

Radiation Biology In The Low Dose-region



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What if...

internally deposited radioactive materials from fallout are more hazardous than external radiation?

**Fallout was on everything
and in everything!**

**My ecological research demonstrated lots of
radioactive material in our bodies. We need to be sure
we have not underestimated risk!!**

What if...



injected or inhaled ^{90}Sr - ^{90}Y was
much more hazardous than acute
radiation?



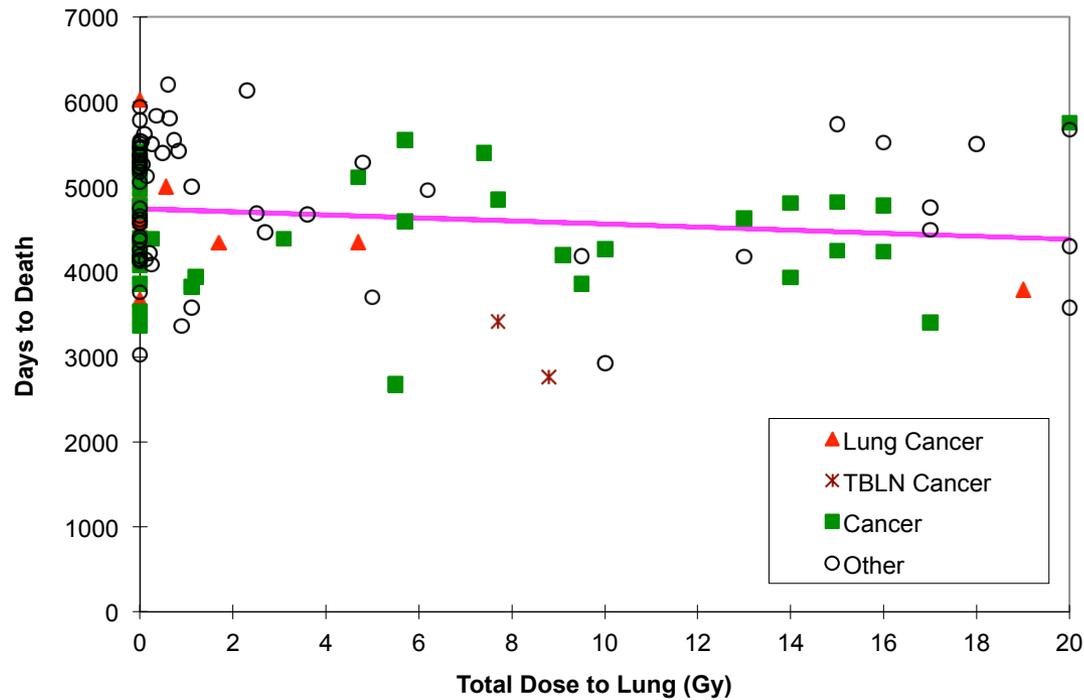
- Samples from the environment were measured in pCi/liter or pCi/Kg range
- Chinese Hamsters were injected with mCi $^{90}\text{Sr/g}$ body weight (5-9 orders of magnitude higher than the environment) to study chromosome aberrations and cancer.



Low-LET Studies

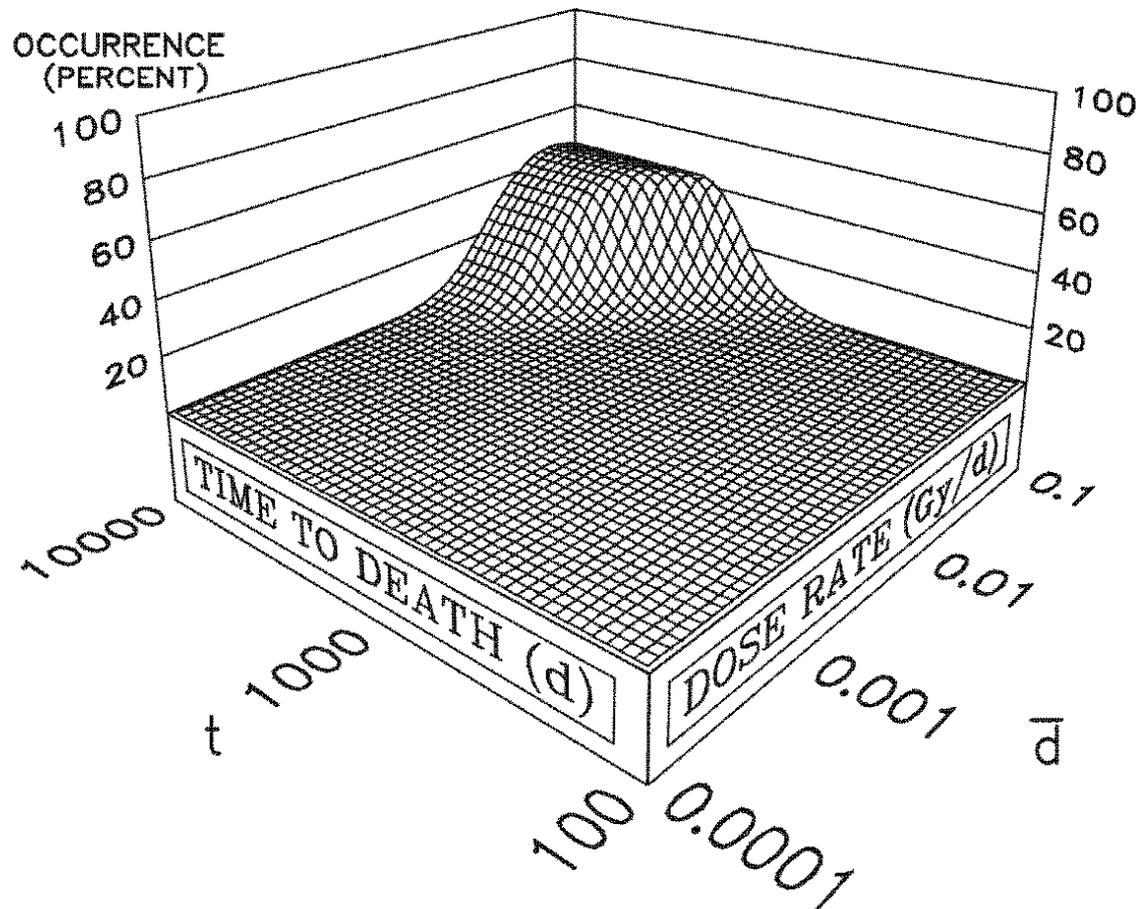
	Utah	Davis	Argonne	ITRI
Injection	1954 ⁹⁰ Sr	1963 ⁹⁰ Sr	1956 ⁹⁰ Sr (Transplacental) 1957 ⁹⁰ Sr (Subcutaneous) 1960 ¹⁴⁴ Ce 1961 ¹³⁷ Cs	
Ingestion		1961 ⁹⁰ Sr		
Inhalation				1970 ⁹⁰ Sr(insol) 1967 ¹⁴⁴ Ce (insol) 1970 ⁹¹ Y (insol) 1969 ⁹⁰ Y (insol) 1965 ⁹⁰ Sr (soluble) 1966 ¹⁴⁴ Ce (soluble) 1972 ¹⁴⁴ Ce (juvenile) 1972 ¹⁴⁴ Ce (aged) 1972 ¹⁴⁴ Ce (multiple exposures) 1968 ¹³⁷ Cs (soluble) 1966 ⁹¹ Y(soluble)

