

Coordination of Low Dose Radiation Research with Armed Forces Radiobiology Research Institute (AFRRI)

Uniformed Services University of the Health Sciences (USU)

Alexandra C. Miller, PhD

Senior Scientist, AFRRI

Adjunct Associate Professor

Department of Radiology and Radiation Science, USU

Alexandra.miller@usuhs.edu

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Declaration: Neither I nor my family members have a financial interest in any commercial product, service, or organization providing financial support for this research.

Overview

- **Introduction to the Armed Forces Radiobiology Research Institute (AFRRI)**
 - **History, mission and leadership**
- **Brief background on radiation exposure within the US military**
- **AFRRI's unique capabilities regarding low dose radiation research and risk communication**
 - **Research areas, Facilities and Technologies**
 - **Education and Training**
 - **Operational Support**
- **AFRRI potential for collaboration and coordination for low dose research program**
 - **Current government interagency partnerships**
 - **Current collaborations, funding sources**

AFRRI History and Mission

- Established in 1961 during the Cold War
- Initially part of the Defense Atomic Support Agency and the Defense Nuclear Agency (DNA) 1961-1992
- Realigned with USU 1992-Present
- Staff includes military officers, military enlisted, government civilians, contractors

AFRRI Mission

The Armed Forces Radiobiology Research Institute (USU/AFRRI), is a unique Department of Defense asset, responsible for preserving and protecting the health and performance of U.S. military personnel operating in potential radiologically contaminated multi-domain conventional or hybrid battle spaces and urban environments; through **research, education, and operational training** that advance understanding of the effects of ionizing radiation in line with the 21st century dynamic threat landscape and national security threats posed by non-state actors, hostile state actors, and near-peer adversaries, as well as providing rapidly deployable radiation medicine expertise in response to a radiological or nuclear event domestically or abroad.

