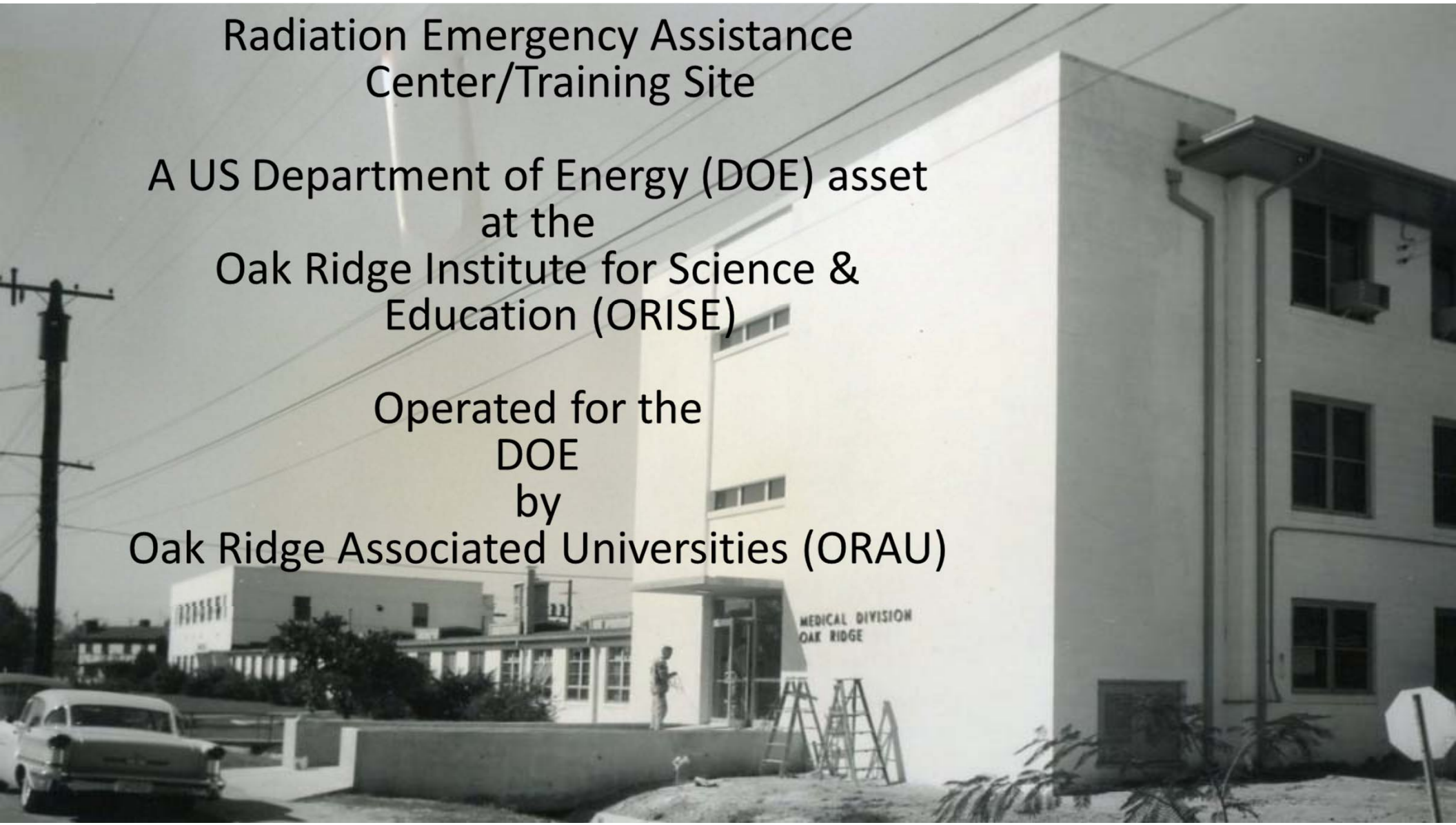
Resources That Could Support Acute and Long-term Health Surveillance in a Radiological / Nuclear (R/N) Incident