Dogs <20 Gy Dose to Lung after Inhalation of FAP



	Lung Cancer	Total Cancer
Control	8/54= 15%	26/54= 48%
Exposed	4/64= 6%	29/64= 45%

OCCURRENCE OF DEATHS FROM BONE CANCER FOR BEAGLES FED ^{90}Sr AT DAVIS



O. RAABE

TIME AFTER BIRTH & AVERAGE BETA DOSE RATE TO SKELETON (LOG SCALES)

What if... Strontium-90 was More hazardous than acute exposure?

Answer:

- Huge doses were required to produce lung cancer from ^{90}Sr . Doses less than 20 Gy had no increase in lung cancer.
- Huge doses and dose rates were required to produce bone cancer from ^{90}Sr .
Low dose rates did not increase bone cancer.

What if Fallout is more Damaging than Acute

External Radiation Exposure?

- Extensive Research on internally deposited radioactive materials, ^{90}Sr , ^{137}Cs , ^{144}Ce , ^{131}I , ^{230}Pu , ^{241}Am .
- All different routes of entry, Ingestion, Inhalation, wounds, injection.
- **Fallout is much less effective** in production of biological damage than single acute exposures (X-rays).
- **Decreased dose-rate decreased biological effects** at all levels of biological organization. Molecular, Cellular, Tissue, Organ, experimental animal.

Heightened concern about Plutonium produced by fallout and nuclear power



- Plutonium is retained in the lung, bone and liver with long physical and biological half-lives.
- Plutonium produces a large dose to the target organs.
- Cells “hit” by a single alpha particle result in a large cellular dose.

What if...

