Radiation Epidemiological Analysis of Late Effects of Population Exposure at Northern Part of East Ural Radioactive Trace

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Population residing in the northern part of the Chelyabinsk oblast and the southeastern part of the Sverdlovsk oblast of Russia affected to accidental exposure since 1957. The territory (East Ural Radioactive Trace - EURT) was contaminated after explosion of container with highly radioactive wastes at the Mayak Production Association [1,2]. Studies of health effects of exposure in the southern, head part of EURT are conducted in the Ural Research and Practical Center of Radiation Medicine (URPCRM). In the 1990s URPCRM formed a cohort of EURT within Chelyabinsk oblast (14,500 cases and 19,400 external controls). The cohort was followed in 1957-1987 and the results of the study are discussed by Crestinina et al. [3]. First results of study on exposure late health effects among rural population in the northern part of the EURT are presented in this paper.

Collection of archive data on causes of death and development of a register

At the first stage of the study the archive data were collected on causes of death among rural population of the Kamensky district, Sverdlovsk Oblast, within the northern part of EURT. Cases of deaths in rural settlements of the area under study which death certificates available in archives of the civilian registry offices of the Sverdlovsk oblast were chosen. The following archive information was copied out and entered into the study database: death certificate ID, sex, dates of death and birth, place of birth, last place and duration of residence and the cause of death. When entering the obtained data into the database additional coding of causes of death according to the International Classification of Diseases (ICD-X) was performed. At present, the cohort includes 15,685 entries (7,749 men and 7,936 women) on deceased within a period 1957-2000. According to demographic statistics [1] the total population of rural settlements in EURT-affected area of the Kamensky district in 1959 was 34 thousand people. The study cohort also includes 3,029 cases migrated to study area after 1957. The analysis showed that 2,660 people migrated from rural areas of the neighboring Sverdlovsk, Chelyabinsk and Kurgan oblasts, and 369 were burn in remote settlements.

General characteristics of death causes

The study cohort were classified by groups of causes of death. Figure 1 shows contribution of three main classes of death causes in the total mortality depending on the age of death: 1) circulatory diseases (class IX, 100-199), 2) traumas and poisonings (class XIX, S00-T98), 3) malignancies (class II, C00-D48).

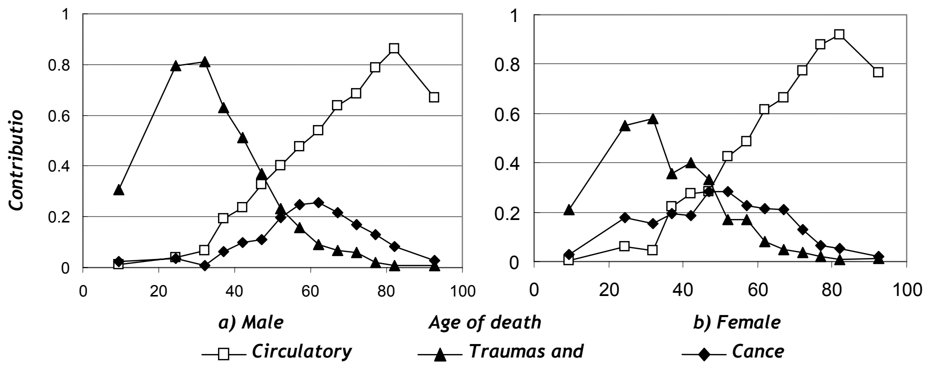


Fig. 1. Contribution of three main causes of death to total

The primary cause of death for young people (<30 years of age) is traumas and poisonings. Number of deaths circulatory diseases increases in the age group of 30-40 and older. Relative contribution of malignancies peaks up at 50-60 years and then declines. The cohort includes 2,118 cases of cancer causes of death including 937 cases of gastrointestinal tract cancer (C15-C26) and 516 cases of respiratory organs cancers.

Dose assessment

Dose assessment was based on Guidelines 2.6.1.024-95 "Reconstruction of doses accumulated by residents of the river Techa basin and the area affected by the accident at the "Mayak" plant in 1957". Methods of dose reconstruction for EURT-exposed population are based on vast experimental materials of research department "Mayak" [4]. According to the approved estimation method the radionuclide composition of depositions for the whole EURT territory is considered invariable ($^{90}Sr+^{90}Y$ - 5.4%, $^{95}Zr+^{95}Nb$ - 24.9%, $^{144}Ce+^{144}Pr$ - 66%, $^{106}Ru+^{106}Rh$ - 3.7%, ^{137}Cs - 0.036%).