Carol J. Iddins, MD, FAADM
Director
Radiation Emergency Assistance Center/Training Site

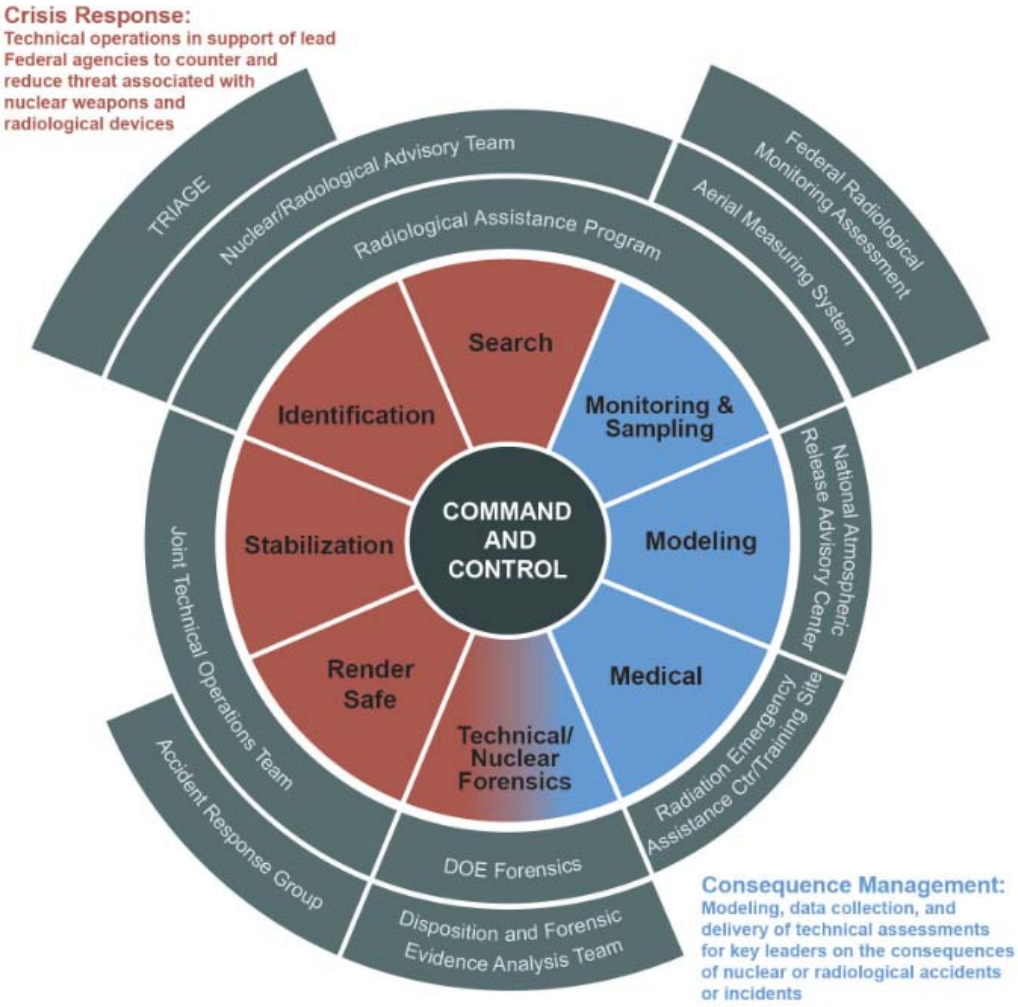


Radiation Emergency Assistance Center/Training Site

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

Provide 24/7 Response and Medical Consultation World-wide

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**

OAK RIDGE INSTITUTE FOR SCIENCE AND EDUCATION
Shaping the Future of Science

Human Subject Health and Protection Surveillance

Protecting Worker Health and Safety

OAK RIDGE INSTITUTE FOR SCIENCE AND EDUCATION
Shaping the Future of Science

- 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

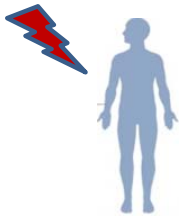
- Dicentric Chromosome Assay (DCA) is most widely used for absorbed radiation dose assessment for individual cases and population triage, **"Gold Standard"**
- DCA formation is dependent on **radiation dose and dose rate**
- **Minimal inter-individual variation** in baseline frequency unlike most "omics" biomarkers
- Lowest level of sensitivity for dicentric detection is ~0.1 Gy of low LET radiation

