Leukemia in the Proximity of a German Boiling-water Nuclear Reactor: Evidence of Population Exposure by Chromosome Studies and Environmental Radioactivity

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Exceptional elevation of children's leukemia appearing 5 years after the 1983 startup of the Krümmel nuclear power plant, accompanied by a significant increase of adult leukemia cases, led to investigations of radiation exposures of the population living near the plant. The rate of dicentric chromosomes in peripheral blood lymphocytes of seven parents of children with leukemia and in 14 other inhabitants near the plant was significantly elevated and indicated ongoing exposures over the years of its operation. These findings led to the hypothesis that chronic reactor leakages had occurred. This assumption is supported by identification of artificial radioactivity in air, rainwater, soil, and vegetation by the environmental monitoring program at the nuclear power plant. Calculations of the corresponding source terms show that emissions must have been well above authorized annual limits. Bone marrow doses supposedly result primarily through incorporation of bone-seeking β- and α-emitters. — *Environ Health Perspect* 105(Suppl 6):1499–1504 (1997)

Key words: chromosome aberration analysis, childhood leukemia, leukemia cluster, ionizing radiation, fission products, nuclear power plant, overdispersion of chromosome aberrations

Introduction

A cluster of childhood leukemia cases was observed in the community of Elbmarsch in northern Germany in 1989 to 1991 (*1–3*). All five cases had been living within a distance of 5 km from the Krümmel nuclear power plant (Kernkraftwerk Krümmel [KKK]) located near the river Elbe about 35 km southeast of Hamburg. Since 1994, four additional cases were identified in the 5-km area surrounding KKK (Figure 1). All these cases were diagnosed at 10 years of age or younger; five were very young: 1.8 to 4 years of age (Table 1). Also, one case of leukemia in a young adult and a case of aplastic anemia in a child were diagnosed.

Between 1986 and 1995 the mean number of children up to the age of 14 living in the 5-km area surrounding KKK was about 5400 (*4*). According to Haaf et al. (*5*), the mean incidence of acute leukemia between 1980 and 1990 was 4.3×10^{-5} a^{-1} in individuals less than 15 years of age. The expected number of leukemia cases in children in the 5-km region around KKK for the period 1990 to 1996 was 1.6; therefore, the incidence of childhood leukemia in that region was elevated by a factor of 5.6.

The Krümmel nuclear power plant is a 1300-mW boiling-water reactor—the largest in the world—and began operation in 1983. The nuclear research institute Gesellschaft für Kernenergieverwertung in Schiffbau und Schiffahrt (GKSS) is located in this plant's vicinity. The GKSS was established in 1958 and operates two research reactors of 5 and 15 mW.

The governments of the Federal States of Lower Saxony and Schleswig-Holstein have established a board of experts to identify possible causes of the observed leukemia cluster. Potential risk factors such as X-rays, chemicals, and previous diseases of the affected families were noted and excluded from the study. None of the parents were exposed to occupational or unusual medical irradiation. One family, however, was living in a house with a mean radon concentration of 450 Bq/m^3. The only common factor among the leukemia cases was their proximity to the two nuclear establishments. With respect to KKK, not only the spatial relationship of the observed leukemia cluster to the nuclear power plant is remarkable but also the temporal correspondence. The first case of malignant blood disease was diagnosed 5 years after KKK was commissioned.

A retrospective epidemiologic study by Hoffmann and Greiser (*6*) in 1994 showed an elevation in the incidence of leukemia in the whole population in the vicinity of KKK. For the period 1984 to 1993 there was a statistically significant elevation for males (+56%) within 5 km of the nuclear power plant. This increase was confined to the period 1989 to 1993; it began 5 years after the KKK startup.

A careful investigation of the possible relationship between the cluster of leukemia cases and the local nuclear facilities appeared imperative even though the whole-body counting of inhabitants performed in 1991 produced negative results and analyses concerning the emission of long-lived fission products failed to demonstrate a consistent pattern of increased radionuclide concentrations in soil and vegetation (*7*). There were, however, several isolated findings of elevated radionuclide activities measured in environmental samples at various times (*8*).

To examine whether the population living in the vicinity of KKK was subjected to elevated exposures of ionizing radiation, analyses of dicentric chromosome aberrations in lymphocytes of the peripheral blood were conducted for a group of inhabitants of the Elbmarsch community. Analyses of data on environmental radioactivity measurements also were conducted.

