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CRITICAL SUPPORT at a crucial time

Since 2011, the Fukushima nuclear reactor incident continues to loom large in people's minds with regard to radiation safety and preparation.

Bob Terbrueggen expands on the critical need for a high throughput radiation biodosimetry test after a mass-scale radiological event

"When we look at the threats against us in chemical, biological, nuclear and radiological, the threat is real. It's evolving in its persistence. Whether the threat comes from rogue states or terrorist groups, our adversaries are interested in creating terror and destruction through the use of chemical, biological, radiological and nuclear weapons"

ELAINE C. DUKE, SEVENTH DEPUTY SECRETARY OF THE DEPARTMENT OF HOMELAND SECURITY, THE FUTURE OF COMBATING TERRORISM AND COUNTERING THE USE OF WMD, DECEMBER 2017

North Korea's recent missile and nuclear tests, along with rising political tensions between the United States and Russia have led to renewed interest in preparedness for a nuclear attack. While significant progress has been made in the development and stockpiling of medical countermeasures to radiation, as well as detailed planning on how and when to use them, a critical unmet need has been the lack of a rapid high throughput radiation biodosimetry test that can be used to determine individualized levels of absorbed radiation post-event.

A nuclear reactor incident like Fukushima, a radiological dispersal device (RDD), and a nuclear detonation ➤

are the three most commonly planned-for nuclear events. A nuclear detonation is by far the most severe in terms of actual medical casualties; however, a deep-set fear of radiation leads these other events to being viewed by the general public as similar, all resulting in large 'worried well' populations that could overwhelm emergency response personnel and hospitals.

Fukushima

The 2011 Fukushima Daiichi Nuclear Power Plant (NPP) disaster shows how even a well-planned-for event can result in a significant need for radiation biodosimetry testing. Fukushima was caused by a magnitude-9 earthquake off the east coast of Japan, leading to a massive tsunami and damage to three of the Fukushima nuclear reactors. Six of the local area hospitals designated as primary radiation emergency facilities prior to the event were closed or failed to function properly owing to evacuation or indoor sheltering orders, damaged facilities and infrastructure disruption caused by the earthquake, or outflow of medical staff in fear of radiation danger.

No lives were lost at Fukushima due to radiation exposure; however, 50 elderly people died during the initial emergency evacuation due to hypothermia, dehydration, and their underlying medical conditions. Some ambulance drivers refused to transport patients out of fear of radiation exposure, and others could not accept or transport contaminated victims because their vehicles and facilities were not properly sanctioned to handle high levels of radiation. People, fearing radiation contamination, flooded the hospital system, which was already dysfunctional due to the damage caused by the earthquake and ensuing tsunami.

In total, the Great East Japan Earthquake and Fukushima disaster led to more than 460,000 people being displaced to 2,400 shelters. According to the report on disaster related deaths, 2,688 people died at shelters and temporary houses in the two years following. About 90% of the disaster-related deaths were elderly, and poor medical care was partially to blame, even though 24,000 medical personnel were actively involved in the response.

According to Japan's Health Ministry, fear of radiation (understandable in Japan) was listed as a primary reason behind medical resources being less than effective. Information on radiation and the situation of vulnerable people was not properly shared – nor was sufficient communication among related personnel established during the disaster response.

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REDI-Dx testing has been demonstrated to be easily integrated into response plans and workflows for government and healthcare agencies tasked with response and recovery efforts from radiological incidents.

Testing for radiation dose

Clinical guidelines for the triage and treatment of individuals following a nuclear event are based on a combination of physical injury, absorbed radiation dose, and availability of resources.

THE GOIÂNIA INCIDENT

The 1987 incident in Goiânia, Brazil shows how discovery of a thimble-sized capsule of the radioactive isotope cesium 137 by two child scavengers can lead to 120,000 people (about 10% of the Goiânia) flooding a local Olympic soccer stadium demanding testing for radiation exposure. This incident overwhelmed the available emergency response resources, and in the end 249 of the triaged 120,000 (0.2%) were diagnosed with ARS (acute radiation syndrome), meaning 99% of the civilians triaged were part of the worried well.