REAC/TS CBL
Retrospective Biodosimetric Dose Assessment Confirmation

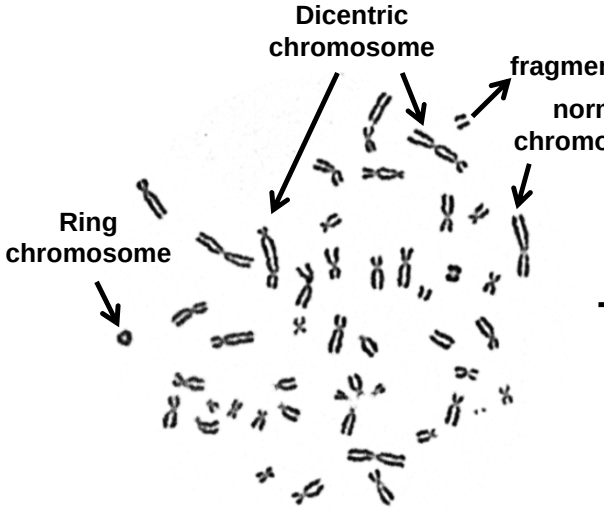
- **Applicable for partial body exposure if the radiation dose is high enough (> 2 Gy)**
- Estimation of exposure requires appropriate **calibration curves**
- Sufficient sensitivity for detecting diagnostic overexposure cases
- Useful for assessing the extent of short and long-term damage to hematopoietic 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

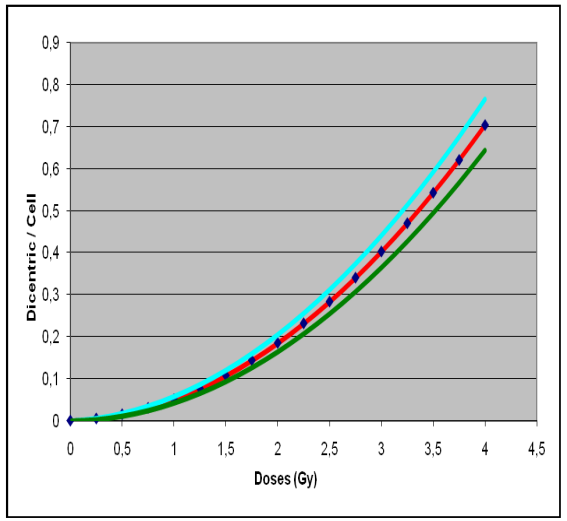
Incidental/accidental exposure



Blood collection, lymphocyte culture and chromosome preparation



Dose-response curve



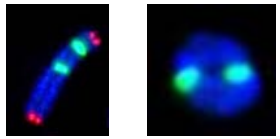
Radiation dose assessment

Long term monitoring for stochastic effects

Application of Radiation Cytogenetic Biodosimetry Tools for Human Population Monitoring

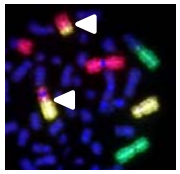
Absorbed radiation dose assessment based on chromosomal aberration frequencies

