Recent Research Results from the Russian Health Studies Program

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JCCRER

- JCCRER is the Joint Coordinating Committee for Radiation Effects Research
- This is a bilateral Government committee representing agencies from the United States and the Russian Federation
- JCCRER's major role is to coordinate scientific research on the health effects of exposure to ionizing radiation in the Russian Federation from the production of nuclear weapons

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JCCRER Member Organizations

U.S. Members:

- Department of Energy (DOE), U.S. Executive Agent
- Department of Defense (DoD), including the Armed Forces Radiobiology Research Institute (AFRRI)
- Department of Health and Human Services (DHHS), including the Centers for Disease Control and Prevention (CDC)
- Environmental Protection Agency (EPA)
- National Aeronautics and Space Administration (NASA)
- Nuclear Regulatory Commission (NRC)

Russian Members:

- Federal Medical-Biological Agency (FMBA), Russian Executive Agent
- Federal Medical Biophysical Center (FMBC)
- State Atomic Energy Corporation (Rosatom)
- State Scientific Center – Institute of Medical and Biological Problems of the Russian Academy of Sciences (IBRAE)
- Mayak Production Association (Mayak)

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Russian Health Studies Program

- The subset of **JCCRER** projects funded by DOE comprise the **Russian** Health Studies Program
- Program's name helped avoid confusion with the Joint Coordinating Committee for Civilian Nuclear Reactor Safety (**JCCCNRS**) Program, which focused on assessing the effects of radiation from the **Chernobyl** nuclear power plant accident of 1986

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Program Purpose and Goals

Purpose

To assess worker and public health risks from radiation exposure resulting from nuclear weapons production activities in the former Soviet Union

Goals

- To better understand the relationship between health effects and chronic, low-to-medium dose rate radiation exposures
- To estimate cancer risks from exposure to gamma, neutron, and alpha radiation
- To provide information to the national and international organizations that determine radiation protection standards and practices

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Current Radiation Protection Standards

- The NRC Annual Dose Limit for Workers is 5 rem (50 mSv)
- The NRC Annual Dose Limit for the Public is 0.1 rem (1 mSv)

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Low Dose Radiation Research

- For purposes of radiation research, 0 to 10 rem (100 mSv) per year are considered to be low doses
- The most crucial issue in radiation research is the determination of the effects on human health of exposures of less than 5 rem (50 mSv) per year (NRC Annual Worker Dose Limit)
- Such exposures are more likely to have been received by DOE workers and surrounding populations

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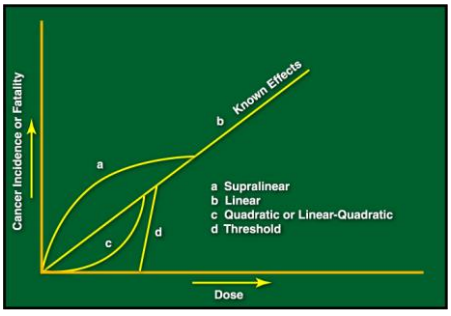
Dose Response Curves Biological Effects of Radiation



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Rationale for Conducting Mayak Worker and Techa River Population Studies

Data Characteristics	Research Focus	Application/ Relevance
Detailed Health and Exposure Records Stationary Worker and Exposed Populations External and Internal Exposures Subjects of both Genders	Close examination of health and doses of Mayak worker and Techa River residents for over 50 years Chronic duration of exposures over a wide range of doses	Research results relevant to understanding radiation risks experienced by nuclear weapons production workers, commercial nuclear workers, and residents of surrounding communities

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Comparison of Plutonium in Bone Tissues from U.S. and Russian Workers

- U.S. worker with highest known plutonium uptake in bone
- Died of heart attack
- Source: USTUR

- Mayak worker plutonium uptake in bone
- Died of lung cancer
- Source: Human Radiobiology Tissue Repository

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Phased Implementation

Completed Phases		
Phase I	**Phase II**	**Phase III**
Coordinating, planning, building infrastructure, providing equipment and supplies, and linking U.S. and Russian researchers	Feasibility studies and data preservation of paper records	Successful feasibility studies resulted in multi-year projects

Current Phases
Phase IV
Refining dosimetry, uncertainty, and cancer risk estimates

Results Published
242 peer-reviewed publications (as of 12/31/2011)

