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SOUL - Southern Urals Radiation Risk Research

(FP6R-516478)

Final report



*Research and
Innovation*



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SOUTHERN URALS RADIATION RISK RESEARCH (SOUL)

Ionizing radiation is widely used in diagnostic medicine, industry and research. The resulting radiation doses of workers and patients are generally low. Nevertheless, potential health risks from these exposures have to be known for radiation protection purposes. Doses result often from some to many small exposure events. Little is known about health effects from such repeated or protracted exposures

A European-Russian consortium studied health effects of protracted exposures to ionizing radiation in the Project 'Southern Urals Radiation Risk Research (SOUL)'. In Southern Urals, the plutonium production for the atomic weapons of the former Soviet Union was started in the late 1940s by the Mayak Production Association. Mayak workers were exposed to plutonium and gamma radiation. For the workers, extensive data on health status and risk factors like smoking, alcohol consumption, obesity, hypertension and radiation exposures have been gathered.

The Mayak Production Association released liquid radioactive waste into the Techa River. Inhabitants of villages located downstream were exposed to external radiation and incorporated strontium with contaminated river water and garden vegetables. The magnitude and time pattern of the exposure of this population are comparable to exposures that can accumulate among workers in the Western nuclear industry and also from medical diagnostic procedures such as CT scans. SOUL explored and started to realize the high potential of Southern Urals cohorts for improving our knowledge of health risks from protracted exposures to ionizing radiation.



Mayak, the plutonium production site for atomic weapons of the former Soviet Union is located in Southern Urals. Liquid radioactive waste was released into the Techa River and exposed habitants of villages located downstream 100 km to the east and further 140 km to the north-east.

Adapted from http://maps.grida.no/go/graphic/russian_federation_topographic_map

SOUTHERN URALS COHORTS

The Mayak Production Association began operations in 1948 as the first and largest nuclear weapons facility in the former Soviet Union. The epidemiological cohort includes all workers first employed before the end of 1972 on one of the reactors, or the radiochemical and plutonium production plants. External radiation was monitored for practically all of the workers. Plutonium body burden was measured for 33% of workers who might have been exposed to plutonium. Workers with acute radiation syndrome, as well as workers exposed to radionuclides other than plutonium, e.g. tritium were excluded from the cohort.

Quality control performed in the frame of SOUL confirmed the high standard of the statistical data for the cohort. The vital status as of 31 December 2005 is known for 95% of the workers. For more than 95% of the deceased cohort members, cause of death is known and autopsies were conducted for about 54%. Medical follow-up for the cohort was conducted on a regular basis according to a specially developed standard program.

The Techa River originates from a small lake near Mayak Production Association. The Techa River Cohort includes all people born prior to 1950, who resided on the river banks at any time between 1950 and 1961. Environmental measurements of radioactivity along the river started in 1951. About one third of the cohort members have at least one measurement of incorporated strontium. The children of the cohort members constitute the Techa River Offspring Cohort, which is of particular importance because of our limited knowledge of radiation risks from prenatal exposure and because of indications from earlier studies that these risks are high.

Cohort	Mayak Worker Cohort	Techa River Offspring Cohort
Number of persons	18 763	24 243
Main pathways of exposure	Protracted external exposure Incorporation of plutonium	Protracted external radiation Incorporation of strontium and caesium
A main organ of interest	Blood vessels and chambers of the heart for cardiovascular diseases	Red bone marrow for leukaemia
Mean organ dose (mGy)	600 (external)* 350 (plutonium)*	12 (in utero) 51 (postnatal)

* dose to the liver as a surrogate for blood vessels and chambers of the heart

EXTERNAL DOSIMETRY FOR MAYAK WORKER COHORT

Mayak Doses 2005, the system for calculating external doses of Mayak workers, is based on occupational dosimetry with film and TLD badges. The calculation of doses in organs that are critical for the development of diseases depends significantly on the energy spectrum of the radiation field and on the directions from which the worker was irradiated.

