NNSA Laboratory Directed Research & Development
Discovery and Innovation for National Security
2012 Symposium

SpinDx™: Rapid Radiation Biodosimetry

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What is the challenge?

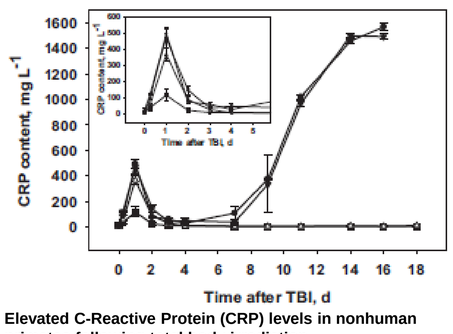
Radiation Biodosimetry

- Existing methods for radiological dose assessment do not meet the needs for rapid triage in mass-exposure scenarios.
- Improved methods are urgently needed that can rapidly discriminate high-priority victims from the "worried well" following potential ionizing radiation exposure.

The Fukushima Daiichi disaster in March 2011 highlights the urgent need for improved radiation dosimetry tools.

Peripheral Blood Biomarkers

- Extensive animal testing has revealed a panel of biomarkers in blood that can be used to estimate exposure dose across broad dose and time windows, including:
  - **Proteins:** up-regulated from different physiological pathways in response to radiation damage
  - **Hematology:** depletion of white blood cells due to hematopoietic damage



Elevated C-Reactive Protein (CRP) levels in nonhuman primates following total body irradiation
1 Gy – squares; 3.5 Gy – open triangles up; 6.5 Gy – triangles down; 8.5 Gy – circles
(Ossetrova et al, 2011, Rad. Meas. 46, 1019-1024)

Objective

- Develop a point-of-care device for detection of multiple radiation dosimetry markers simultaneously using finger puncture volumes of whole blood
- **Key Requirements:**
  - Combined protein quantification and cell counting capability
  - Less than 15 minute sample-to-answer
  - Fully automated, limited user interaction
  - Portable, hand-carried device

What is our innovation?

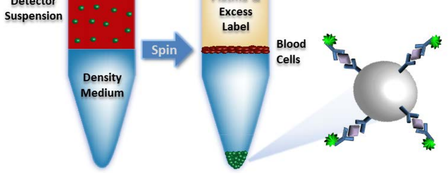
SpinDx™ Salient Features

- Fully automated, field-deployable biodosimetry device
- Multiplexed protein immunoassays and hematology assays from 20-µL blood samples
- 15 minute sample-to-answer time
- No up-front sample preparation required
- Inexpensive: ~$500 per reader, ~$2.00 per consumable disk

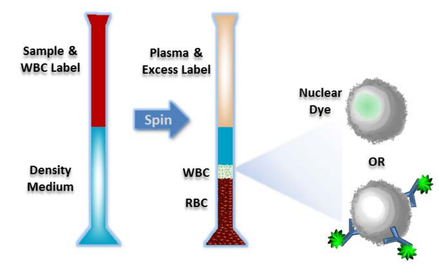
Approach

- Novel sedimentation assays upon single-use centrifugal microfluidic disks
- Fluorescent readout and biomarker quantitation
- Algorithm-based dose estimation based on multi-parameter biomarker panel

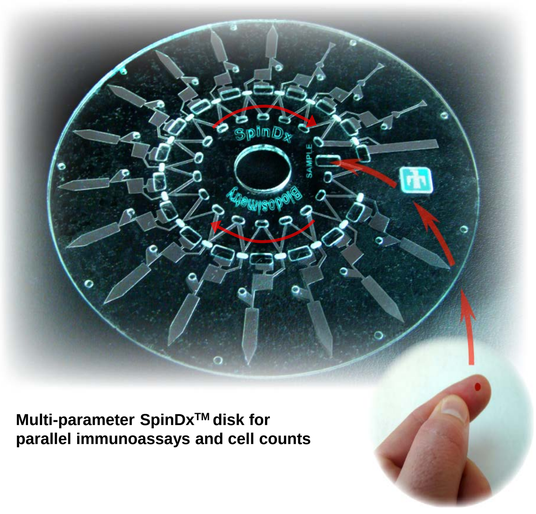
SpinDx™ prototype reader



On-disk sedimentation-based immunoassay scheme
(Schaff and Sommer, *Clin Chem* 57, 753-761, 2011)



On-disk WBC separation and quantitation



Multi-parameter SpinDx™ disk for parallel immunoassays and cell counts

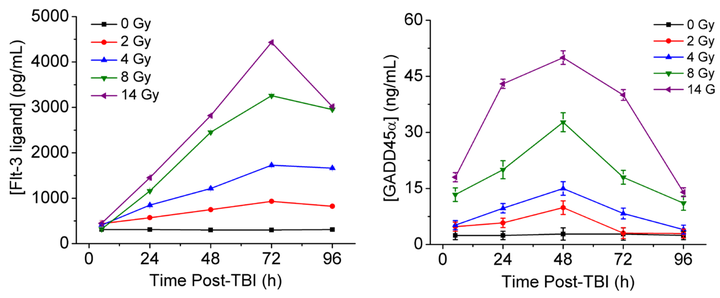
What have we learned so far?