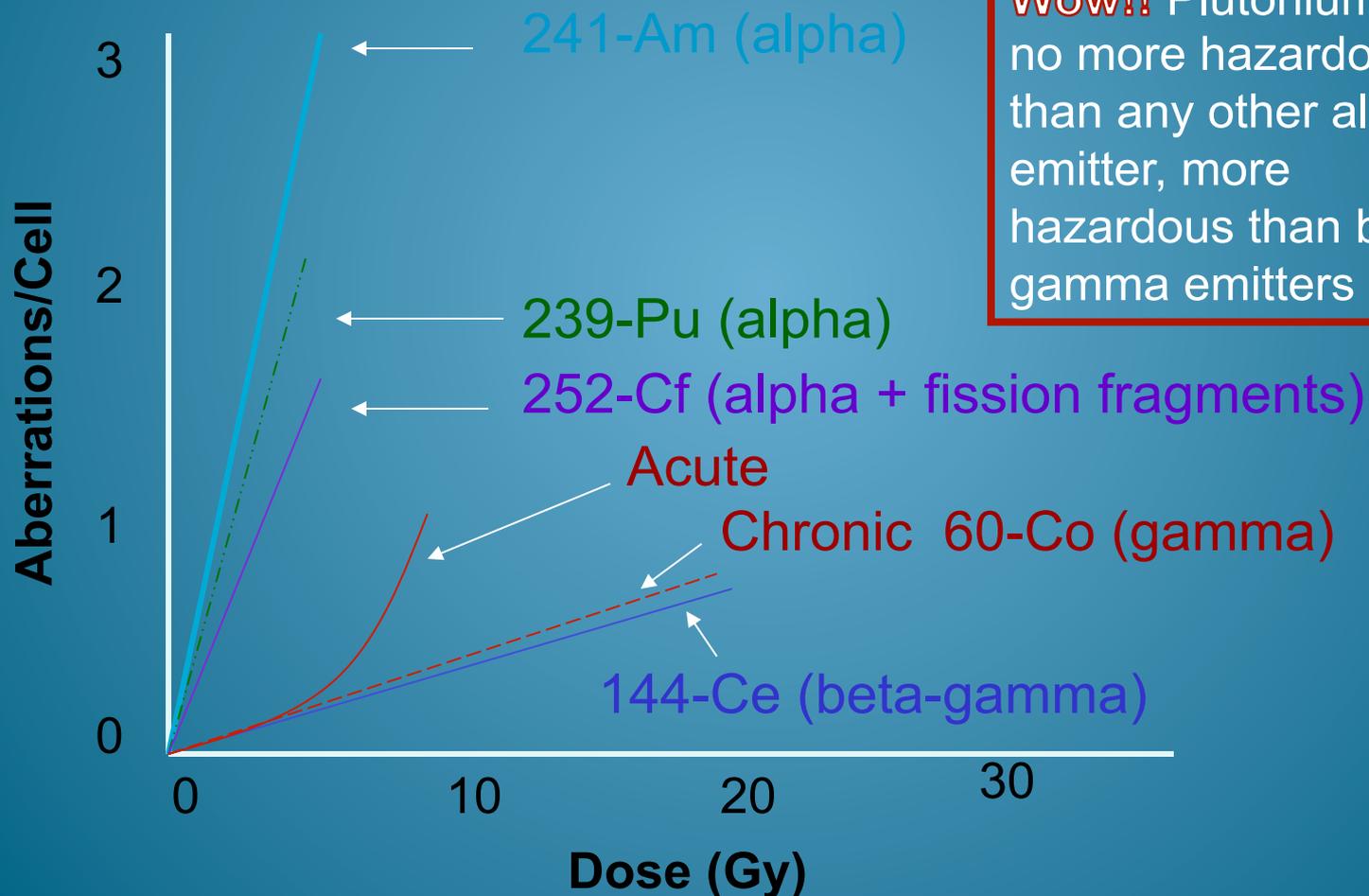


^{239}Pu



is the most
hazardous substance
known to man?

