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Dosimetry Support of the Ukrainian-American Case-Control Study of Leukemia and Related Disorders among Chornobyl Cleanup Workers

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Abstract

This paper describes dose reconstruction for a joint Ukrainian-American case-control study of leukemia that was conducted in a cohort of 110,645 male Ukrainian cleanup workers of the Chornobyl (Chernobyl) accident, who were exposed to various radiation doses over the 1986-1990 time period. Individual bone-marrow doses due to external irradiation along with respective uncertainty distributions were calculated for 1,000 study subjects using the RADRUE method, which employed personal cleanup history data collected in the course of an interview with the subject himself if he was alive or with two proxies if he was deceased. The central estimates of the bone-marrow dose distributions range from 3.7×10^{-5} to 3,260 mGy, with an arithmetic mean of 92 mGy. The uncertainties in the individual stochastic dose estimates can be approximated by lognormal distributions; the average geometric standard deviation is 2.0.

Keywords

Chernobyl; cleanup workers; radiation; bone marrow; dose; leukemia

Introduction

The accident at the Chornobyl (Chernobyl) nuclear power plant (NPP), which occurred on April 26, 1986, resulted in the destruction of the reactor unit #4 and severe damage to the reactor building as well as heavy radioactive contamination of the environment.

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Immediately after the accident, increasing numbers of responders and emergency workers (police, military, firefighters, civilian specialists, etc.), usually called cleanup workers or liquidators, were engaged in activities associated with high exposure to external irradiation. The operation officially called “liquidation of the consequences of the accident” technically lasted till the end of 1990, so that all workers who worked within the restricted (30-km) zone until the end of 1990 are designated ‘liquidators’. The total number of cleanup workers from all former Soviet Union republics was about 540,000; in Ukraine, more than 300,000 persons have the official status of “liquidator” (Chumak and Bakhanova 2011), of whom 229,219 are registered in the Chornobyl State Registry of Ukraine (SRU) (UNSCEAR 2011).

This large population of workers with radiation exposures delivered in a protracted manner has prompted several epidemiological studies, including the joint Ukrainian-American case-control study of leukemia and other hematological cancers. This study was conducted in a cohort of 110,645 male Ukrainian workers who were registered in the SRU, resided at the time of registration in Kyiv City or in any one of five study regions (Cherkasy, Chernihiv, Dnipropetrovsk, Kharkiv, and Kyiv Oblasts), and were 18–62 years old during cleanup activities at the Chornobyl NPP in 1986–1990. The epidemiological analysis covered cases of various forms of leukemia diagnosed between 1986 and 2006 (Zablotska et al. 2013). The study consisted of two phases. Phase 1 included 71 cases diagnosed in 1986–2000 while Phase 2 covered 66 leukemia cases diagnosed in 2001–2006. The numbers of controls were 501 in Phase 1 and 362 in Phase 2. Epidemiological findings of Phase 1 were presented by Romanenko et al. (2008), while epidemiological results of the Phases 1 and 2 combined analysis were recently published by Zablotska et al. (2013). This paper describes the manner in which the bone-marrow dose estimates were obtained in Phases 1 and 2 of the study.

Methods

The population of Ukrainian cleanup workers was extremely heterogeneous and encompassed a broad variety of occupational groups (military, nuclear workers and specialists, construction workers, support staff), affiliations (different ministries and organizations), types of work performed (decontamination, repair and maintenance of NPP equipment, construction, scientific support and research, supply and logistics, etc.), and locations of workplace (from roofs of the reactor building to remote locations at the edge of the restricted “30-km zone” and beyond up to 70 km from the reactor site). The cleanup workers mainly received doses from external irradiation, which were monitored by means of personal dosimeters, group dosimetry (one personal dosimeter per group of liquidators), or group assessment (when the same value of “individual” dose was assigned to all members of a group who performed the same task, based on a dose assessment carried out prior to the implementation of the task). The results, were called “official doses”, and were recorded in the SRU when they became available. The percentage of cohort members with official doses in the SRU varies from 29% for those exposed in 1986 (when radiation exposures were highest) to 70% for later periods.

The reliability and validity of the official doses depend on the time period considered and the type of work performed (Ilyin 1995; Chumak 2007; Bouville and Kryuchkov 2014).

