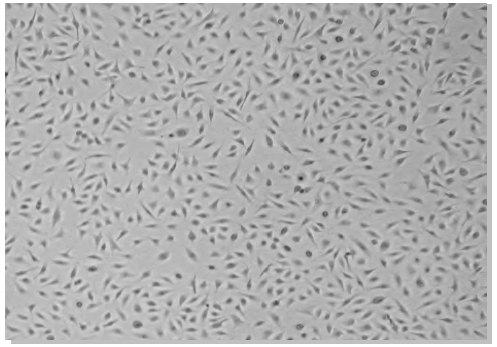
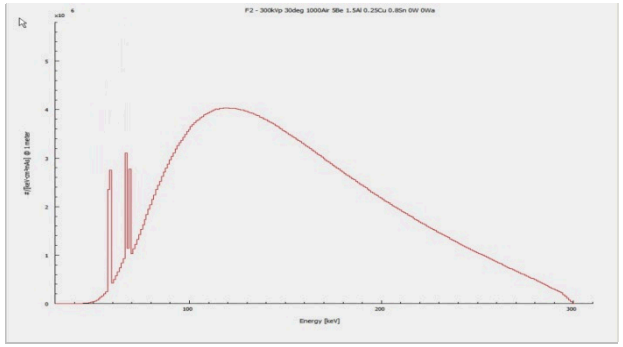
SAND2018-0624PE






# A Study Comparing the Efficacy of Gamma and X Rays in Biological Research

Charles “Gus” Potter
Sandia National Laboratories

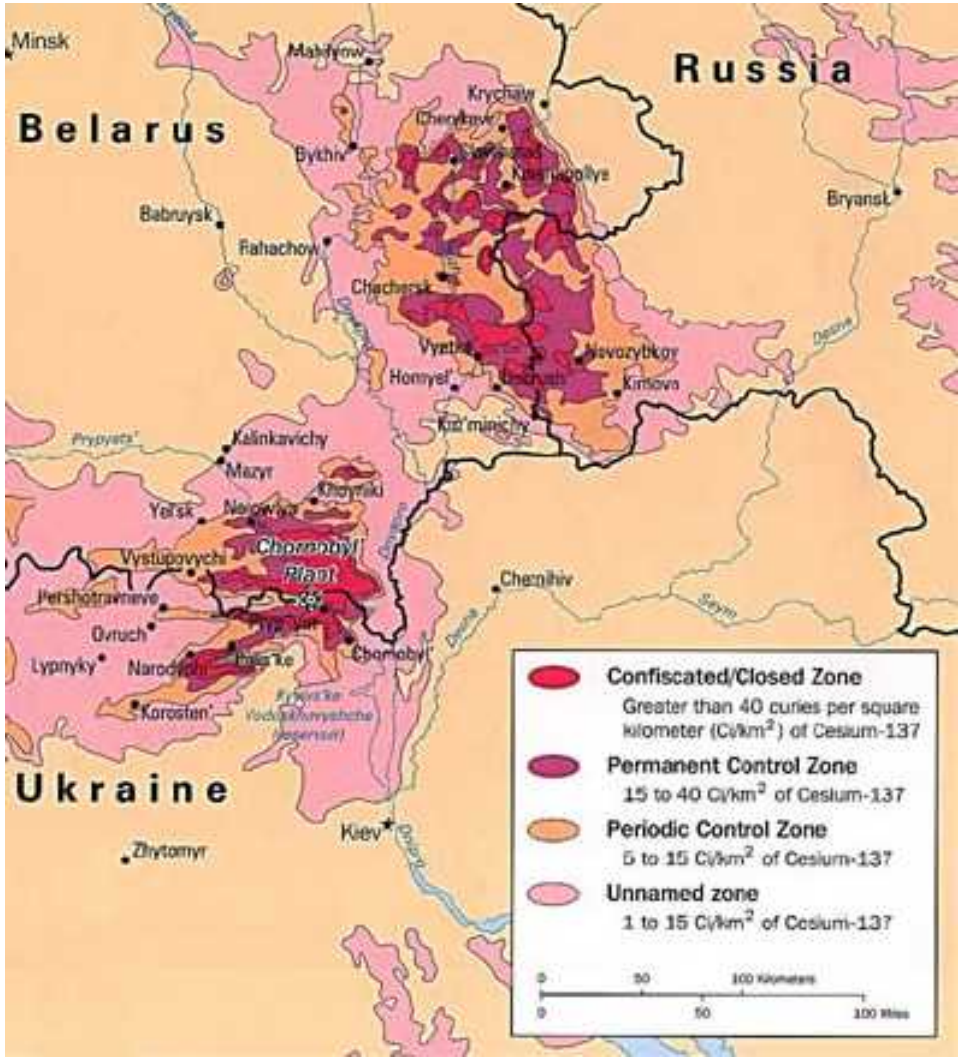
Sandia National Laboratories is a multimission laboratory managed and operated by National Technology and Engineering Solutions of Sandia, LLC, a wholly owned subsidiary of Honeywell International, Inc., for the U.S. Department of Energy’s National Nuclear Security Administration under contract DE-NA0003525. SAND NO. 2017-XXXXP

