

Compromised Warfighter Success in a Near Peer Radiation Conflict: Operational Capability Impacted by Non-Lethal Behavioral and Neurological Deficits

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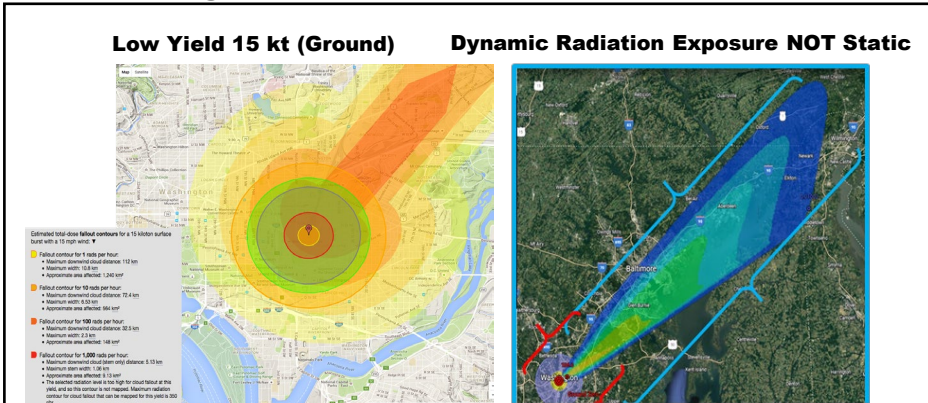
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Abstract

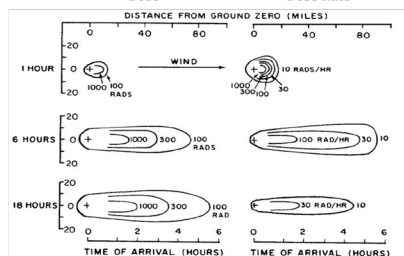
The US faces an increasing weapons of mass destruction (WMD) threat from actors of concern who may conduct activities throughout the operational environment (OE). The greatest and least understood challenge confronting the joint U.S. military force in a nuclear conflict is how to operate in a post-nuclear detonation (NUDET) radiological environment. Medical readiness challenges to sustained operations, will include exposure to multiple radiation qualities, i.e., mixed field neutron gamma, followed by chronic gamma exposure during "Fallout" at changing dose rates over time. The health effects of high dose exposures are well documented and research has been done on developing medical countermeasures to the acute radiation syndromes (ARS). In contrast, low-dose and low-dose-rate radiation health effects are not fully understood with most low-dose research focusing on stochastic effects like cancer. Of importance to military planners in a NUDET environment is increasing evidence that low-dose radiation exposure may be associated with deterministic low-dose outcomes including neurological disorders. These health issues are very relevant to military operations in a NUDET environment and if their development is rapid but difficult to detect, they can adversely compromise military operations.

Recent *in vivo* studies in our lab have shown that non-lethal neutron radiation (5-50 cGy) can cause neurological damage that is associated with a significant increase in early anxiogenic behavior, a decrease in cognition, and an increase in risk aversion within 48-72 hr post radiation. Mechanistic studies using murine neurological tissues demonstrated that these behavioral changes were associated with an increase in blood brain barrier permeability and an increase in cerebral inflammation. Importantly, studies with the ARS medical countermeasure, Ketone Ester (R3KE), showed that prophylactic or post-radiation oral administration of R3KE can inhibit neurological damage and reverse these adverse neurological effects. The extent of the health risks stemming from exposure to low-dose ionizing radiation is unclear. These potential risks have important implications for combat power and readiness in a dynamic post-NUDET environment. Development of compounds like ketone ester that are effective as both ARS and non-lethal countermeasures can be used to assist the warfighter and improve readiness and resilience during ongoing combat operations in a NUDET.

