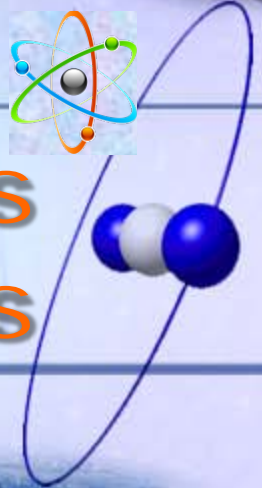



International Nuclear Energy Academy 2015 Annual Meeting, Vienna, Sep 14

**Beneficial radiation effects
contradict the LNT model's
cancer predictions**

**Jerry M. Cuttler D.Sc., P.Eng.
Cuttler & Associates Inc.
Toronto, Ontario, Canada**





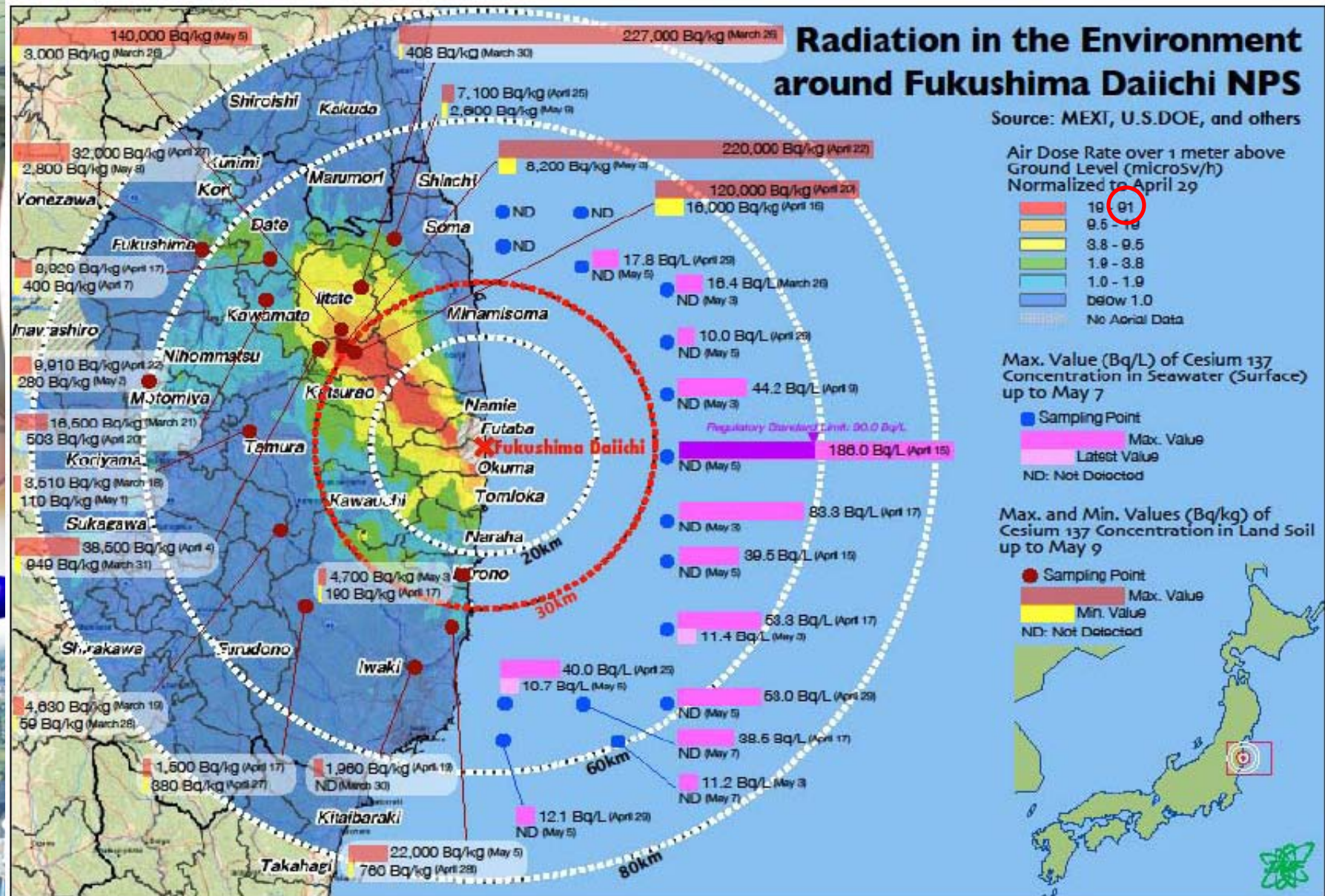
**“Nothing in life is to be feared;
it is only to be understood.”**

Maria Sklodowska Curie

Two-time Nobel laureate and
discoverer of radium and polonium

**Now is the time to use our knowledge and wisdom
to understand more, so that we may fear less.**

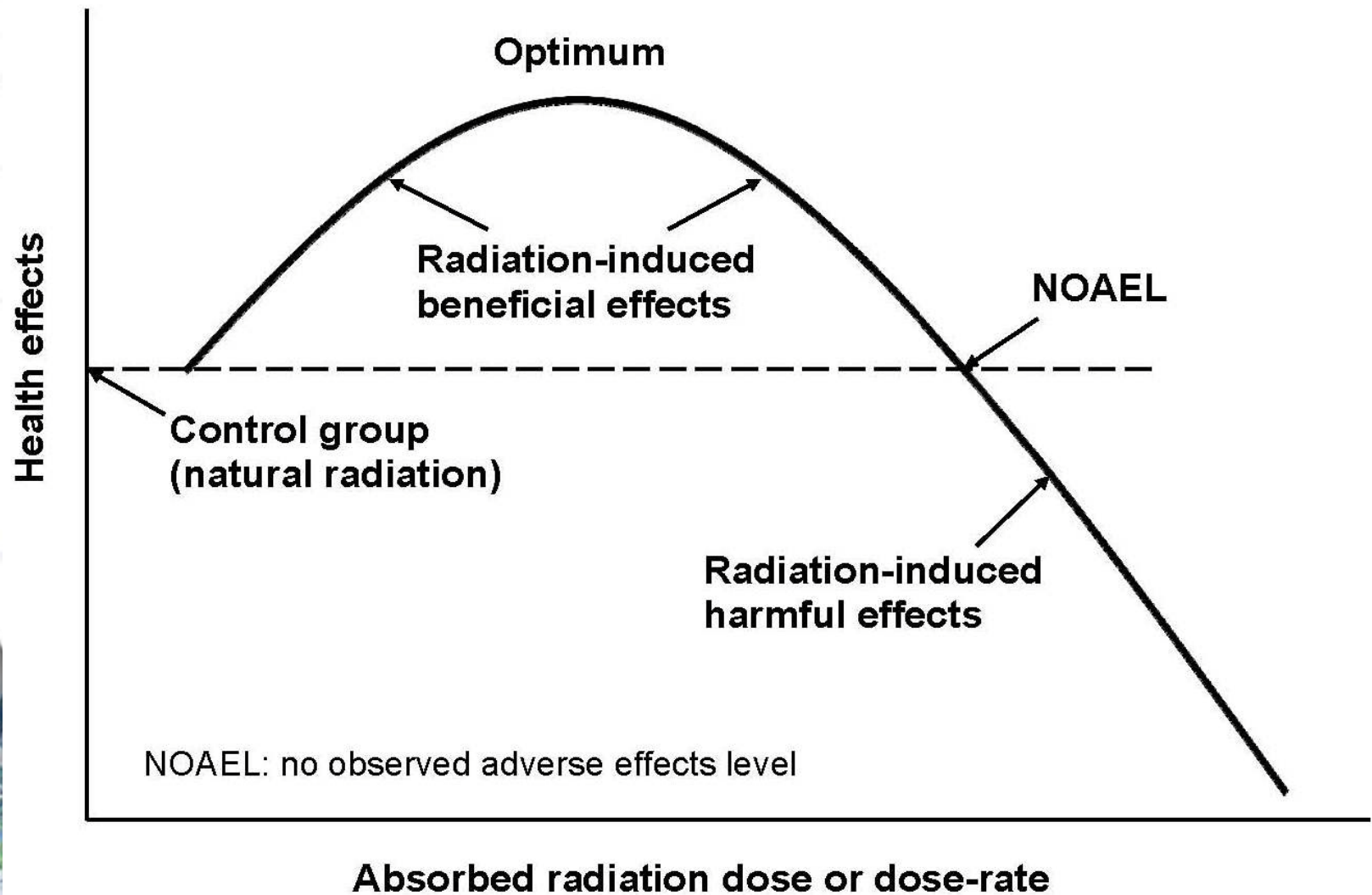
$$91 \mu\text{Sv/h} \times 8766 \text{ h/y} = 798 \text{ mSv/y} \sim \text{natural HBRAs}$$



The basic problem of nuclear energy

- People are *afraid* of nuclear power plants because we are still telling everyone that any *radiation* exposure they receive increases their risk of fatal *cancer*.
- This is a 1950s antinuclear health scare, and it is *false*.
- A *low* radiation dose or dose-rate *stimulates* adaptive protection systems, more than 150 genes in humans.
- But *high* radiation *inhibits* or *damages* these systems.
- For every exposure scenario, there is a dose *threshold* at which the health effects change from net benefit to net harm.
- Longevity is best measure of health effect, not cancer

Radiation dose-response model



How did the LNT model happen?

- Early geneticists (Muller) observed mutations in germ cells of fruit flies induced by very high dose-rate & dose
- When the dose-rate and the dose are both very high, then *mutation frequency* is roughly proportional to dose
- Caspari used “low” dose-rate 2.5 R/day x 21 d (52.5 R); observed a threshold; *experimentals* same as *controls*
<http://www.genetics.org/content/33/1/75.full.pdf+html?sid=cb861a39-fb63-48c4-bcbe-2433bb5c8d6a>
- Muller put aside Caspari’s evidence and proclaimed in his 1946 Nobel prize *political* lecture that there is “no escape from the conclusion that there is no threshold”
- Genetics Panel of NAS BEAR Committee recommended in 1956 the LNT model to assess risk of genetic harm;
NCRP extended LNT model to assess risk of cancer in normal somatic cells; they had *no cancer evidence*

Calabrese on scientific misconduct of NAS in recommending LNT for risk assessment

Arch Toxicol

DOI 10.1007/s00204-015-1455-3

LETTER TO THE EDITOR, NEWS AND VIEWS

Cancer risk assessment foundation unraveling: New historical evidence reveals that the US National Academy of Sciences (US NAS), Biological Effects of Atomic Radiation (BEAR) Committee Genetics Panel falsified the research record to promote acceptance of the LNT

Edward J. Calabrese

Received: 15 December 2014 / Accepted: 6 January 2015
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Abstract The NAS Genetics Panel (1956) recommended a switch from a threshold to a linear dose response for radiation risk assessment. To support this recommendation, geneticists on the panel provided individual estimates of the number of children in subsequent generations (one to ten) that would be adversely affected due to transgenerational reproductive cell mutations. It was hoped that there would be close agreement among the individual risk estimates. However, extremely large ranges of variability and uncertainty characterized the wildly divergent expert

Keywords Mutation · Cancer · Risk assessment · Linear no-threshold (LNT) · Threshold dose response

In 1956, the US National Academy of Sciences (NAS) published their long-awaited reports addressing national concerns about how ionizing radiation may affect such entities as oceans/fisheries, agriculture/food supply, meteorology/atmosphere, medicine/pathology, genetics and disposal of radioactive wastes. As it turns out, the report that domi-

Failure of regulators to assess LNT model recommended by NAS prior to their acceptance

Arch Toxicol

DOI 10.1007/s00204-015-1454-4

LETTER TO THE EDITOR, NEWS AND VIEWS

An abuse of risk assessment: how regulatory agencies improperly adopted LNT for cancer risk assessment

Edward J. Calabrese

Received: 15 December 2014 / Accepted: 6 January 2015
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Abstract The Genetics Panel of the National Academy of Sciences' Committee on Biological Effects of Atomic Radiation (BEAR) recommended the adoption of the linear dose–response model in 1956, abandoning the threshold dose–response for genetic risk assessments. This recommendation was quickly generalized to include somatic cells for cancer risk assessment and later was instrumental in the adoption of linearity for carcinogen risk assessment by the Environmental Protection Agency. The Genetics Panel failed to provide any scientific assessment to sup-

The most significant event in the history of environmental risk assessment was the recommendation by the United States National Academy of Sciences (NAS), Biological Effects of Atomic Radiation (BEAR) Committee, Genetics Panel in 1956 to switch from a threshold to a linear dose–response model for the assessment of genomic mutation risk (Anonymous 1956; NAS/NRC 1956). Within a brief period of time, this recommendation became generalized to somatic cells by other governmental advisory committees and was eventually applied to cancer risk assess-

Calabrese on NAS Genetics Panel scandal

Environmental Research 142 (2015) 432–442



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Environmental Research

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On the origins of the linear no-threshold (LNT) dogma by means of untruths, artful dodges and blind faith

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ABSTRACT

This paper is an historical assessment of how prominent radiation geneticists in the United States during the 1940s and 1950s successfully worked to build acceptance for the linear no-threshold (LNT) dose–response model in risk assessment, significantly impacting environmental, occupational and medical exposure standards and practices to the present time. Detailed documentation indicates that actions taken in support of this policy revolution were ideologically driven and deliberately and deceptively misleading; that scientific records were artfully misrepresented; and that people and organizations in positions of public trust failed to perform the duties expected of them. Key activities are described and the roles of specific individuals are documented. These actions culminated in a 1956 report by a Genetics Panel of the U.S. National Academy of Sciences (NAS) on Biological Effects of Atomic Radiation (BEAR). In this report the Genetics Panel recommended that a linear dose response model be adopted for the purpose of risk assessment, a recommendation that was rapidly and widely promulgated. The paper argues that current international cancer risk assessment policies are based on fraudulent actions of the U. S. NAS BEAR I Committee, Genetics Panel and on the uncritical, unquestioning and blind-faith acceptance by regulatory agencies and the scientific community.

Japanese repeat fruit fly study

Reduction in Mutation Frequency by Very Low-Dose Gamma Irradiation of *Drosophila melanogaster* Germ Cells

Keiji Ogura,^{a,b,1} Junji Magae,^{a,b} Yasushi Kawakami^b and Takao Koana^{a,2}

^a Radiation Safety Research Center, Central Research Institute of Electric Power Industry, Iwado-Kita 2-11-1, Komae, Tokyo 201-8511, Japan; and

^b Biotechnology Department, Institute of Research and Innovation, Takada 1201, Kashiwa, Chiba 277-0861, Japan

Ogura, K., Magae, J., Kawakami, Y. and Koana, T. Reduction in Mutation Frequency by Very Low-Dose Gamma Irradiation of *Drosophila melanogaster* Germ Cells. *Radiat. Res.* 171, 1–8 (2009).

To determine whether the linear no-threshold (LNT) model for stochastic effects of ionizing radiation is applicable to very low-dose radiation at a low dose rate, we irradiated immature male germ cells of the fruit fly, *Drosophila melanogaster*, with several doses of ⁶⁰Co γ rays at a dose rate of 22.4 mGy/h. Thereafter, we performed the sex-linked recessive lethal mutation assay by mating the irradiated males with nonirradiated females. The mutation frequency in the group irradiated with 500 μ Gy was found to be significantly lower than that in the control group ($P < 0.01$), whereas in the group subjected to 10 Gy irradiation, the mutation frequency was significantly higher than that in the control group ($P < 0.03$). A J-shaped dose-response relationship was evident. Molecular experiments using DNA microarray and quantitative reverse transcription PCR indicated that several genes known to be expressed in response to heat or chemical stress and *grim*, a positive regulator of apoptosis, were up-regulated immediately after irradiation with 500 μ Gy. The involvement of an apoptosis function in the non-linear dose-response relationship was suggested. © 2009 by Radiation Research Society

for the estimation of cancer risks, because cancer risk was considered to be proportional to mutation rate, and the mutation rate was found to be proportional to radiation dose in high dose ranges. Therefore, cancer risk was considered to be proportional to radiation dose at high doses.

Much later, the mutation frequency in murine spermatogonia was found to be dependent not only on the total radiation dose but also on the dose rate (3). It was inferred that the repair function of irradiated cells was sufficient with chronic irradiation and that the cells are able to repair radiation-induced DNA damage without errors. However, doses exceeding the repair capacity would cause incomplete repair and/or misrepair, which would occasionally result in mutations. Although Russell *et al.* (3) indicated that a low dose rate resulted in a low inclination of the dose-response curve, a threshold dose was not found at any dose rate.