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6 Current Projects

Community Studies	Worker Studies
1.1, Techa River Population Dosimetry	2.2, Mayak Worker Cancer Mortality
1.2b, Techa River Population Cancer Morbidity and Mortality	2.4, Mayak Worker Dosimetry
1.4, Ozersk Population Dose Reconstruction	2.8, Human Radiobiology Tissue Repository

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Principal Investigators (PIs) and Organizations

Project Number	Title	Russian PI	Organization	U.S. PI	Organization
1.1	Techa River Population Dosimetry	Marina Degteva	Urals Research Center for Radiation Medicine (URCRM)	Lynn Anspaugh Bruce Napier	University of Utah Pacific Northwest National Laboratory (PNNL-Battelle)
1.2b	Techa River Population Cancer Morbidity and Mortality	Alexander Akleyev Ludmila Krestinina	URCRM	Faith Davis	University of Illinois at Chicago
1.4	Ozersk Population Dose Reconstruction	Yuri Mokrov	Mayak Production Association (Mayak)	Lynn Anspaugh Bruce Napier	University of Utah PNNL-Battelle
2.2	Mayak Worker Cancer Mortality	Mikhail Sokolnikov	Southern Urals Biophysics Institute (SUBI)	Vacant	
2.4	Mayak Worker Dosimetry	Alexander Efimov Vadim Vostrotin Mikhail Gorelov	SUBI Mayak	Bruce Napier	PNNL-Battelle
2.8	Human Radiobiology Tissue Repository	Evgeniya Kirillova	SUBI	Christopher Loffredo	Georgetown University

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Project 1.1 Scope of Research

- Techa River Population Dosimetry provides the dosimetry data for:
  - Project 1.2b, Techa River Population Cancer Morbidity and Mortality
  - NCI and EC-funded studies (SOUL and SOLO Programs)
- Techa River Dosimetry System (**TRDS**) 2009 provides individual dose estimates for:
  - Techa River Cohort (**TRC**), which consists of 30,000 persons born before the start of contamination
  - Post-natal doses to the Techa River Offspring Cohort (**TROC**), which consists of 21,000 persons born after the start of contamination
  - East Urals Radioactive Trace Cohort (**EURT**), which consists of 18,000 evacuees from the "Kyshtym explosion"
- 14,000 (35%) of 30,000 TRC members have direct whole body counting measurements
- 14,000 (35%) of 30,000 TRC members have data from relatives from the same households

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Project 1.1 Status

- Added doses to residents of evacuated EURT villages
- Adding additional organs for medical doses (complete set the same as environmental pathways)
- Updating dose conversion factors for organs of skeleton and gastrointestinal tract using recently developed dosimetric models
- Calculations of individual doses of environmental exposure for all cohort members planned for September 2014:
  - Will provide household-specific rather than village average external doses
  - Results evaluated by separating shared/unshared and measurement/grouping (Classical/Berkson) types of uncertainties

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Project 1.2b Scope of Research

- Techa River Population Cancer Morbidity and Mortality and companion Project 1.1 address cancer incidence in residents downstream from Mayak
  - Residents exposed to both internal and external radiation (less than 1 rem or 10 mSv per year) over a long period (20 to 30 years)
  - Published results with doses from TRDS 2000 use follow-up through 12-31-2002 (46 years) for solid cancer and breast cancer and 12-31-2005 (49 years) for leukemia
  - Current analyses with new doses from TRDS 2009 use follow-up through 12-31-2007 (51 years)

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Project 1.2b Description of Cohort

- Techa River Cohort (TRC):
  - 30,000 exposed permanent residents of villages on the Techa River born before 1-1-1950
  - Lived in riverside villages up to 120 miles downstream at any time between 1-1-1950 and 12-31-1960
- Techa River Incidence Cohort (TRIC):
  - 18,420 exposed permanent residents of villages on the Techa River born before 1-1-1950
  - Lived in the riverside villages at any time between 1-1-1956 and 12-31-1960

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Project 1.2b Follow-up

- Follow-up through 12-31-2007:
  - 21% lost to follow-up (due to migration from the catchment area)
  - Vital status is unknown for an additional 8% of the cohort who are not known to have migrated
  - Among catchment area residents with known vital status (71% of the cohort):
    - 25% were alive; and
    - 75% were known to have died
    - Cause of death is known for 91% of the decedents