Dose Response for Radiation-Induced Chromosome Aberrations

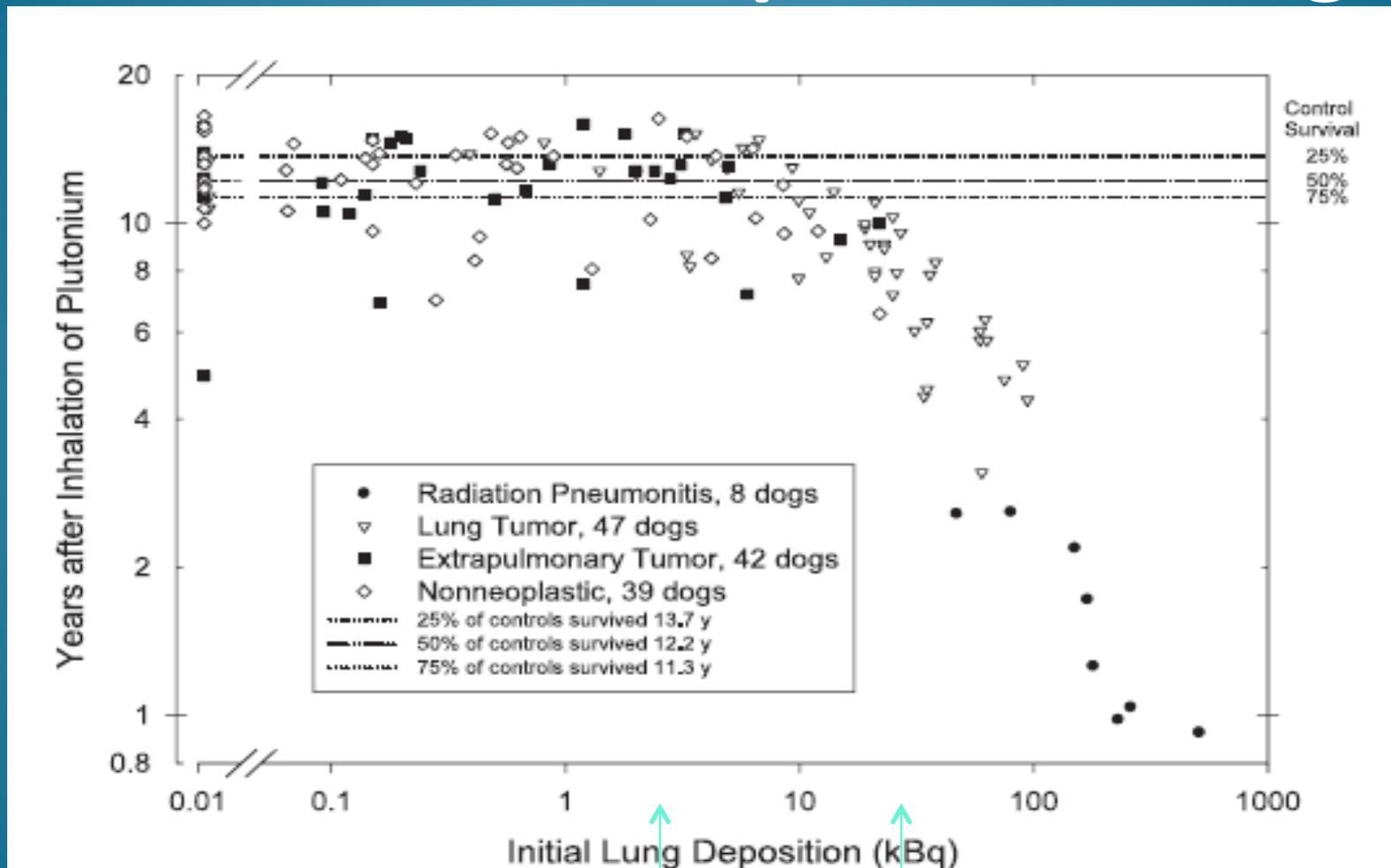


Wow!! Plutonium is no more hazardous than any other alpha emitter, more hazardous than beta-gamma emitters

Human and Dog Experience with Plutonium

- Experimental Animal Studies
 - University of Utah (Injected)
 - Pacific Northwest National Laboratory (inhaled)
 - Inhalation Toxicology Research Institute (Inhaled)
- Human Exposures (LANL)
- Human Exposures (Hanford)
- Mayak Production Workers
- Human Exposures (INL)

Inhaled ^{239}Pu Responses in Dogs



2012 Park et al.

Dose 2.6-10 Gy = 6.3-24 Sv = (630,000 – 2,400,000 mrem)

UPPU Club Los Alamos

- Here we interviewed ten men who agreed to share their stories of plutonium intakes. It is their belief that open communication will help the Laboratory, the community and the whole of society to understand the human factors associated with managing our plutonium legacy.
- “On the Front Lines, Plutonium workers past and present share their experiences”

Past Human Exposures

(UPPU) Club Los Alamos, TU, (ZPPR) INL

Class	Number of Workers	Committed Effective dose equivalents (rem)
1 (UPPU)	4	10-30
2	1	30-100
3	4	100-300
4	1	300-1000
Case 269 (TU)	1	36
INL	4	0.0-0.001
	4	0.002-0.08
	5	0.08-0.35
	2	0.35-2.22
	1	16.1
Background dose (US Population)		15 with Medical 30

What is the risk for cancer, genetic effects or life shortening?

- Cancer risk for protracted exposures= 5% per Sv.
 - Top dose was 16 rem or 0.16 Sv
 - $0.16 \text{ Sv} \times 5\% \text{ risk/Sv} = \text{an increase risk of } 0.8 \%$
 - Background risk for cancer is 40% and deaths from cancer 25%
- No genetic effects detected in human exposures following high doses.
- No life shortening detected in dogs given less than 6.0 Sv or 600 rem (600,000 mrem) dose to the lungs

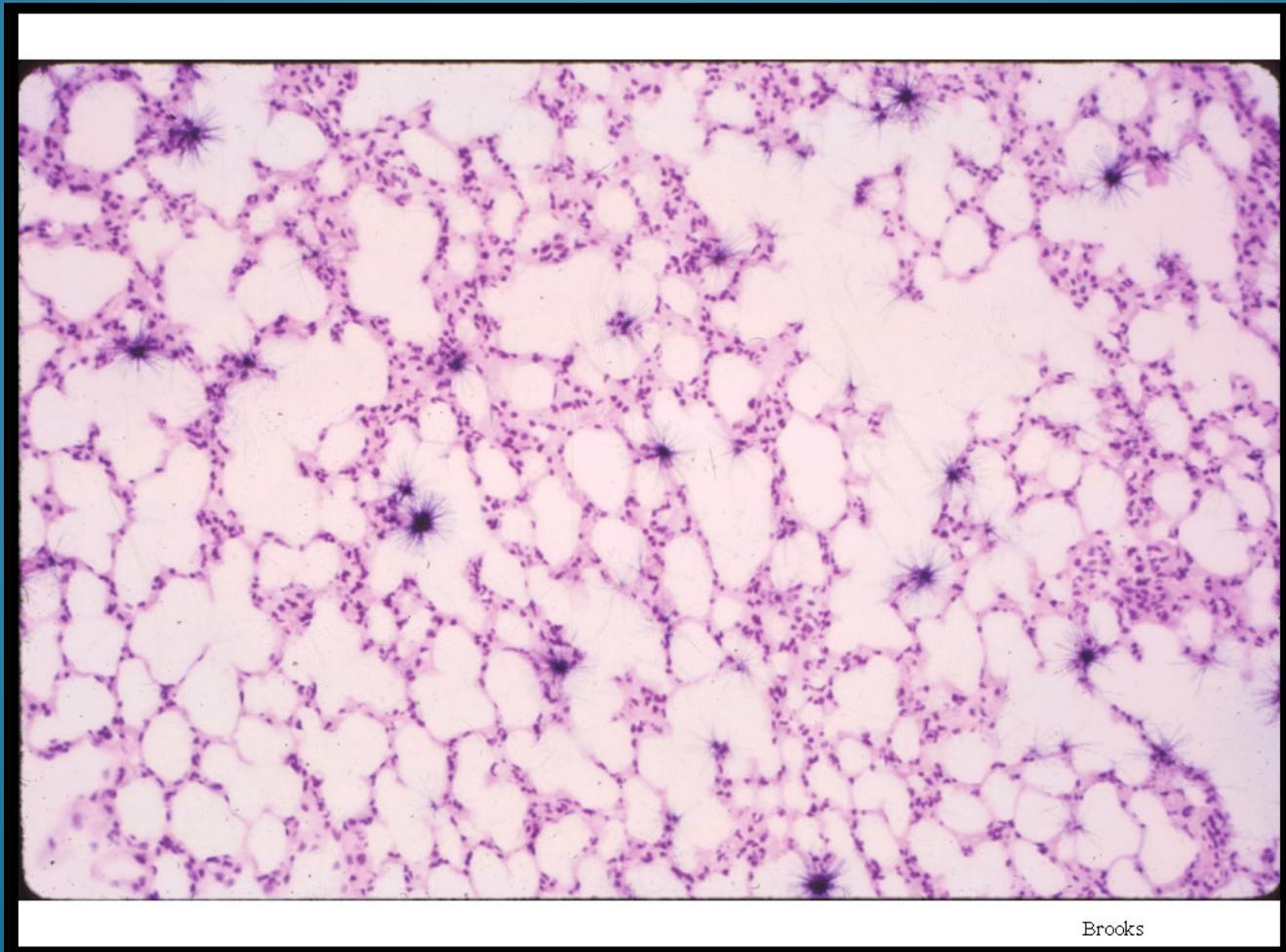
What if...