# There are three general categories of radiological terrorism.

| Device Type | Dispersal Form | Economic Effects | Health Effects | Comments |
|---|---|---|---|---|
| **Radiation Exposure Device (RED)** | None | Low | Deterministic effects including acute radiation syndrome (radiation sickness) | Could impact thousands;<br>Lethality difficult;<br>No lasting economic impact |
| **Food or Water poisoning** | Dissolve or mix | Medium | Serious health effects over large population | **Not unique**<br>Other poisons more readily available |
| **RDD for "Area Denial"** | Many | High | Few (if any) prompt health effects;<br>Slight increased cancer risk | **Unique** aspect of radiological material |

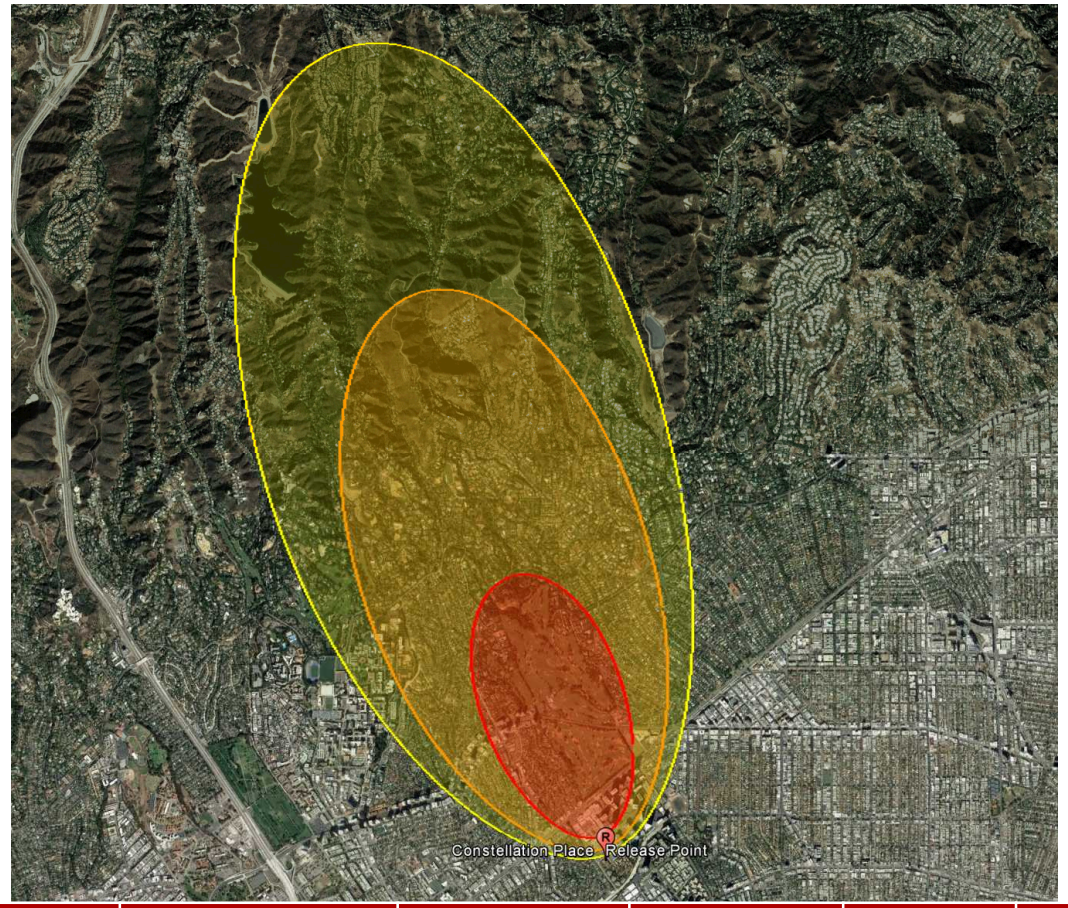
# Cesium contamination can result in considerable consequences.