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Project 1.2b Significant Research Outcomes

- Current Results:
  - Based on TRDS-2000 and follow-up through 2002:
    - $ERR_{Solid\ cancer}$ = 1.0/Gy 95%CI (0.3-1.9)
    - ERR_{Breast} = 5.0/Gy 95%CI (0.8-12.8)
  - Based on TRDS-2000 and follow-up through 2005:
    - ERR_{nonCLL} = 4.9/Gy 95%CI (1.6-14.0)
  - Analysis of chronic lymphoid leukemia incidence did not reveal any dose effect relationship
  - Risk estimates with revised environmental and medical doses are in progress
- Future Results: TRC leukemia incidence: 1953-2007 using TRDS-2009

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Project 1.2b Comparison of TR and LSS Cohorts

- No significant differences between the Techa River cohort and the Japanese Atomic Bomb Survivor cohort in:
  - ERR/Gy time-constant point estimates from solid cancer morbidity or mortality
  - ERR/Gy time-constant external dose point estimates from solid cancer mortality
  - Risks from solid cancer whether acute or chronic exposure to gamma radiation

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Project 1.4 Scope of Research and Status

- Ozersk Population Dose Reconstruction was the first study to provide data on the monthly releases of radionuclides from Mayak stacks from 1948-1982
- Will provide doses to the thyroid for representative individuals
- When individual-specific information becomes available, dosimetry system may be used for computing thyroid radiation doses as inputs to estimation of cancer risk for Ozersk residents from ^{131}I
- Delayed but will be completed by September 30, 2013

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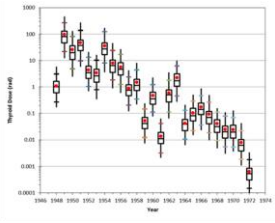
Project 1.4
Initial Results

- Prior research has provided information on releases, regional agriculture, and food consumption patterns
- Preliminary scoping indicates that doses could be large
- Example: 5 year-old children in Ozersk with a "backyard cow"
- Annual thyroid doses in rads for a representative individual



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Project 2.2
Description of Cohort

- Mayak Worker Cancer Mortality was the first study to demonstrate in humans significantly increased incidence of lung, liver, and bone cancer related to internal deposition of plutonium
- 26,000 workers hired from 1948-1982
- 25% female
- Exposed to both external and internal radiation
- Protracted low dose rate exposure similar to that of interest for radiation protection

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Project 2.2
Scope of Research

- Published cancer risk estimates using the Mayak Worker Doses 2005 database for 17,740 Mayak workers hired between 1948 and 1972
- Will publish new cancer risk estimates using the Mayak Worker Dosimetry System (MWDS) 2008 completed in September 2010 for about 26,000 workers hired between 1948 and 1982
- A paper on lung cancer risks based on MWDS 2008 has been submitted for publication

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Project 2.2 Follow-up

- Follow-up through 9-30-2010:
  - 5% lost to follow-up
  - Vital status is known for 95% of the cohort
  - Among the cohort with known vital status:
    - 44% were alive; and
    - 56% were known to have died
    - Cause of death is known for 94% of the decedents

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Project 2.2 Significant Research Outcomes

- Results for internal plutonium dose using Doses 2005:
  - Analyses adjusted for external dose
  - Highly significant dose-response for lung, liver, and bone cancer
  - For lung and liver cancer, the dose-response is well-described by a linear function
  - Source: Sokolnikov et al., Int. J. of Cancer, 2008

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Project 2.2 Significant Research Outcomes, Continued

- Summary of ERR per Gy for plutonium dose from Doses 2005 using 95% confidence intervals :

Organ	Gender	
	Males	Females
Lung	7.1 (4.9 – 10)	15 (7.6 – 29)
Liver	2.6 (0.7 – 6.9)	29 (9.8 – 95)
Bone	0.8 (<0 – 5.2)	3.4 (0.4 – 20)

Sokolnikov et al., 2008

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Project 2.2: Lung Cancer Risk Compared with Atomic Bomb Survivors

- Mayak ERR/Gy 7.0 (4.8 – 10)
- Mayak ERR/Sv (QF=20) 0.35 (0.24 – 0.50)
- LSS mortality 0.36 (0.05 – 0.72)
- LSS incidence 0.34 (0.05 – 0.72)

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Project 2.2: Summary Comments