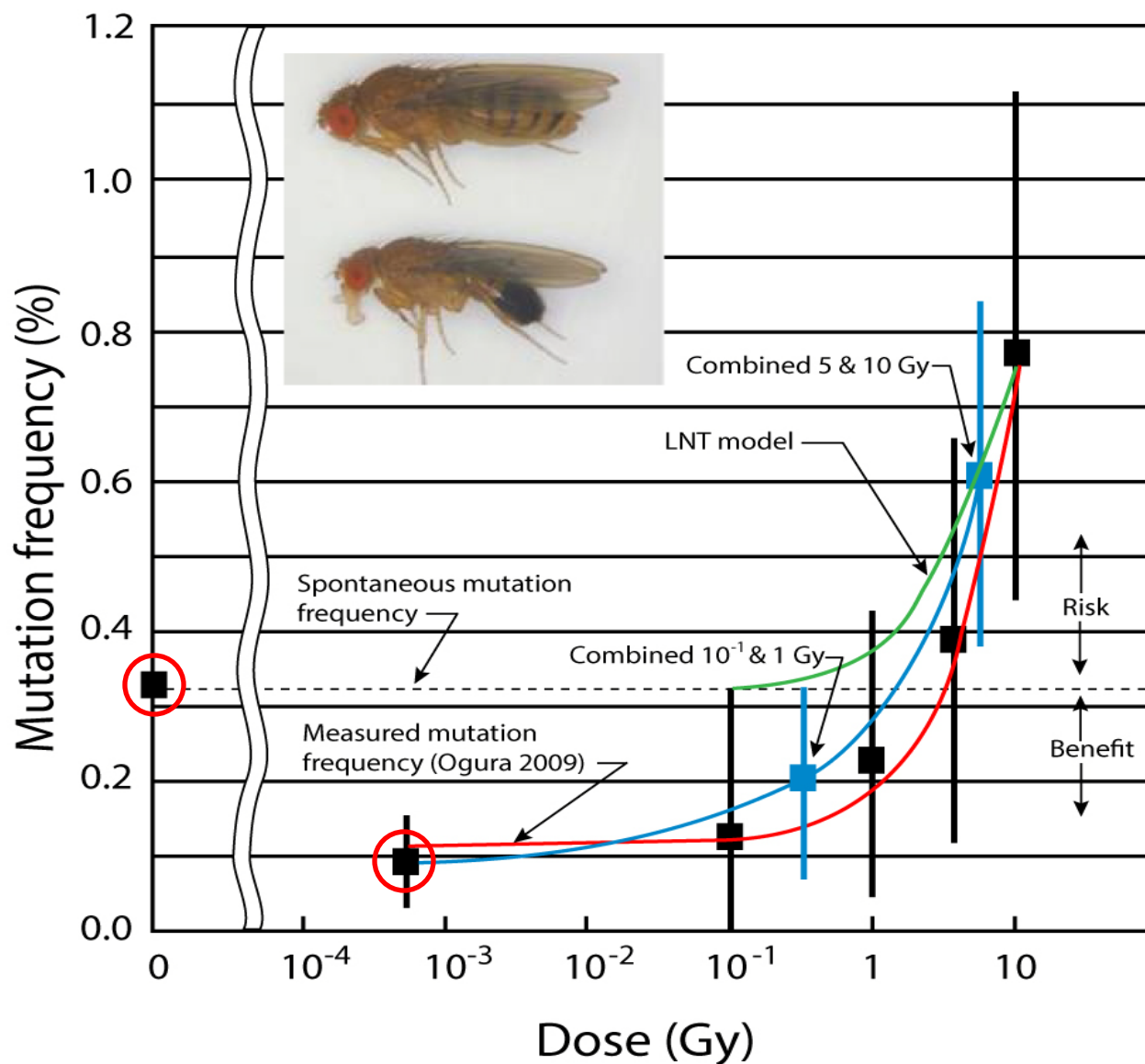
In contrast, we reported previously that in the somatic mutation assay using *Drosophila*, there was a threshold dose at approximately 1 Gy and that a mutation in the DNA repair function decreased the threshold value (4). The existence of a threshold, as determined in the sex-linked recessive lethal assay, using repair-proficient immature germ cells (spermatogonia and spermatocytes), was also indicated, and it was inferred that the excision repair function was

Binomial statistics applied to fruit fly mutation data measured by Ogura et al. 2009

Dose Gy	Number Lethals y	Chromo somes n	Mutat'n Freq. p = y/n	q = 1-p	Var σ^2 n•p•q	Std. dev. σ	2 σ /n %	p + 2 σ /n %	p - 2 σ /n %
0.0005	9	10,500	0.0009	0.9991	9.441	3.07	0.06	0.15	0.03
0.1	2	1507	0.0013	0.9987	1.957	1.399	0.186	0.32	-0.06
1	6	2662	0.0023	0.9977	6.109	2.472	0.186	0.42	0.04
5	8	2055	0.0039	0.9961	7.983	2.825	0.27	0.66	0.12
10	21	2730	0.0077	0.9923	20.86	4.567	0.33	1.10	0.44
0.3	8	4169	0.0019	0.9981	7.906	2.81	0.13	0.32	0.06
7	29	4785	0.0061	0.9939	29.01	5.386	0.225	0.84	0.38

Mutation frequency for controls = 0.0032

Germ cell mutation frequency - 22.4 mGy/h



Beneficial effects of low radiation

Medical practitioners used radiation ~1900 to ~1960, to:

- Eliminate metastases or slow cancer growth
- Accelerate healing of wounds
- Stop infections: gas gangrene, carbuncles and boils, sinus, inner ear, etc.
- Treat arthritis and other inflammatory conditions
- Treat swollen lymph glands
- Cure pneumonia
- Cure asthma

with no apparent increase of cancer incidence

Longevity is best measure of health effects

- Radiation scare: an increased risk of *cancer* with dose
- It is the ideal antinuclear scare because cancer is: very complex, many causes, confounding factors, uncertain, not well understood, difficult to predict, and *we dread it*
- *Best* measure of health effects of radiation is *longevity*
- Cameron: early radiologists, Nuclear Shipyard Workers
- Calabrese-Baldwin: gamma radiation increases *median* life span of low-dose group by 10 to 30% over “controls”
- Radiation stimulates the adaptive protection systems, which act against the enormous endogenous rate of cell damage and against the damage by all causes

Mortality of 1338 British radiologists 1897-1957

Smith and Doll 1981, Br J Radiology 54(639) 187-194

Cause of death	Observed (O) and expected (E) numbers of deaths					
	Entry prior to 1921			Entry after 1920		
	O	E	O/E	O	E	O/E
All causes	319	(1) 334.42 (2) 308.03 (3) 327.97	0.95 1.04 0.97	411	541.77 461.14 469.97	0.76*** 0.89* 0.87**
All neoplasms	62	(1) 49.11 (2) 43.07 (3) 35.39	1.26* 1.44** 1.75***	72	114.93 91.07 68.65	0.63*** 0.79* 1.05
Other causes	257†	(1) 285.31 (2) 264.96 (3) 292.58	0.90* 0.97 0.88*	339†	426.84 370.07 401.32	0.79*** 0.92 0.84**

(1) Based on rates for all men in England and Wales.

(2) Based on rates for social class 1.

(3) Based on rates for medical practitioners.

† includes one death with unknown cause.

*P < 0.05
**P < 0.01
***P < 0.001

} One sided in direction of difference.

Nuclear Shipyard Workers Study

John Cameron, APS, Physics and Society, Oct 2001

Table 1

Deaths from All Causes, Person-years and Death Rates¹ for high-dose nuclear workers ($NW_{>0.5 \text{ rem}}$); low-dose nuclear workers ($NW_{<0.5 \text{ rem}}$); and non-nuclear workers (NNW) (after Matanoski 1991 p. 333)

	<u>High dose</u>	<u>Low dose</u>	<u>Zero dose</u>
Workers in Subset	27,872	10,348	32,510
Person-years	356,091	139,746	425,070
Deaths	2,215	973	3,745
Death Rates Per 1,000 ²	6.4	7.1	9.0
Death Rate (SMR) ³	0.76	0.81	1.00
95% C.I. ⁴	(0.73, 0.79)	(0.76, 0.86)	(0.97, 1.03)

1 Rates calculated per 1000 person-years.

2 Adjusted for deaths excluded from analysis due to unknown date of death.

3 Using age-calendar time specific rates for U.S. white males.

4 C.I. = 95% Confidence intervals.

Blood system very sensitive

HEMOPOIETIC RESPONSE TO LOW DOSE-RATES OF IONIZING RADIATION SHOWS STEM CELL TOLERANCE AND ADAPTATION

Theodor M. Fliedner, Dieter H. Graessle □ Radiation Medicine Research Group and WHO Liaison Institute for Radiation Accident Management, Ulm University, Germany

Viktor Meineke □ Bundeswehr Institute of Radiobiology Affiliated to the University of Ulm, Germany;

Ludwig E. Feinendegen □ Heinrich-Heine-Universität Düsseldorf, Germany, and Brookhaven National Laboratory, Upton, NY, USA

□ Chronic exposure of mammals to low dose-rates of ionizing radiation affects proliferating cell systems as a function of both dose-rate and the total dose accumulated. The lower the dose-rate the higher needs to be the total dose for a deterministic effect, i.e., tissue reaction to appear. Stem cells provide for proliferating, maturing and functional cells. Stem cells usually are particularly radiosensitive and damage to them may propagate to cause failure of functional cells. The paper revisits 1) medical histories with emphasis on the hemopoietic system of the victims of ten accidental chronic radiation exposures, 2) published hematological findings of long-term chronically gamma-irradiated rodents, and 3) such findings in dogs chronically exposed in large life-span studies. The data are consistent with the hypothesis that hemopoietic stem and early progenitor cells have the capacity to tolerate and adapt to being repetitively hit by energy deposition events. The data are compatible with the “injured stem cell hypothesis”, stating that radiation-injured stem cells, depending on dose-rate, may continue to deliver clones of functional cells that maintain homeostasis of hemopoiesis throughout life. Further studies perhaps on separated hemopoietic stem cells may unravel the molecular-biology mechanisms causing radiation tolerance and adaptation.

Blood system response to chronic radiation

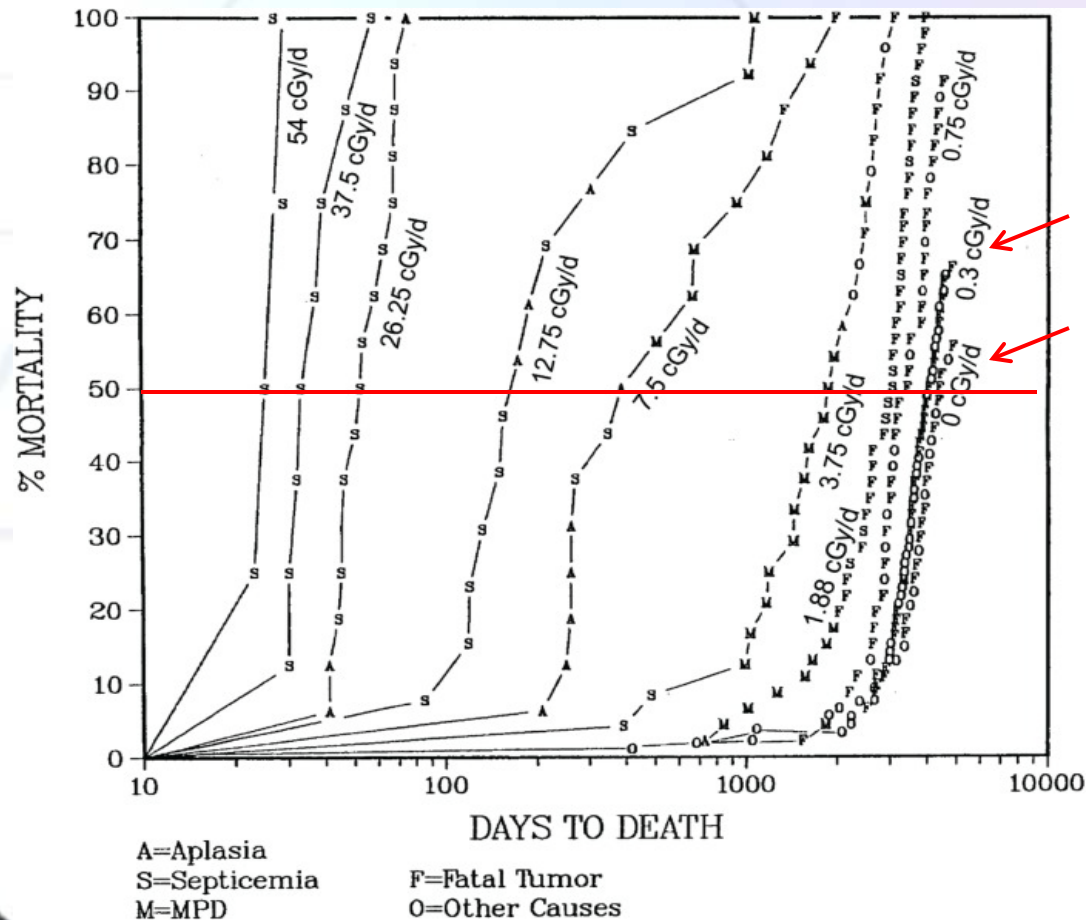
- Fliedner et al. paper in Dose-Response Journal, Dec 2012
- Reviewed histories of *humans* in 10 radiation accidents (including 28,000 in Techa and 1,800 in Mayak) and studies on rats and dogs
- Radiation effect is a function of dose-rate *and* total dose
- Blood stem cells are usually very radiosensitive, but they tolerate and adapt to *chronic* radiation --- adapt better at *lower* dose rate.
- Deliver clones of functioning cells; maintain a lifetime of service
- Beagle dogs at 0.3 rad/day had *same* cancer rate as control dogs
- ICRP standard 1934: a tolerance dose of 0.2 r/day or 50 rad/y is ok
- Present-day ICRP recommendations (LNT & ALARA) not justified