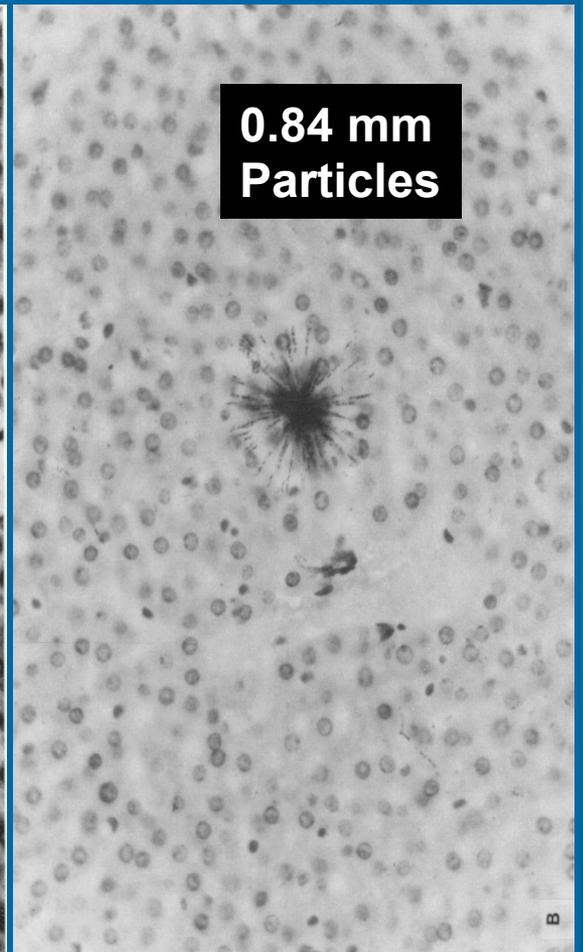
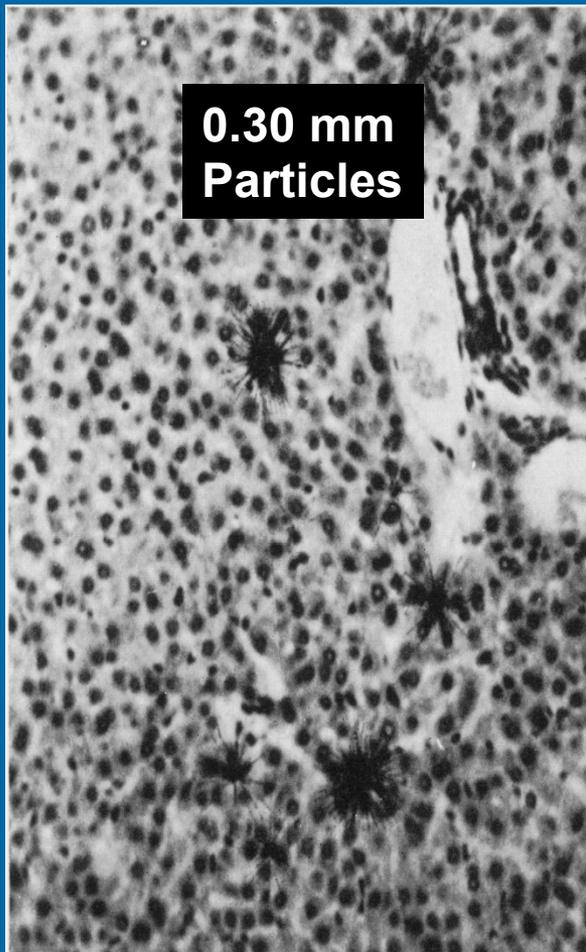
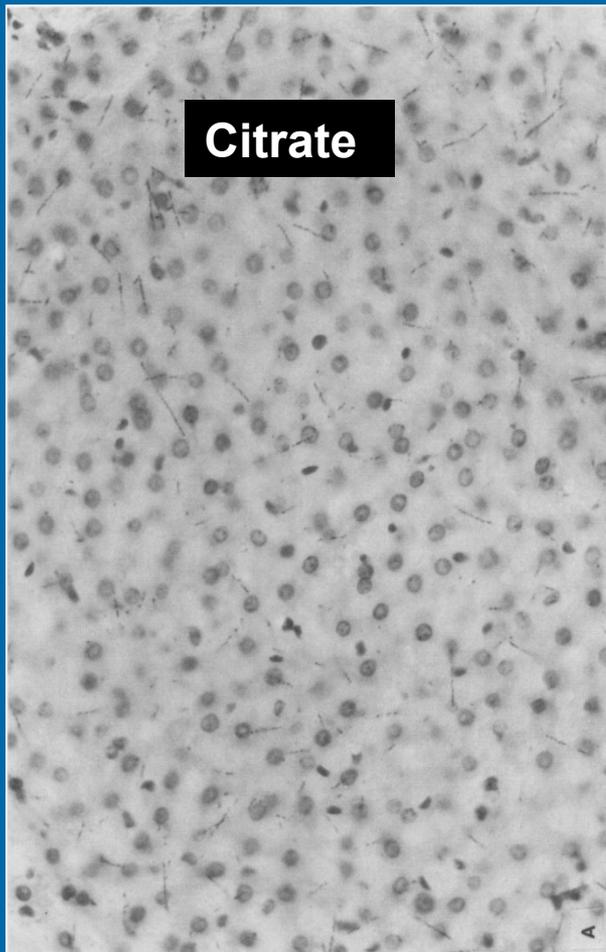
a single $^{239}\text{PuO}_2$ particle
deposited in the lung
can cause cancer?