The main factors contributing to exposure of EURT affected population include:

- *external exposure from the radioactive cloud;*
- *external exposure due to radioactive contamination of territory;*
- *inhalation of radionuclides from the radioactive cloud;*
- *internal exposure of organs and tissues due to ingestion of contaminated food and water.*

Assessment of external exposure is based on dose coefficients relating the dose to the location in the radiation field. When estimating internal doses, intake of radionuclides during the whole period under study is considered. For the early phase of the accident the internal exposure related to inhalation of radionuclides is assessed on the assumption that the median activity aerodynamic diameter of radioactive aerosols was 1 μm. Dose coefficients recommended by ICRP were applied to estimate doses from inhalation and ingestion.

Dose estimation is based on the consideration as follows: external and internal dose rate is in proportion to the initial (in 1957) ^{90}Sr surface contamination. Levels of initial radioactive contamination of EURT area are taken in agreement with the State EURT Map considering contamination of both settlements and agricultural lands. Table 1 shows distribution of cohort by levels of initial ^{90}Sr surface contamination. The maximum ^{90}Sr surface contamination of a settlement and agricultural land were 160 and 190 kBq/m^2 (5.2 and 4.2 Ci/km^2), respectively.

Table 1. Distribution of cohort by levels of initial ^{90}Sr surface contamination.

^{90}Sr surface contamination, Bq/m^2 (Ci/km^2)	Distribution by levels of settlement contamination	Distribution by levels of agricultural lands contamination
0-11 (0-0.3)	68%	67%
11-37 (0.3-1)	16%	14%
37-74 (1-2)	7%	8%
>74 (>2)	9%	11%

Accumulated doses were estimated for members of cohort depending on sex, age at first exposure, duration of exposure and level of initial ^{90}Sr surface contamination. Results of individual dose reconstruction along with the epidemiologic cohort compose the epidemiologic dosimetric register of deceased at northern part of EURT (Register). Table 2 shows mean and maximum values of the accumulated doses of different organs and tissues due to exposure at EURT in Register. The mean accumulated effective dose is 12 mSv, whereas the mean effective doses within subgroups of least (2/3 of Register) and most (1/3 of Register) exposed members of Register are 1 and 33 mSv, respectively.

Table 2. Register average and maximum organs and tissues accumulated doses due to exposure at EURT, mGy

Organs and tissues	Average dose	Maximum value
Bone surface	61	1545
Red bone marrow	26	440
Upper part of large intestine	34	549
Lower part of large intestine	19	215
Small intestine	6.0	93
Stomach	2.2	29
Liver	1.9	22
Lungs	1.6	58
Upper airways	0.89	11
Female genital organs	0.87	7.0
Urinary bladder	0.83	7.2
Pancreas	0.67	5.8
Kidneys	0.64	5.7
Thyroid gland	0.62	5.6
Esophagus	0.61	5.5
Male genital organs	0.58	5.0
Mammary gland	0.29	5.4

Selection of the control group and estimation of background solid cancer mortality

Taking into account insignificant accidental exposure within considerable part of Register, the cohort was divided into groups of low (10,726) and high exposure (4,959). The division was based on the following criteria: effective dose value, colon dose (reference organ), age at first exposure, duration of exposure. The low and high exposure groups were utilized as the internal control and case or critical group of the radiation epidemiological study respectively. The advantage of the internal control group as a reference group in an epidemiologic study is supposed homogeneity of case and control groups considering possible confounders, while disadvantage is limited size. Mean colon doses in the internal control and case groups were 3 and 80 mGy, respectively.