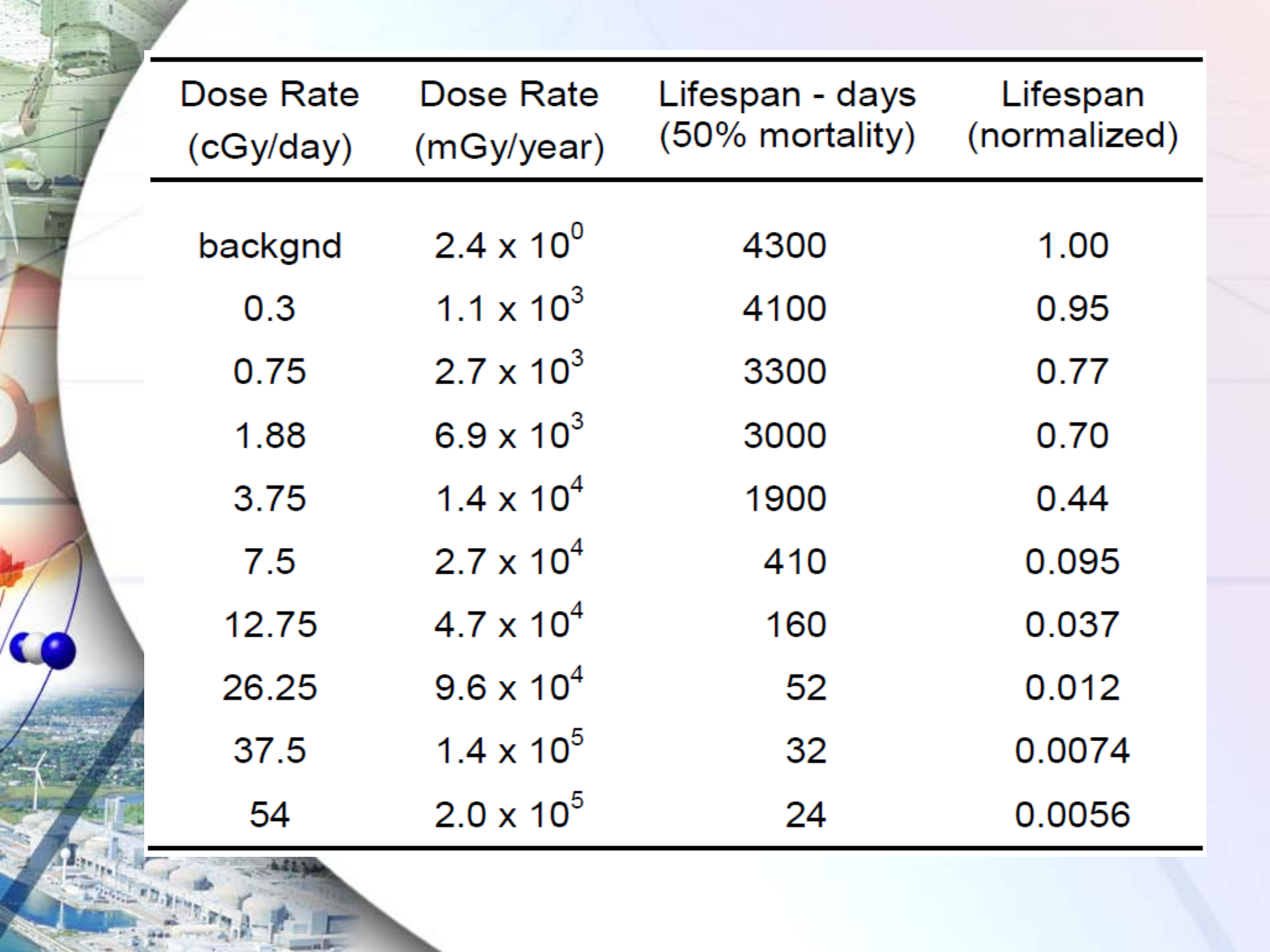
Continuous Co-60 irradiation of dogs

0.3 cGy/d = 1100 mGy/year = 110 rad/year

Blood counts of 0.3 cGy/d same as 0 cGy/d

Fatal tumors of 0.3 cGy/d same as 0 cGy/d

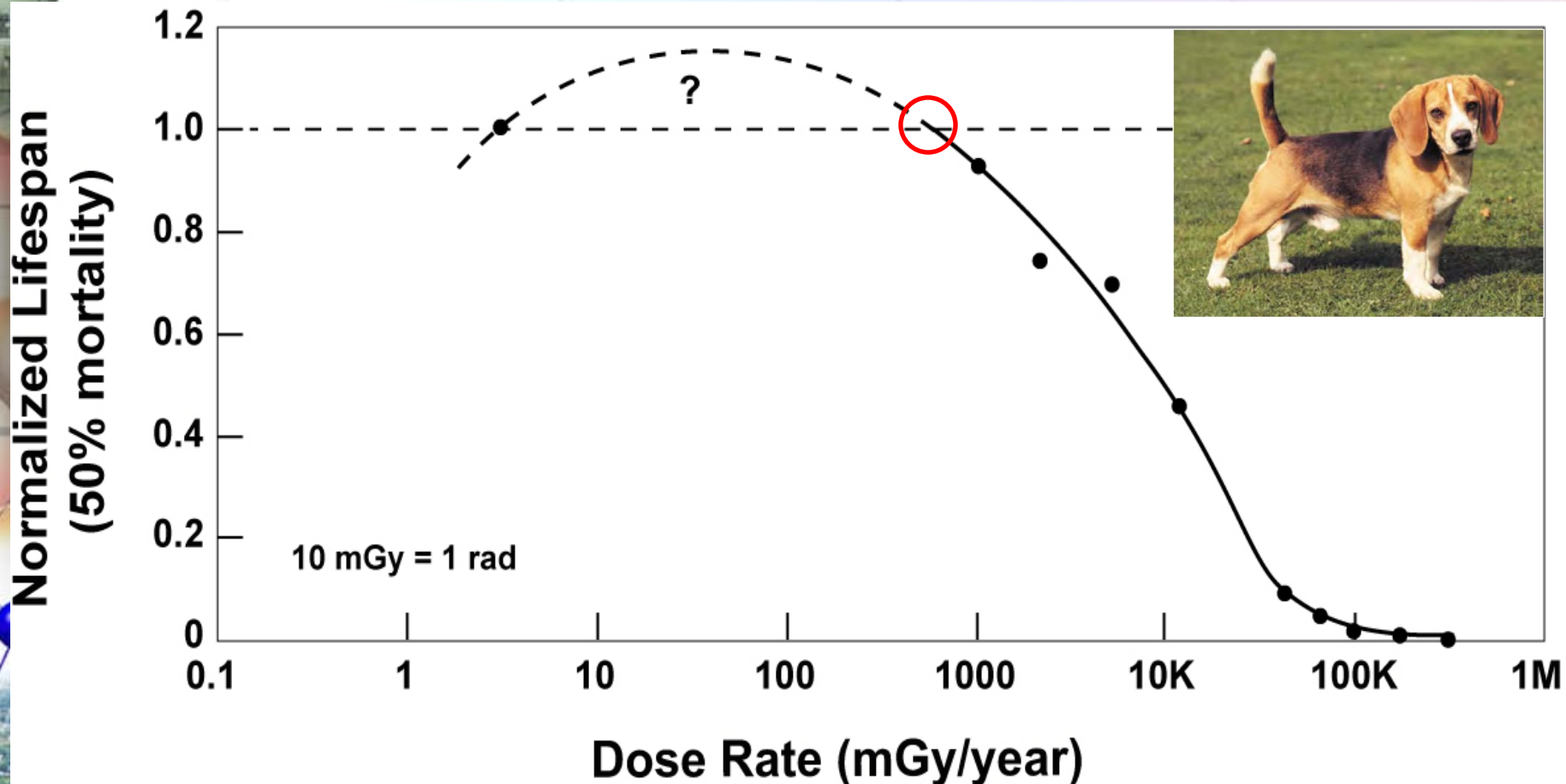




Dose Rate (cGy/day)	Dose Rate (mGy/year)	Lifespan - days (50% mortality)	Lifespan (normalized)
backgnd	2.4×10^0	4300	1.00
0.3	1.1×10^3	4100	0.95
0.75	2.7×10^3	3300	0.77
1.88	6.9×10^3	3000	0.70
3.75	1.4×10^4	1900	0.44
7.5	2.7×10^4	410	0.095
12.75	4.7×10^4	160	0.037
26.25	9.6×10^4	52	0.012
37.5	1.4×10^5	32	0.0074
54	2.0×10^5	24	0.0056

Median lifespan versus Co-60 radiation level

Threshold for shorter lifespan ~ 700 mGy/year



Radiotoxicity of Inhaled $^{239}\text{PuO}_2$ in Dogs

Bruce A. Muggenburg,^a Raymond A. Guilmette,^a Fletcher F. Hahn,^a Joseph H. Diel,^a Joe L. Mauderly,^a
Steven K. Seilkop^b and Bruce B. Boecker^{a,1}

^aLovelace Respiratory Research Institute, Albuquerque, New Mexico 87108; and^bSKS Consulting Services, Siler City, North Carolina 27344

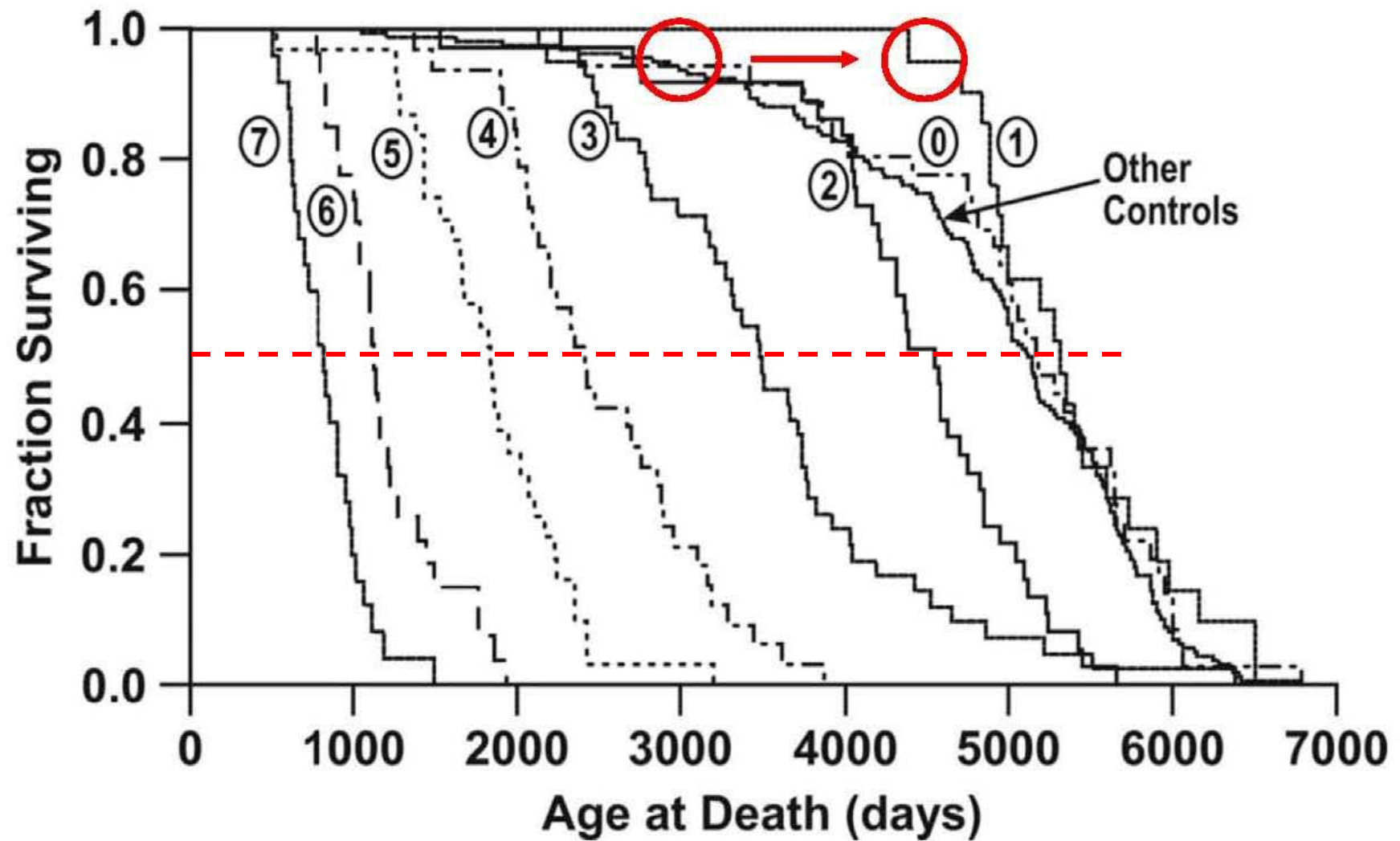
Muggenburg, B. A., Guilmette, R. A., Hahn, F. F., Diel, J. H., Mauderly, J. L., Seilkop, S. K. and Boecker, B. B. Radiotoxicity of Inhaled $^{239}\text{PuO}_2$ in Dogs. *Radiat. Res.* 170, 736–757 (2008).

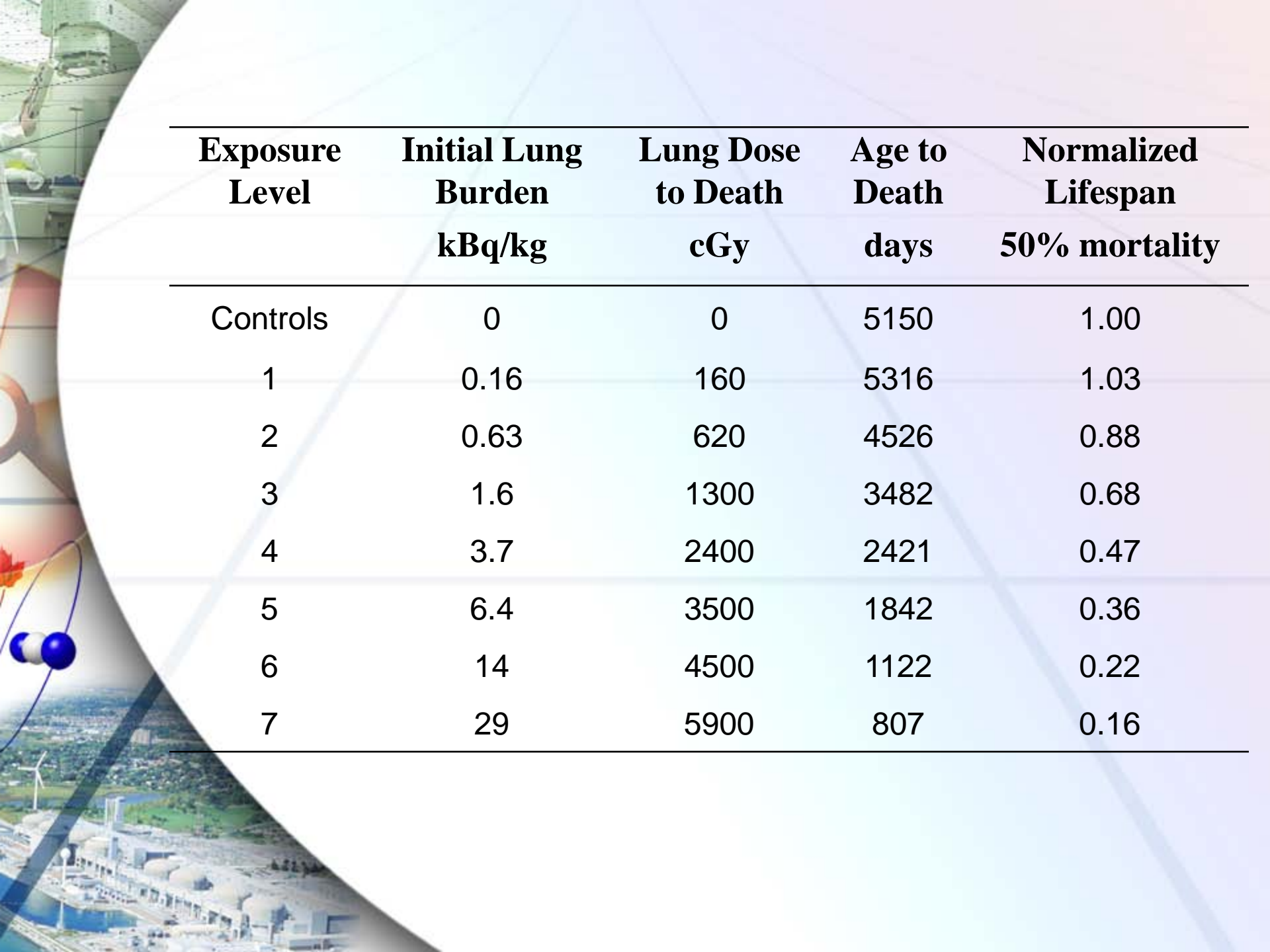
Beagle dogs inhaled graded exposure levels of insoluble plutonium dioxide ($^{239}\text{PuO}_2$) aerosols in one of three monodisperse particle sizes at the Lovelace Respiratory Research Institute (LRRI) to study the life-span health effects of different degrees of α -particle dose non-uniformity in the lung. The primary noncarcinogenic effects seen were lymphopenia, atrophy and fibrosis of the thoracic lymph nodes, and radiation pneumonitis and pulmonary fibrosis. Radiation pneumonitis/pulmonary fibrosis occurred from 105 days to more than 11 years after exposure, with the lowest associated α -particle dose being 5.9 Gy. The primary carcinogenic effects also occurred almost exclusively in the lung because of the short range of the α -particle emissions. The earliest lung cancer was

erations, the possibility of plutonium environmental exposure exists through a severe reactor accident such as that at Chernobyl, various nuclear weapons testing activities, and waste disposal practices at various nuclear sites. Of increasing concern is the possible use by terrorists of ^{239}Pu in an improvised nuclear device (IND) or in a radiological dispersal device (RDD). The inventories of ^{239}Pu that exist around the world are mainly in the metallic or dioxide form. ^{239}Pu has a radioactive half-life of about 24,000 years and decays primarily by α -particle emissions. Due to its abundance and long half-life, accidental and intentional human exposures continue to be important concerns.