Reviews of official doses have revealed their possible bias and low accuracy, to degrees strongly correlated with the affiliation of the cleanup worker and, therefore, the type of dosimetric monitoring received at the time of cleanup (Chumak 2007). For instance, military liquidators, who account for about 50% of the cohort, have the most imprecise and biased dosimetric data (Chumak et al. 2008, Skaletsky 2007). Atomic workers in general had adequate dosimetric monitoring, although it is not comprehensive for the early cleanup period (from the time of the accident until mid-June 1986), primarily due to failure of routine dosimetric monitoring and partial loss of recorded data.

For the purposes of the case-control epidemiological study, the conclusion was made that the application of official dose records (ODR), as found in the SRU, to assign individual doses to the Ukrainian liquidators was not defensible. Therefore, a new approach to dose estimation had to be used to estimate individual doses from external irradiation to all study subjects. A method called RADRUE (Realistic Analytical Dose Reconstruction with Uncertainty Estimation) was developed and extensively tested by an international group of experts (Kryuchkov et al. 2009). The main idea of dose calculation by the RADRUE technique is very straightforward: it is based on the calculation of external dose as a product of the exposure rate and irradiation time, with shielding taken into account. It should be noted that at the time of the Chernobyl cleanup work in 1986–1990, all the radiation measurement devices used for monitoring were calibrated in terms of exposure rate ($R \text{ h}^{-1}$, mR h^{-1}) and it is therefore convenient to use exposure rates (in those units) in the retrospective dose calculations. Mathematically the external dose D (mGy) absorbed in red bone marrow during a liquidator's trip can be inferred from the summation of the products of exposure rate, duration, and shielding factor during each time interval when the person was exposed to radiation:

$$D = \sum_{i=1}^n C_i P[x(t_i), y(t_i), t_i] \Delta t_i L_i,$$

where C_i is the conversion coefficient from exposure to bone-marrow dose (mGy h^{-1} per mR h^{-1}); $P[x(t_i), y(t_i), t_i]$ is the exposure rate (mR h^{-1}) at the location $[x(t_i), y(t_i)]$ and at time t_i , where and when the liquidator was present; Δt_i is the time interval during which the liquidator performed a relatively brief but complete task; L_i is the shielding factor for the working conditions (sometimes called “location factor”); and n is the number of (usually unequal) time intervals considered in the calculation. Any time that an individual spent working, traveling, sleeping, or resting within the 70-km zone was included in the analysis.

The RADRUE method includes both point estimates of dose and the uncertainties in the dose estimates caused by uncertainties of the input parameters, estimated from 10,000 dose realizations for each cleanup worker. Details of the RADRUE method can be found elsewhere (Kryuchkov et al. 2009).

In brief, implementation of the RADRUE method requires information on the work histories of the liquidators, exposure rates at the locations visited by the liquidators, shielding factors for devices that reduced the liquidators' exposures, and appropriate exposure-to-dose

conversion coefficients, which depend on workplace environment. Information about a liquidator's work history was obtained from personal interviews with use of a standard questionnaire, complemented with maps, photographs and other information designed to help the liquidator remember his activities in the Chornobyl area. The interviewers were handpicked among liquidators, preferably dosimetrists at the time of cleanup. This approach facilitated the contacts between the study subjects and the interviewers both being Chornobyl veterans. In addition, good knowledge of the cleanup routines, topography, and history of the Chornobyl cleanup helped to collect essential information regarding the personal histories of the study subjects.

The questionnaire included detailed questions regarding (a) liquidator's routes to and from his work place(s) in the 30-km zone, (b) details about the work he performed, including duration and special shielding from radiation, and (c) locations of residence and rest quarters during the mission. In the case of deceased, or otherwise incapacitated subjects, proxies were interviewed: (1) a next-of-kin (usually the spouse or a grown-up child), who provided information on personal and health data of the subject, and also gave the names of colleagues, who may have worked together with the subject during his cleanup mission, and (2) one (or several, if work periods overlapped only partially) identified colleague(s), in order to retrieve information on the cleanup activities that were carried out by the subject.