	Complexity	Sensitivity	Specificity	Time to Result	Testing Capacity
Radiation survey meter	+	–	–	< 1 Day	High
Personal dosimetry device	+	–	–	< 1 Day	High
Clinical symptoms alone	+	–	–	7+ Days	High
Dicentric chromosome assay	–	+	+	7+ Days	Low
Lymphocyte depletion kinetics	–	–	+	3+ Days	Medium

Comparison of traditional biodosimetry tests: radiation survey meters can only detect if a person has external contamination but they are not able to measure the level of absorbed dose. The current gold-standard absorbed dose biodosimetry test is the Dicentric Chromosome Assay (DIC) - but it takes three days to deliver results. Blood samples must be tested within 24 hours post-collection, and there is insufficient throughput to respond to a mass-scale radiation event.

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RADIATION BIODOSIMETRY

Estimated population numbers of victims following a given radiological event based upon projections within the centre of a densely populated city.

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	RADIOLOGICAL EVENT		
	Nuclear Reactor Incident	Radiological Explosure/ Dispersal Device	Military Nuclear Device Detonation
Population requiring medical treatment	10 – 1,000	100 – 1,000	10,000 – 250,000
Population worried about explosure "worried well"	10,000 – 250,000	10,000 – 500,000	500,000 – 2,000,000

Absorbed dose is measured in Gray (Gy), and individuals receiving a dose of greater than 0.7 Gy are likely to experience ARS.

Doses above 2.0 Gy start to require medical treatment, and 50% of people receiving 5 Gy will die without medical treatment. A total body dose of 8 Gy or higher is usually fatal even with intensive medical treatment.

Unfortunately, accurately determining an individual's absorbed radiation dose, especially in the immediate wake of a radiological event, is not a simple task. ARS can be asymptomatic for days to weeks after initial exposure, and the clinical symptoms of exposure are irregular and non-specific, making accurate diagnosis difficult.

Today, the most commonly referenced radiation biodosimetry test is the dicentric chromosome assay, which has been in use for more than 50 years. This cytogenetic test examines chromosome breaks from a cultured blood sample and has proven effective at helping to understand the long-term effects of radiation exposure. However, the dicentric protocol is labour intensive, requires highly skilled cytologists, has limited worldwide capacity, and requires rapid, controlled transport of samples to the testing laboratory.

First CE-IVD test

Recognizing the critical unmet need for radiation biodosimetry testing, BARDA (Biomedical Advanced Research and Development Authority), a division of Health and Human Services of the US Government, has invested more than $365 million since 2009 in the development of next-generation radiation biodosimetry tools. These efforts have evaluated traditional cytogenetic techniques, as well as advanced proteomic and genomic methods.

Gene expression testing has been shown to be particularly promising, and in 2016 BARDA awarded DxTerity Diagnostics up to $150 million for the advanced development and delivery of REDI-Dx,* a gene expression-based biodosimetry test, for potential placement in the US Strategic National Stockpile (SNS) through 2026.

REDI-Dx estimates absorbed radiation dose from a post-event-collected blood sample, which is shipped ambient and ➤

The REDI-Dx assay has been designed to be fully compatible with today's high throughput lab automation systems, allowing for high volume and fast turnaround of test results for rapid response.