In the early years after plutonium was discovered, data on the possible long-term health effects in humans were absent. Therefore, numerous studies of the dosimetry and health effects of internally deposited ^{239}Pu were conducted in laboratory animals since its discovery more than 60

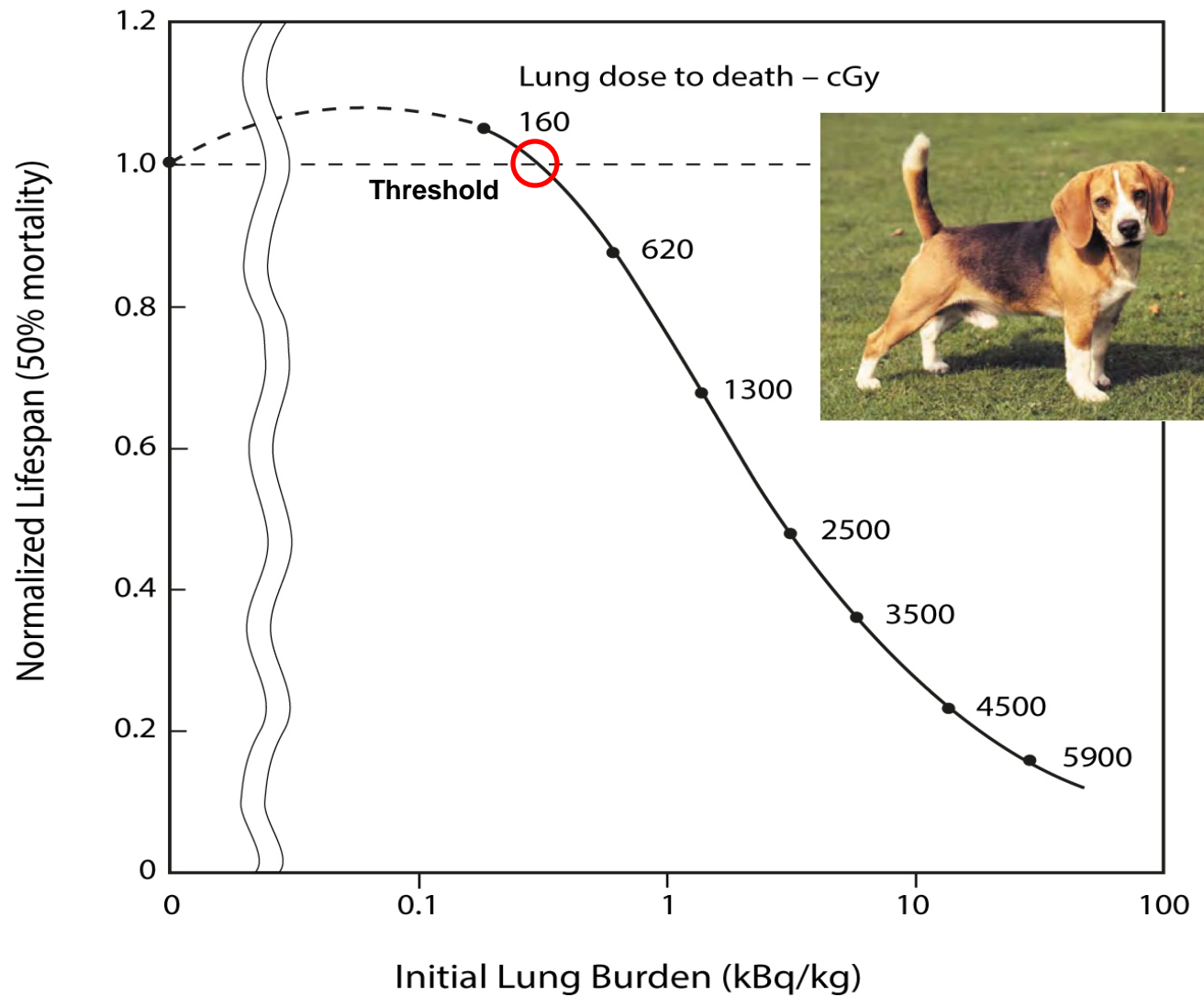
Radiotoxicity of inhaled $^{239}\text{PuO}_2$ in beagle dogs





Exposure Level	Initial Lung Burden kBq/kg	Lung Dose to Death cGy	Age to Death days	Normalized Lifespan 50% mortality
Controls	0	0	5150	1.00
1	0.16	160	5316	1.03
2	0.63	620	4526	0.88
3	1.6	1300	3482	0.68
4	3.7	2400	2421	0.47
5	6.4	3500	1842	0.36
6	14	4500	1122	0.22
7	29	5900	807	0.16

Median lifespan versus $^{239}\text{PuO}_2$ lung burden



CARCINOGENESIS FROM INHALED $^{239}\text{PuO}_2$ IN BEAGLES: EVIDENCE FOR RADIATION HOMEOSTASIS AT LOW DOSES?

Darrell R. Fisher and Richard E. Weller*

Abstract—From the early 1970's to the late 1980's, Pacific Northwest National Laboratory conducted life-span studies in beagle dogs on the biological effects of inhaled plutonium ($^{238}\text{PuO}_2$, $^{239}\text{PuO}_2$, and $^{239}\text{Pu}[\text{NO}_3]_4$) to help predict risks associated with accidental intakes in workers. Years later, the purpose of the present follow-up study was to *reassess* the dose-response relationship for lung cancer in the $^{239}\text{PuO}_2$ dogs compared to controls—with particular focus on the dose-response at relatively low lung doses. A $^{239}\text{PuO}_2$ aerosol (2.3 μm activity-median aerodynamic diameter, 1.9 μm geometric standard deviation) was administered to six groups of 20 young (18-mo-old) beagle dogs (10 males and 10 females) by inhalation at six different activity levels, as previously described in Laboratory reports. Control dogs were sham-exposed. In dose level 1, initial pulmonary lung depositions were $130 \pm 48 \text{ Bq}$ ($3.5 \pm 1.3 \text{ nCi}$), corresponding to 1 Bq g^{-1} lung tissue ($0.029 \pm 0.001 \text{ nCi g}^{-1}$). Groups 2 through 6 received initial lung depositions (mean values) of 760, 2,724, 10,345, 37,900, and 200,000 Bq (22, 79, 300, 1,100, and 5,800 nCi) $^{239}\text{PuO}_2$, respectively. For each dog, the absorbed dose to lungs was calculated from the initial lung burden and the final

each. However, the incidence of lung tumors at zero dose was significantly greater than the incidence at low dose (at the $p \leq 0.053$ confidence level), suggesting a protective effect (radiation homeostasis) of alpha-particle radiation from $^{239}\text{PuO}_2$. If a threshold for lung cancer incidence exists, it will be observed in the range 15 to 40 cGy.

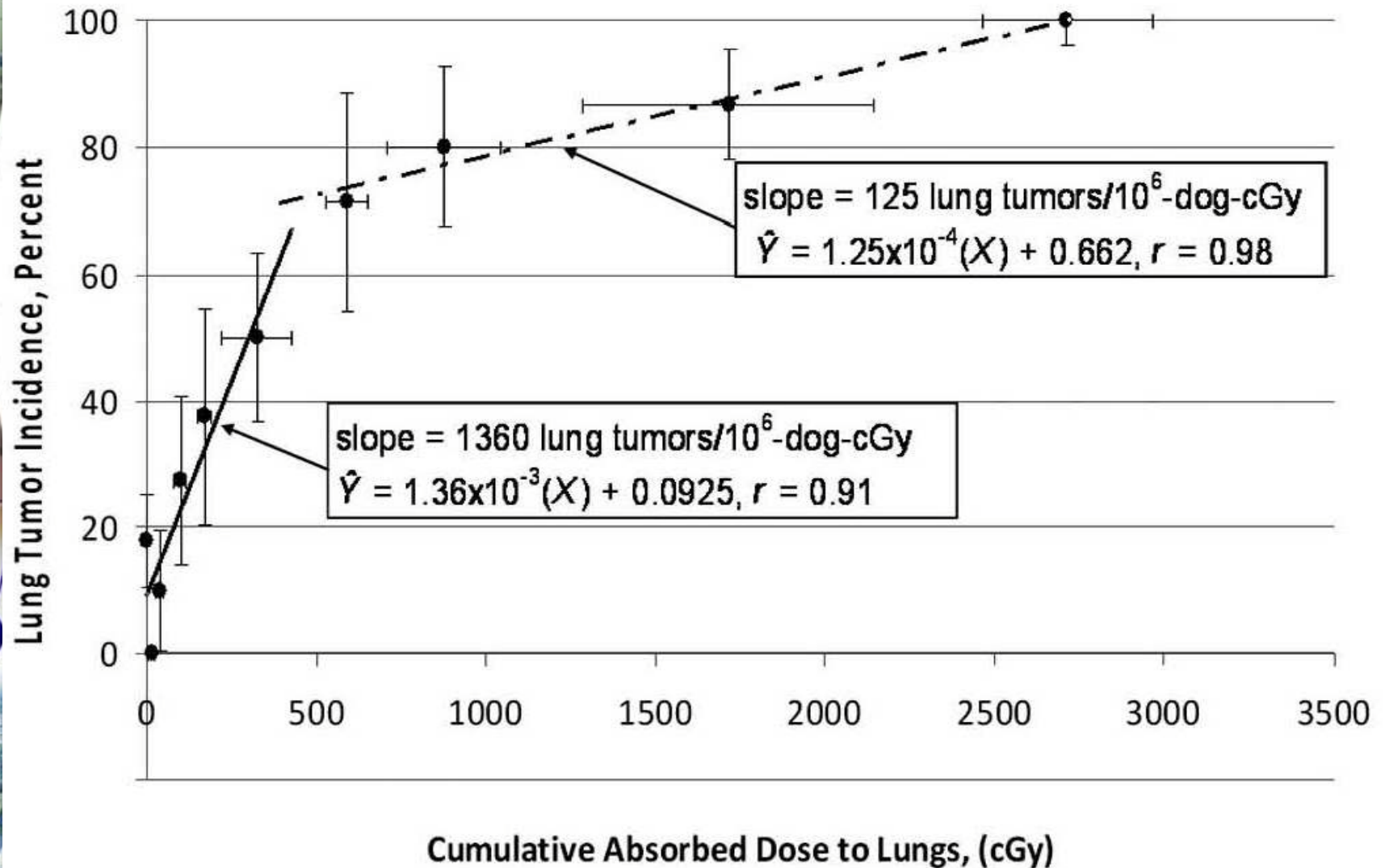
Health Phys. 99(3):357–362; 2010

Key words: alpha particles; analysis, risk; dogs; ^{239}Pu

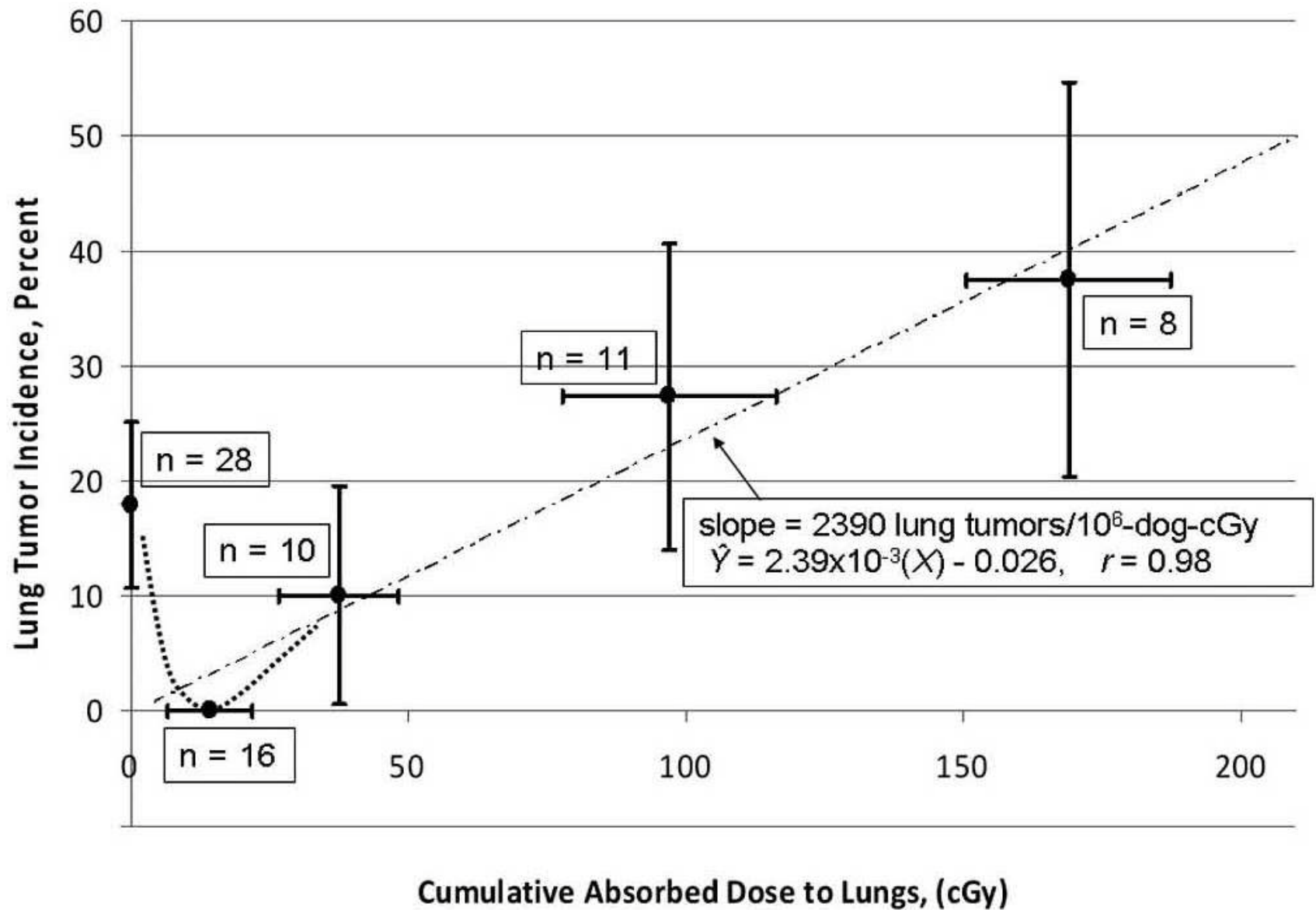
INTRODUCTION

INHALED PLUTONIUM dioxide (insoluble) deposits with high efficiency and is retained for long times (years) in the lungs (ICRP 1994). Desire to understand the health effects of internally deposited, alpha-particle-emitting plutonium isotopes stimulated a vast amount of research involving several research institutes and universities (Standard 1988). Life-span studies in beagle dogs have provided