SOUL developed a methodology for validating *Mayak Doses 2005* with two experimental methods of dose reconstruction: electron paramagnetic resonance (EPR) spectrometry of teeth and fluorescence in situ hybridisation (FISH) with peripheral lymphocytes.

EPR measurements of 335 teeth from 238 workers were evaluated. Different teeth from the same worker gave consistent results. However, even after exclusion of workers with doses below the detection limit (100 mGy) or with potential strontium exposures, dose estimates for 29% of the workers were significantly lower (8% were higher) than expected on the basis of *Mayak Doses 2005*. FISH measurements were performed for 102 workers. Also for this method a similarly large number of measurements were different from dose values in the dosimetry system.

A relatively good agreement was found for dose estimates based on EPR and FISH methodologies. An analysis of results specific for special working conditions indicates that the treatment of the relative high doses from radiation incidents could be improved in the dosimetry system.

Dose to teeth is measured by electron paramagnetic resonance (EPR) spectrometry: An enamel sample (in the glass tube) is introduced into the strong magnetic field of the spectrometer. The absorption of a microwave field in the cavity is proportional to the amount of radicals that have been created by past radiation exposures in the crystal lattice of hydroxyapatite, the main mineral constituting the enamel.



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INTERNAL DOSIMETRY AND HEALTH EFFECTS IN MAYAK WORKER COHORT

Doses to workers at Mayak from plutonium incorporated into the body were calculated and the accuracy and reliability of the system for calculating internal doses was enhanced. An integrated bioassay/dosimetry model was developed that could accommodate multiple exposures. Uncertainties associated with radiochemical methods, sampling techniques and interpretation of bioassay data were addressed. This assisted in developing *Mayak Doses 2008* for use in future analyses.

The epidemiological analyses focussed on circulatory disease and cancer incidence, based on *Mayak Doses 2005*. A key strength of this study is the availability of incidence data for cancer and non-cancer disease, as well as on smoking and alcohol consumption. Statistically significant increasing trends in the incidence of both, ischemic heart disease and cerebrovascular disease, with increasing external dose were found among workers first employed at one of the main plants during 1948-1958 and followed to the end of 2000. Much of the evidence for raised risks arose at external doses greater than 1 Gy, although the findings are consistent with a linear trend in risk with dose. The possible impact of internal exposures on circulatory disease was less clear; on-going research is addressing this issue and lower doses.

Initial analyses of cancer incidence among Mayak workers first employed in 1948-1982 and followed to the end of 2004 showed statistically significant increasing trends in lung cancer incidence with both external dose and with internal dose to the lung from intakes of plutonium. Analyses of lung tissue collected at autopsy from workers with specific types of lung cancer showed a significantly lower rate of recurrent alterations in oncogenes associated with these types of lung cancer in other populations. Statistically significant associations were also found between liver cancer and internal dose, and between leukaemia and external dose.

Relative risks with 95% confidence ranges for incidence rates in the Mayak Worker Cohort 1948-58

Exposure	Cerebrovascular diseases	Ischemic heart diseases
External dose:		
500 – 1000 mGy	1.14 (1.04, 1.25)	1.02 (0.92, 1.13)
greater than 1000 mGy	1.60 (1.47, 1.75)	1.20 (1.09, 1.32)

DOSIMETRY FOR TECHA RIVER COHORTS

Validation of the Techa River Dosimetry System is important, especially because contributions of short lived radionuclides to potentially high doses in 1950 and 1951 are not fully known.

In the framework of SOUL, external doses at the shoreline of the Techa River in Muslyumovo, a village 70 km downstream from the Mayak Production Association, were reconstructed. Bricks were sampled from a former mill. Luminescence methods were applied to measure the dose in the samples accumulated since the production of the bricks. Computer simulations of the radiation transport in the river plain were used to calculate the dose at various locations at the shore line. Doses were found to be quite heterogeneous with an average value that confirmed the Techa River Dosimetry System.