Centromere/telomere FISH



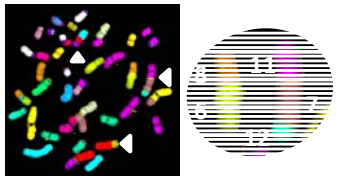
Dicentric chromosomes | Ring

Whole chromosome specific paints



Translocations

Multicolor FISH



Simple and complex translocations

Multicolor Band

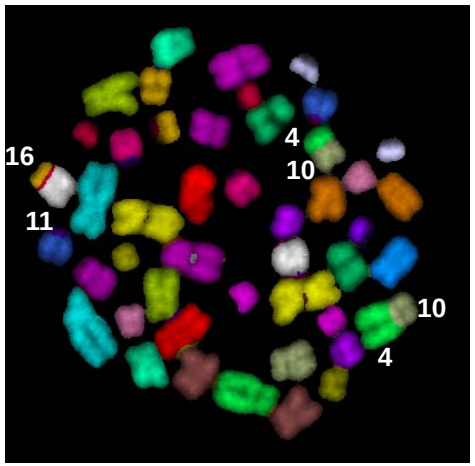
Normal | Inverted

Inversions

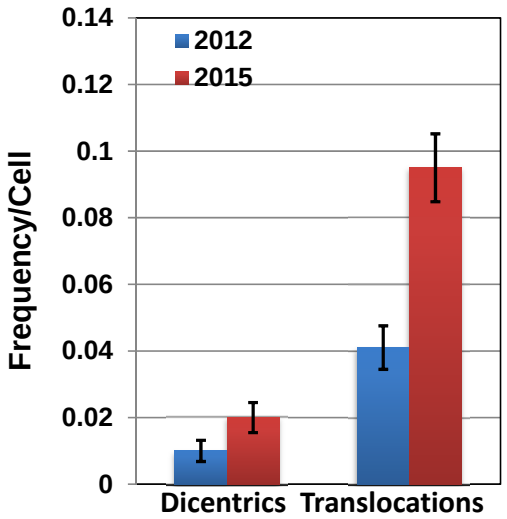
Unstable — **Stable and Persistent Changes for Retrospective Dosimetry**

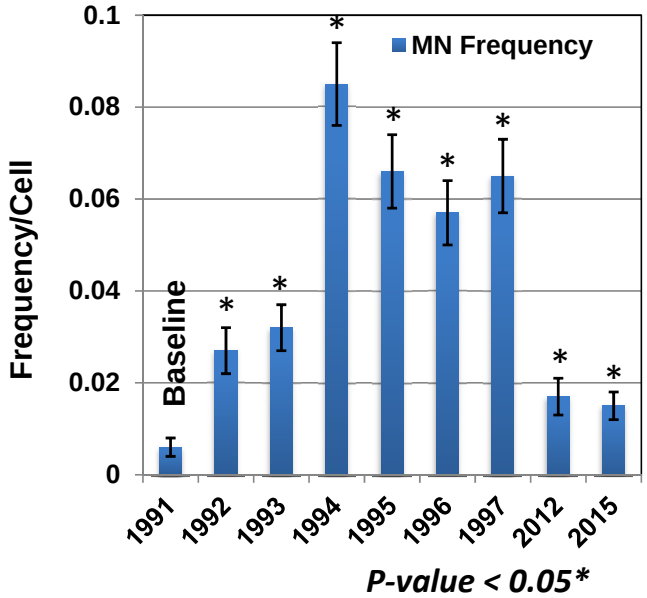
Short-term monitoring → **Genomic instability** ← **Long term monitoring for stochastic effects**