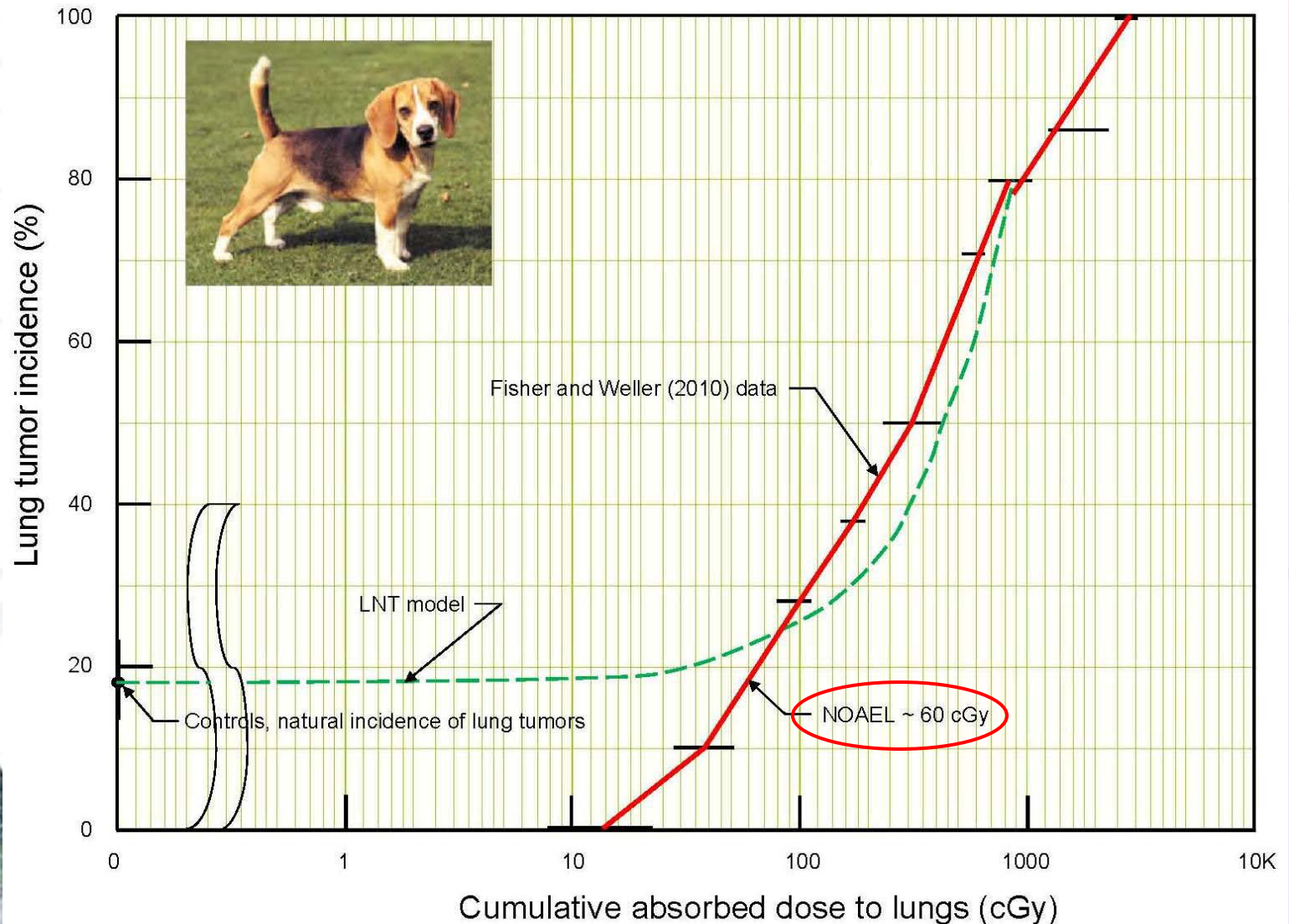
PuO_2 in beagle dog lungs



PuO_2 in beagle dog lungs: low-dose range



Inhaled PuO_2 in dogs, dose on log scale

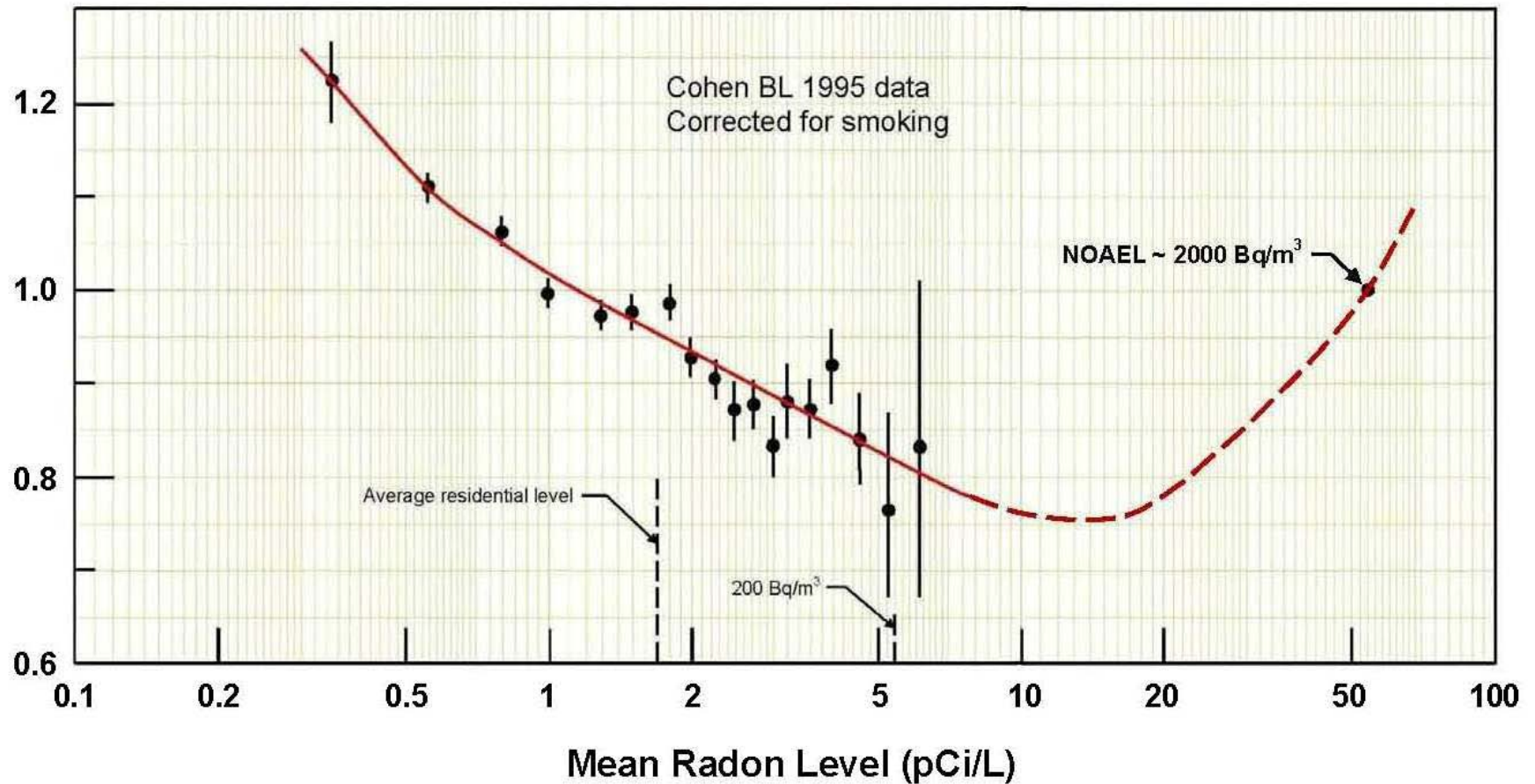


Threshold-NOAEL for radon-induced cancer

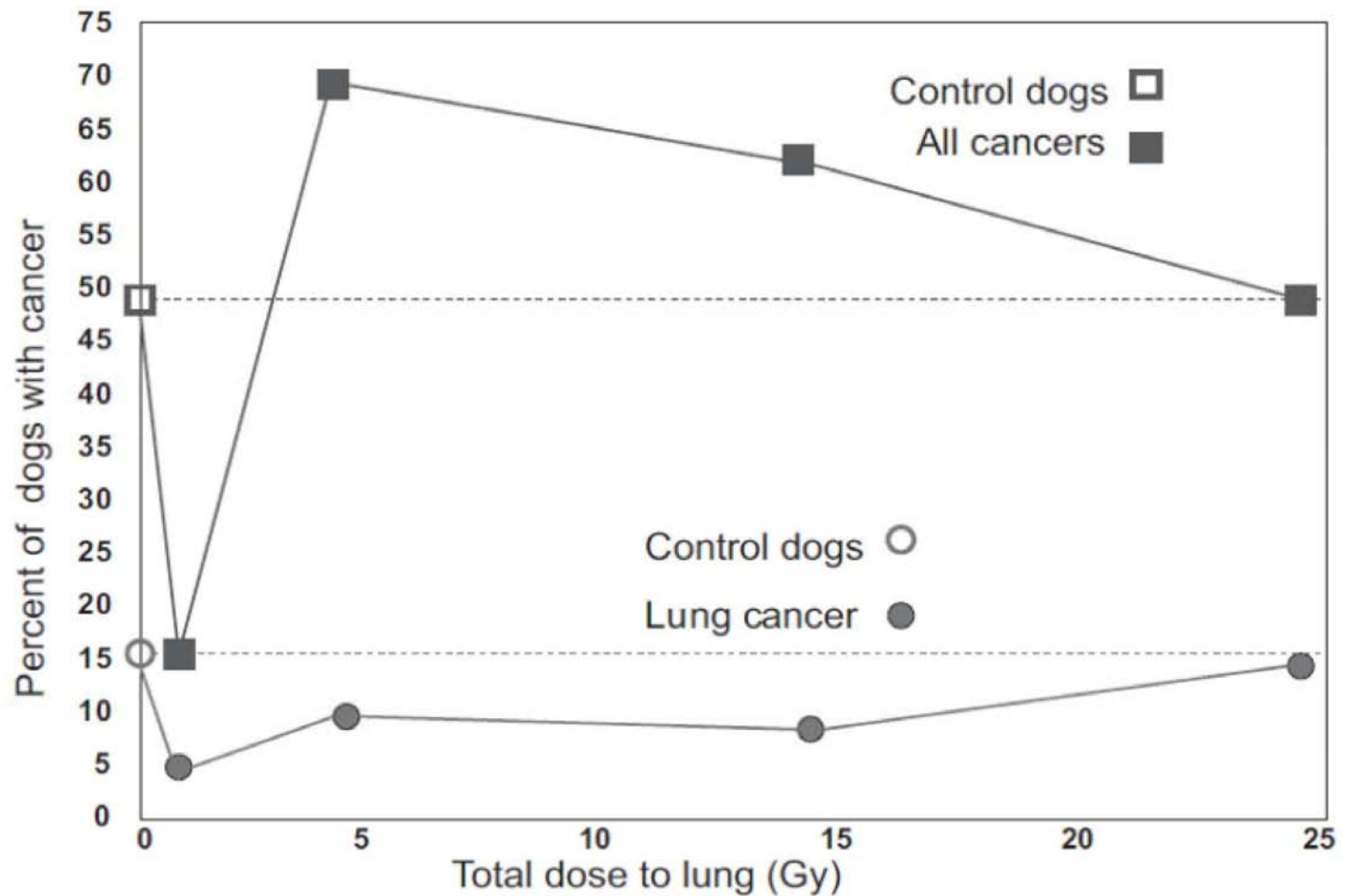
- Raabe (2011): The average dose rate determines the cancer risk
- Dose rate of inhaled $^{239}\text{PuO}_2$ NOAEL = **60 cGy** \div 12.5 year = **4.9 cGy/y**
- ICRP-115 (2010) gives 17 mSv/year as effective dose for 300 Bq/m³ of radon in homes with 0.4 equilibrium factor and 80% occupancy factor
- Absorbed dose $D_{T,R} = E/(w_R \times w_T)$; 17 mSv/y \div (20 \times 0.12) = 7.1 mGy/y
- Radon level of $300 \times 4.9 \div 0.71 =$ **2000 Bq/m³** or 54 pCi/L is the radon NOAEL that corresponds to 4.9 cGy/year NOAEL of inhaled $^{239}\text{PuO}_2$
- EPA action level is 150 Bq/m³, which is 13 times below 2000 Bq/m³
- Recommend radon limit of 1000 Bq/m³, which gives optimum benefit

Inhaled radon in homes

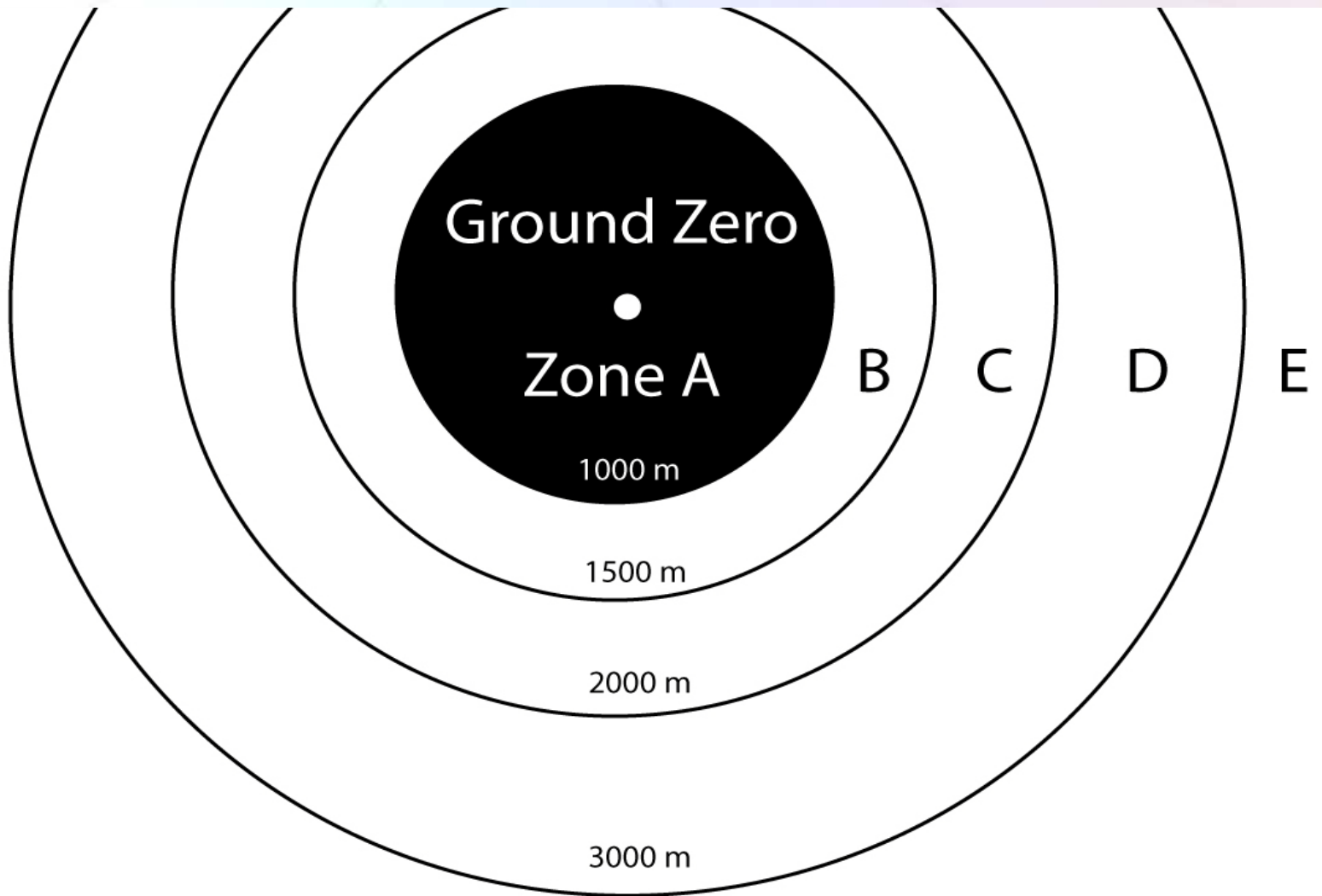
Normalized Lung Cancer Mortality (m/m₀)



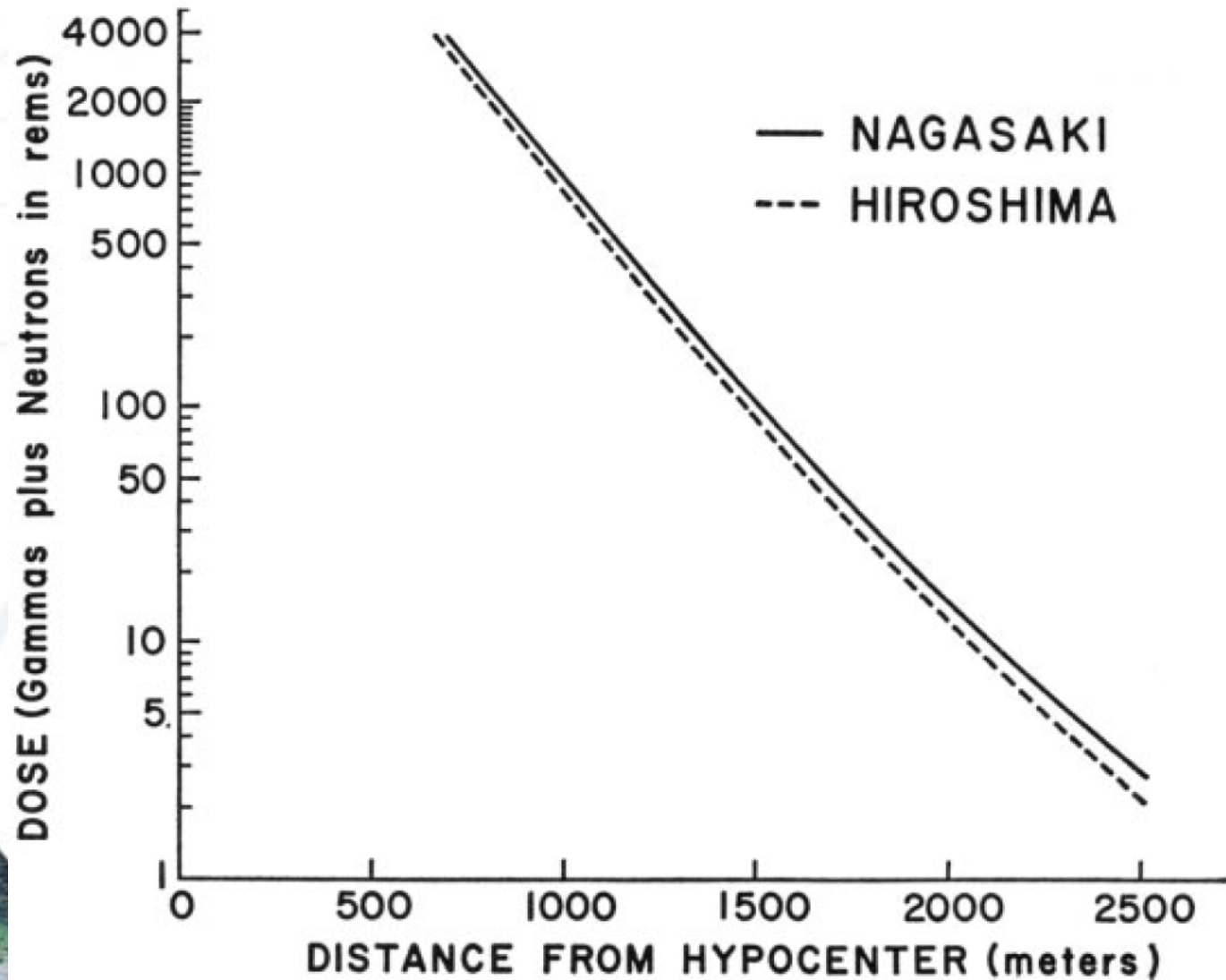
Brooks-2009: Summary of cancer frequency for inhaled beta-gamma emitting ^{90}Sr , ^{144}Ce , ^{91}Y and ^{90}Y