Chernobyl, USSR April 1986
2 Million Ci, Cs-137




70 g Cs-137 resulted in 40 tons of rad-waste

# Dispersal from medical irradiator source could contaminate a large area.




| Range | TED | Area (sq mi) | Population | Cancers | Fatal |
|---|---|---|---|---|---|
| | 2 rem/1st year | 2 | 10,000 | 158 | 107 |
| | 0.5 rem/2nd year | 7 | 30,000 | 173 | 118 |
| | 5 rem/50 yrs | 14 | 47,000 | 269 | 183 |

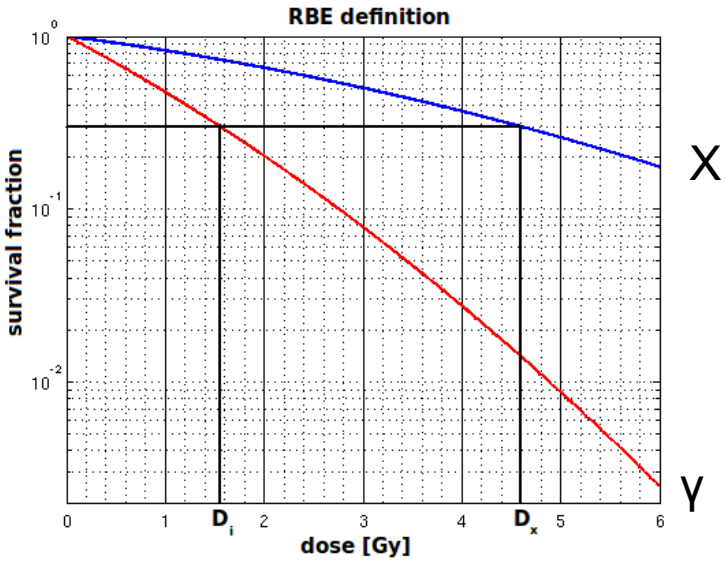

| Range | TED | Area (sq mi) | Population | Cancers | Fatal |
|---|---|---|---|---|---|
| | 5.87 | 2 | 79000 | 1370 | 942 |
| | 0.5 rem/2nd year | 9 | 147000 | 1420 | 978 |
| | 5 rem/50 yrs | 19 | 214000 | 1810 | 1025 |

# The study objective was to demonstrate a source replacement option for medical research irradiators.

- SNL/LRRI Team, Dr. Bobby Scott, PI
- Perform comparisons between gamma and X-ray systems for common experiments.
  - Cells – compare relative biological effectiveness (RBE) for different cell lines
  - Mice – bone marrow cell ablation capability
  - Model mouse data
- Results published in peer-reviewed journals