National Security
Strategy

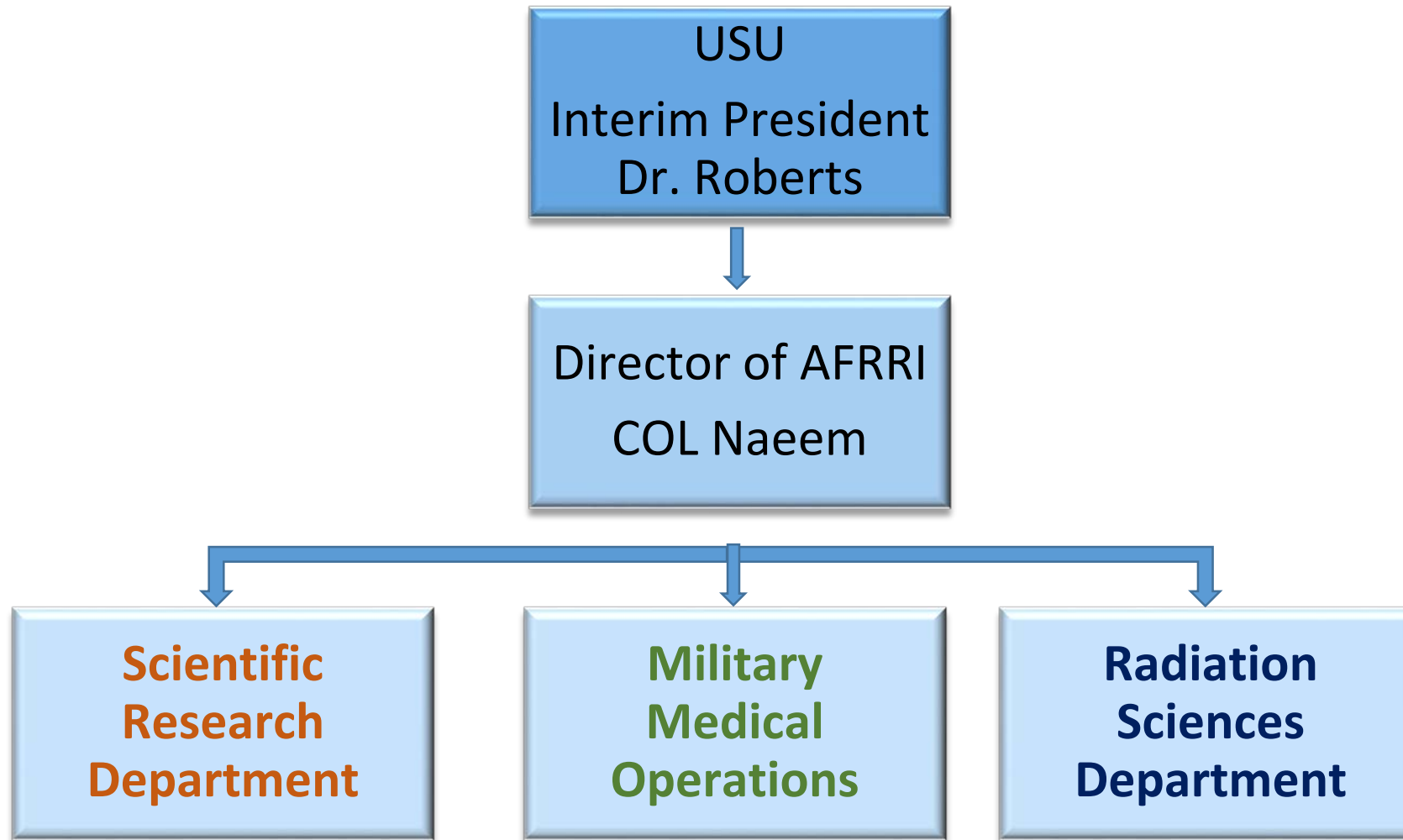
National Defense
Strategy

National Military
Strategy

National Strategy
for Countering
WMD Terrorism

Nuclear posture
Review

AFRRI Leadership Structure



AFRRI Departments and Capabilities

Scientific Research Department

Low Level Radiation

Medical Countermeasures

Cellular Radiobiology

Internal Contamination

Radiation Combined Injury

Biodosimetry

Military Medical Operations

MEIR

MRAT

EMP Testing

Radiation Sciences Department

Radiation Sources

Radiation Generators

Imaging Systems

Radiation Physics

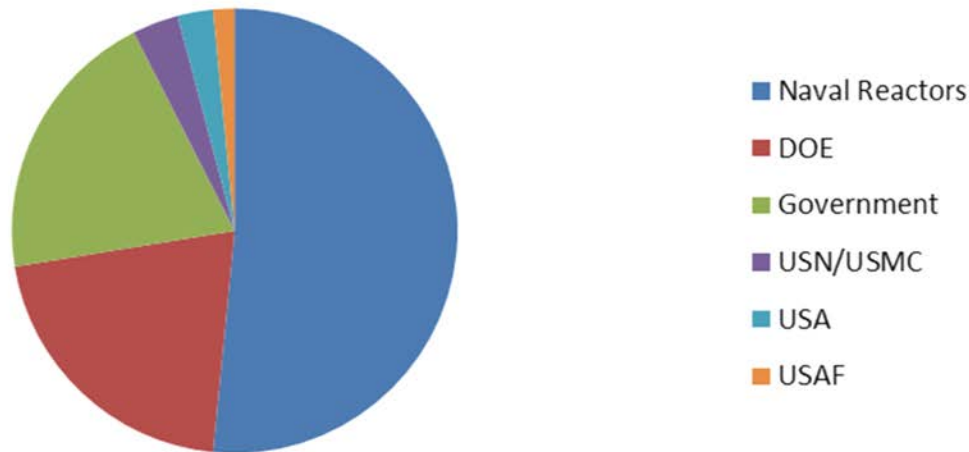
Computational Modeling

Nuclear Weapons Effects

DTRA Liaison

DOD is Largest Federal Component of Occupational Radiation Exposure

**2006 Government Collective Effective Dose
 (person-Sv)**



Cohort	Individuals	person-Sv
Naval Reactors	45,964	20.0
DOE	91,280	8.1
Government	122,367	7.8
USN/USMC	5,965	1.3
USA	12,018	1.0
USAF	<u>6,598</u>	<u>0.6</u>
	284,192	38.8

