Negative trends for *in utero* Chernobyl exposure and early childhood leukaemia in Western Germany

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Abstract
A recent report in Nature linked increased incidence of early infant leukaemia in Greece with ^{137}Cs fallout density, attributing the effect to an increased *in utero* exposure to ionising radiation from the Chernobyl accident. As a validation exercise in a similarly affected region, we performed an analysis based on the data of the Childhood Cancer Registry for Western Germany. Using the same definitions as Petridou et al. we also observed an increased incidence of infant leukaemia in a cohort of children who were born after the Chernobyl accident. More detailed analyses of embryonic/foetal doses regarding areas of different contamination levels and dose rate gradients with time since the accident showed non-significant negative trends with exposure. Therefore, we conclude that the observed effect was not caused by exposure to ionising radiation due to the Chernobyl accident. Dosimetric considerations per se, based on careful assessments of *in utero* doses in three different exposure categories, show doses much too small relative to natural radiation exposures to account for a significant effect on leukaemia rates.

Introduction
Petridou et al. [1] reported about infant leukaemia after *in utero* exposure from the Chernobyl accident in April 1986. The authors defined two birth cohorts: The first cohort consisted of children who were born in the second half of 1986 and all children born in 1987. These were considered to be exposed and were compared with a combined cohort of children born between January 1980 and December 1985 and of children born between January 1988 and December 1990. The authors found that infants exposed *in utero* by this definition had an increased incidence of leukaemia compared to the „unexposed“ children (rate ratio = 2.6, 95%-confidence interval 1.4 to 5.1). In addition, the authors described that children born in regions with increased radioactive contamination had a higher incidence of leukaemia. For children diseased at an age of 1 to 4 years no significant results were found. Until this publication no increase in incidence or mortality of childhood leukaemia had been reported, neither for areas near Chernobyl nor for other European countries.
Due to different regional weather situations in the end of April 1986 in West Germany there was a heterogeneous contamination by the Chernobyl fallout with a south-north gradient. About 2 to 50 kBq m^{-2} ^{137}Cs were deposited on the soil with maxima greater than 100 kBq m^{-2}. A similar distribution was observed for other radionuclides [2]. The United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) estimated an effective dose equivalent of 0.49 mSv due to the Chernobyl accident (1st year) for the population in southern Germany and of 0.33 mSv for the greatest part of Greece [3].
We therefore decided to perform an analysis comparable with that of Petridou et al. in order to check whether their observation could be confirmed by an independent study.

Material and Methods
Since 1980 the German Childhood Cancer Registry has recorded all malignant diseases for children diagnosed under the age of 15 in West Germany [4]. Information on gender, date of birth, date of

diagnosis, type of disease, place of residence at time of diagnosis and a large number of clinical parameters are collected. The same birth cohort definitions as Petridou et al. were used. Children born between 1 July 1986 and 31 December 1987 were considered as being exposed during pregnancy to radiation due to the accident (cohort B). The first cohort (cohort A) and the third cohort (cohort C) covering all children born between 1 January 1980 and 31 December 1986, resp. 1 January 1988 to 31 December 1990 were considered as unexposed. For further methodological details see Kaletsch et al. [5].

For an estimate of the *in utero* exposure of children in the region around Munich, the external gamma radiation due to the ground deposition of radionuclides and the internal radiation originating from radionuclides incorporated by the mother was considered. The external gamma dose rate at Munich-Neuherberg had been monitored by the Institute for Radiation Hygiene and the National Research Centre for Environment and Health GSF using a scintillation dosemeter and a proportional counter with a filter for energy compensation, respectively. To estimate external shielding, the assumptions of the German Commission on Radiological Protection were adopted: Shielding factors for buildings range from 0.03 to 0.3. Our calculations are based on a value of 0.15. The mother is supposed to stay indoor 80% of time. The internal shielding factor was calculated taking the ground deposition of radionuclides at Munich-Neuherberg [6] and the resulting gamma spectrum into account. It was derived from Ref. [7] which refers to a female adult according to ICRP Publication 23.

To estimate foetal doses for areas with different ground depositions, available data on mean soil contamination of the 328 administrative districts with ^{137}Cs in May 1986 were used to subdivide West Germany into regions of low (less than 6 kBq m^{-2}), intermediate and high contamination (more than 10 kBq m^{-2}). For 28 of the 328 districts no measurements were available and the contamination was estimated by using the measurements from the neighbourhood areas.

Internal radiation predominantly arose from ^{134}Cs, ^{137}Cs, and to a lesser extent from ^{131}I. In view of large-distance distribution of foodstuff, data for the whole of Germany were used for the monthly intake of ^{137}Cs [8]. The intake rate of ^{134}Cs was estimated from ingestion data of Chernobyl ^{137}Cs and the isotopic ratio $^{137}Cs/^{134}Cs = 1.75$ of the Chernobyl fallout at Munich-Neuherberg [6].

Ingestion of ^{131}I is only significant for May and June 1986. It was derived from the specific activity of ^{131}I in raw milk in southern Bavaria assuming a consumption rate for dairy produce of 120 kg/a. Foetal doses due to ingested radionuclides were derived from an elaborate model which takes into account morphology and growth during pregnancy and appropriate biokinetic models for different gestational stages [9].

Estimates of inhalation doses were based on measurements of activity concentrations of radionuclides in air at Munich-Neuherberg using a filter unit which consisted of aerosol filter, molecular sieve and charcoal.

Results

In utero exposure of children was estimated for a hypothetical high-exposure period of pregnancy. It starts at 1 May 1986 and lasts until 31 January 1986. The embryonic/foetal doses originating from external gamma radiation and from radionuclides incorporated by the mother were evaluated.

