Resources That Could Support Acute and Long-term Health Surveillance in a Radiological / Nuclear (R/N) Incident

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A US Department of Energy (DOE) asset at the
Oak Ridge Institute for Science & Education (ORISE)

Operated for the DOE by
Oak Ridge Associated Universities (ORAU)
DOE/NNSA Office of Counterterrorism and Counterproliferation (CTCP)
REAC/TS Mission

Radiation Medicine
- Provide advice and consultation on diagnosis and management of ionizing radiation-related injuries
- Deployment capabilities in US in support of DOE NNSA and internationally

Education and Expertise
- Provide state-of-the-science educational opportunities for the emergency preparedness and response community in the US and throughout the world (FY19: ~6,000 participants)
- Maintain a robust Radiation Accident Registry

Radiation Dose Assessment Capability
- Provide timely dose estimation for external exposures or internal contamination
- Perform cytogenetic dicentric chromosome assay (DCA) as “gold” standard of biodosimetry
REAC/TS Radiation Accident Registry

• The 1st and 2nd accidents chronicled: Las Alamos National Lab Criticality events in 1945 and 1946
• Contains consultations done on-site and off-site
• 2,787 Entries
• Complete history and physical examinations, laboratory, imaging, pathology, post-mortem reports, and tissue for many cases
• Many patients have been followed from the accident to present day, including the last survivor of the Y-12 Criticality Accident, 1958
• A US DOE Registry
  – Not an open access registry
  – Not de-identified (has Personal Identifying Information and Personal Health Information)
Human Subject Health and Protection Surveillance
Protecting Worker Health and Safety

• Began in Early 1960’s
• Secure Quality and Integrity of Data
• Protection of Sensitive Data (Personal Identifying Information)
• Dissemination of Results in Wide Range of Platforms
• Radiation Exposure Monitoring of DOE Employees, Contractors, Subcontractors and Members of the Public (in controlled, monitored areas)
• Million Person Study
Human Subject Health and Protection Surveillance
Protecting Worker Health and Safety

• 725,000 Workers With More Than 4 Million Occupational Radiation Exposure Records (30 DOE sites)
• Analytical Data for More Than 80 Health Studies of More Than 1 Million Workers (de-identified data)
• All Occupational Radiation Exposure Records on Workers Submitted to NRC, + 7 Million Records for More Than 1 Million Workers

12.5 Million Health Records
REAC/TS Cytogenetic Biodosimetry Laboratory (CBL) Retrospective Biodosimetric Dose Assessment Confirmation

• Dicentric Chromosome Assay (DCA) is most widely used for absorbed radiation dose assessment for individual cases and population triage, “Gold Standard”

• DCA formation is dependent on radiation dose and dose rate

• Minimal inter-individual variation in baseline frequency unlike most “omics” biomarkers

• Lowest level of sensitivity for dicentric detection is ~0.1 Gy of low LET radiation
REAC/TS CBL
Retrospective Biodosimetric Dose Assessment Confirmation

- Applicable for partial body exposure if the radiation dose is high enough (> 2 Gy)
- Estimation of exposure requires appropriate **calibration curves**
- Sufficient sensitivity for detecting diagnostic overexposure cases
- Useful for assessing the extent of short and long-term damage to hematopoietic system
- **Stable chromosome changes** (translocations and inversions) can be used for retrospective dosimetry and for predicting stochastic effects
Application of Cytogenetic Biodosimetry for Individualized Absorbed Radiation Dose Assessment

Incidental/accidental exposure

Blood collection, lymphocyte culture and chromosome preparation

Dicentric chromosome

fragments normal chromosome

Ring chromosome

Dose-response curve

Radiation dose assessment

Long term monitoring for stochastic effects
Application of Radiation Cytogenetic Biodosimetry Tools for Human Population Monitoring

Absorbed radiation dose assessment based on chromosomal aberration frequencies

- **Centromere/telomere FISH**
  - Dicentric Ring chromosomes
- **Whole chromosome specific paints**
  - Translocations
- **Multicolor FISH**
  - Simple and complex translocations
- **Multicolor Band**
  - Normal Inverted Inversions

Unstable Short-term monitoring

Stable and Persistent Changes for Retrospective Dosimetry

Long term monitoring for stochastic effects

Genomic instability
Long-term Cytogenetic Follow-up Study on a Radioiodine Therapy Patient

- **Case History:** Received two rounds of ablative radioiodine therapy for thyroid cancer
  - 1\textsuperscript{st}: 48 mCi of $^{131}$I in mid-January, 1992; 2\textsuperscript{nd}: 392 mCi in mid-March, 1994
  - **Cytogenetic follow up study was performed for micronuclei, dicentric chromosomes and translocations**

Fluoroscopy-induced Cutaneous Injury - REAC/TS

* Received 1 h of fluoroscopy in September 2007 to locate a coronary blockage
* Another 1 h in January 2008
* ~5 h procedure in April 2008 (Exact time undetermined)
* Referred to REACTS in December 2008
* X rays with an approx. voltage of 140kVp
* Intermittent exposure, total beam time?

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**Translocation frequency/Cell**

- 10 months
- 96 months

(Time after fluoroscopy)

**Dicentric chromosome frequency/Cell**

- 1.13 Gy
- 1.05 Gy
- 0.34 Gy

(Time after exposure)

Total Cells
Analyzed - 215
Translocations - 95
Frequency/Cell - 0.44/Cell
Y-12 Criticality Patient, 1958

June 16, 1958 occurred at Oak Ridge, TN.
86 years old

Cytogenetic Studies:
2008
2015
2016

No marked increase in chromosomal aberrations

Dicentrics: 2 in 934 cells
Translocations: 3 in 250 cells
Inversions: None

Normal base line frequencies for aberrations
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Absorbed radiation dose assessment based on chromosomal aberration frequencies

- Centromere/telomere FISH
  - Dicentric chromosomes
  - Ring chromosomes

- Whole chromosome specific paints
  - Translocations

- Multicolor FISH
  - Simple and complex translocations

- Multicolor Band
  - Normal
  - Inverted
  - Inversions

Unstable
- Short-term monitoring

Stable and Persistent Changes for Retrospective Dosimetry
- Long term monitoring for stochastic effects

Genomic instability
Summary

- REAC/TS has 43 years experience in emergency response and consultation on radiation injuries and illnesses
- REAC/TS Registry has 74 years of accidents and health surveillance
- ORISE Registries have 60 + years of registries/databases for worker health surveillance and population monitoring with 12 Million health records
- Our registries are ongoing for population research purposes
- REAC/TS CLIA Cytogenetic Biodosimetry Lab is actively operational in retrospective cytogenetic biodosimetric dose assessment
Thank You!

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Recent Registries Bibliography

2019


2018


Recent CBL Bibliography