Reference: NCRP Report 160, Chap.7, "Ionizing Radiation Exposure of the Population of the United States"

DOD Radiation Repository Radiation Exposure Repositories

- DoD has five repositories of occupational radiation exposure that maintain records from 1945-present:
 - Army Dosimetry Center
 - Naval Dosimetry Center
 - Air Force Dosimetry Center
 - Operation Tomodachi Registry
 - Includes dependents
 - Defense Threat Reduction Agency's (DTRA) Nuclear Test Personnel Review
 - Includes atomic vets, underground test participants, and pacific atoll cleanup participants

Cohort	Unique Individuals (x1000)
Army	700
Navy-Marine Corps	800
Air Force	150
Coast Guard	3
Op. Tomodachi Registry	75
DTRA-Atmospheric Test Participants	500
DTRA-Underground Test Participants	55
DTRA-Pacific Atoll Cleanup Participants	7
Total:	2,290

**Used Extensively in the Million Person Study
Low Dose Epidemiology Research**

AFRRI Capabilities

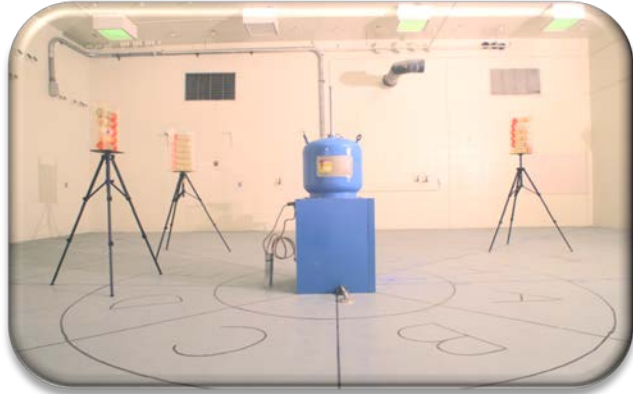
Useful to Low Dose Research

Personnel	Technologies	Radiation Sources	USU/AFRRI Facilities	Support	Partners
•Radiobiologists •Neuro-chemists •Physiologists •Behaviorists •Biochemists •Immunologists •Toxicologists •Clinicians •Physicists •Nuclear engineers •Veterinarians •Pathologists	•Cytogenetics •Proteomics •3D Bioprinting •Cell Culture •Animal models •Genomics •Epigenomics •ICPMS •Discovery Platforms	•TRIGA Nuclear Reactor •Low Level Gamma Facility •High Level Gamma Facility •LINAC •SARRP •Cs-137 •X-ray irradiator	•Dosimetry •USU DLAR •AFRRI Vivarium •Rad Sources •USU BIC •Genomics core •Imaging core •USU Centers •Global Health •Neuroscience	•JPC-7 •NIAID •BARDA •NIH •DTRA •NASA •CDMRP •JWMRP	•DTRA •NATO •NIH •NASA •Academic •Pharma •IARPA