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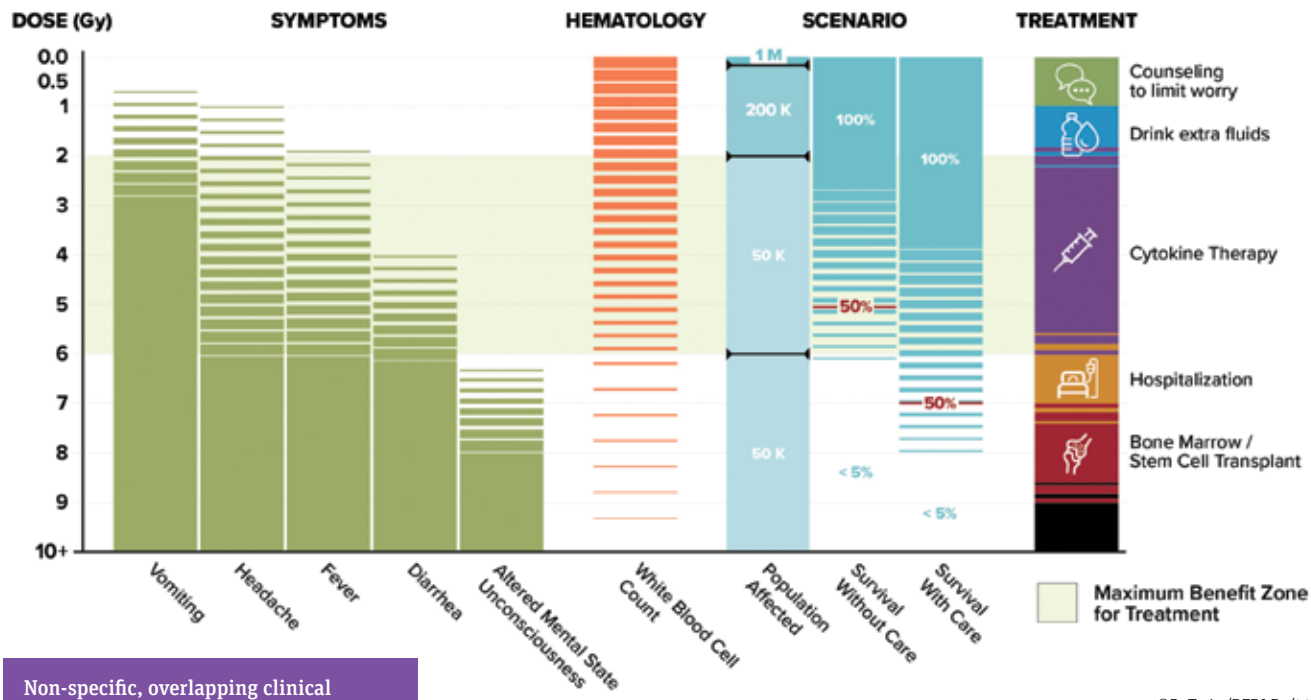
Effective management of civilians following a mass-scale nuclear event requires a high throughput way to estimate absorbed radiation dose.



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Non-specific, overlapping clinical symptoms (vomiting, headache, fever, diarrhoea, confusion) and haematology are currently used to prioritize victims of absorbed radiation for potentially life-saving medical interventions.

stable for up to 14 days, greatly simplifying response logistics over the dicentric chromosome assay. The REDI-Dx test can be analysed using Thermo Fisher's existing install base of ABI 3500xL Dx Genetic Analyzers with associated REDI-Dx Biodosimetry Interpretive Software. Each high throughput instrument can process over 1,000 samples per day, enabling a capacity of tens of thousands per week on existing infrastructure.

While radiological response to an unknown disaster will still present challenges and difficulties we must all overcome, past events like Fukushima and Goiânia have taught us there is still a need for a next-generation radiation biodosimetry solution like REDI-Dx: a test that could help provide critical support to emergency responders and clinicians when they – and those affected – need it the most.

REDI-Dx®

REDI-Dx is CE-IVD marked.
Not for Sale in the USA. Limited by United States law to investigational use only.

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Bob Terbrueggen, PhD is the Founder and CEO of DxTerity, a Los Angeles-based diagnostics company specializing in the development of cost-effective, high-precision genomic tests. REDI-Dx is a product of DxTerity Diagnostics and the first and only radiation biodosimetry test with CE-IVD mark.