Background - Nuclear Detonation Scenario



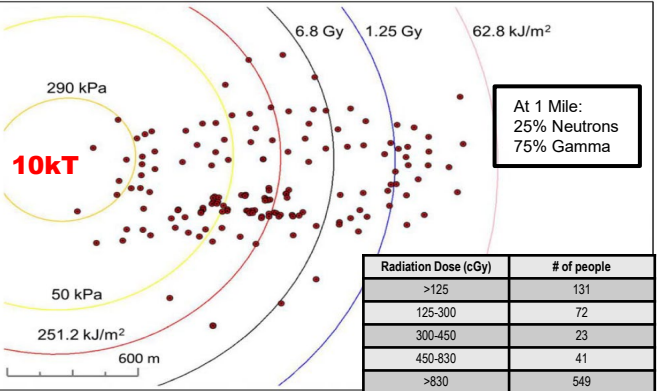
Dose and Dose Rate Estimates Post-Mixed Field Neutron Weapon Exposure



- 1) Military personnel at a distance from a nuclear detonation could receive a low dose of mixed field neutrons: gamma that does not cause development of acute radiation syndrome (ARS). They are presumed to have a "negligible" exposure.
- 2) There will be a constant change in gamma dose rate and exposure resulting from nuclear fallout. This is dynamic radiation exposure scenario and has not been widely studied.

Military Casualty Analysis

Institute for Defense Analysis - Casualty Estimation for Nuclear and Radiological Weapons, 2015 DTRA-TR-21-027, DTRA-TR-19-002

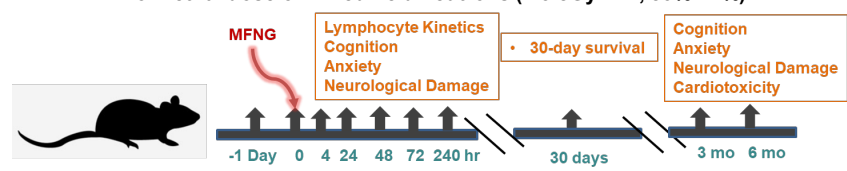


Post NUDET
16% Combat Ready
OR
Are They

Research Design/Objectives

Mixed Field Neutron Study

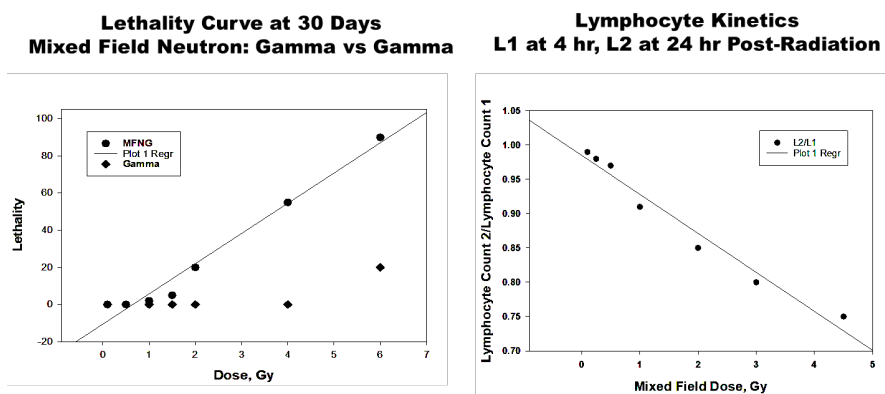
- Establish a murine model in which there are no clinical signs or symptoms of acute radiation syndrome (ARS)
- Non-lethal dose of mixed field neutrons (2.5 cGy/min, 83%:17%)