Radiation Sources & Generators

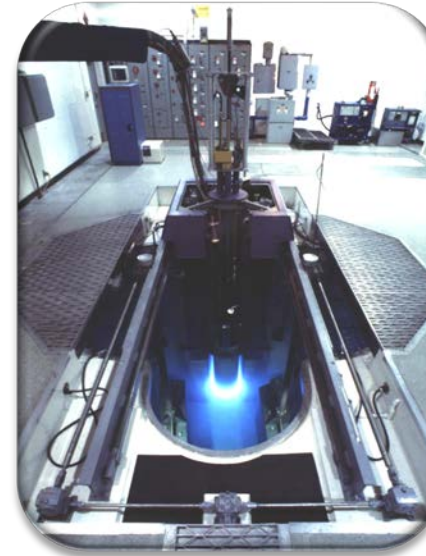
Support Low Dose Research

Low Level Cobalt-60



Range of:
 Dose Rates
 Total Doses
 Radiation Qualities
 Neutron Spectra
 Chronic & Prompt
 Exposures

TRIGA Reactor



SARRP



High Level Cobalt-60



Cs-137



X-ray 120 kV



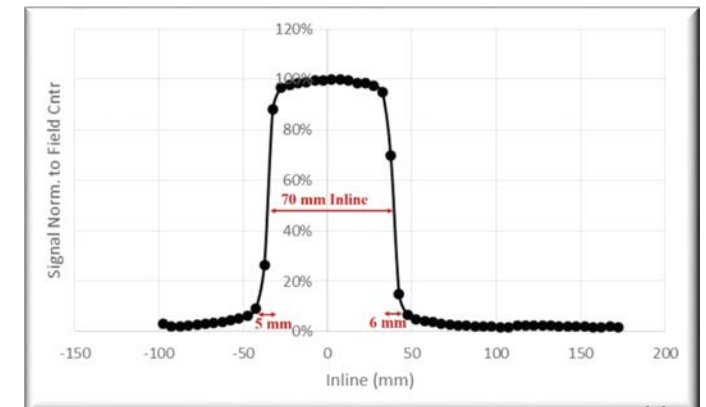
Linear Accelerator



AFRRI is Unique Having All Sources in One Infrastructure

Radiation Physics and Dosimetry Support Low Dose Research

- Computational Modeling and dosimetry
- Ionization chambers
- Gafchromic™ film (EBT-XD)
- Optically stimulated luminescent (OSL) dosimeters
- IBA Star Track Detector and Sun Nuclear 3D Scanner
- Use of animal specific phantoms and consensus dosimetry protocols
- All measurements are **traceable to national metrology institutes** and standards
- **Independent quality assurance tests with Accredited Dosimetry Calibration Labs**



Department of Laboratory Animal Research (DLAR) and DLAR Vivarium at AFRRRI (DVA)

USU



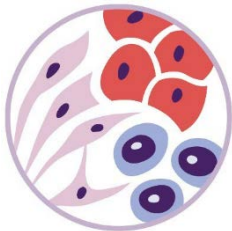
AFRRRI



AAALAC Accredited

**Regulatory Compliance
IACUC**

**Comparative
Pathology**



GLP



72 personnel strong

Veterinarians and Technicians: 39

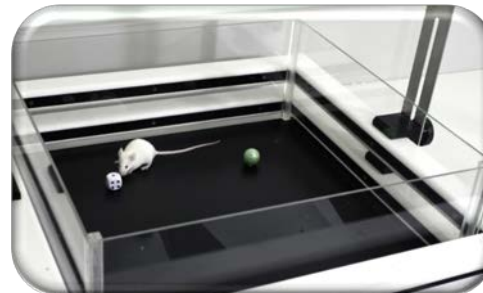
Animal Husbandry Personnel: 25

Behavioral Core Scientists: 4

Administrators: 4



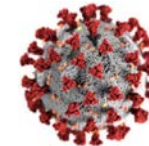
Behavior Core



DLAR Vivarium AFRRRI (DVA)

- Close Proximity to radiation sources
- Updated surgical suites, large animal housing
- GLP-rodent housing
- Support for radioactive animal studies