A methodology was developed to reconstruct external doses of residents of the banks of the Techa River by applying EPR spectrometry to teeth and FISH measurements to peripheral lymphocytes. The EPR measurements indicated that the dose did not decrease monotonically with the distance from the Mayak Production Association. Instead, relatively high external dose values were found for inhabitants of Nadyrovo, a village about 50 km downstream of Mayak.

Major steps were achieved in the reconstruction of radiation exposures of the offspring of members of the Techa River Cohort. A worldwide unique set of computerized phantoms of foetuses and new-borns were used to calculate dose distributions from exposure to strontium. Also, a new model for the intake of strontium with breast milk was developed.



Dose in bricks is measured by optically stimulated luminescence (OSL). Typically a few hundred milligram of quartz grains are extracted from a brick sample and funnelled into a measurement carousel in aliquots of about 10 mg. Illumination with blue light stimulates recombination of electron-hole pairs. The intensity of the resulting luminescence is proportional to the dose from the past exposure to ionizing radiation.

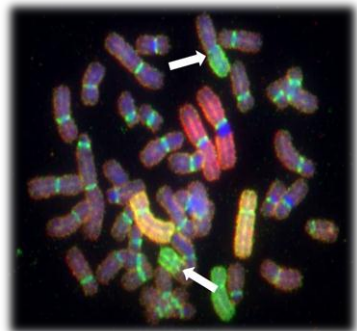
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HEALTH EFFECTS IN TECHA RIVER COHORTS

Analyses of non-cancer mortality during 1950-2005 were conducted in the Extended Techa River Cohort (ETRC), which contains 29 737 persons. Through further data collection and quality control checks, the proportion of persons with unknown vital status or unknown cause of death was reduced. Using estimates of doses from the recently-developed TRDS-2009 dosimetry system, there were statistically significant increasing trends with increasing dose in mortality from all non-cancer causes taken together and specifically for circulatory diseases and, in particular, ischemic heart disease. This analysis took account of factors such as ethnicity, although information on smoking and alcohol was not available.

The Techa River Offspring Cohort was expanded and now contains 24 243 persons born from 1950 onwards to born to parents who resided in the contaminated villages along the Techa River. Dose estimates (total parental gonadal dose, foetal dose and postnatal dose) based on TRDS-2009 are available for 20 501 of these persons. Based on follow-up to the end of 2003 of the 14 427 persons who continued to live close to the Techa River or in Chelyabinsk city, there was little evidence of associations between these doses and the incidence of solid cancers taken as a whole, leukaemia or lymphoma. However, the precision of the analysis of cancer following exposure in utero was relatively low.

Metaphase analysis in human peripheral blood lymphocytes derived from one Mayak worker. Multi-colour fluorescence in situ hybridization (FISH): Using chromosomes specific paint probes for #1 (red), #4 (yellow), #8 (green) and all other chromosomes painted with DAPI (blue-colour), and a pan-centromeric probe for whole genome. Arrows indicate the position of one reciprocal translocation between chromosome #8 and one DAPI-painted chromosome.



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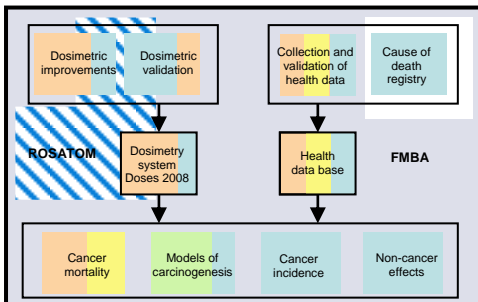
CONSORTIUM SOUL AND INTERNATIONAL COLLABORATION

The project Southern Urals Radiation Risk Research (SOUL, www.helmholtz-muenchen.de/SOUL) started in August 2005 and ended in December 2009. The consortium consisted of 15 partners from Germany, UK, the Russian Federation, Sweden, Italy, Greece, the Netherlands and USA and was coordinated by the Helmholtz Zentrum München in Germany. The budget was 11.5 M€ with a contribution from the 6th framework programme of the European Commission of 6.8 M€. In total, 2500 person-months were invested to achieve the objectives of the project.