“Hot Particle Hypothesis”

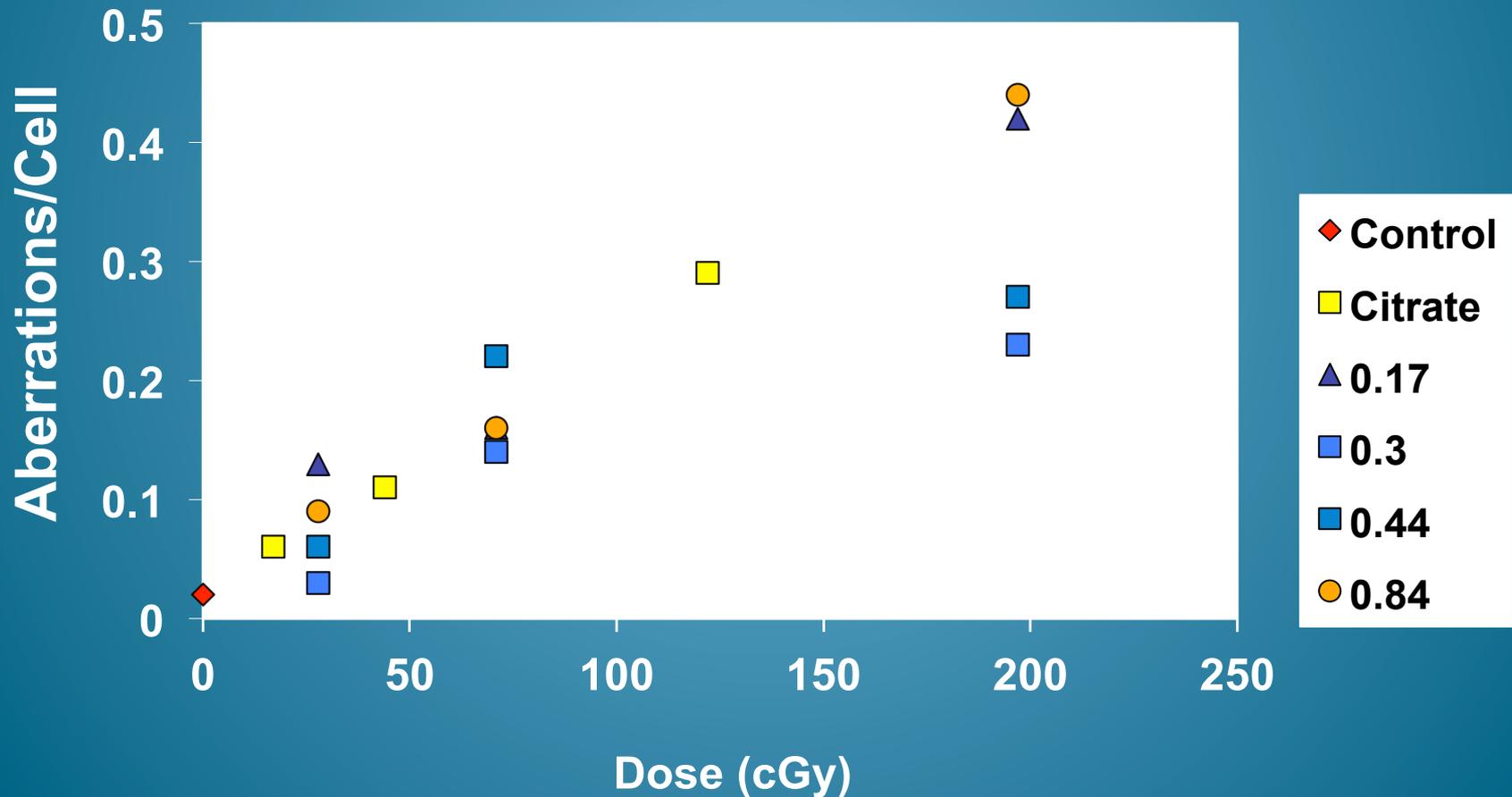
Non-Uniform Dose Distribution from Plutonium Inhalation