BSL2 Corridor



Surgery

6 Operating Rooms:

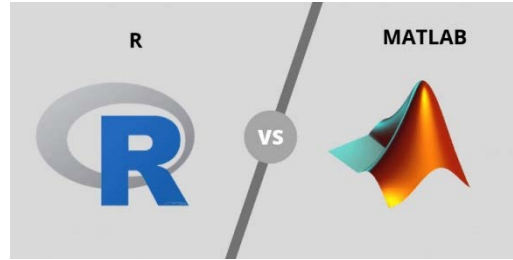
- OR-A : Small Rodent
- OR-B : Small Rodent
- OR-C : Robotics Room
- OR-D : Large Animal
- OR-E : Large Animal



Selected Discovery Technology Platforms Support Low Dose Research



**MESO (MSD)
 Sector S 600 System**



**Machine Language
 Software Algorithms**



**CellWriter S
 BioDot**



**Metafer
 MetaSystems Inc**



**3D
 Bioprinting**



**NovaSeq*
 6000 System**



**Biomark HD*
 Fluidigm**



**QIAasymphony SP*
 Qiagen**



**HiSeq 300 Sequencing System*
 Illumina**

*USU Genomics Center – Selected Core Equipment

AFRRI Mission

Research

- Biodosimetry
- Internal Contamination/
Heavy Metal
- Low Dose Radiation
- Radiation Combined Injury
- Radiation Countermeasures
Prophylaxis and treatment

Education and Training

- Medical Effects Ionizing Radiation
(MEIR) Course
- Radiobiology Course at USU
- USU 1st PhD Candidate with
Radiobiology Training
- Internship and SMART
Scholarship Programs

Support Operational Forces

- MRAT
- Fukushima
- Reach-back Support

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Combat Operations At Low Level Radiation

COALL-R

“To determine the effects of low dose ionizing radiation exposure (other than cancer) on multiple organ systems including cardiovascular, neurological, pulmonary, hematological and gastrointestinal that could compromise operational performance and resilience.”

Radiation sources

- Low Level Cobalt-60
- Chronic exposure
- Fallout mimic
- High Level Cobalt-60
- Dose rates mGy/hr- kGy/min
- TRIGA Reactor
- LINAC/SAARP

Animal Models

- Mice
- Rats
- Mini-pigs

Applied Research Focus

- Biomarkers of Effect
- Risk Assessment Improvement
- Countermeasure development
- Optimize neurological responses

Model Systems/Platforms

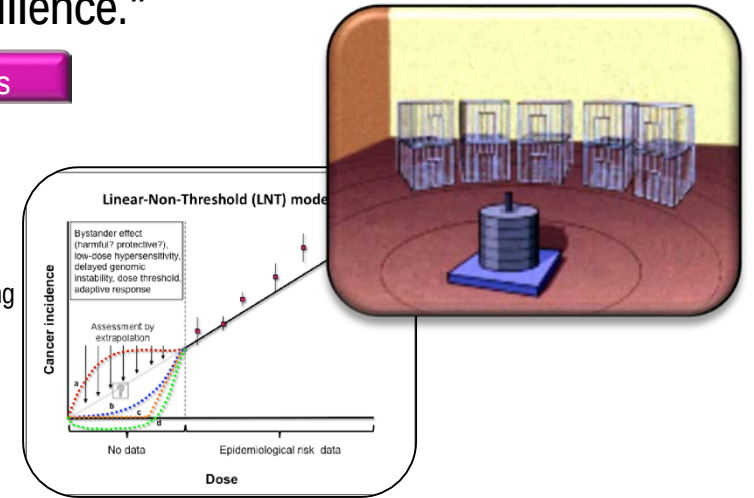
- Multiple In Vivo models
- 3D Bioprinted Models
- IPS derived cells
- Primary human cultures
- Immortalized cell culture

Dose Response Assessments

- Chronic exposure - Long-term survival
- Cardiac function/histology
- Hematological function/characterization
- Neurological/chemistry/histology
- Behavior characterization (anxiety, comprehension)
- Pulmonary function/chemistry
- Organ Fibrosis