# The $^{137}$Cs gamma ray was considered the standard in this research.

$$RBE = \frac{D_\gamma}{D_X}$$




$$\frac{4.6}{1.6} = 2.9\ (@30\%)$$

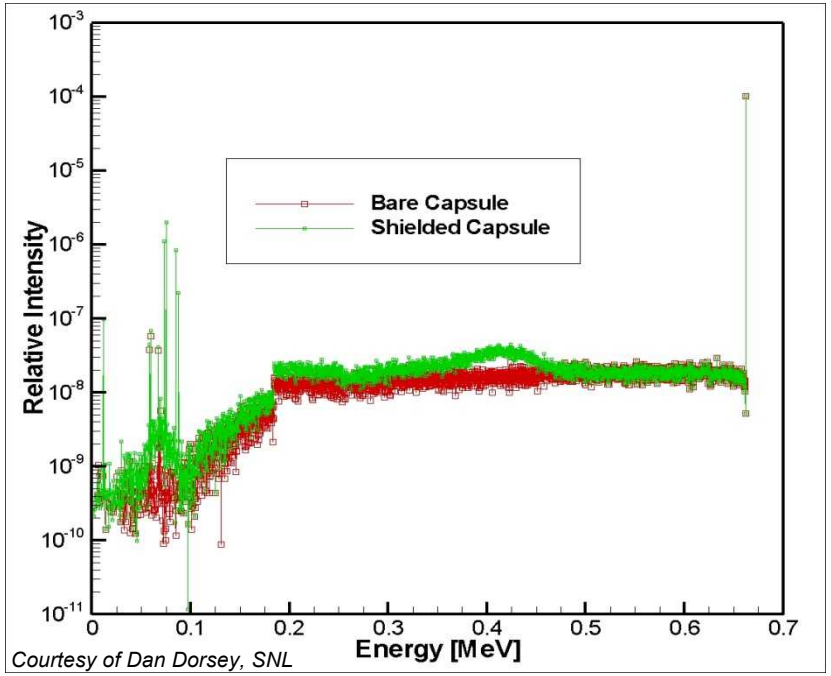
- $D_\gamma$ = absorbed dose of γ-ray standard
- $D_X$ = absorbed dose of X ray that causes same damage