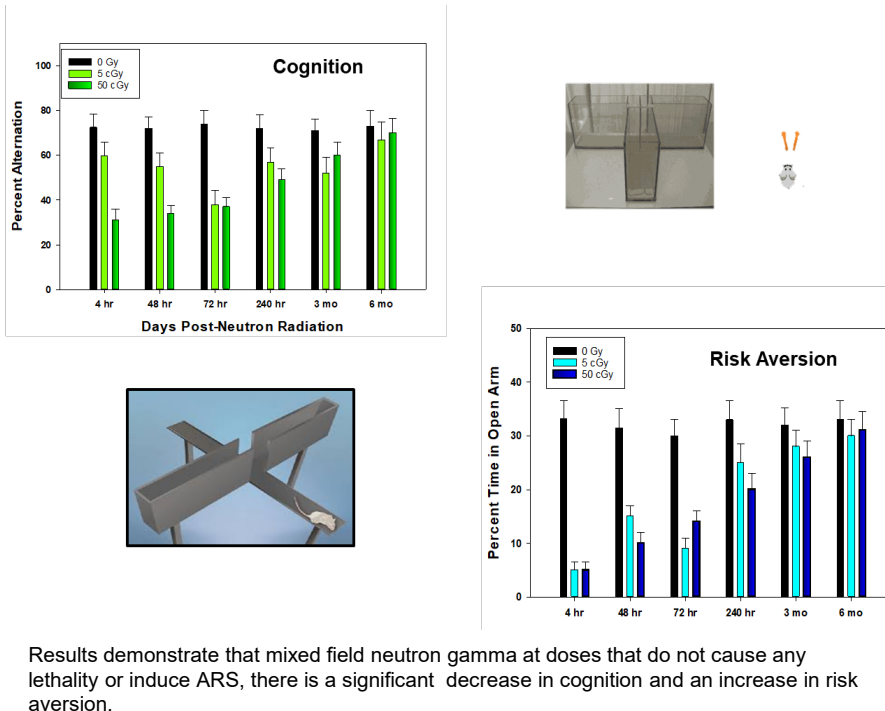
- Dose
- Dose Rate
- Mixed Field Neutron: Gamma Ratio

Results

Mixed Field Neutron: Gamma Radiation Model (2.5 cGy/min 150 cGy/hr)

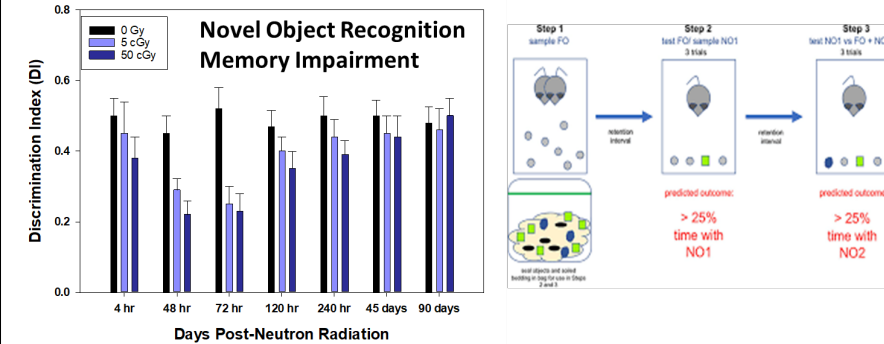


Mixed Field Neutron-Induced Effects in Mice Behavioral Effects (Non-Lethal Dose; 2.5 cGy/min)

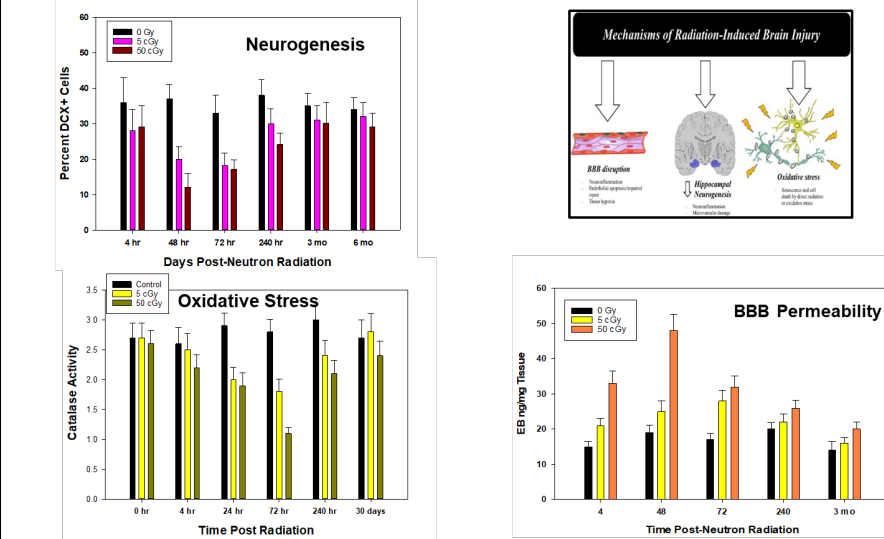


Results

Mixed Field Neutron-Induced Effects in Mice Behavioral Effects (Non-Lethal Dose; 2.5 cGy/min)