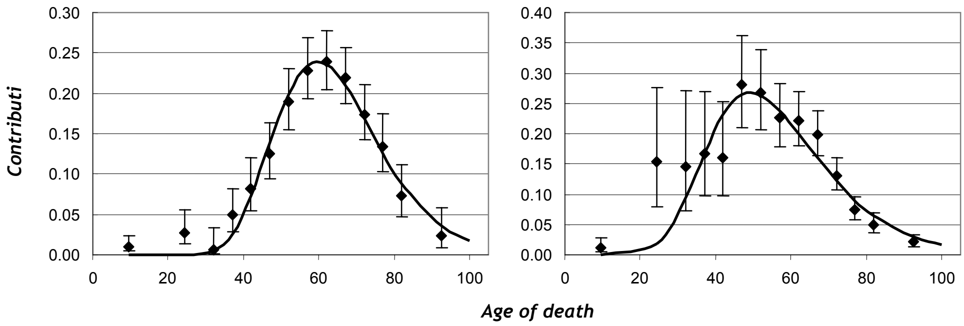
Relative contribution of solid cancers as a cause of death to all-cause mortality in the internal control group is estimated. Cancer of the eye (C69), brain (C70, C71), gastrointestinal tract (C15-C26), skin (C43, C44), mammary gland (C50), urinary tract (C64-C68), male genital organs (C60-63), female genital organs (C51-C58), respiratory organs (C30, C32-C34, C39), thyroid gland (C73), and unspecified sites have been referred to the group of solid cancers. Relative contribution of solid cancers in the internal control group was applied to estimate the expected background mortality due to solid cancers in the critical group. The background relative contribution has been estimated with adjustment for sex and age of death (stratified by 14 age groups: 0-19, 20-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84, and 85-100). Figure 2 demonstrates the relative contribution of solid cancers to all-cause mortality depending on age of death for time period 1957-2000 in control group.

The relationship between the background relative contribution of solid cancers to total mortality and age of death is well fitted by the following function:

$$\hat{I}\,\hat{A}(a) = X_1 \exp\left(X_2 \log\left(\frac{a}{60}\right) - X_3 \log\left(\frac{a}{60}\right)^2 \right), \qquad (1)$$

where, a - age at death, and X_1, X_2, X_3 - model parameters.

Taking into account a global tendency of cancer mortality increasing the model (1) was applied for four time periods 1957-1966, 1967-1976, 1977-1986, and 1987-2000. Thus the background relative contribution of solid cancers to total mortality standardized by sex, age and date for the region under study was obtained. The results of model (1) parameters estimation are provided in Table 3.



a) Male b) Female

Fig. 2. Relative contribution of solid cancers to all-cause mortality registered in 1957-2000 in control group (with 95 % confidence intervals).

Table 3. Model (1) parameters estimation by sex and four time periods

Time period	X_1	X_2	X_3	R^2
Male				
1958-1966	0.2407	-0.1755	8.421	0.83
1967-1976	0.2329	-0.2026	11.60	0.76
1977-1986	0.2361	0.05864	11.14	0.94
1987-2000	0.2411	-0.2197	9.273	0.96
Female				
1958-1966	0.4250	-1.965	8.409	0.63

1967-1976	0.2064	-2.153	7.115	0.76
1977-1986	0.2007	-1.757	9.807	0.79
1987-2000	0.1867	-2.324	4.046	0.85

RESULTS AND DISCUSSION

Expected number solid cancers deaths in the critical group of the register was estimated and compared with observed number through a cross-table. The cross-table includes data on the total number of deaths from all causes, the expected and the observed number of deaths from solid cancers depending on sex, the year (1957-2000), age of death (14 age groups), age at first exposure (in 1957, for the categories of <20, 20-39, 40-60, >60 and of those born after 1957). Shortened cross-table with additional categorization by four time period, three groups of age of death and five groups of age at first exposure is presented in Table 4. Value of mean colon dose due to accidental EURT exposure within each subgroup is also included to Table 4.

The register contains information about 691 cases of death from solid cancers in critical group while the expected number of solid cancer deaths is 626. Observed 65 excess deaths from solid cancer could be attributed to accidental EURT exposure. Considering 90% confidence interval from 18 to 144 deaths this excess is statistically significant. Relative risk of radiation induced solid cancers (RR) is 1.1 and excess relative risk normalized to colon dose (ERR) is 1.3 Gy^{-1} (90% CI 0.36-2.9 Gy^{-1}).