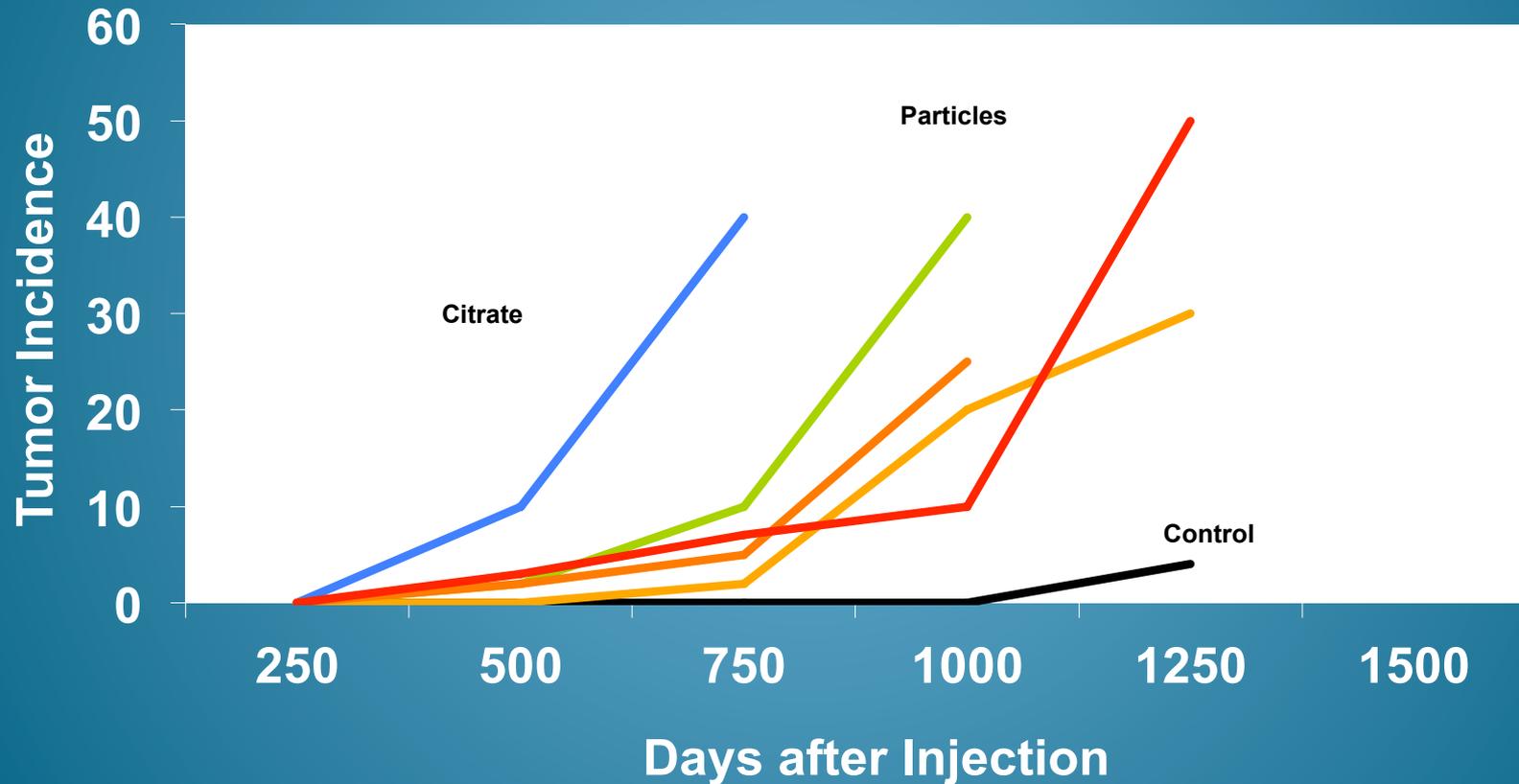
Non-Uniform Distribution of ^{239}Pu in the Liver of Chinese Hamsters following injection with citrate or oxide particles



The Influence of ^{239}Pu Dose-Distribution on Chromosome Aberration Frequency



Cumulative Liver Tumor Incidence After $^{239}\text{PuO}_2$ or ^{239}Pu Citrate Exposure

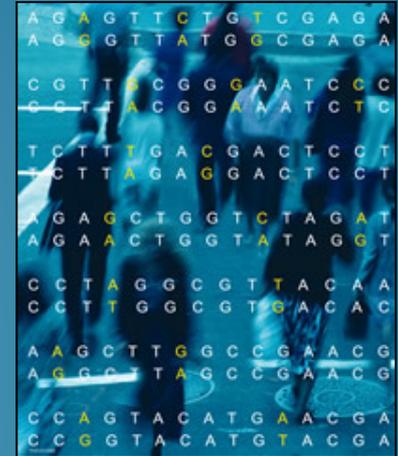


Answers:

- What if Plutonium is the most hazardous substance known to man? **It is not!!!**
- What if a single Plutonium particle will cause cancer. **It will not!!!**
- To get cancer from Plutonium, it is necessary to expose as many cells to alpha particles as possible.

New Technologies

- The Human Genome was sequenced
- New technologies, such as microbeams, were now available to test health risks in the low dose region, where it couldn't be measured before.



Can health risks in the low dose region now be understood?

What if...