The measured external gamma dose rate at Munich-Neuherberg, corrected for the contribution of natural radionuclides, reached values of about 0.9 mSv/h beginning of May 1986. For the gestation period mentioned above a total dose due to external gamma radiation of 447 mSv is calculated. Taking a shielding factor of 0.15 for buildings and assuming that the mother stays indoor 80% of time, an external shielding factor of 0.32 is derived. For the internal shielding by mother's body, a shielding factor of 0.66 is deduced from Ref. [7]. The internal shielding factor is based on a reference female adult according to ICRP Publication 23. To give a rough idea about the possible variation of this value, it should be mentioned that an additional layer of 1 cm adipose tissue would reduce the intensity of incident 600 keV photons to about 92% and hence the internal shielding factor would be lowered from 0.66 to 0.61. Variations in mother's dimensions may appreciably change the internal shielding factor. In summary, the foetal dose due to external sources is calculated to be about 95 mSv for the hypothetical gestation period.

Concerning ingestion, only ^{134}Cs, ^{137}Cs, and ^{131}I (during May and June 1986) significantly contribute to the embryonic/foetal dose. The embryonic/foetal doses due to ingestion of ^{134}Cs, ^{137}Cs, and ^{131}I were calculated from the intake rates using the gestation-stage-dependent dose conversion factors listed in Ref. [9]. For the period May 1986 to January 1987, the foetal dose due to ingestion is about 23 mSv, approximately a fourth of the shielded external gamma dose.

To estimate foetal doses in parts of Germany with considerably different ground depositions, an approximate relation between ground deposition in Germany and foetal doses can be derived. Deposition of Chernobyl ^{137}Cs at Munich-Neuherberg amounts to 20 kBq/m^2. The contribution of external gamma radiation to the foetal dose roughly scales linearly with ground deposition within Germany. Hence, for the hypothetical period of pregnancy the total foetal dose is given by

$$H_{foetal} \approx 4.8 \cdot D_{137Cs} + 23 \qquad \text{(for period May 1986 to January 1987)} \qquad (1)$$

where D_{137Cs} denotes the ground deposition of Chernobyl ^{137}Cs in kBq m^{-2} and the foetal dose H_{foetal} is calculated in mSv. The constant term refers to the ingestion pathway. Contributions arising from inhaled activity are not significant.

Table 1 shows the incidence rates and rate ratios for children with acute leukaemia in the first year of life. The incidence of infant leukaemia in cohort B compared to the combined cohorts A and C is significantly increased. The rate ratio is 1.48 with a 95%-confidence interval from 1.02 to 2.15. Calculation of incidence rates for regions with different exposure levels revealed that the greatest difference between the exposed and unexposed birth cohorts is observed for children living in areas with lowest exposure (rate ratio 1.84, 95%-confidence interval 1.21-2.78).

Table 1: Numbers, incidence rates and rate ratios of children with acute leukaemia in the first year of life for the exposed and unexposed birth cohorts in West Germany and regions according to three levels of contamination. In the last column the 95%-confidence intervals are given.

Areas with mean ground deposition of ^{137}Cs	Exposed birth cohort		Unexposed birth cohorts			
	Number	Incidence rate*	Number	Incidence rate*	Rate ratio	95% CI
< 6 kBq m^{-2}	29	41.6	96	22.7	1.84	1.21-2.78
6 - 10 kBq m^{-2}	1	8.9	24	35.1	0.26	0.03-1.89
>10 kBq m^{-2}	5	41.5	23	32.1	1.29	0.49-3.40
total West Germany	35	37.7	143	25.4	1.48	1.02-2.15

* per 10^6 new-born

Radiation exposure after the Chernobyl accident showed quite steep dose rate gradients with time in West Germany. Therefore, a potential excess of infant leukaemia due to intrauterine radiation exposure should be more clearly marked in times of higher exposure. In order to study a potential time trend, the birth cohort B is divided into two parts. The subcohorts comprise children born in the 9 months from 01.07.1986 to 31.03.1987 and from 01.04.1987 to 31.12.1987, respectively. The results of the corresponding calculations showed a trend which was opposite to the hypothesis: The rate ratio for the first subcohort of B in comparison to cohorts A and C is smaller (1.29, 95%-CI 0.76-2.20, based on 15 cases in the exposed time interval) than the corresponding value for the second subcohort (1.67, based on 20 cases in the exposed subcohort).

Discussion

Based on data of the German Childhood Cancer Registry it was analysed whether similar to the observation of Petridou et al. an increase of infant leukaemia for children born after the Chernobyl accident could be shown. Comparable effective dose equivalents resulting from the contamination due to the accident were calculated for children in Greek and parts of West Germany, so that many children in both countries had comparable risks.

The analyses of the German incidence rates are based on a population at risk in the exposed time period which is about six times as large as that in the study of Pertridou et al.. Therefore estimates of a potential risk may be more precise.

Similar to the results of Petridou et al. the analyses of the West German data showed an increase in the incidence of infant leukaemia for children of a birth cohort born after the Chernobyl accident in comparison to two unexposed cohorts. However, the highest rate ratios were observed in regions of lowest contamination and a partition of the „exposed" birth cohort in an early and a late subset showed higher rate ratios in the less exposed late subset. These findings do not support a causal relationship between intrauterine exposure and the occurrence of infant leukaemia.

Although the observed increase of the incidence of infant leukaemia cannot be attributed to an *in utero* exposure to ionising radiation originating from the Chernobyl accident, it may still be explained as an effect of the accident. Possibly, the accident has caused an increased diagnostic awareness of physicians who may have diagnosed the disease somewhat earlier. A similar mechanism was also discussed in relation to an incidence peak of neuroblastoma following the Chernobyl accident [10].

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