Excess cancer mortality in comparison with the external control group was also noted in the EURT cohort formed and followed during 30 years by URPCRM [3]. Cancer mortality per 100 000 population was 162.6 (95% CI, 149.3 - 176.8) and 137.1 (95% CI, 125.9 - 149.0) in the study cohort and external control group, respectively, consequently RR=1.19. Differences in RR values for the northern and south parts of EURT observed in two studies might be explained by different doses of accidental exposure. Unfortunately, direct comparisons of ERR normalized to dose are impossible due to some differences in approaches to dose assessment and applying different reference doses (dose of external exposure and a red bone marrow dose were used in the URPCRM study).

According to radiation induced cancers risk assessments using linear no-threshold models of radiation carcinogenesis the expected total number of radiation induced solid cancer deaths in the EURT within the Sverdlovsk oblast (population 300 000) ranges from 94 to 240 by the year 2002 [5,6]. While the critical group of our study matches to most exposed population of the region the results of the study are in general agreement with the previous radiation risk assessments.

Table 4. Shortened cross-table (male/female).

Time period	Age of death	Age in 1957	Total deaths	Observed solid cancer deaths	Expected solid cancer deaths	Mean colon dose, Gy
1958-1962	0-40	<20	15/23	0/0	0/0	0.104/0.094
		20-39	53/17	3/2	1/1.1	0.078/0.104
	40-60	20-39	1/5	0/3	0/1.5	0.082/0.063
		40-60	48/46	12/20	9/20	0.093/0.093
	>60	40-60	21/11	5/4	5/4.3	0.085/0.065
		>60	145/207	18/24	21/36	0.086/0.093
1963-1975	0-40	<20	82/30	3/3	0/0.3	0.095/0.08
		20-39	99/32	5/5	1/3.1	0.089/0.077
	40-60	20-39	119/58	19/11	13/14	0.087/0.078

		40-60	97/61	29/19	21/20	0.09/0.079
	>60	40-60	239/260	63/61	46/43	0.086/0.079
		>60	191/414	15/30	19/32	0.095/0.086
1976-1988	0-40	Unborn	3/0	0/0	0/0	0.037/-
		<20	74/28	1/3	0/1.2	0.13/0.13
		20-39	2/1	0/0	0/0.1	0.022/0.017
	40-60	<20	18/4	5/1	2/0.6	0.067/0.114
		20-39	196/92	32/16	31/19	0.07/0.077
	>60	20-39	48/58	16/12	11/10	0.076/0.07
		40-60	245/481	34/57	39/44	0.079/0.068
		>60	53/177	1/8	2/4.2	0.08/0.078
1989-2000	0-40	Unborn	3/1	0/0	0/0.2	0.015/0.004
		<20	17/2	2/0	0/0.4	0.109/0.067
	40-60	<20	130/30	16/10	21/7.2	0.087/0.105
		20-39	47/18	6/6	11/3.8	0.066/0.082
	>60	20-39	248/250	52/38	50/30	0.077/0.067
		40-60	95/348	10/11	9/18	0.076/0.062

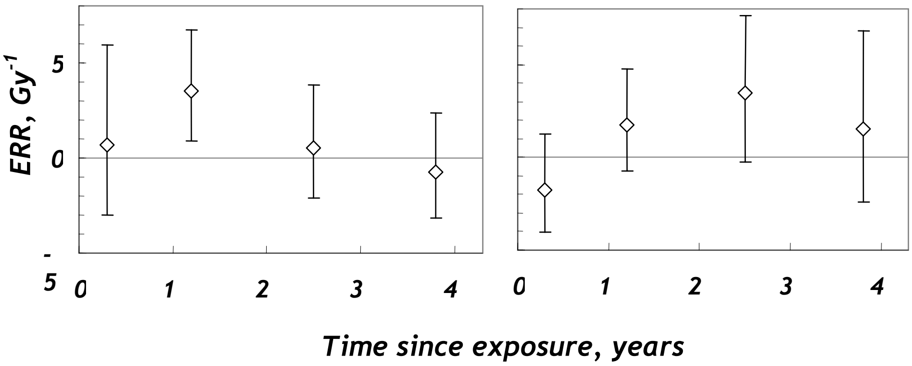
Results of recent radiation epidemiological studies demonstrate a substantial dependence of radiation risk on sex and various time and age factors. For example, in the Hiroshima and Nagasaki cohort ERR declined with the increase in age at exposure and attained age [7]; in the cohort of uranium miners risk declined with the time since exposure [8]. Therefore, we carried out a detailed analysis to establish the relationship between the risk of death from radiation-induced solid cancers and different temporal and age factors in the register under study.