Hiroshima atomic bomb survivor zones



Radiation dose vs. distance from ground zero



UNSCEAR 1958 Table VII

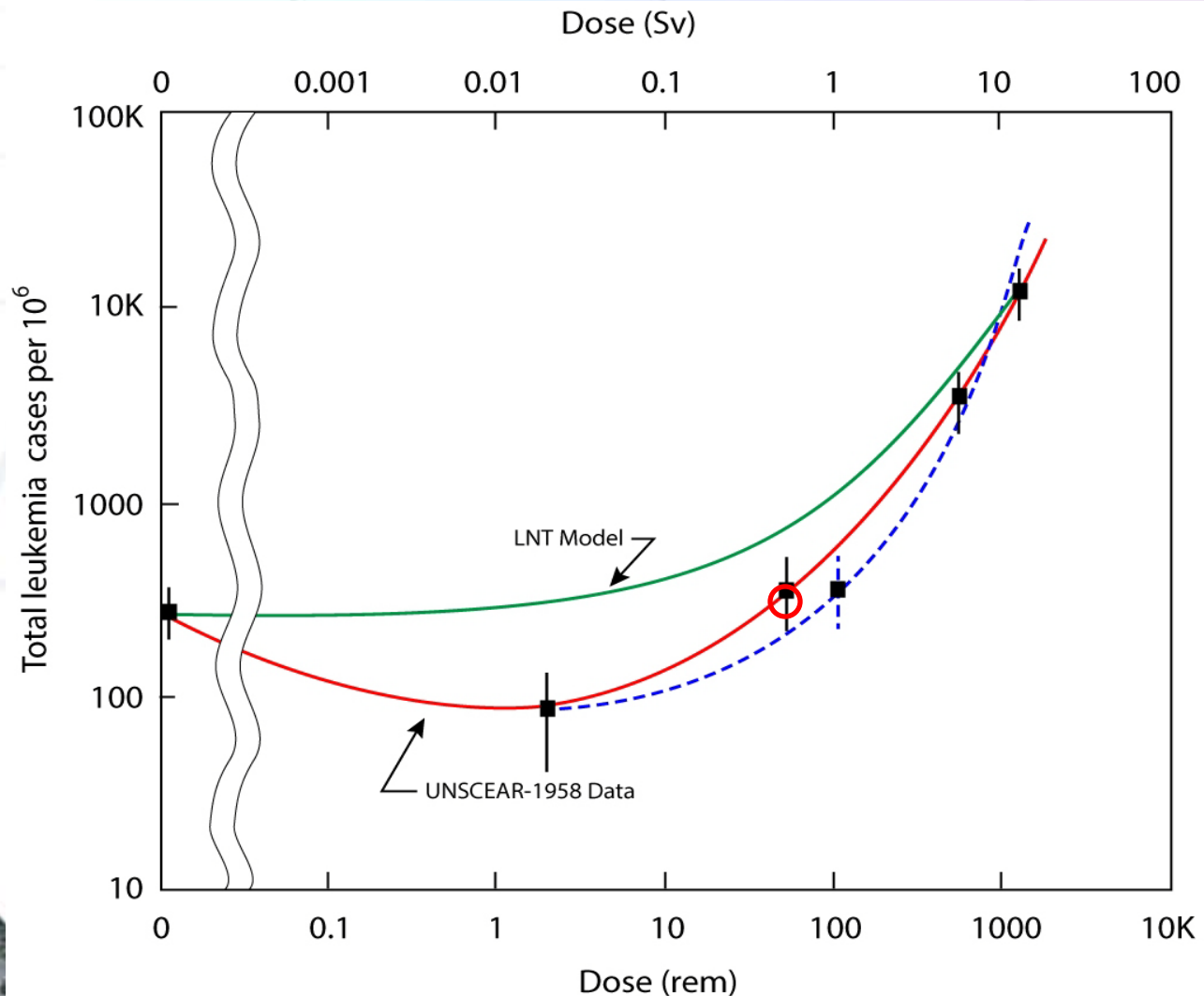
Leukemia incidence for 1950–57 after exposure at Hiroshima^a

Zone	Distance from hypocentre (metres)	Dose (rem)	Persons exposed	L (Cases of leukemia)	\sqrt{L}	N ^b (total cases per 10 ⁶)
A	under 1,000	1,300	1,241	15	3.9	12,087 \pm 3,143
B	1,000–1,499	500	8,810	33	5.7	3,746 \pm 647
C	1,500–1,999	50 ^c	20,113	8	2.8	398 \pm 139
D	2,000–2,999	2	32,692	3	1.7	92 \pm 52
E	over 3,000	0	32,963	9	3.0	273 \pm 91

^c It has been noted (reference 15, 16) that almost all cases of leukemia in this zone occurred in patients who had **severe radiation complaints**, indicating that their **doses were greater than 50 rem**.

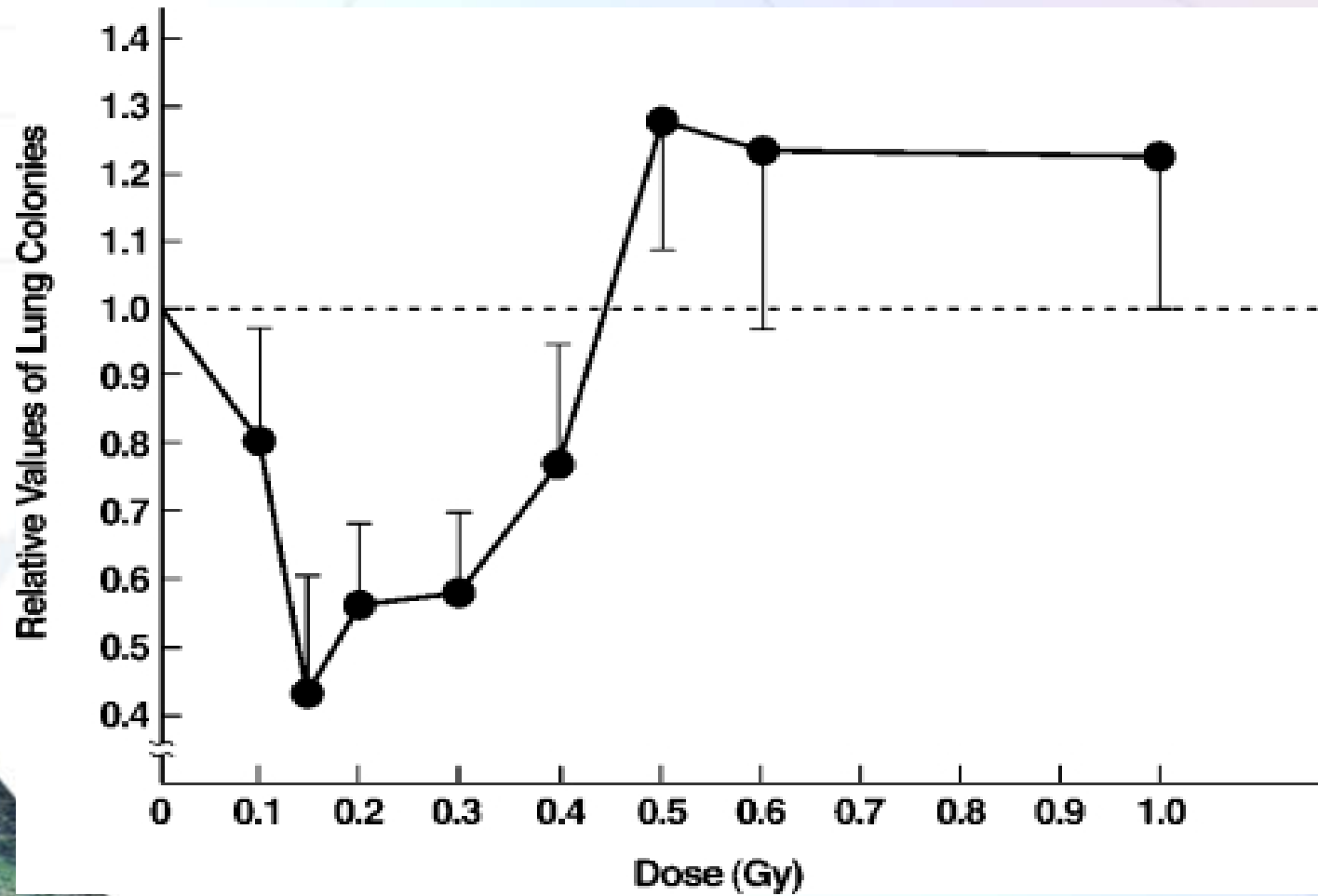
Threshold level at ~ 50 rem (500 mSv)

J-curve, not LNT model



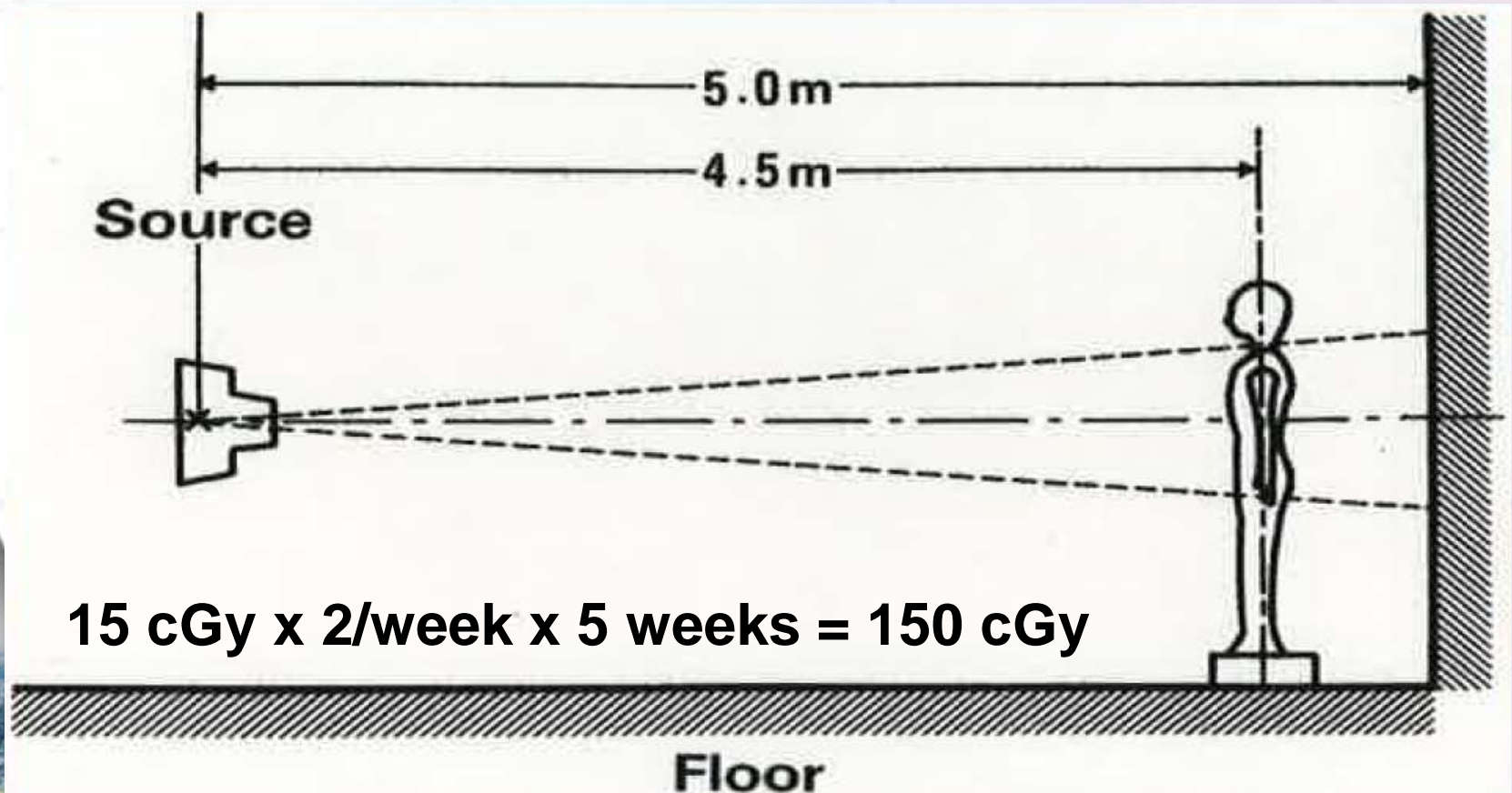
Results of one Sakamoto study

Spontaneous lung metastasis vs. total-body dose



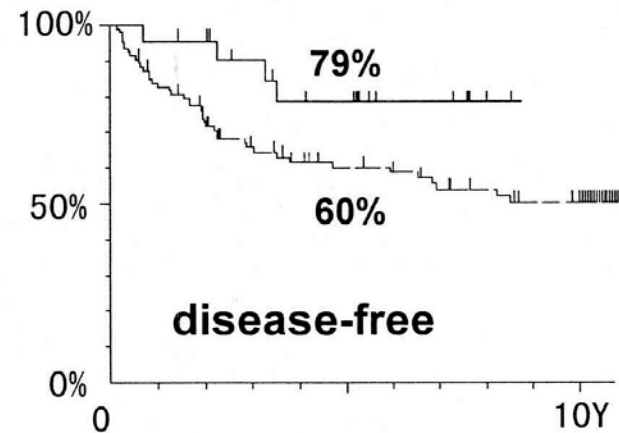
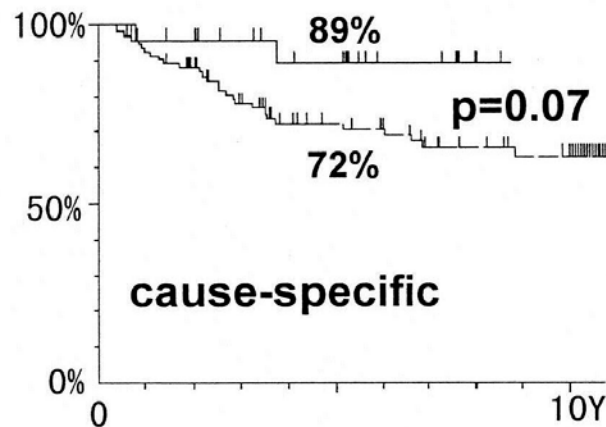
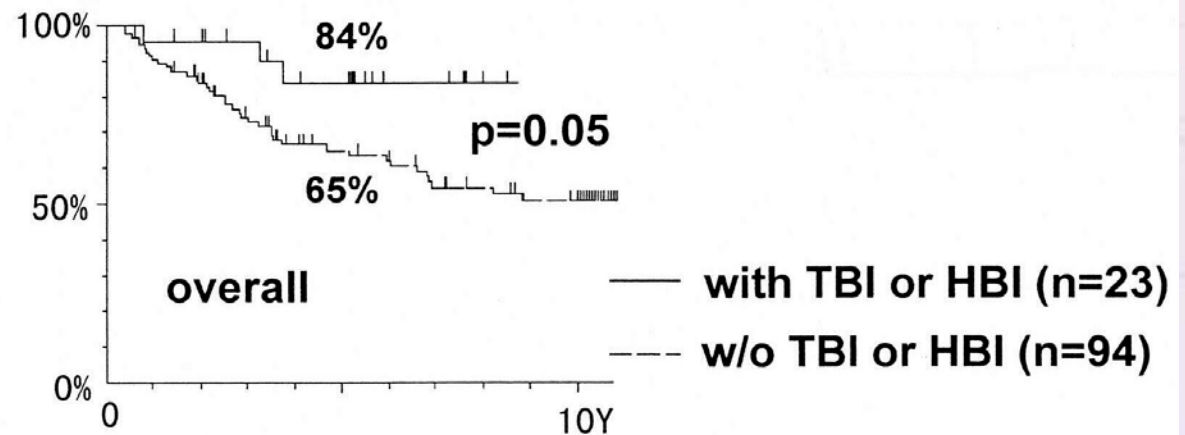
Source – patient schema for half-body LDR

“Observed the total removal of tumors in all regions of the body of a patient with advanced ovarian cancer.”