Responses to the questionnaires were reviewed by an expert-dosimetrist to identify and account for (or clarify) possible inconsistencies. The work history of the liquidator that was obtained by means of the questionnaire was combined with the exposure rates, shielding factors, and exposure-to-bone-marrow-dose conversion coefficients at the locations visited by the liquidator to derive his bone-marrow dose estimate and its uncertainty. However, RADRUE takes into account only the so-called 'intrinsic' component of uncertainty in the dose estimate (related to the uncertainties in the dose-rate data due to interpolation and extrapolation and uncertainty of the expert-dosimetrist's decisions while converting the questionnaire data into personal histories with RADRUE data format), while uncertainty of recollection and reporting of the events related to the cleanup activities of the subject (so-called 'human factor uncertainty') is not quantified (Kryuchkov et al. 2009). Estimation of the human factor uncertainty remains topical and is the subject of separate ongoing study.

RADRUE was used to estimate the bone-marrow doses and intrinsic uncertainties for all subjects of Phase 1 and Phase 2. There was no substantial difference in the methodology used in Phases 1 and 2, except for the quality control procedures:

- In Phase 1, the dosimetric interviews were repeated by another interviewer for 10% of randomly selected subjects. Similarly 10% of the questionnaires were reanalyzed by a different expert-dosimetrist. In addition, the quality of the interviews was reviewed by a senior interviewer while an expert dosimetrist evaluated the completeness and quality of the information collected in the course of the interview setting ranks to each of the processed questionnaires. Extensive details of this approach are given in (Chumak et al. 2008).
- In Phase 2, interviews were not repeated because of stringent bioethical considerations. Quality control procedures during Phase 2 focused on the independent

inspection of all processed histories by a third party expert-dosimetrist (i.e., the developer of the RADRUE code, based in Moscow). Some consistency tests were done in automated mode using specially devised routines, while conclusive inspection was done by hand. Mistakes and deficiencies were communicated to the expert-dosimetrist in Kyiv and necessary corrections were introduced into data files. This system of triple check (expert-dosimetrist's self-check, automated consistency check, and manual final inspection) proved to be quite efficient.

In summary, the dose calculation methods used during Phases 1 and 2 are completely compatible, so that the bone-marrow dose estimates and their associated intrinsic uncertainties that were obtained during the two phases of the study are entirely consistent.

Results and Discussion

During Phase 1 individual bone-marrow doses to 572 study subjects (71 cases and 501 controls) were reconstructed using the RADRUE method. The same dosimetry method was used to calculate the bone-marrow doses received by the 428 subjects (66 cases and 362 controls) of Phase 2. For the approximately 14% of Phase 1 and 8% of Phase 2 study subjects who were deceased, their bone-marrow doses were estimated based on interviews of proxies (colleagues in the Chornobyl 30-km zone). Table 1 summarizes the mean bone-marrow doses and their ranges for the cases and controls of Phases 1 and 2. All doses were reconstructed in a blind manner, i.e. the status of the subject (case or control) was unknown to the dosimetrists. This information was only made available after the completion of the epidemiological analysis (Zablotska et al 2013).

Dose distributions (arithmetic means of 10,000 stochastic dose values) are presented in Table 2. It can be seen that the dose distributions among the subjects of both Phase 1 and 2 are extremely broad covering seven and five orders of magnitude, respectively. The lowest dose of 0.037 μGy was received by a person who briefly passed the contaminated area onboard the radiation reconnaissance airplane (Chumak et al. 2008). When this atypical 'liquidator' exposure itinerary is excluded, both dose distributions have ranges of about five orders of magnitude. The maximum dose values in both study phases, taking into account uncertainties in dose estimates, are comparable (3,260 and 1,763 mGy) and were received by controls.

The summary of dosimetric parameters for both Phase 1 and 2 subjects, broken down according to their affiliation, is presented in Table 3. It can be seen that for the most populated and relatively uniform categories of cleanup workers (military and early liquidators), the parameters of the dose distribution are quite similar. For less abundant categories of workers, the parameters of the dose distribution are inconsistent and, therefore, do not demonstrate any kind of robustness. This is also true for the second most populated but extremely heterogeneous category of Sent on Mission to the 30-km zone: their dose estimates are very variable, although their intrinsic uncertainty, expressed in terms of geometric standard deviation (GSD) is relatively low, about 2.0, because of the usually short and simple itineraries of the liquidators in this category. On average, they spent 75 days in the Chornobyl 30-km zone, compared to 69 and 501 days for the military and ChNPP personnel, respectively.