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



Multicolor FISH





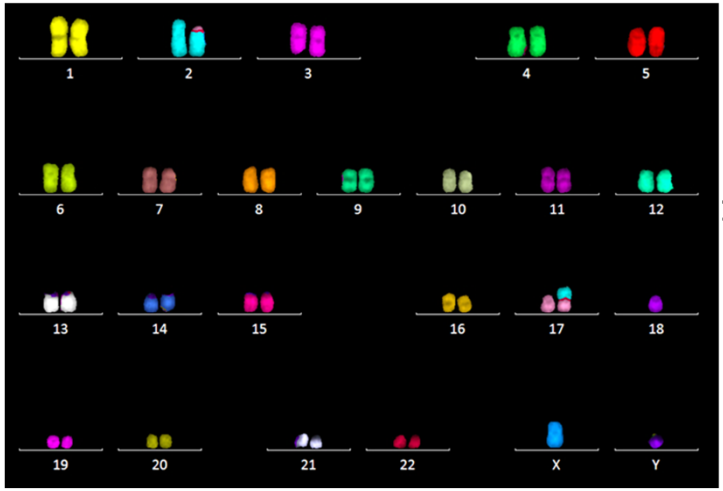
*P-value < 0.05**

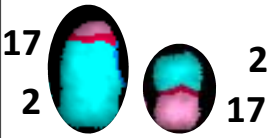
- Case History: Received two rounds of ablative radioiodine therapy for thyroid cancer
- 1st: 48 mCi of ^{131}I in mid-January, 1992; 2nd: 392 mCi in mid–March, 1994
- Cytogenetic follow up study was performed for micronuclei, dicentric chromosomes and translocations

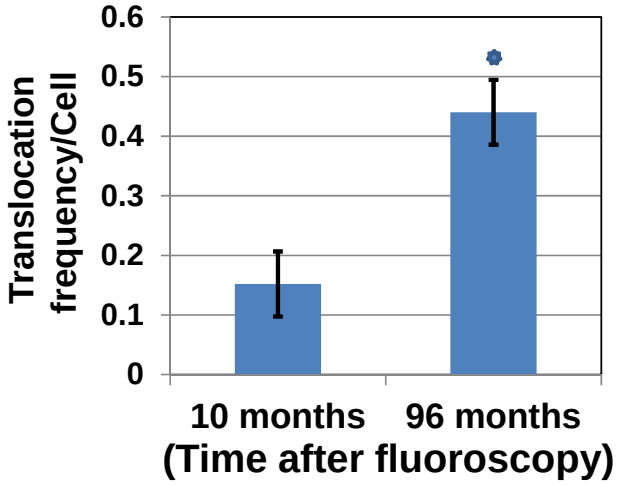
Livingston, G. K., M. Escalona, A. Foster, A. S. Balajee. Persistent In Vivo Cytogenetic Effects of Radioiodine Therapy: A 21 Year Follow-up Study Using Multicolor FISH. Journal of Radiation Research 59(1):10–17 (January 2018). doi: 10.1093/jrr/rrx049.

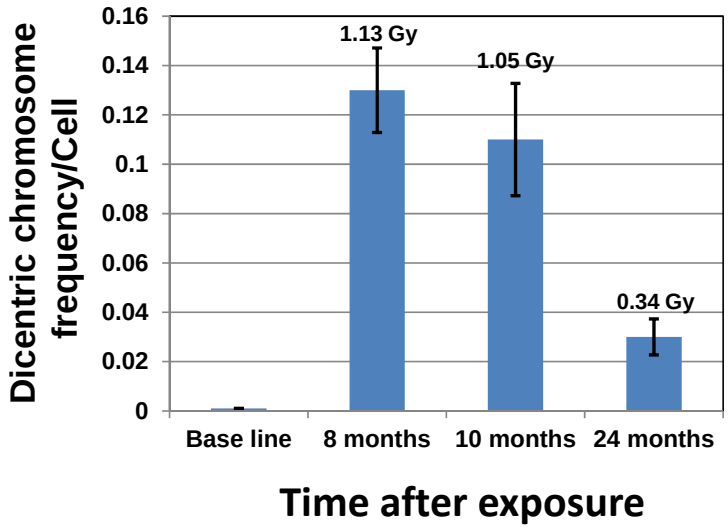
Fluoroscopy-induced Cutaneous Injury - REAC/TS

* 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 ?









Total Cells Analyzed - 215
Translocations - 95
Frequency/Cell - 0.44/Cell

Y-12 Criticality Patient, 1958

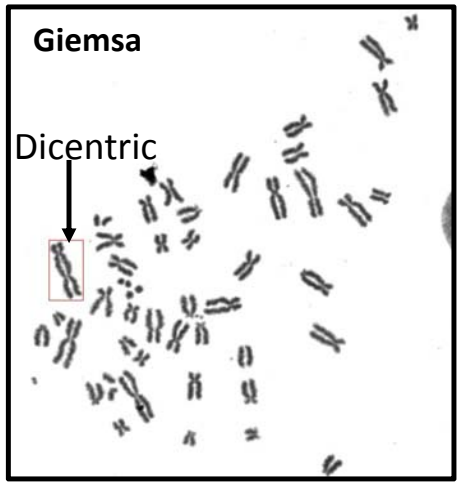
June 16, 1958 occurred at Oak Ridge, TN.
86 years old