Mechanistic approaches

- Epigenomic markers
- Genomics/cytogenetics
- Neoplastic Transformation
- Single-cell technology
- Flow cytometry
- qPCR, Next Gen Sequencing
- Markers of organ system decrements
- Microbiome Analysis

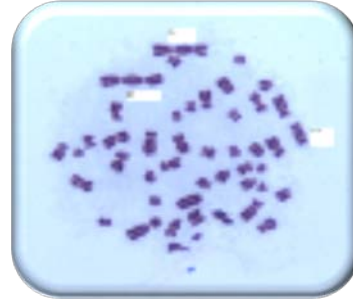


CAPABILITY AREA	WHAT SRD IS DOING	HOW WE'RE DOING IT
Prompt low dose radiation induced early-delayed cardiotoxic and hematological effects in vivo.	Studying cardiotoxic radiation effects within days to months following low dose gamma radiation exposure.	Mouse survival, body weight measurement, Heart weight/body weight ratio Cardiac function, Echocardiography, electrocardiography., coronary vessel morphology measured by histological examination; pre-atherosclerosis.
Low dose neutron and gamma effects on neutron-induced neurobehavioral deficits affecting operational performance in vivo	Evaluating low dose radiation effects on neurobehavioral outcomes that could impact combat operations during nuclear event/Fallout	Within-subject studies assessing multiple neurological, cardiac- and hematological endpoints in the same animals for ≥ 6 months following radiation.
Use of 3D bioprinted blood brain barrier models and others to examine complex cellular responses to chronic low dose radiation	Assessing BBB changes that impact radiation sensitivity of brain to low dose radiation	Apply 3D human cell models to measure astrocyte, pericyte, brain microvascular endothelial cell proteomic and epigenomic responses; establishing single-cell assessments.
Utilize molecular biology techniques to evaluate epigenomic and genomic responses (biomarkers) to low dose radiations	Evaluate primary human cells cultures to establish very low dose epigenomic changes as biomarker of exposure to less than current detectable exposure levels	Using a multiplex "omics" approach to investigate low dose radiation effects on human cells, also employing DNA sequencing, gene expression evaluations
Low dose multi-ion exposure	Studying neurobehavioral outcomes	Translational behavioral tests of operational performance, such as the rodent psychomotor vigilance test. In addition to gold-standard and state-of-the-art neuroscience techniques.

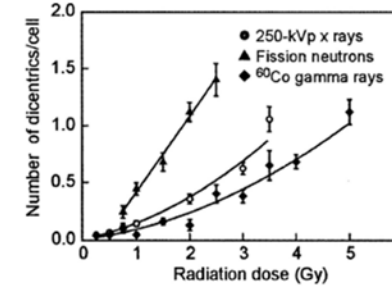
Low Dose Program Can Expand in these areas



Combined Injury



Biodosimetry



Countermeasures

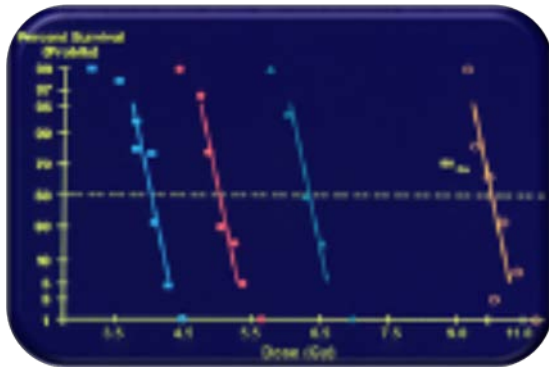
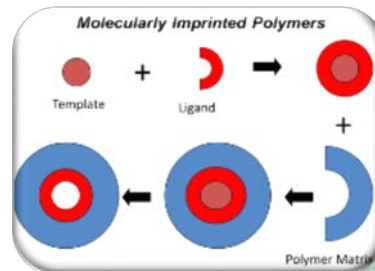