**the LNTH overestimates
risk??**

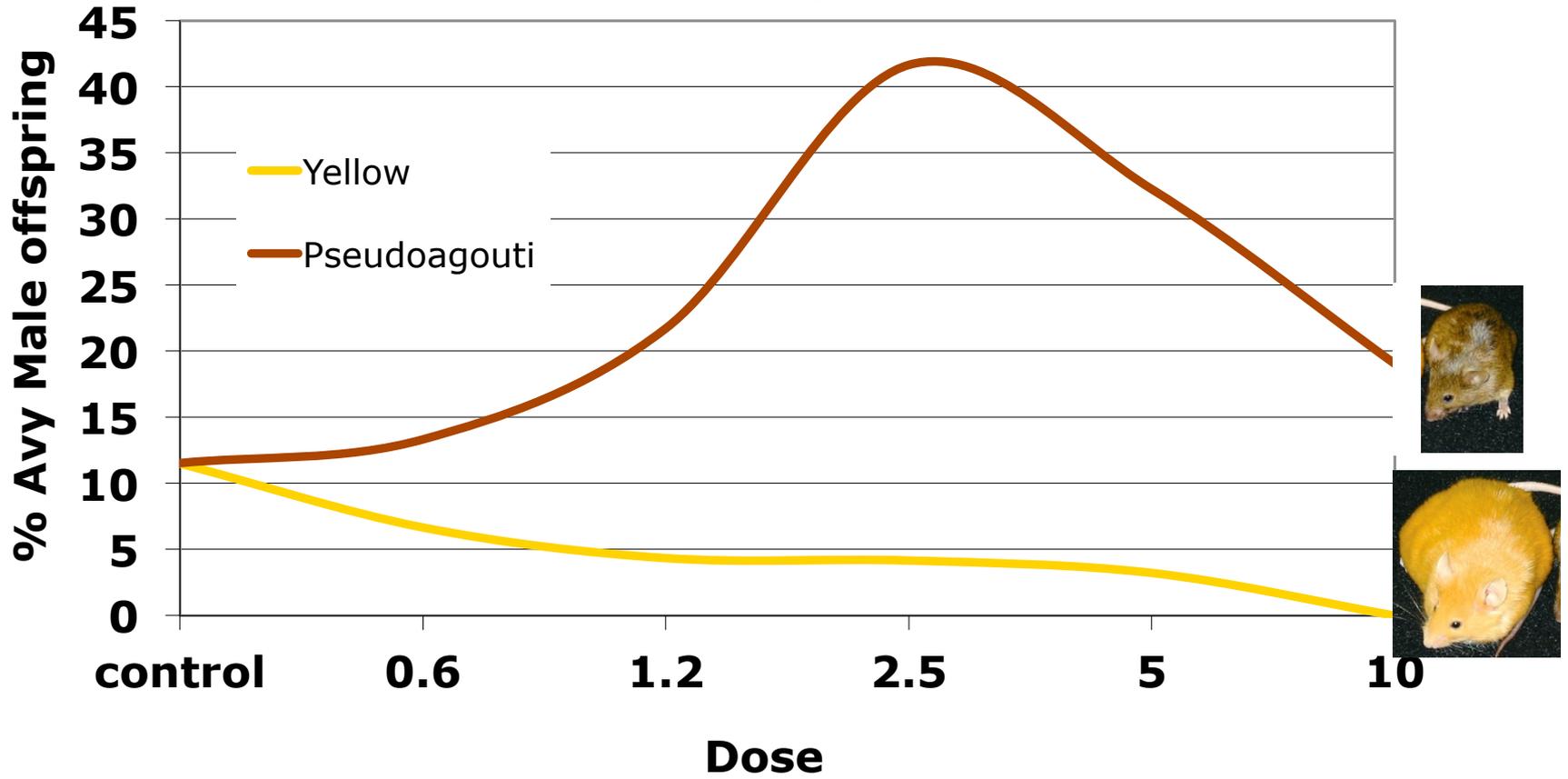


- Are the mechanisms of action the same for low and high doses of radiation?
- Do we need to change current paradigms in radiation biology?
- Is the LNTH an accurate scientific description for the dose-response relationship for cancer in the low dose region?

Research in Low Dose Region

- Extensive research on biological effects of low dose radiation resulted in many new observations making paradigm shifts in radiation biology essential.
 - Hit theory vs Bystander and tissue effects
 - Linear dose-responses vs Protective adaptation
 - Mutation theory vs Genomic instability
- The mechanisms of action of these phenomena are being carefully documented and understood.
- Low-dose responses are non-linear at all levels of biological organization (Molecular, Cellular, Tissue, Organism, Humans?) and suggest that LNT overestimates risk.

Fetal Radiation Exposure and Coat Color Change in Male Avy Mice



What if...

mechanisms of action are
different at high and low doses
of radiation?

Differences between High- and Low-Dose Radiation Responses

High Dose > 0.2 Sv

Cell killing high

DNA damage high

Gene Expression (Damage?)

Epigenetic Effects?

Free Radical Increased

Direct Action

- ↑ Apoptosis (Increased)
- ↑ Mutation Frequency
- ↑ Cell Transformation
- Immune response (-)
- Cancer increased (5%/Sv)

Low Dose < 0.2 Sv

Cell killing low

DNA damage low/not detected

Gene Expression (Protective?)

Epigenetic Effects (Protective)

Free Radicals decreased

Indirect Action

MnSOD

Glutathione

- ↑ Selective Apoptosis
- ↓ Mutation Frequency
- ↓ Cell Transformation
- Immune response? (+)
- Cancer (mSv)?