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Epidemiological cohorts in Southern Urals have a large potential to allow a direct study of health risks from protracted exposures as they are typical for higher occupational exposures in the European Union or for exposures from several CT scans in medical diagnostics. The importance of these cohorts for radiation protection has not only been recognized by the European Commission but also by key funding organizations in the Russian Federation and in the USA. A number of projects are conducted on the cohorts in Southern Urals. SOUL had a leading role in organizing a network of these projects. International groups of experts have been convened, e.g. on general questions of dose reconstruction or epidemiology in Southern Urals. The collaboration is achieved by telephone conferences and international workshops that have been organized every second year.



Southern Urals radiation risk research is a network of projects funded by the European Commission (SOUL, blue), the Russian Federal Medical-biological Agency (grey), the US Department of Energy (JCCRER, rose), the Russian Atomic Energy Agency (hatched), the US National Cancer Institute (yellow), and the German Federal Ministry of Environment (green)

PERSPECTIVES AND CONSORTIUM SOLO

The key achievements of SOUL include:

- Validation of existing dosimetry systems for the Mayak and Techa River cohorts and input to the development of new dosimetry systems;
- Identification of raised risks of circulatory disease and of the incidence of specific cancers among Mayak workers;
- Expansion of the Techa River cohorts and improvements in follow-up, which have permitted analyses of non-cancer mortality in the Extended Techa River Cohort and of cancer incidence in their offspring;
- Close collaboration with those involved in other radiation research projects in the Southern Urals.

Looking forward, it is planned to focus on the following topics.

Low Doses: Study of more recent workers at Mayak, who tended to receive lower doses than early workers, together with longer follow-up should provide more information at doses below 1 Gy.

Specific Cancers: Continued follow-up for cancer incidence among Mayak workers should provide more information on risks for specific cancers.

Non-Cancer Diseases: As well as continuing to follow-up circulatory diseases among Mayak workers, analyses of respiratory disease are planned in view of the raised risks seen among the Japanese atomic bomb survivors.

Plutonium exposure: For the first time ever, there is the potential opportunity to produce preliminary results for mortality and cancer incidence risks from the pooled cohorts of plutonium workers at Mayak and Sellafield (UK). The feasibility of such an analysis would first need to be established.

In utero exposure: A pooled analysis of the Mayak and Techa in utero cohorts would provide stronger evidence on risks of cancer than analysis of either cohort alone. The compatibility of these data would be addressed in a feasibility study.



These topics will be considered in SOLO (Epidemiological Studies of Exposed Southern Urals Populations), a new project supported by the EC under its 7th Framework Programme. SOLO began on 1 March 2010 and will run for 4 years. More details can be found at: <http://www.solo-fp7.eu/>

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The FP6 project SOUL collected essential information on people exposed to radiation in Southern Urals due to occupational exposure at plutonium production facilities and environmental exposure to radioactive discharges from these facilities. Thanks to a remarkable record keeping of radiation doses and morbidity as well as the use of upfront technology to cross checking data quality on these doses and other information, several projects are conducted on Epidemiological cohorts in Southern Urals. They are useful for the study of health risks from protracted exposures as they are typical for higher occupational exposures in the European Union or for exposures from several CT scans in medical diagnostics. Beyond the European Union, the importance of these cohorts for radiation protection is internationally recognized and their follow-up supported by key funding organizations in the Russian Federation and in the USA. The methodology and practice from SOUL will develop with the FP7-SOLO project and form with this latter project an essential element of knowledge to be further exploited by the Multidisciplinary European Low Dose Initiative-MELODI. The project was coordinated by the Helmholtz Zentrum Muenchen and cost 11,5 M€.

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