Time since exposure. Three time intervals covering the period 1963-2000 and corresponding to 6-18, 19-31, 32-43 years after first exposure in 1957 were studied. The first 5-year interval 1957-1962 was excluded from the analysis. Table 5 shows an excess number of solid cancer cases and relative risk as compared to the internal control depending on the time since exposure. With such approach the estimated number of radiation induced solid cancers for the period 1963-2000 is 72. Figure 3 demonstrates dependence of EER normalized to colon dose depending on time since exposure. ERR estimated for males decreases with time within period 6-43 years after the accident (p=0.047). Highest statistically significant risk was registered for period 6-18 years after the accident, and by the year 2000 the risk of death from radiation induced solid cancers become negligible. The trend was not statistically significant for female (p=0.44) though the risk of radiation induced cancer diseases considerably reduces by the end of the study period as well.

Table 5. Excess number of solid cancers and relative risk of death from radiation induced cancers in the critical group compared to internal control by time since exposure.

Time period	Male		Female	
	Excess number of solid carcinomas	Relative risk (CI, 90%)	Excess number of solid carcinomas	Relative risk (CI, 90%)
1963-1975	32 (8 - 62)	1.32 (1.08 - 1.61)	16 (-7 - 44)	1.14 (0.94 - 1.39)
1976-1988	4 (-15 - 27)	1.04 (0.83 - 1.32)	19 (-1 - 45)	1.24 (0.98 - 1.58)

1989-2000	-5 (-22 - 17)	0.94 (0.75 - 1.18)	6 (-10 - 27)	1.11 (0.83 - 1.47)



a) Male b) Female

Fig. 3. ERR of radiation induced solid cancers normalized to colon dose vs. time since exposure.

Age at first exposure (in 1957). The dependence of relative risk the age at first exposure was studied for the period of 6-18 years after irradiation (1963-1975) for male and the period of 6-31 (1963-1988) for female. The dependence of radiation risk on the time since exposure appeared to be most significant for these time periods. Data were grouped by age of 0-60 years and >60 years in 1957. A more detailed grouping by age resulted in insufficient number of cases for analysis. Excess number of solid cancers and relative risk values are presented in Table 6 and the dependence of ERR on the age at exposure is shown in Fig.4.

Table 6. Excess number of solid cancers and relative risk of death from radiation induced cancers in the critical group compared to internal control by age at first exposure (in 1957).

Age at first exposure	Male		Female	
	Excess number of solid carcinomas	Relative risk (CI, 90%)	Excess number of solid carcinomas	Relative risk (CI, 90%)
0-60	37 (14 - 66)	1.45 (1.16 - 1.8)	33 (5 - 67)	1.22 (1.03 - 1.43)
>60	-4 (-11 - 6)	0.78 (0.45 - 1.33)	2 (-10 - 19)	1.05 (0.73 - 1.52)

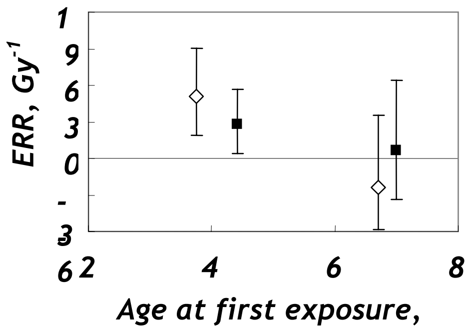


Fig. 4. ERR of radiation induced solid cancers normalized to colon dose vs. age at first exposure (in 1957) for male (rhombuses) and female (squares).

Both Table 6 and Figure 4 demonstrate statistically significant risk of radiation induced solid cancer in the age group under 60 at exposure, whereas in the age group over 60 the risk was not revealed (for both sexes). Decline in ERR with the age at first exposure was statistically significant for male (p=0.047) and not significant for female (p=0.25).

Age of death (attained age). As above, the periods of 6-18 years after radiation exposure (1963-1975) for male and 6-31 (1963-1988) for female were considered. Additionally, the analysis was limited to the age at exposure <60 and the age of death >40. Death cases under 40 were excluded from the analysis since the evaluation of the expected number of deaths from solid cancers for this age range is quite uncertain and possibly underestimated. We considered two ranges of age of death 40-60 and >60. Results of analysis are presented in Table 7 and Figure 5.