Risk Communication



**Applicable
 Research for
 Low Dose**

**Internal Contamination/
 Heavy metal**



AFRRI Mission

Research

- Biodosimetry
- Internal Contamination/
Heavy Metal
- Low Dose Radiation
- Radiation Combined Injury
- Radiation Countermeasures
Prophylaxis and treatment

Education and Training

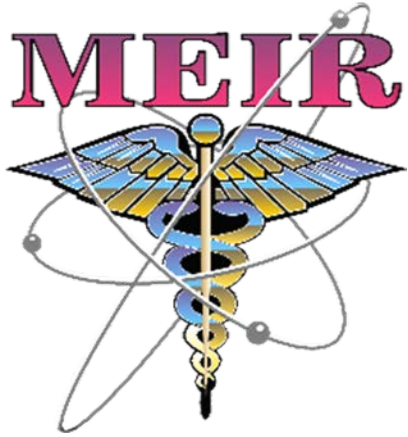
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Scholarship Programs

Support Operational Forces

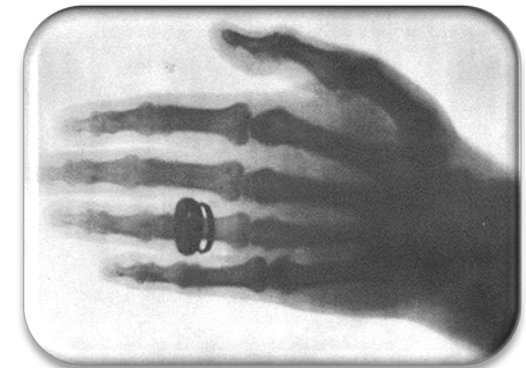
- MRAT
- Fukushima
- Reach-back Support

AFRRI Operational Training Mission

Reach-back and Operational Support and Training

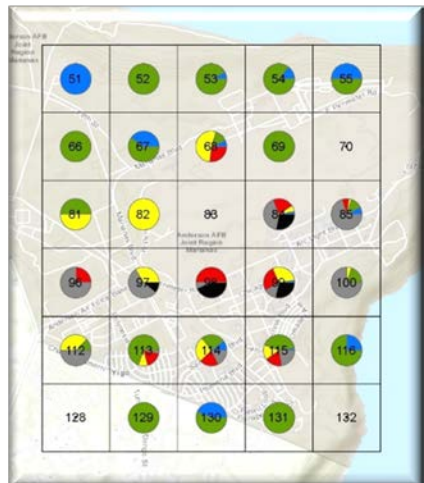
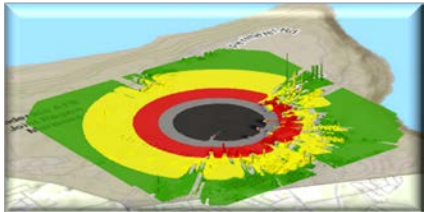


- Mobile training team
- 3 or 4 days of instruction
- SME instructors
- CME and CNE credits provided
- Topics include: Radiological Fundamentals, Current Threats, Radiation Biology, Dosimetry, Medical Management, Radiation Detectors, Accident Response
- Scenarios and culminating discussion-based workshop
- Risk Communication



Medical Radiobiology Advisory Team (MRAT)

Provides Operational Reach-Back & Support



- Three deployable, multi-service teams
- One health physicist and one radiation trained physician per team
- SME advice to Combatant Commanders, DoD agencies, allied forces, federal agencies, state and local governments
- Accidents and incidents involving nuclear weapons, nuclear reactors, radiological dispersal devices, and industrial and/or medical sources
- Advice on radiation protection, incident modelling for plume prediction and health physics interpretation of the results, personnel dose estimation, detection of ionizing-radiation and radionuclide identification, contamination control, decontamination, medical countermeasures, diagnosis and treatment of acute radiation syndrome and internal contamination and radiation risk communication