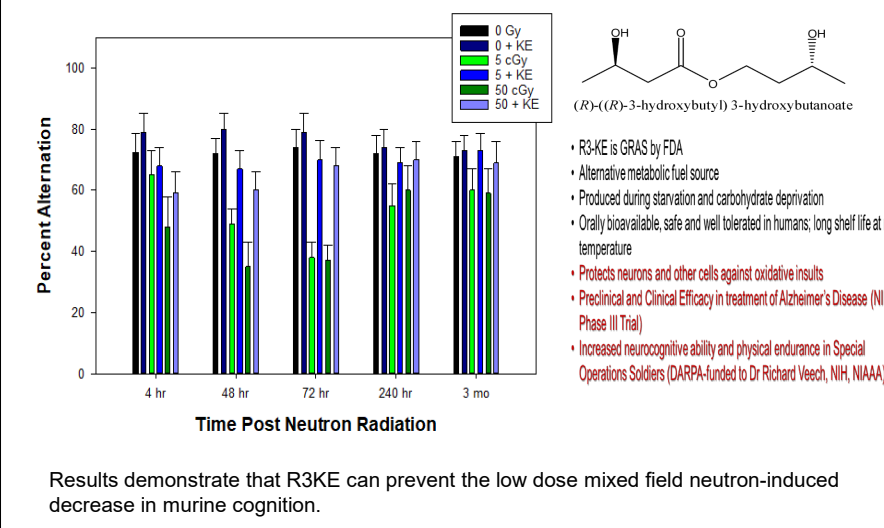


Mixed Field Neutron-Induced Effects in Mice Neurobiology Effects (Non-Lethal Dose; 2.5 cGy/min)



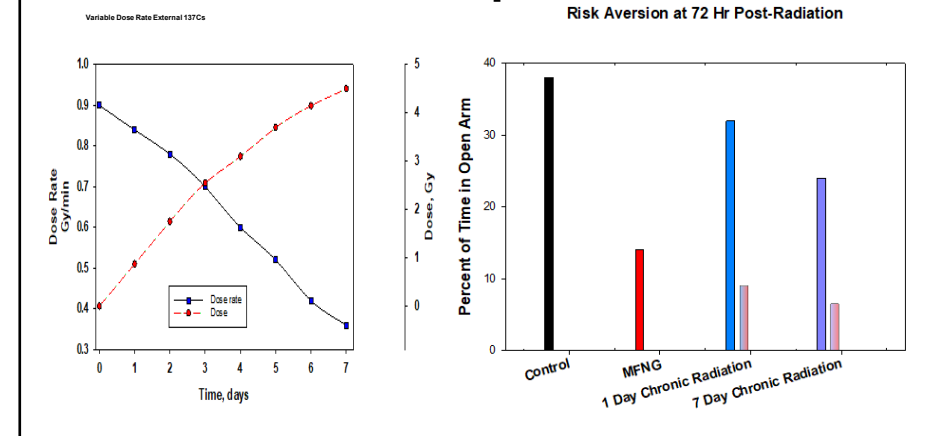
Results: Medical Countermeasure Study

Mixed Field Neutron-Induced Effects in Mice Behavioral Effects (Non-Lethal Dose; 2.5 cGy/min) With Ketone 1X (pre- 4 hr)



Results

Mixed Field Neutrons Followed by Chronic ¹³⁷Cs Exposure



Summary

- Non-lethal, Non-ARS mixed field neutron dose resulted in a decrease in cognition, increase in risk aversion, and an increase in memory impairment.
- Non-lethal, Non-ARS mixed field neutron dose resulted in a decrease in neurogenesis, increase in oxidative stress, increase in blood brain barrier permeability, and increased inflammatory response.
- Treatment with the ketone ester, R3KE, prophylactically significantly ameliorated the decrease in cognition and risk aversion (not shown).
- Preliminary data suggest that low dose mixed field neutron gamma radiation followed by a chronic dose of ¹³⁷Cs (mimicking fallout) caused a significant and additive decrease in cognition in comparison to chronic radiation alone.
- Nonlethal radiation effects may compromise military operations.

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