Biological Dosimetry by Investigation of Dicentric Chromosome Aberrations

The retrospective investigation by chromosome aberration analysis included 21 individuals (19 females and 2 males), all inhabitants or former inhabitants of the Elbmarsch community. All were residing within 5 km of KKK in a southern direction. At the time the blood samples were

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Abbreviations used: GKSS, Gesellschaft für Kernenergieverwertung in Schiffbau und Schiffahrt; KKK, Kernkraftwerk Kruemmel; LET, linear energy transfer; mSv, millisieverts; TLD, thermolumiscence dosimeter(s).

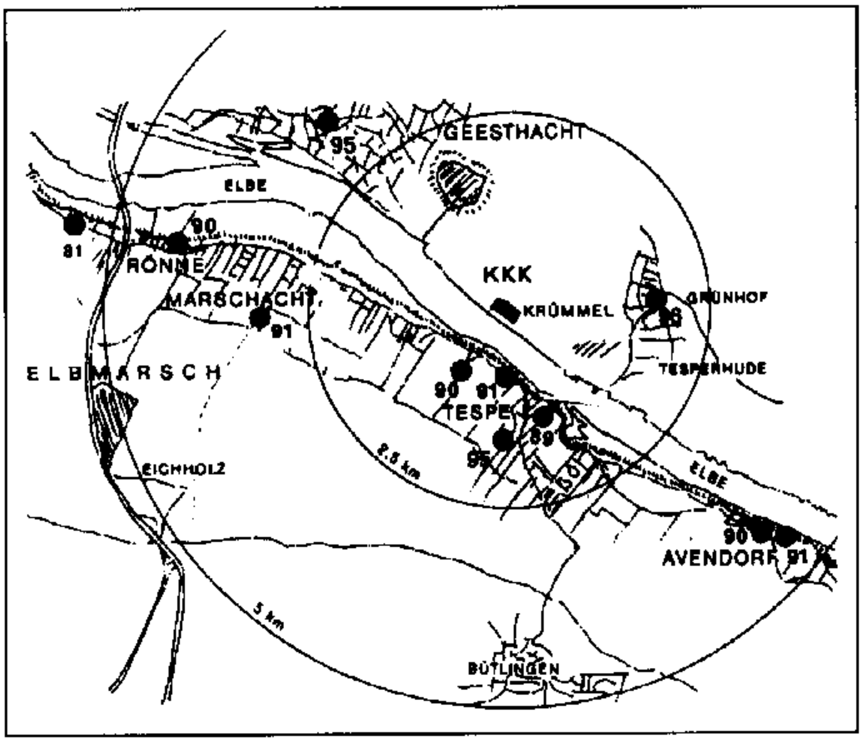

Figure 1. Map of the area around the Krümmel nuclear power plant. Black circles indicate homes of leukemia and aplastic anemia cases with year of diagnosis since 1980. The only case before the start-up of KKK was diagnosed in 1981. Circles show the distance to KKK. An additional case diagnosed in 1994 is not indicated on the map because the location is not known.

Table 1. Cases of leukemia and aplastic anemia observed in a 5-km radius of the Krümmel nuclear power plant

Case no	Month and year born	Sex	Disease	Date of diagnosis	Age at diagnosis
1	9/1982	F	AA	12/1989	7
2	8/1986	F	ALL	2/1990	3.5
3	2/1981	M	ALL	3/1990	9
4	3/1981	M	AML	4/1990	9
5	3/1989	F	ALL	1/1991	1.8
6	1970	M	AML	4/1991	21
7	9/1988	M	ALL	5/1991	2.7
8	?	M	ALL	1994	?
9	ca 1991	M	ALL	1995	4
10	1985	M	ALL	6/1995	10
11	1993	M	ALL	6/1996	3

Abbreviations: ?, not known; AA, aplastic anemia. ALL, acute lymphatic leukemia; AML, acute myeloid leukemia; F, female; M, male.

taken (in 1992, 1993, and 1995) these volunteers were 28 to 45 years of age. Four women were selected because they had settled in the village after 1986 (Table 2, cases 8–11), as had one of the leukemia families (Table 2, case 5). Seven subjects were parents of the children who were diagnosed with leukemia in Elbmarsch.