In Vivo Validation: Mouse Total Body Irradiation (TBI) Studies

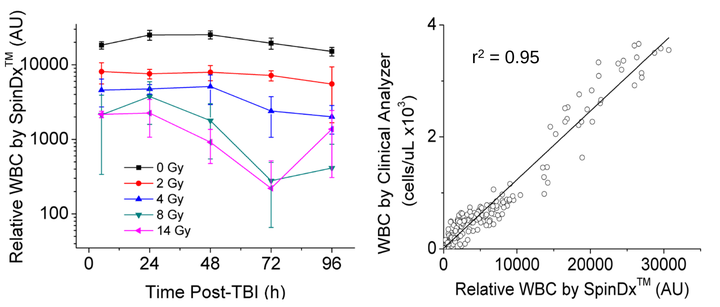
- CD2F1 male mice (n = 204) exposed to doses ranging from 0 to 14 Gy with ^{60}Co γ-rays at dose rate 0.6 Gy/min.
- Blood samples were taken from 5h – 4d post-exposure.
- Samples analyzed with SpinDx™ for the following radiation-responsive biomarkers:
  - **Proteins:** Flt-3 Ligand, GADD45α, Serum Amyloid A (SAA), and Interleukin 6 (IL-6)
  - **Hematology:** Total white blood cell count (WBC)
- Results compared with gold standard measurements (ELISA and clinical hematology analyzer) performed at AFRRI

Results

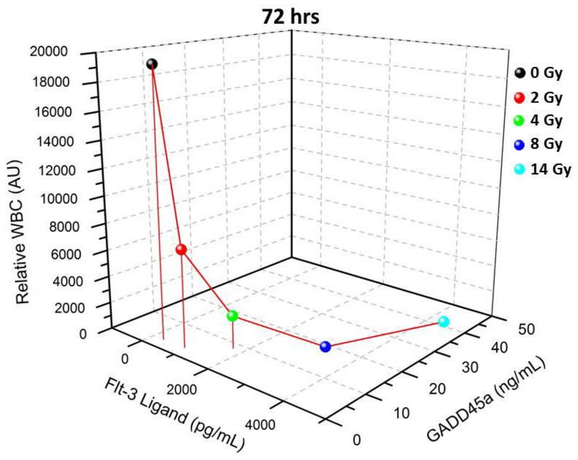
Dose and time course response for protein biomarkers Flt-3 ligand and GADD45α.
Method comparison with ELISA show strong correlation: $r^2 = 0.96$ and $r^2 = 0.98$, respectively



Dose and time course response for total WBC, and method comparison with clinical hematology analyzer.



Multi-Parameter Dose Discrimination



Three-dimensional graphical representation of multi-parameter biomarker response at 3 d post-exposure.
Algorithm-based dose assessment will be fully automated within final product.

(Manuscript in preparation)

Why is this important for our nation?

Radiological/Nuclear Threats

- Our nation is not prepared for mass radiological exposure scenarios.
- New tools are urgently needed to assist in medical triage following radiation release.
- Growing threats of intentional or accidental releases from radiological dispersal devices (RDDs), improvised nuclear devices (INDs), nuclear weapons (NWs), and nuclear power plants.

Mass Casualty Projections (10-kiloton detonation in city of 2 million people)

Patient Category	Number of Patients
Immediate fatalities	**> 13,000**
Expectant care (>10 Gy)	**45,000**
Intensive care (5 – 10 Gy)	**79,400**
Critical care (3 – 5 Gy)	**108,900**
Normal care (1 – 3 Gy)	**70,000**
Ambulatory monitoring (0.5 – 1 Gy)	**139,000**

(Waselenko et al, Clinical Guidelines 2004)

Multi-Use Capability

- Biodosimetry devices will be of greatest value if the technology also translates to more routine clinical use (lower barrier to adoption for rare emergency events).
- SpinDx™ has broad applicability for both biodefense and clinical needs:
  - We have demonstrated rapid, ultra-sensitive quantitation of toxins and pathogens of biodefense concern.
  - Furthermore, we are exploring utility for routine clinical assays such as Complete Blood Counts (CBC) and infectious disease screening.

Funding: Sandia LDRD #10-0104