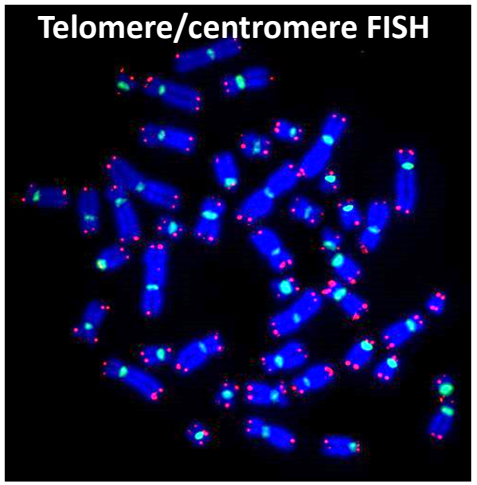
Cytogenetic Studies:
2008
2015
2016

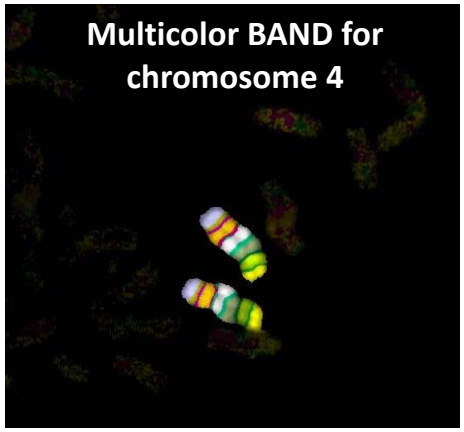
No marked increase in chromosomal aberrations

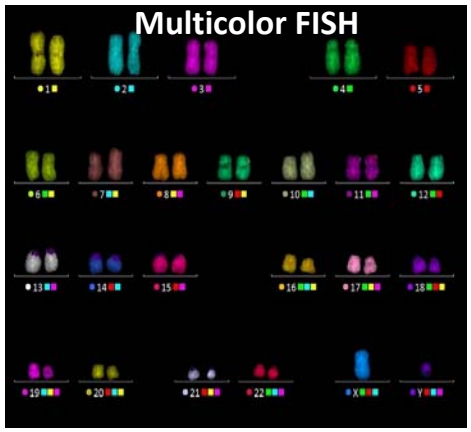
Dicentrics: 2 in 934 cells
Translocations: 3 in 250 cells
Inversions: None

Normal base line frequencies for aberrations





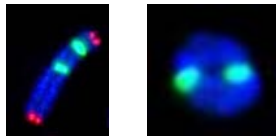




Application of Radiation Cytogenetic Biodosimetry Tools for Human Population Monitoring

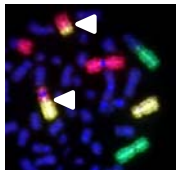
Absorbed radiation dose assessment based on chromosomal aberration frequencies

Centromere/telomere FISH



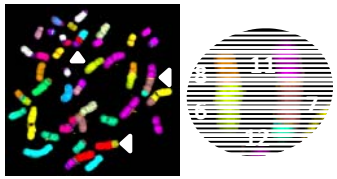
Dicentric chromosomes | Ring

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


Special Thanks to Dr. Donna Cragle and Dr. Adayabalam Balajee
reac/ts
150 East Vance Road
ORISE
OAK RIDGE INSTITUTE FOR SCIENCE AND EDUCATION
Radiation Emergency Assistance Center/Training Site
Managed for the U.S. Department of Energy by Oak Ridge Associated Universities
150 East Vance Road
Thank You!
CAROL.IDDINS@ORAU.ORG
https://orise.orau.gov/

Recent Registries Bibliography

2019

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