The control group consisted of 25 healthy adults (9 females and 16 males) living in the city of Bremen, about 100 km southwest of Hamburg. At the time of blood sampling (1988 to 1994) these individuals were 17 to 57 years of age.

Each subject completed a detailed questionnaire. Exclusion criteria were previous occupational exposures, greater than average diagnostic medical irradiation, or exposure to chemical mutagens. Smokers (those who smoked more than 10 cigarettes per day) were also excluded.

To evaluate the rate of dicentric chromosomes and centric ring chromosomes, lymphocyte cultures and slide preparations were made according to standard cell cycle controlling methods (*9*). Collection of metaphases was facilitated by a semiautomatic computerized system that included data management (Metasystems, Sandhausen, Germany). Only first-division metaphases with 46 centromeres were analyzed and all structural aberrations were registered. The results are given in Table 2.

Compared to the laboratory control (0.46×10^{-3}), the investigated population of Elbmarsch showed a highly significant elevation of dicentric chromosomes, with a rate of 1.77×10^{-3} dicentric chromosomes/metaphase [$p < 0.01$ (*10*)]. The highest individual number of dicentrics (excluding case 3 in Table 2) was 5 dicentric chromosomes in 1000 metaphases.

Particularly noteworthy was the existence of cells with two dicentrics in the Elbmarsch group (Table 2, cases 5, 8, 10, and 12) in contrast to the control group (no cells with more than one dicentric). Additionally, there was one metaphase with six dicentrics (Table 2, case 3). The aberrations did not follow Poisson distribution but showed a significant overdispersion (*11*). This was true for the entire Elbmarsch population investigated, even when the multiaberrant cell was excluded (Table 3). Although the results of the chromosome aberration analysis indicate that the population of the Elbmarsch community has been severely exposed to ionizing radiation in the past (*12*), extrapolation of the entire accumulated dose is not adequate because exposure conditions are not known.

Gamma Dose in the Surrounding Area

The major focus of the environmental monitoring program of KKK and GKSS is γ dose rate and accumulated γ dose (*7,8,13,14*). The annual external γ dose is controlled by 80 thermoluminescence dosimeter(s) (TLD) distributed at different locations (*13*). We analyzed the results by regarding two zones: 0 to 2.5 km (a total of 11 locations excluding measurements at the KKK site) and 7.5 to 15 km (34 dosimeters). By calculating annual averages for each of the zones it was determined that there was systematic elevation of γ exposure in the internal zone since the beginning of operation in 1983 to about 1992 (Figure 2). In the 2 years before the KKK startup the external γ doses in the two zones were statistically similar.

The difference in γ exposures corresponds to a mean additional exposure of

Table 2. Results of chromosome aberration analysis in adult residents of Elbmarsch and in controls.

Case Number	Parent of child with leukemia	Length of residence in Elbmarsch	Date of blood sampling	Analyzed metaphases, number	Dicentrics, number	Rate of dicentrics $\times 10^{-3}$
Elbmarsch						
2	Yes	Since before 1984	January 1992	1005	2	2.0
2	Yes	Since before 1984	January 1992	390	2	5.1
3	Yes	Since before 1984	January 1992	1000	3[a]	3.0
4	Yes	Before 1984 1991	January 1992	1001	2	2.0
5	Yes	Since May 1988	January 1992	664	2[b]	3.0
6	Yes	Since before 1884	October 1995	1010	2	2.0
7	Yes	Since before 1984	October 1995	1010	0	0.0
8	No	Since 1988	April 1993	1002	5[c]	5.0
9	No	Since 1987	April 1993	1014	0	0.0
10	No	Since 1987	April 1993	1097	4[c]	3.6
11	No	Since 1987	April 1993	1034	1	1.0
12	No	Since before 1984	June 1993	1005	3[c]	3.0
13	No	Since before 1984	June 1993	1110	0	0.0
14	No	Since before 1984	June 1993	1003	1	1.0
15	No	Since before 1984	June 1993	1005	1	1.0
16	No	Since before 1984	June 1993	1002	2	2.0
17	No	Since before 1984	June 1993	1011	2	2.0
18	No	Since before 1984	June 1993	1008	0	0.0
19	No	Since before 1984	June 1993	1007	2	2.0
20	No	Since before 1984	June 1993	1004	2	2.0
21	No	Since before 1984	June 1993	1009	0	0.0
Total				20,391	36	1.77±0.33[d]
Control						
1–25	—	—	1988–1995	19,775	9	0.46±0.15[d]

[a]Excluding one multiaberrant cell with six dicentrics. [b]One cell contained one tricentric, which was counted as two dicentrics. [c]Including one cell with two dicentrics. [d]Standard error of the mean.