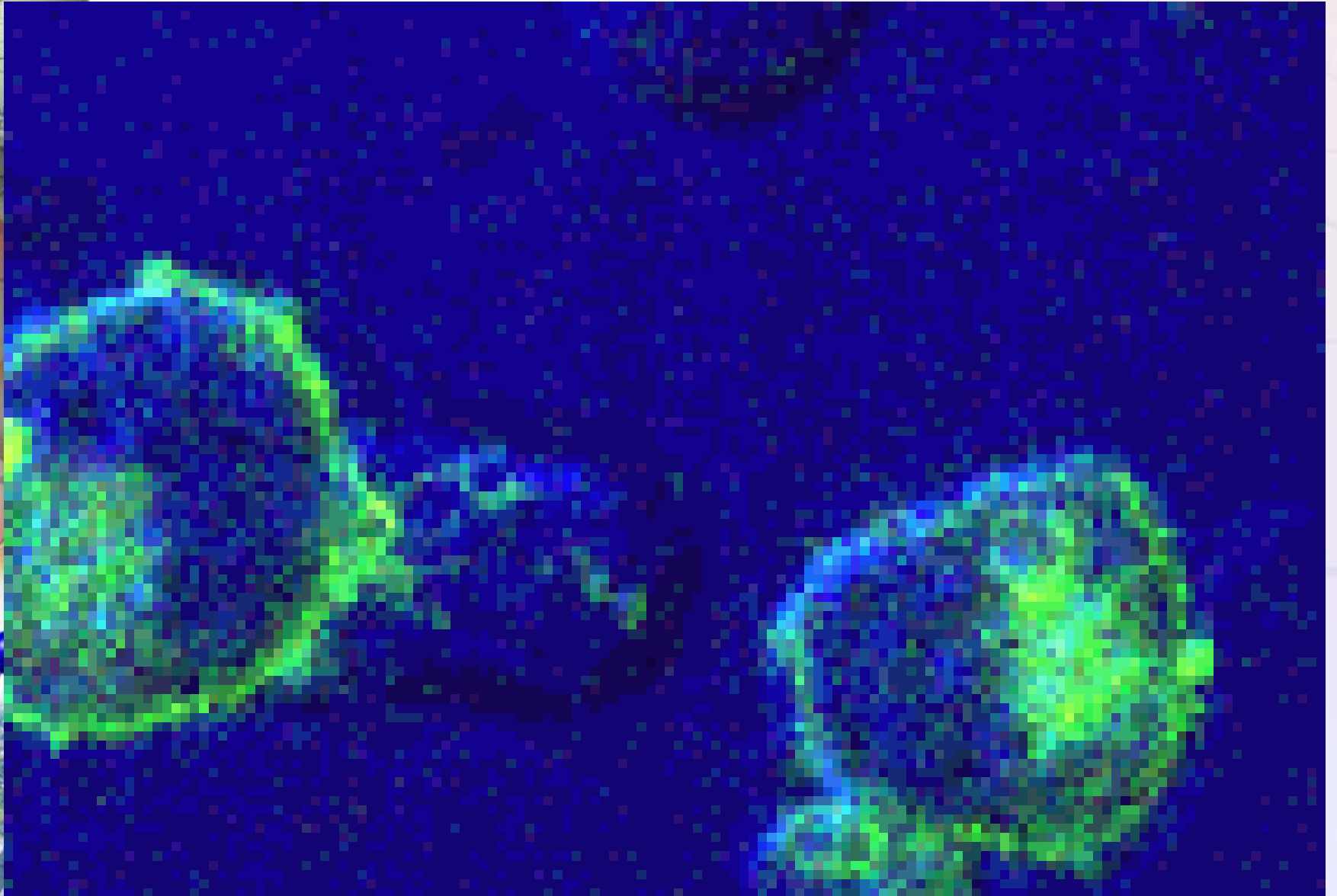
HBi or TBI for non-Hodgkin's lymphoma

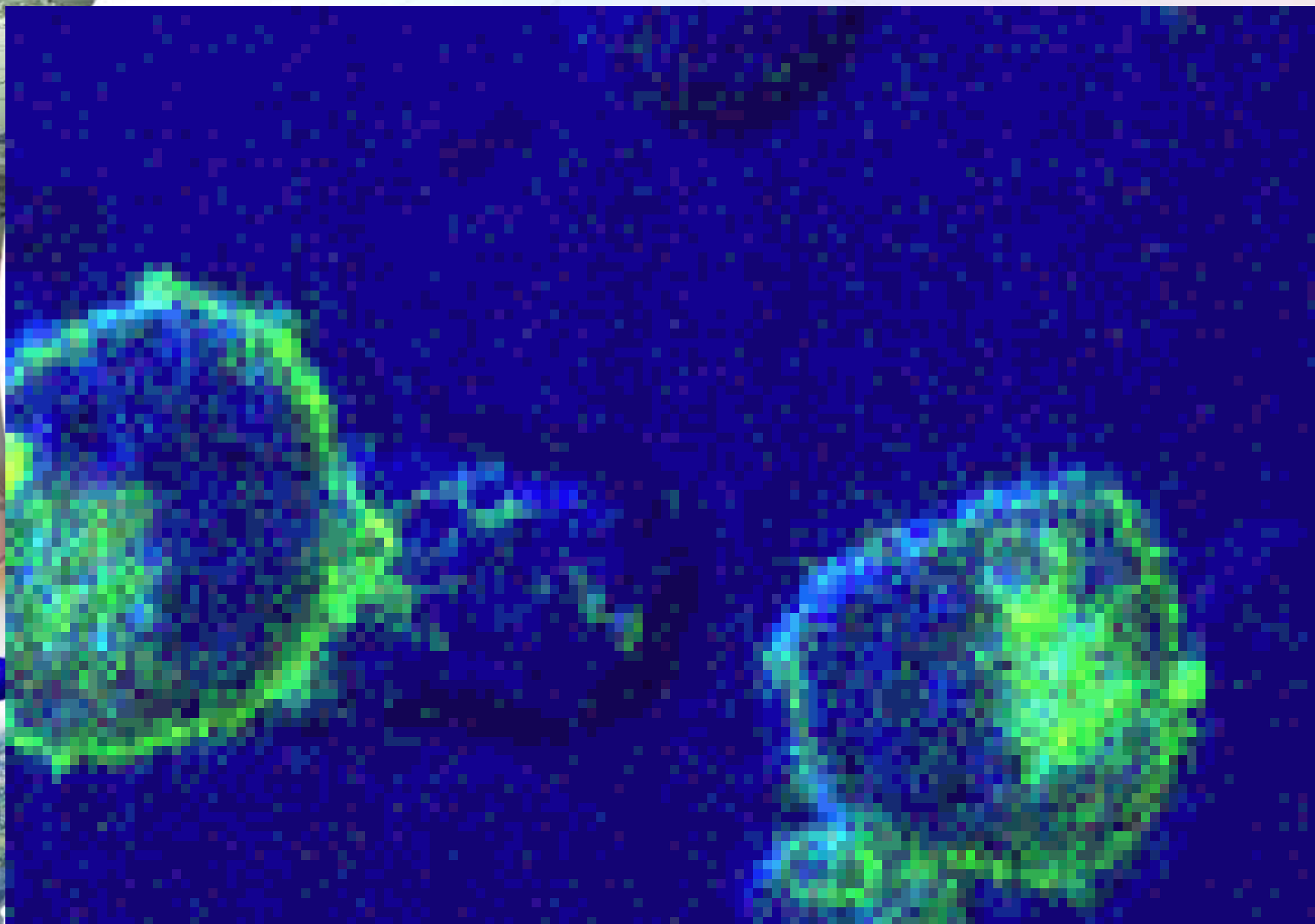
Survivals of Stage I,II Non-Hodgkin's lymphoma



Shu-Zheng Liu and Jerry Cuttler in Mississauga







LDR therapy for Hurthle cell carcinoma

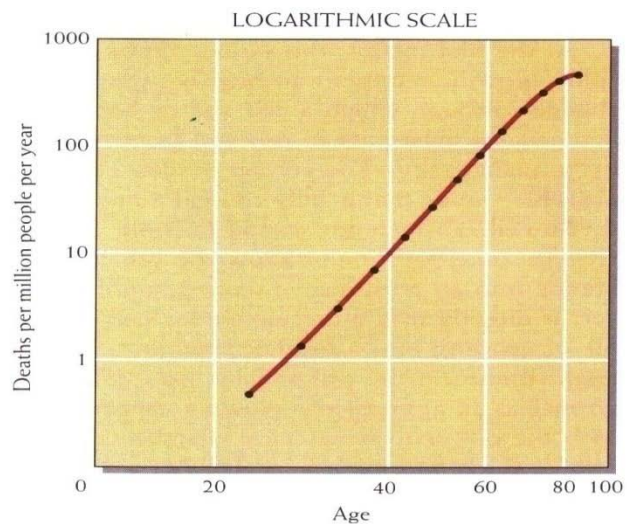
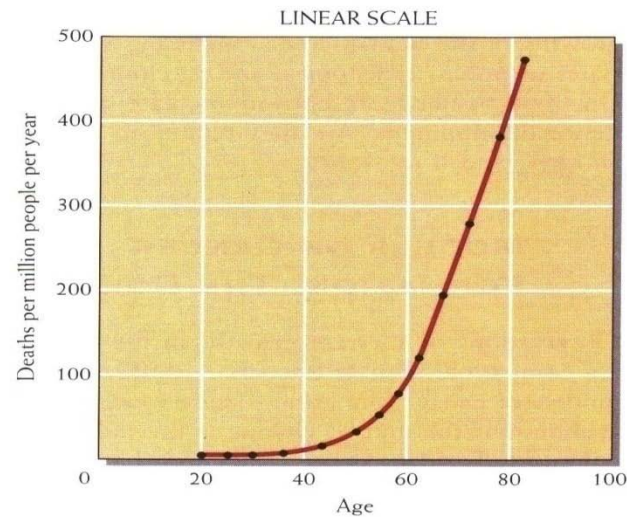


HB-LDI therapy; prophylaxis against cancer

150 mGy x twice/week x 5 weeks = 1500 mGy



Cancer death rate rises exponentially with age



Actual annual U.S. death rate from colon cancer in relation to age, 1986.

Cancer cells from where?

Spontaneous DNA damage:
free radicals, reactive oxygen species, thermal effects

Why the increase?

Protection systems age, i.e.,
immune system gets weaker

Can we do something?

Low radiation doses stimulate
adaptive protection systems

Hormesis by Low Dose Radiation Effects: Low-Dose Cancer Risk Modeling Must Recognize Up-Regulation of Protection

Ludwig E. Feinendegen, Myron Pollycove, and Ronald D. Neumann

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2	The Meaning of Absorbed Dose in the Low Dose Region.....
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11	Conclusion.....
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Abstract

Ionizing radiation primarily perturbs the basic molecular level proportional to dose, with potential damage propagation to higher levels: cells, tissues, organs, and whole body. There are three types of defenses against damage propagation. These operate deterministically and below a certain impact threshold there is no propagation. Physical static defenses precede metabolic-dynamic defenses acting immediately: scavenging of toxins;—molecular repair, especially of DNA;—removal of damaged cells either by apoptosis, necrosis, phagocytosis, cell differentiation-senescence, or by immune responses,—followed by replacement of lost elements. Another metabolic-dynamic defense arises delayed by up-regulating immediately operating defense mechanisms. Some of these adaptive protections may last beyond a year and all create temporary protection against renewed potentially toxic impacts also from nonradiogenic endogenous sources. Adaptive protections have a maximum after single tissue absorbed doses around 100–200 mSv and

Ludwig Feinendegen et al.

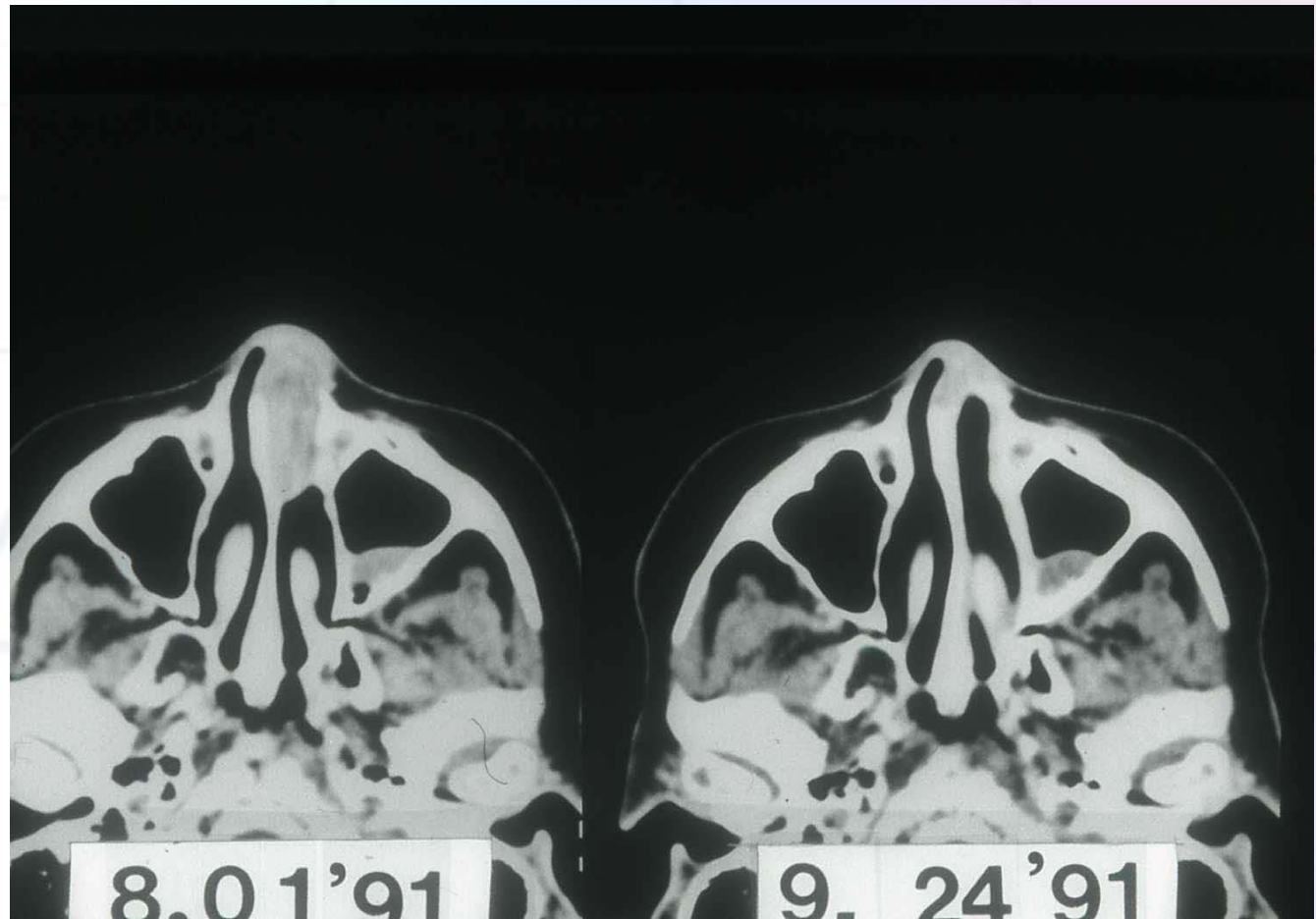
- Studies ignore spontaneous (endogenous) DNA *damage* rate
- Endogenous rate is very high compared with radiation-induced rate
- Average number of DNA alterations per average cell, per day
Endogenous (mainly due to metabolic ROS): total $\sim 10^6$, DSB $\sim 10^{-1}$
Radiation-induced (1 mGy/yr, γ background): total $\sim 10^{-2}$, DSB $\sim 10^{-4}$
- Ratio of DNA alterations (endogenous/rad'n): total $\sim 10^8$, DSB $\sim 10^3$