Table 4 shows the percentages of liquidators who worked in the Chornobyl 30-km zone in different years. As can be seen from the table, the percentages are similar between Phase 1 and Phase 2. This means that observed differences in mean doses for all study subjects between Phase 1 and 2 (Table 3) could be due to variability of the dose rates in the locations of their work rather than due to any potential bias from non-random selection of the subjects. This statement is based on the fact that the dose rates within the 30-km zone varied by 6 orders of magnitude (Kryuchkov et al. 2012), depending upon specific location and time elapsed since the accident.

It should be noted that other methods of dose estimating were also used in epidemiological studies among Chornobyl liquidators. Reconstruction of individual doses due to external gamma-irradiation for the subjects of Ukrainian-American Chornobyl Ocular Study (UACOS) (Worgul et al. 2007) was based on retrospective assessment of reliability and possible bias of ODRs and their recalibration against EPR dosimetry with tooth enamel in this case (Chumak et al. 2007). Results suggested that ODRs of military liquidators overestimate EPR doses by a factor of 2.2, and that ODRs should be adjusted (recalibrated) prior to use in risk analysis.

Official doses of Russian liquidators were broadly used in the risk analyses for various endpoints (leukemia, thyroid, cerebrovascular diseases) conducted in the cohort of cleanup workers registered in the Russian National Medical Dosimetric Registry (Ivanov et al. 2006, 2008, 2012). Despite some reservations on the applicability of these dosimetric data (Illyin 1995, Pitkevich 1996), ODRs from the Russian registry were used without modification. This application could be justified in view of the large proportion of professional atomic workers possessing relatively higher quality of ODRs; however, interpretation of results should be cautious because of the unreliability and bias of ODRs for military liquidators (Chumak et al. 2008, Skaletsky 2007).

The RADRUE method also was used for dose assessment in the study of hematological malignancies in cohorts of cleanup workers from Belarus, Russian Federation and Baltic countries that provided (Kesminiene et al. 2008) risk estimates quite compatible to those obtained in Ukrainian-American study. Both studies had a case-control design, included alive and deceased cases of leukemia, and used the same questionnaire that had been developed jointly. In view of similar study designs, it was decided to use RADRUE as a common dosimetry method. Although RADRUE was applied in both studies, its application differed in some aspects. For example, in the Belarus-Russian-Baltic study, where subjects were distributed over a large territory including several countries, local interviewer teams were composed of persons with medical background (nurses as a rule) who had to be trained about the details of the cleanup activities related to the Chornobyl accident – contrary to Ukrainian-American study interviewers, who were well informed Chornobyl dosimetrists.

Obviously, RADRUE method has some limitations. The primary limitation of RADRUE is that the resulting dose estimates may be fraught with large ‘human factor’ uncertainties that are currently the subject of a separate study. A second limitation is the ‘intrinsic’ uncertainty related to imperfect knowledge of the exposure rates at the locations visited by the clean-up worker at specific times. However, as shown in a series of validation exercises described in

Kryuchkov et al. (2009), these ‘intrinsic’ uncertainties do not appear to be large. Also, in the absence of reliable dose records obtained by physical or biological techniques, RADRUE seems to be the method of choice because it can be applied to any clean-up worker, whether alive or deceased, and because it is conceptually very simple to analyze its results.

Conclusions

Individual bone-marrow doses were estimated in the framework of a case-control study of leukemia among Ukrainian cleanup workers of the Chernobyl accident, who were exposed to external irradiation in 1986-1990. The group of subjects consisted of 1,000 Ukrainian liquidators, including 137 leukemia cases and 863 randomly assigned controls, matched by age and region of residence. The study was conducted in two phases: Phase 1 included 71 cases diagnosed in 1986-2000 while Phase 2 covered 66 leukemia cases diagnosed in 2001-2006. All individual doses along with respective uncertainty distributions were calculated using the same RADRUE method, which employed personal cleanup history data collected in the course of an interview with the subject himself if he was alive or with proxies if he was deceased. The process of RADRUE dose estimation relies on high quality interviews (provided by training of interviewers with the appropriate professional background as well as a series of quality-control procedures), a proper interpretation of the questionnaire data, which was performed by an extremely knowledgeable expert-dosimetrist, and calculation (including stochastic modeling) of individual dose by means of a specialized RADRUE software. Application of this methodology in Phases 1 and 2 of the leukemia study provided consistent results for the respective categories of liquidators and yielded dose estimates that were used in the risk analysis. The proposed methodology could be applied in other epidemiological studies, either related to Chernobyl cohorts or to other circumstances in which individual doses need to be reconstructed retrospectively.