Table 3. Intercellular distribution of dicentric chromosomes in Elbmarsch inhabitants.

	Dicentric chromosomes per cell, no								
	0	1	2	3	4	5	6	s^2/Y[a]	u*
Includes multiaberrant cell									
Observed	20,358	28	4	0	0	0	1	1.90	92.76
Expected	20,349	41.91	0.04	0	0	0	0		
Excludes multiaberrant cell									
Observed	20,358	28	4	0	0	0	0	1.22	22.58
Expected	20,354	35.94	0.03	0	0	0	0		

[a]Relative variance (Y is the mean value). *$u > 1.96$: overdispersion is significant ($p < 0.05$).

0.09 mSv per year and cannot be explained by small-scale spatial variation of the background external γ radiation field. Although the γ exposure rate is well below the German permissible limit of 0.3 mSv per year, the influence of the reactor operation is well demonstrated. This result is remarkable because a safety assessment report (*15*) predicted a possible maximum reactor dose of only 0.04 mSv per year. This dose would be incurred partly by inhalation and ingestion of radionuclides, which are not registered by TLD dosimetry.

Cesium Isotopes in Rainwater and Air

Long-lived γ emitters are routinely measured in the vicinity of KKK (*13,14*). Concentrations in rainwater are measured periodically at three locations. Figure 3 shows ^{137}Cs activity in precipitation at these sampling stations. The Grünhof station, which is 2.2 km downwind of KKK, has shown a decreasing but permanent elevation of isotopes ^{134}Cs and ^{137}Cs since 1986. These isotopes were elevated compared to isotope incidence at other locations of the KKK monitoring program and the ^{137}Cs concentration was at least 10 fold higher than that at other measuring points in northern Germany from the third quarter of 1986 until 1993 (*16*). Thus, Chernobyl fallout can be excluded as a cause of such elevations. In addition, the presence of the ^{134}Cs isotope in these samples indicates that the contaminations cannot be attributed to the fallout from nuclear weapons testing because of the short half-life of ^{134}Cs (2.1 years).

Calculations and measurements demonstrate that the releases of radioactivity permitted by German nuclear facilities do not lead to detectable contamination in the surrounding areas (*17*). Therefore, findings of Cs in rainwater appear to be an indication of repeated releases of nuclides above permitted limits.

Elevated Cs emissions have been confirmed by measurements of dry fallout at different locations near KKK (*13*). Compared to that in other locations in Germany, the ^{137}Cs aerosol concentration in air near the ground in the vicinity of KKK was significantly elevated in different quarters in the period 1985 to 1995 (Table 4). It should be noted that these measurements were carried out by three different laboratories; therefore, repeated measurement errors can be discounted. Additionally, remarkable concentrations of ^{90}Sr were found in 1984 and 1988, which also cannot be explained by any other sources than KKK emissions (^{90}Sr in rainwater was not measured).

Fission and Activation Products in Soils and Green Plants

Measurements of environmental samples show elevated activities of the nuclides ^{137}Cs and ^{90}Sr in soil and plants since the startup of KKK (*13,14*). The Chernobyl accident led to only marginal increases of ^{90}Sr in the German environment (*17*). Nevertheless, concentrations of this isotope rose repeatedly by several Bq/kg (dry mass) compared to the background fallout in the grass around KKK. The highest ^{90}Sr contamination—30 Bq/kg (dry mass)—was registered in August 1987 at a location 10 km from KKK; this is more than 10-fold the normal concentration in Germany at that time (*18,19*). The highest concentration of ^{137}Cs in grass (103 Bq/kg) was measured in 1988 2 km from KKK (*13*). This is an approximately 100-fold increase over the normal value in local vegetation (*19*).

