cohort is surprising, although the cancer sites with an increased incidence correspond to those observed among the atomic bomb survivors [4]. Still, it cannot be ruled out that either the decrease in 1975 or part of the second increase might be due to an artefact. The decrease in 1975 could be a chance finding or result from a strong underreporting. The second increase might be due to more intensive investigation in the main area, between 1975 and 1990. This would not, however, explain the steady increase during the time period. A similar continuous decrease or increase can also be observed when reviewing the annual data, which are available for the years 1970–1980. The second increase can be taken as real and not as an artefact.

Both the small number of observed cases and the multiple cross-sectional nature of the present analysis make it necessary to interpret the results with caution. Although there is evidence of the elevated risk in the main area being due to radiation exposure, no dose-response relationship can be calculated from the present data. More information will arise from an envisaged cohort analysis of the underlying data, which is being prepared now. Since this work will take some time and it is important to obtain a first impression of the data set, the results are presented here. For breast cancer, thyroid cancer, and leukemias, more intensive research has been done in the past years on the basis of cross-sectional data. It would have been beyond the scope of this first survey to give these more detailed results here. They will be published later.

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