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Table 1 Categories of cleanup workers: numbers and bone-marrow dose estimates.^a

Category	Number of subjects	Bone-marrow dose (mGy)		
		Arithmetic mean	Range	
			Min	Max
Cases (Phase 1/Phase 2)	71 / 66	150 / 120	3.7×10^{-5} / 0.031	3170 / 1546
Controls (Phase 1/Phase 2)	501 / 362	78 / 96	0.007 / 0.005	3260 / 1763
Deceased subjects (Phase 1/Phase2)	78/ 34	126 / 151	3.7×10^{-5} / 0.26	3170 / 1063
Alive subjects (Phase 1/ Phase 2)	494 / 394	81 / 95	0.007 / 0.005	3260 / 1763

^aData are presented for both phases as Phase 1 / Phase 2

Table 2

Distribution of the arithmetic means of 10,000 individual stochastic bone-marrow dose estimates for the 1,000 study subjects.

Interval of the means of stochastic bone-marrow doses (mGy)	Phase 1		Phase 2		Entire study	
	N	%	N	%	N	%
<0.01	4	0.7	1	0.2	5	0.5
0.01 – 0.1	12	2.1	5	1.2	17	1.7
0.1 – 1.0	75	13.1	59	13.8	134	13.4
1.0 – 10	156	27.3	106	24.8	262	26.2
10 – 100	203	35.5	149	34.8	352	35.2
100 – 1000	118	20.6	103	24.1	221	22.1
1000	4	0.7	5	1.2	9	0.9
Entire study	572	100	428	100	1000	100

Table 3

Parameters of dose distributions and estimates of intrinsic uncertainty for Phase 1 and Phase 2^a subjects.

Name of category	Number of subjects	Arithmetic mean of stochastic bone-marrow doses (mGy)			Mean GSD
		Mean	Minimum	Maximum	
Witnesses of the accident	3 / 5	160 / 208	38 / 4.7	377 / 840	2.3 / 2.3
Victims of the accident	2 / 0	2878 / -	2584 / -	3171 / -	3.4 / -
Early liquidators	66 / 47	97 / 84	0.5 / 0.2	1014 / 630	2.0 / 2.2
ChNPP personnel	9 / 1	234 / 121	23 / 120	966 / 120	1.7 / 3.3
Sent to assist the ChNPP staff	1 / 3	44 / 103	44 / 1.9	44 / 205	1.9 / 1.6
Staff of AC-605	5 / 4	110 / 272	1 / 16	295 / 483	2.0 / 1.7
Staff of Kurchatov Institute	2 / 2	129 / 244	15 / 150	242 / 337	2.7 / 2.4
Military liquidators	220 / 157	71 / 89	0.01 / 0.2	554 / 831	2.1 / 2.1
Sent on Mission	181 / 137	30 / 50	3.7×10 ⁻⁵ / 0.005	694 / 1444	2.0 / 2.0
Staff of Combinat	4 / 3	16 / 126	3 / 18	45 / 240	1.7 / 2.0
Mixed ^b	79 / 69	164 / 206	0.4 / 0.5	3260 / 1763	1.7 / 1.8
All	572 / 428	87 / 99	3.7×10 ⁻⁵ / 0.005	3260 / 1763	2.0 / 2.0
Total	1000	92	3.7×10 ⁻⁵	3260	2.0

^a As in Table 1, the data for the phases are separated: Phase 1 / Phase 2.

^b Mixed refers to a set of liquidators who worked at the Chernobyl site several times as members of different categories.

Table 4 Distribution of subjects by years of their cleanup activities.^a

Year of beginning of work	Year of completion of work					
	1986	1987	1988	1989	1990	All
1986	51% / 54%	9% / 10%	3% / 3%	1.9% / 1.4%	6.3% / 7.7%	71% / 76%
1987	-	11% / 10%	3% / 4%	0.7% / 0.9%	0.9% / 1.2%	15% / 16%
1988	-	-	8% / 4%	0.7% / 1.2%	0.0% / 0.2%	9% / 5%
1989	-	-	-	3.1% / 1.9%	0.5% / 0.7%	4% / 3%
1990	-	-	-	-	0.9% / 0.5%	0.9% / 0.5%
1986-1990	51% / 54%	20% / 20%	14% / 11%	6% / 5%	9% / 10%	100% / 100%

^a As in Table 1, the data for the phases are separated: Phase 1 / Phase 2.