The KKK environmental monitoring program does not call for nuclide-specific and continuous measurements of pure β-and α-emitters in the controlled media except for ^{90}Sr in the air. Measurements of short-lived γ and β emitters are also not required. Nevertheless, there have been occasional findings of short-lived fission and activation products as well as radioactive corrosion products, none of which can be explained by the Chernobyl accident (Table 5). Only after damage to the fuel rods would these nuclides be detectable outside the plant. In these cases leakages of primary cooling water would be

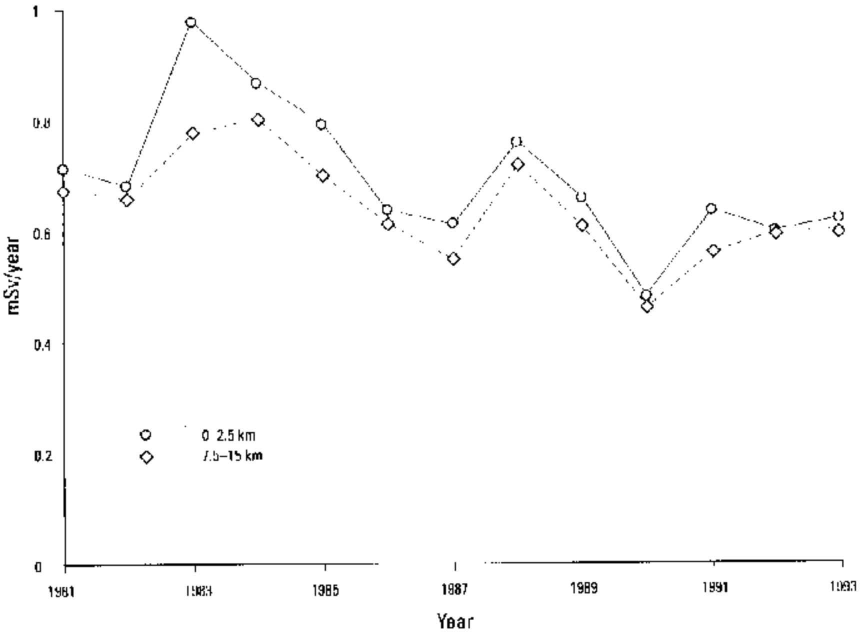

Figure 2. Annual γ dose measured by TLD in two radial zones around the Krümmel nuclear power plant. The values given are averages taken at 11 locations in the 0 to 2.5 km zone and at 34 locations in the 7.5 to 15 km zone.

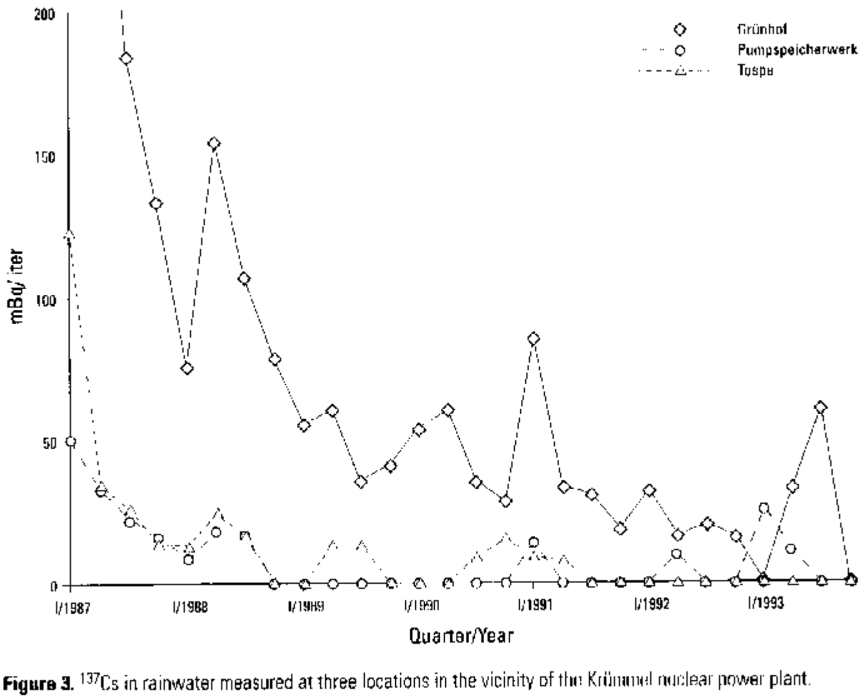

Figure 3. ^{137}Cs in rainwater measured at three locations in the vicinity of the Krümmel nuclear power plant.

accompanied by releases of Pu and other transuranium isotopes (*20*).