# Commercial gamma and X-ray devices were used in the comparison.

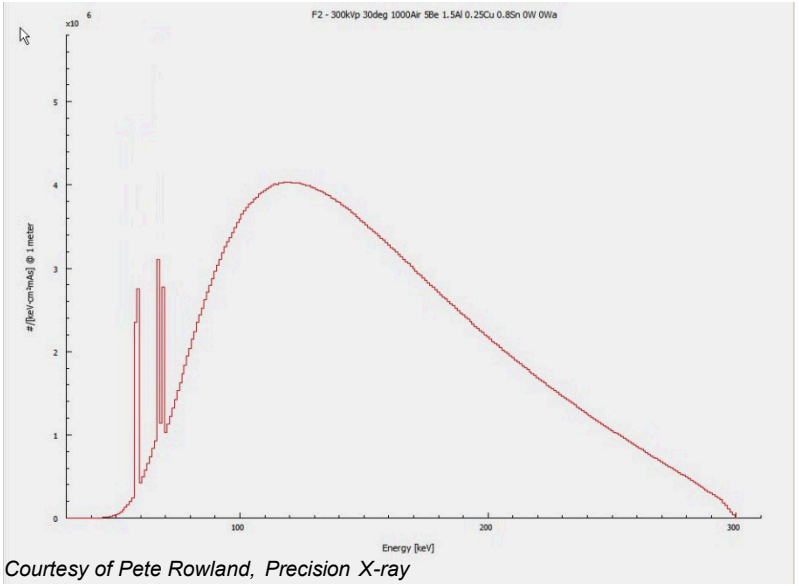
Gammacell 1000


X-RAD 320

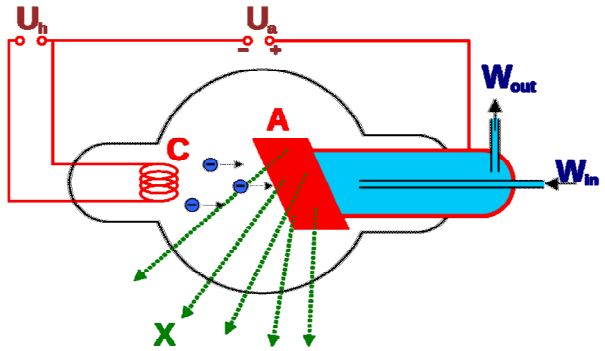
# The energy profile of the two devices is quite different.

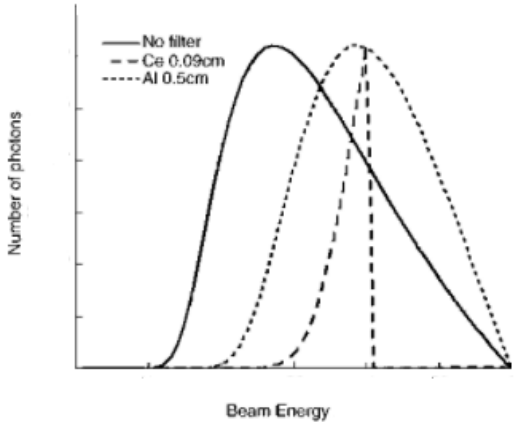


*Courtesy of Dan Dorsey, SNL*



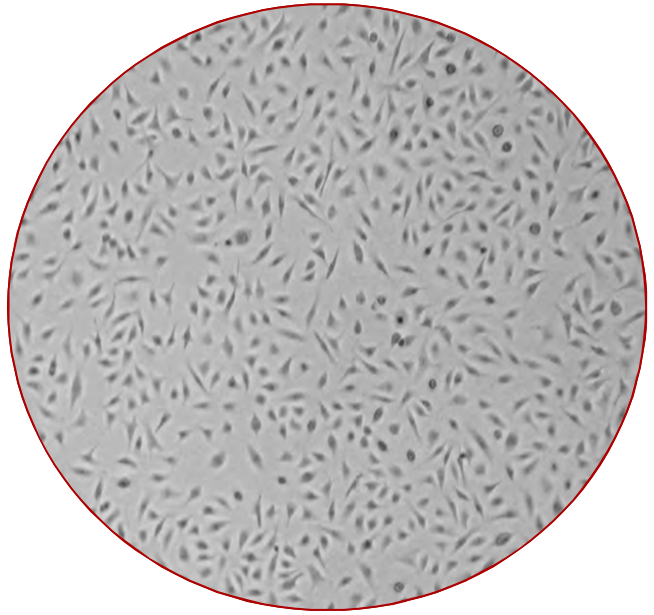
*Courtesy of Pete Rowland, Precision X-ray*



# Several assays and cell lines were used in cell experiments.

- MTT – colorimetric assay for cytotoxicity
  - Color indicates reduction in metabolic activity
  - Used in this work to estimate RBE
- Other common assays used
  - Cell migration – viability by observing migration towards stimulant
  - Colony formation – ability of single cell to form colony
  - Western blot – uses antibodies to detect specific proteins



# Results of cell experiments indicate capability with increase in dose.

| Assay | Cell Lines | X/γ Dose Responses Similar? |
|---|---|---|
| MTT (cytotoxicity) | HBEC-2, HBEC-13, HFL-1, A549, HeLa, MCF-7 | Yes |
| Cell Migration | A549, HeLa | Yes |
| Colony Formation | A549 | Yes |
| Western Blot | HBEC-2 | Yes |