- Mayak worker cohort is a unique resource for evaluating:
  - Risk of cancer from exposure to plutonium
  - Risk of cancer from extended external exposure
- Recognize limitations
  - Dosimetry uncertainties
  - Applicability to populations with different smoking habits
- Future Work:
  - Need information on magnitude of measurement (classical) errors
  - Include dose uncertainties in dose-response analyses
    - Extremely challenging task
    - Without adjustment, likely to underestimate risks

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Project 2.4 Scope of Research

- Mayak Worker Dosimetry, provides the dosimetric data for companion Project 2.2
  - Enhanced the understanding of plutonium metabolism in the human body and improved the biokinetic models for assessing dose from plutonium uptakes
  - Mayak Worker Doses 2005 database superseded by Mayak Worker Dosimetry System (MWDS) 2008
  - MWDS 2008 delivered to Project 2.2 epidemiologists and SOLO researchers and now being used for computing cancer risks
  - MWDS 2013 due in June 2013
    - Will include uncertainty analyses
    - Will include health status

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Project 2.4
Recent Research

- Papers on ^{238}Pu investigations recently published in *Health Physics*
- Whole-body counting results have been compared to autopsy data
- ^{241}Am in Mayak workers recently published and a proposed new ^{241}Am model in humans is in press
- The hyper-model approach is a paradigm shift
  - The whole distribution of parameters is used, avoiding issues of parameter selection while providing a defensible distribution of uncertainty on the results

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Project 2.4
Future Plans

- For MWDS-2013, dosimetrists will calculate internal and external organ doses in a completely different way than in Doses-2005 and MWDS-2008 by:
  - Directly considering uncertainties in the model parameters and measurement data by creating multiple realizations
  - Differentiating those parameters which are shared and unshared between members of the cohort
- MWDS-2013 target completion date is June 2013
- Negotiating with Mayak for later enhancements to external dose models

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Project 2.8
Scope of Research

- Russian Human Radiobiological Tissue Repository is the first facility to preserve and make available to the scientific community unique biospecimens of Russian nuclear facility workers
- Contains over 3 million information storage units and about 200,000 biological specimens from 8,018 registrants in storage
- Includes samples from Mayak workers and Ozersk residents without occupational exposure to ionizing radiation
- The contents facilitate molecular epidemiology studies designed to assess the relationship between disease and radiation exposure

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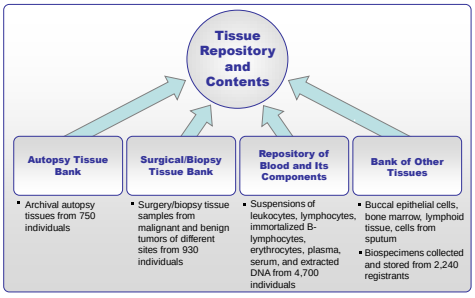
Project 2.8 Repository Structure and Contents



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Scientific Oversight

- External Scientific Review Group (SRG)
- Eminent U.S. and Russian radiation effects research scientists
- Ad hoc external expert scientific reviewers
- Internal DOE scientific experts
- Expertise in radiation epidemiology and dosimetry, dose reconstruction, radiation shielding, radiation measurements, health physics, and public health

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Future Plans

- Re-engage Mayak scientists on Projects 1.4 and 2.4 (external dosimetry)
- Recruit a new U.S. PI for Project 2.2; RFA to be issued soon; new award anticipated in June 2013
- Participate in the joint Russian-U.S. SRG Meeting in Ozersk and Chelyabinsk on June 24-27, 2013 to perform an on-site critical review and evaluation of current projects
- Complete MWDS-2013 by June 30; prepare articles for peer-reviewed journals by September 30, 2013

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Future Plans, Continued

- Participate in programmatic and scientific discussions as part of the 10th International Russian-U.S. JCCRER Meeting in St. Petersburg, Russia on September 9-11, 2013
- Conduct a site visit and prepare an assessment of the databases, infrastructure, and organizational capabilities to conduct radiation health effects research at the Seversk Chemical Combine (Seversk)
- Enhance coordination and engagement with international standard-setting organizations

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Future Plans, Continued

- Continue current projects to their completion as appropriate and as budget will permit
- Identify additional research topics which can benefit from the economy of scale and the existing scientific network
- Continue to work with NCI and EC to better coordinate research, leverage resources, and disseminate results

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