In 1984 Pu isotopes were found in surface water of the Elbe River and in fish in the river (*8*). When the activity ratios of isotopes ^{238}Pu and $^{239/240}Pu$ are compared, it is concluded that they were generated in a reactor and are not the result of weapons fallout. No Pu measurements were available after 1984. A further indication of Pu releases is in the discovery of ^{239}Np in soil in 1993 because ^{239}Np is a precursor of ^{239}Pu (Table 5).

Discussion

Elevated rates of leukemia among populations in the vicinity of nuclear establishments have been found repeatedly (*21–23*). For example, in the case of the Pilgrim nuclear reactor in Massachusetts, a correlation between the leukemia rates in the vicinity of the plant and official information on releases of radioactivity was established and a cause–effect relationship derived (*24*). In western Germany, an incidence study of childhood leukemia near nuclear establishments in the former countries of the Federal Republic had negative results (*25*). However, with respect to populations residing in a radius of less than 5 km from a nuclear establishment and children less than 5 years of age at diagnosis, there was a 3-fold significant elevation in leukemia incidence compared to that in control regions (*25*).

The study by Keller and co-workers (*25*) was restricted to the period 1980 to 1990; therefore, most of the cases of childhood leukemia near KKK were not included. Most of these children became ill at very young ages (Table 1). The hypothesis of radiation induction is thus supported by the well-known fact that individuals in the prenatal stage and at very young ages have a higher sensitivity to radiation. Furthermore, the predominance of illnesses among boys (Table 1) corresponds to the findings among A-bomb survivors in which the male:female ratio is 2:1 for radiation-induced cases (*26*); the normal ratio for such illnesses is 1.3:1 (*5*).

Further support for the hypothesis of radiation-induced leukemia in the Elbmarsch region has been found through investigations of the latency periods for leukemia in exposed cohorts. Children 0 to 15 years of age receiving X-ray therapy for ringworm of the scalp showed a maximum rate of leukemia about 4 years after irradiation; 50% of all cases occurred by this time (*27,28*). This corresponds to the distribution in the Oxford Survey of Childhood Cancers for leukemia after prenatal exposure to diagnostic X-rays (*29*), and to age correlations in latent cases of radiation-induced illnesses among Japanese A-bomb survivors (*30*).

Assuming 4 years of latency and realizing that the first appearance of childhood leukemia in the proximity of KKK was in 1990 (Table 1), a single exposure event in

Table 4. ^{137}Cs aerosol concentrations in air above soil in μBq/m³ at different measuring points in the vicinity of KKK in comparison to other locations in Germany. Values of the year of the Chernobyl accident (1986) are not reported.

Year	Quarter, location	KKK surrounding[a]	Braunschweig[b]	Berlin[b]	Freiburg[b]
1985	III, GKSS	31 ± 6	0.59	0.72	
1987	I, GKSS	55 ± 1	32.0	112	–
	II, GKSS	14 ± 3	17.6	17.1	–
	III, GKSS[c]	78 ± 1	57.1	33.0	–
	III, GKSS[d]	110 ± 28	57.1	33.0	–
	IV, GKSS[c]	22 ± 3	15.3	26.5	–
	IV, GKSS[d]	121 ± 3	15.3	26.5	–
1988	III, Tespe	20 ± 3	3.4	3.6	–
	III, GKSS	29 ± 4	3.4	3.6	–
	IV, Pumpspeicherwerk	28 ± 4	2.8	6.0	–
	IV, Tespe	19 ± 3	2.8	6.0	–
1989	I, GKSS	18 ± 3	2.0	3.7	2.7
	I, Tespe	13 ± 2	2.0	3.7	2.7
	III, Pumpspeicherwerk	22 ± 3	2.5	4.0	1.3
	III, Tespe	14 ± 2	2.5	4.0	1.3
	IV, GKSS	21 ± 3	1.9	2.8	1.2
1990	I, Pumpspeicherwerk	13 ± 2	1.7	3.1	2.4
	I, Tespe	21 ± 0.3	1.7	3.1	2.4
	I, GKSS	25 ± 4	1.7	3.1	2.4
	II, Pumpspeicherwerk	15 ± 2	2.4	2.6	2.0
	II, Grünhof	15 ± 2	2.4	2.6	2.0
	III, GKSS	27 ± 4	1.9	1.9	0.9
1991	III, GKSS	25 ± 5	1.2	1.4	0.7
1991	II, Pumpspeicherwerk	19	1.5	2.2	1.1
	II, Grünhof	31	1.5	2.2	1.1
1992	II, Freischaltanlage	16	2.2	3.0	2.4
	II, Pumpspeicherwerk	27	2.2	3.0	2.4
1995	I, Pumpspeicherwerk	26	–	–	0.6