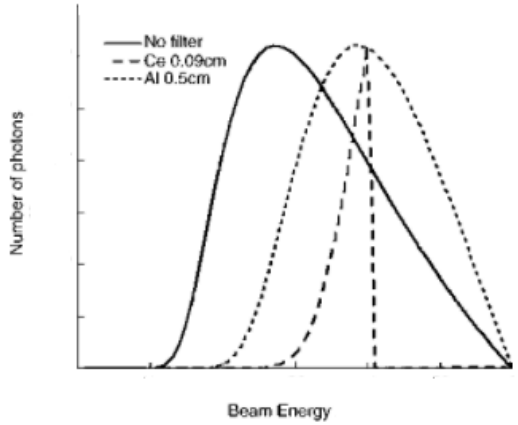
- RBE Estimates (cytotoxicity)
  - Normal Cells: 1.5 (HBEC-13) – 1.6 (HBEC-2), HVL=1 mm Cu
  - Cancer Cells: 1.2 (HeLa) – 1.5 (A549), HVL=3.7 mm Cu

# Two studies were performed to determine bone marrow ablation effectiveness.

- Bone Marrow Transplantation
  - Used for leukemia, solid tumors, other metabolic diseases.
  - High-dose therapy used to ablate bone marrow.
  - *Syngeneic* or *allogeneic* bone marrow is grafted.

- Incomplete ablation → host marrow out-competes donor

- Two studies, both irradiators used in each
  - X-Rad 320:  HVL = 3.7 mm Cu



# Whole-body irradiation did not completely ablate.

- Study 1: Whole-body irradiation only
  - Bone marrow & spleen cell depletion
  - Body weight loss & recovery
  - Reconstitution of spleen & bone marrow – 6 weeks
  - Designed for RBE = 1.3

| Gammacell 1000 | X-Rad 320 |
|---|---|
| 2.03 Gy | 1.56 Gy |
| 4.01 Gy | 3.09 Gy |
| 6.0 Gy | 4.62 Gy |

# Bone marrow and spleen reconstituted.

- Study 2: Whole-body irradiation & transplant
  - Body weight loss and recovery
  - Reconstitution of spleen & bone marrow – 6 weeks

| Gammacell 1000 | X-Rad 320 |
|---|---|
| 2.03 Gy | 1.56 Gy |
| 4.01 Gy | 3.09 Gy |
| 6.0 Gy | 4.62 Gy |

# Additional dose is likely required for ablation and splenocyte killing.

- Bone marrow ablation was similar at each dose level.
- Viable splenocytes at 24 hrs and 6 weeks significantly lower for gamma vs. X rays
- RBE for splenocyte killing less than 1.3
- Allogeneic bone marrow engraftment unsuccessful for X rays.

# Splenocyte modeling confirms need for additional dose.

- Models developed to predict if higher doses would successfully ablate spleen tissue.
- Mouse study 1 data modeled.
- Results:
  - RBE for splenocytes closer to 0.94
  - More data at higher doses needed

# Both irradiators experienced maintenance issues during research.

- X-RAD 320
  - Maintenance costs higher than Gammacell
  - Room temperature buildup
  - Throughput may be issue in large transfusion programs

- Gammacell 1000
  - Aging units also expensive to maintain

# Publications


- B. R. Scott, J. Hutt, Y. Lin, M. T. Padilla, K. M. Gott, and C. A. Potter. Biological microdosimetry based on radiation cytotoxicity data. *Radiation Protection Dosimetry*, 153(4): 417-424, 2013.

- B. R. Scott, K. M. Gott, C. A. Potter, and J. Wilder. A comparison of in vivo cellular responses to Cs-137 gamma rays and 320-kV X rays. *Dose Response*, 11:444-459, 2013.

- B. R. Scott and C. A. Potter. Stochastic threshold exponential (TE) model for hematopoetic tissue reconstitution deficit after radiation damage. *Dose Response*, 12:415-428, 2014.