Table 7. Excess number of solid cancers and relative risk of death from radiation induced cancers in the critical group compared to internal control by age of death.

Age of death	Male		Female	
	Excess number of solid carcinomas	Relative risk (CI, 90%)	Excess number of solid carcinomas	Relative risk (CI, 90%)
	1.38 (0.96 - 1.99)	13 (-1 - 34)	0.88 (0.64 - 1.23)	-6 (-19 - 12)
	1.37 (0.99 - 1.88)	17 (0 - 41)	1.34 (1.08 - 1.67)	33 (7 - 65)

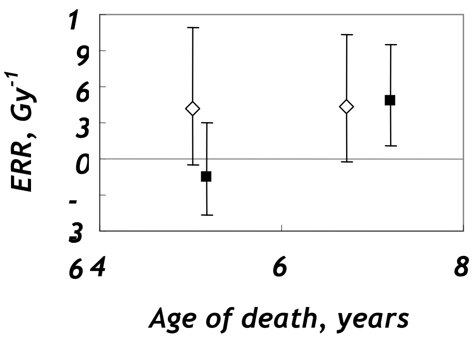


Fig. 5. ERR of radiation induced solid cancers normalized to colon dose vs. age of death for male (rhombuses) and female (squares).

According to the results of analysis the relationship between radiation risk and age of death the ERR for male remains constatnt (p=0.5, with the null hypothesis of "increasing dependence") whereas for female the ERR significantly rises with age (p=0.019). It should be noted that the radiation risk for female older 60 is statistically significant and it is close to 0 in the age group under 60.

Uncertainty assessment

When analyzing results of study of cancer mortality association with accidental EURT radiation exposure in the northern part of EURT based on a created register, the following sources of uncertainty should be taken into consideration:

- possible mistakes in cancer diagnostics and establishing causes of death;

- possible mistakes in documentation and data collection;
- insufficient data of registration archive documents for reconstruction of residence history, absence of individual data on consumed foodstuffs and other characteristics necessary to assess intake of radionuclides and other possible mistakes leading to erroneous estimates of doses;
- non-uniform radioactive contamination of settlements and agricultural lands;
- statistical uncertainty in estimating background relative contribution of solid cancers to total mortality;
- confounder influence (environmental, social and occupational factors);
- other uncertainties.

Though it was impossible to completely avoid the sources of uncertainty, the methods of the study were chosen to minimize a possible impact of the above uncertainties. Thus, approaches applied to estimating confidence intervals for above-mentioned parameters of radiation risk reflect only the statistical errors associated with a probability of event (risk of death from a given cause).

CONCLUSIONS

1. For the period 1958-2000 a statistically significant increase in cancer mortality associated with accidental exposure at EURT area was observed in the critical group of population of the Kamensky district, Sverdlovsk Region (65 cancer deaths among 691 cases, 90% CI 18-144). The finding is in agrrement with the results of a radiation epidemiological study in the southern head part of EURT and model radiation risk assessments. ERR normalized to colon dose is 1.3 Gy^{-1} (90 % CI 0.36-2.9 Gy^{-1}).

2. Analysis of the age and temporal factors influence on solid cancers radiation risk allows conclusion on decline of radiation risk in time. At present considerable number of additional radiation-induced cancer deaths are unlikely to appear. Radiation risk of solid cancers realizes at most during 30 post-accident years. Radiation risk declines with age at first exposure and not appeared in the age group >60. Derived age and time dependencies generally agree with results of other radiation epidemiological studies.

3. Continuation and development of radiation epidemiological study of the population residing in the northern part of EURT is of a certain interest for investigating radiation induced heath effects. The retrospective epidemiologic dosimetric register of the deceased in the northern part of EURT presented here may be considerably expanded by data on Kamenst-Uralsky and other districts of the Sverdlovsk Region contaminated following the accident of 1957 in "Mayak" plant.

5. When continuing the studies based on the register, potential sources of uncertainty should be considered in a more detail and it is necessary to conduct special studies to improve dosimetric methods of dose reconstruction for the territory under study.

The work is supported by Russian Foundation for Basic Research (grant RFBR 05-08-01401-□)

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