[a]All values except the last five entries in column 3 are derived by air filter measurements and contain all results above the detection limits (*13,14*). Values for the last five entries of column 3 are measurements of the dry fallout by deposition, which have been converted into air concentrations. [b]The data from the locations Braunschweig (northern Germany), Berlin and Freiburg (southern Germany) are taken from the annual reports on environmental radioactivity and radiation of the Federal Ministry of Environment (*19*). [c]Measurements made by KKK. [d]Measurements made by an independent second laboratory.

Table 5. Short-lived fission and activation products found near KKK.

Nuclide	$T_{1/2}$	Time	Concentration, Bq/kg	Location
^{65}Zn	250 days	September 1985	1.5	Grass, Tesperhude, 1.5 km east
^{95}Nb	35 days	June 1984	0.36	Grass, Tespe, riverside opposite KKK
		October 1984	0.01	Surface water, 10 km west
^{106}Ru	1 year	May 1988	24.0	Suspended material, Geesthacht
		June 1988	1.9	Soil, Dassendorf, 10 km north
		August 1988	1.6	Soil, Tespe, riverside opposite KKK
^{141}Ce	33 days	May 1985	2.3	Sediment, near Geesthacht
		February 1987	0.004	River Elbe, above KKK
		May 1991	0.16	Soil, Schwinde, 6 km west
		July 1991	0.2	Sediment, 4 km southeast
		January 1995	0.2	Four samples of soil in 3-km region
^{239}Np	2.3 days	January 1993	53.0	Soil, near transformer station KKK

about 1986 could be suspected. However, the ongoing occurrence of malignancies in Elbmarsch points to continuous contamination and/or incorporation of radioactivity with a long biological half-life.

From the medical and biological findings discussed in this paper, we conclude that the population was affected by repeated exposures for the following reasons. First, at least four of the children with leukemia were born after 1987 (Table 1). Second, the repeated exposures are indicated by the results of the chromosome aberration analysis. Dicentric chromosomes are unstable aberrations with a decline of about 40%/year (*12*). Therefore, backdating the measured rates of dicentric chromosomes to a single event in 1986 or earlier would yield unrealistically high original rates of exposure. Third, the elevated rate of dicentric chromosomes is similar for persons who settled in Elbmarsch both before and after 1986 (Table 2).

Dose estimations based on the observed rate of dicentric chromosomes in Elbmarsch inhabitants are not reliable because neither the time nor the conditions surrounding the exposures are known. The findings about overdispersion of the distribution of aberrations per cell, however, give additional information about the kind of exposure. Overdispersion of dicentric chromosomes can be caused by either nonuniform or high linear energy transfer (LET) irradiation. Such distributions have been found in blood samples of persons occupationally exposed to plutonium (*31*), tritium (*32*), or uranium (*33*). This cannot be proven through available data or measurements for the Elbmarsch population. The overdispersion observed in the present study also is unexplainable by external γ irradiation or other kinds of low-dose low LET exposure.

The supervising ministry in Schleswig-Holstein has denied that KKK is responsible for exposing the population in the vicinity of the plant and refers to the results of the extensive γ monitoring of the surrounding area. Although there is no indication of a severe overexposure to external γ irradiation in that region, the supposed bone marrow dose may have been a result of incorporation of α- and β-aerosols, whereas the γ submersion was negligible. Scenarios that lead to such organ doses are described in connection with accidents caused by cooling water effluent (*20*). In addition, fuel-rod failures are a well known problem in nuclear reactors. Because it has the largest boiling-water reactor in the world, the Krümmel nuclear power plant is a unique installation. A recent television documentary reported severe problems encountered during construction of the pressure vessel with regard to the welding of single elements. The leukemia study researchers learned of significant leakages of cooling media from the pressurized system during almost all the years of operation (*34*). The quantities rose to 300 liters/hr in 1986 and increased to more than 200 liters/hr in 1993 and 1996. Further investigations will consider the relevance of these leakages by analyzing the pattern of observed nuclides in the areas surrounding KKK.

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