AFRRI Structures To Coordinate Research And Funding Agencies

Research Coordination

- **USU Office of Research**
- **USU Office of Sponsored Programs**
- **Henry M Jackson Foundation for Military Medicine**
- **Geneva USA**

Research Funding

- **JPC-7**
- **NIAID**
- **BARDA**
- **NIH**
- **DTRA**
- **NASA**
- **CDMRP**
- **JWMRP**

Interagency Coordination

- **Office of Science and Technology – The White House**
- **NATO Science Technology Organization**
- **DTRA**
- **Walter Reed National Military Medical Center**

Academic

University of Kentucky
Bundeswehr Institute of Radiobiology
Columbia University, Radiological Research Center
Hirosaki University
New York University, SOM
Harvard University,
Massachusetts General Hospital
University of California, Los Angeles
Johns Hopkins University, SOM
The College of New Jersey
Hamilton College
University of Maryland, SOM
University of Oxford
University of Wisconsin
University of Georgia
Ohio State University
Georgetown University
Nebraska University

Government

National Academy of Science
National Institute of Health, NIAAA
National Institute of Allergy, & Infectious Disease
National Aeronautics and Space Administration
Department of Veterans Affairs,
Baltimore Medical Center
Intelligence Advance Research Projects Activity
Defense Advance Research Projects Agency
Intelligence Advanced Research Projects Activity

Pharma & Co.

Cleveland BioLabs, Inc
Onconova Therapeutics
Cellerant Therapeutics
Humanetics Pharmaceuticals
ChromoLogic LLC
Bolder Biotechnology
Zymeron Corporation
Technology Holding LLC
Frontier Supplements
ASELL

Department of Defense

Joint Program Commtee-7
Defense Threat Reduction Agency
Defense Health & Human Services
Defense Health Agency
Naval Medical Research Center
Walter Reed Army Institute of Research
Walter Reed National Military Medical Ctr
U.S. Army Medical Research Institute for Infectious Diseases
U.S Army Nuclear and Countering Weapons of Mass
Destruction Agency
Office of Science & Technology Policy
National Strategic Research Institute

International

North Atlantic Treaty Organization
World Health Organization
National Council of Radiation Protection and
Measurements
International Standards Organization WG-18 & 25
Health Canada

AFRRI Subject Matter Expertise

Low Level Radiation

Dr. Catherine Davis-Takacs
Dr. Alexandra C. Miller

Biodosimetry

Dr. William F. Blakely
Dr. David L. Bolduc
Dr. Adarsh Ramakumar

Countermeasures

Dr. Lynnette Cary
Dr. Sanchita P. Ghosh
Dr. Greg Holmes-Hampton
Dr. Vidya P. Kumar
Dr. Alexandra C. Miller
Dr. Mang Xiao
Dr. Vijay Singh

Cellular Radiobiology

Dr. Sergey Iordanskiy
Dr. Robert Lowy

Internal Contamination and Heavy Metal

Dr. John Kalinich
Dr. Lynnette Cary
Dr. Alexandra C. Miller

Radiation Physics

Dr. Alia Weaver
Ms. Alena Tsioplaya
Mr. Greg Kim
Dr. David Schauer

Radiation Combined Injury

Dr. Juliann Kiang
Dr. David Burmeister
Dr. Mang Xiao

Radiation Sciences

LTC Omololu Makinde
Mr. Andrew Cook
Dr. Mathieu Brener
Mr. Tim Ayers
Dr. Inseok Baek

Clinicians

COL Naeem, MD
LTC Senchak, MD
MAJ Olsen, MD

Summary

- AFRRI is uniquely positioned to conduct low dose radiation research, training, and risk communication
 - Variety of radiation sources, generators and imaging systems operated and maintained by Radiation Sciences Department
 - Cutting-edge research and technology development
 - Employ multiple *in vitro* and *in vivo* models – from cells to non-human primates
- AFRRI is a strong interagency partner and academic collaborator

Questions and Thank you