Adapted from Pollycove and Feinendegen 2003

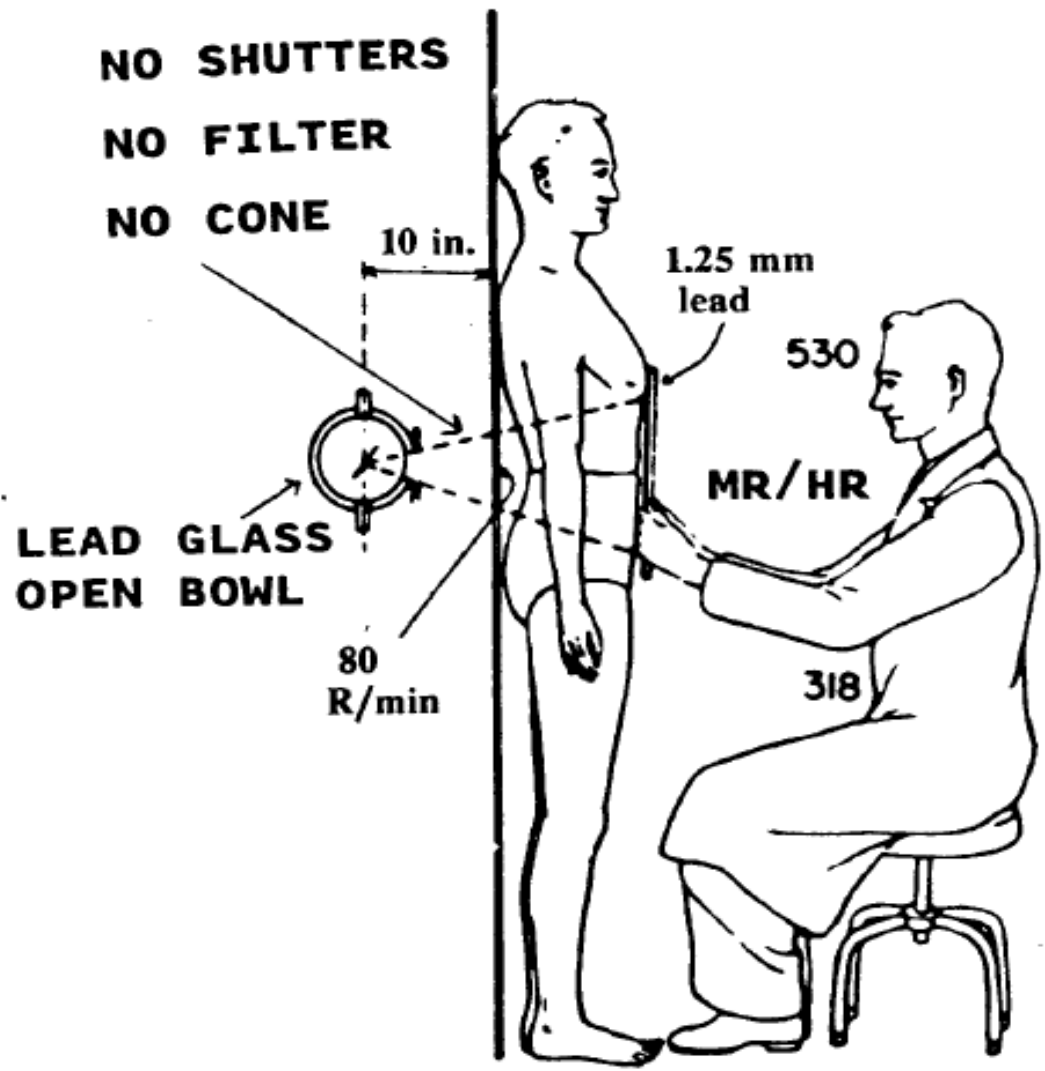
Ludwig Feinendegen et al. #2

- Low doses of radiation up-regulate adaptive protection systems
- *Fast defences* act immediately to remove toxins, repair molecules (DNA), remove/replace damaged cells and tissue, followed by ...
- *Delayed defences* of up-regulated adaptive systems (> 150 genes) that may last more than a year and protect against renewed toxic impacts from *both* radiation sources and non-radiation sources
- Adaptive protections are highly stimulated by 150 mGy acute dose
- Chronic or repetitive radiation initiates protection at lower level
- Adaptive protections **reduce risks \Rightarrow less cancer, extends life span**

Abscopal effect 54 days after HB LDI



Fluoroscopy circa. 1930



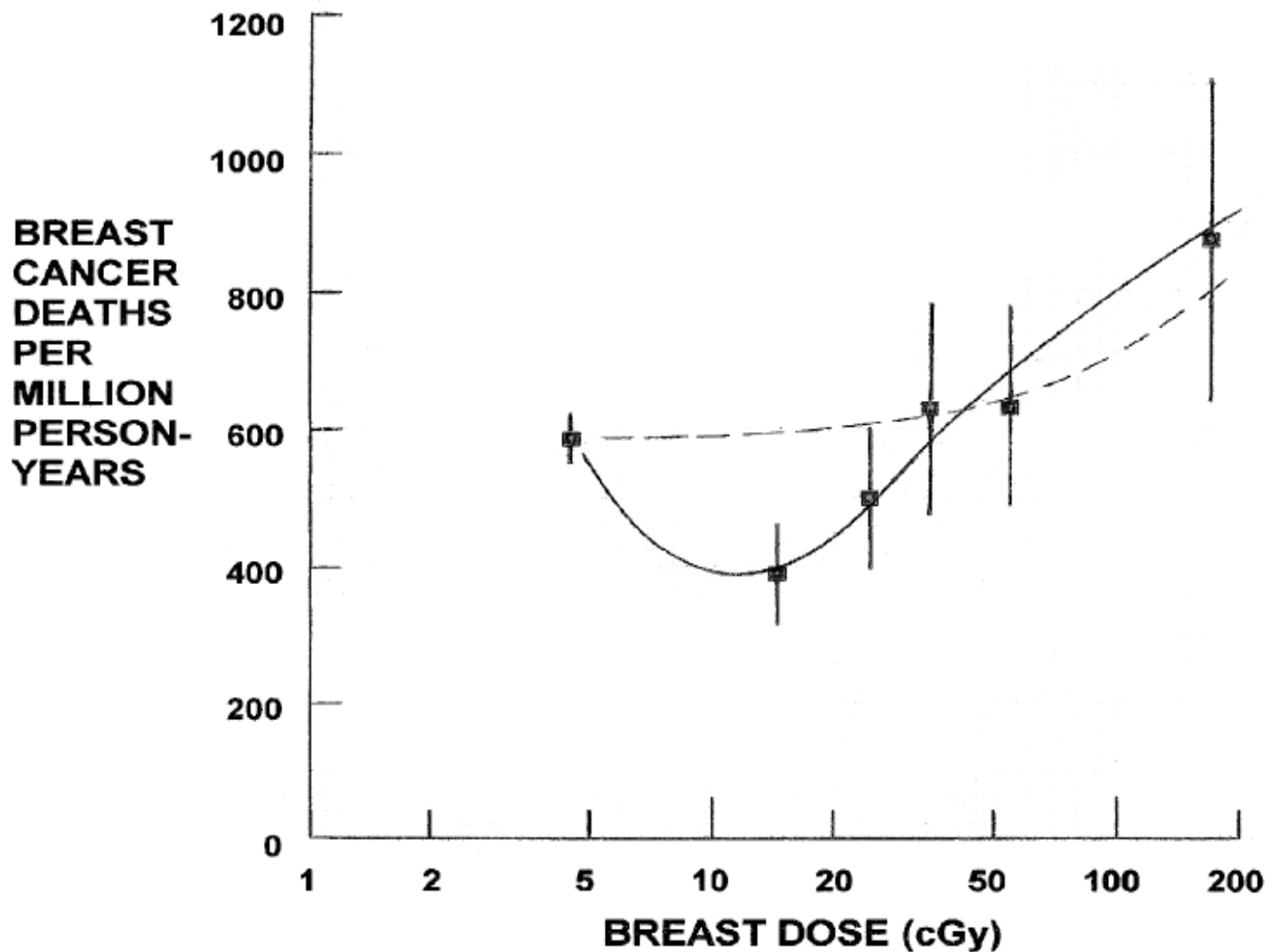
Canadian Breast Cancer Study

Table 1. Observed Rates of Death from Breast Cancer, According to the Dose of Radiation Received.

Dose (Gy)	STANDARDIZED RATE PER 10 ⁶ PERSON-YEARS*		
	NOVA SCOTIA	OTHER PROVINCES	ALL PROVINCES
0-0.09	455.6 (13)	585.8 (288)	578.6 (301)
0.10-0.19	}	389.0 (29)	421.8 (32)
0.20-0.29		497.8 (24)	560.7 (26)
0.30-0.39		630.5 (17)	650.8 (18)
0.40-0.69		632.1 (19)	610.0 (19)
0.70-0.99			1362 (13)
1.00-2.99	2060 (14)		1382 (17)
3.00-5.99	2811 (13)	873.1 (14)	2334 (14)
6.00-10.00	7582 (8)		8000 (9)
≥10.00	21,810 (12)		20,620 (13)

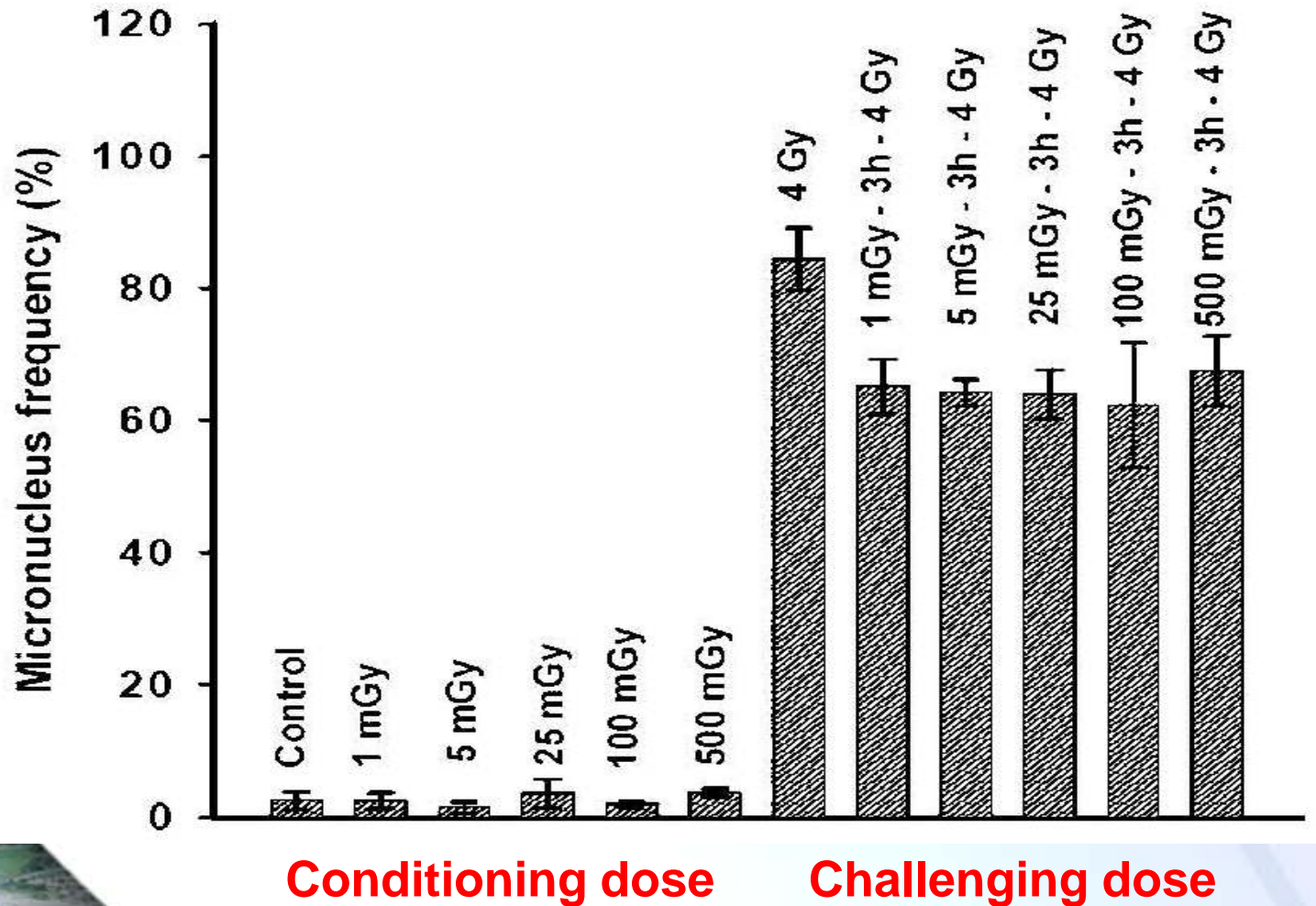
*The number of deaths is shown in parentheses. The calculations exclude the values for 10 years after the first exposure and have been standardized according to age at first exposure (10 to 14, 15 to 24, 25 to 34, and ≥35 years) and time since first exposure (10 to 14, 15 to 24, 25 to 34, and ≥35 years) to the distribution for the entire cohort.

Breast cancer mortality of TB patients



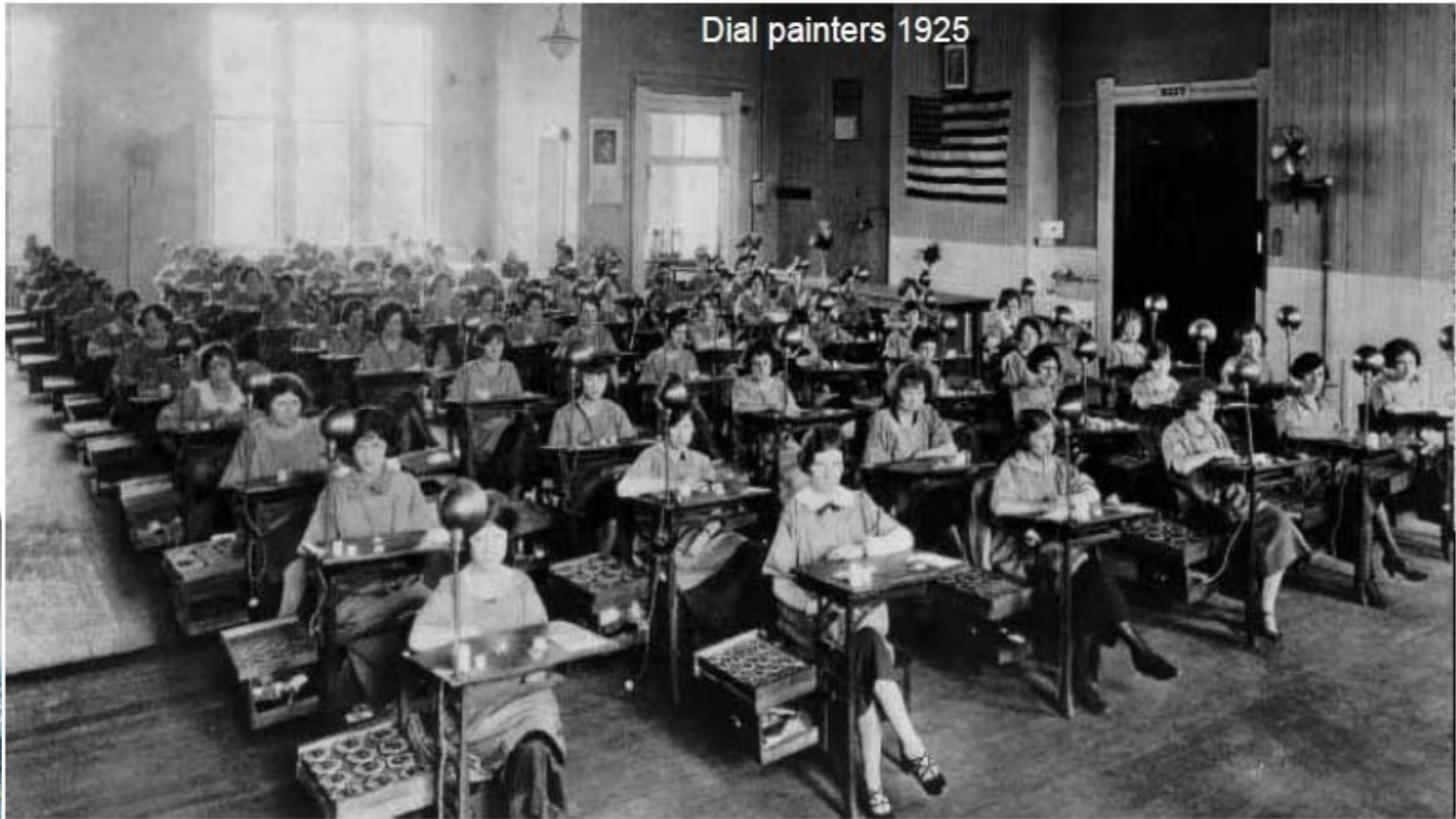
Adaptive response

Low radiation dose up-regulates cell repair capability
Decreases risk of 4 Gy challenging dose



4133 identified radium dial painters in USA

Bone cancer *threshold* at 10 Gy (1000 rad) radium alpha radiation



1000cGy threshold radium-induced bone cancer

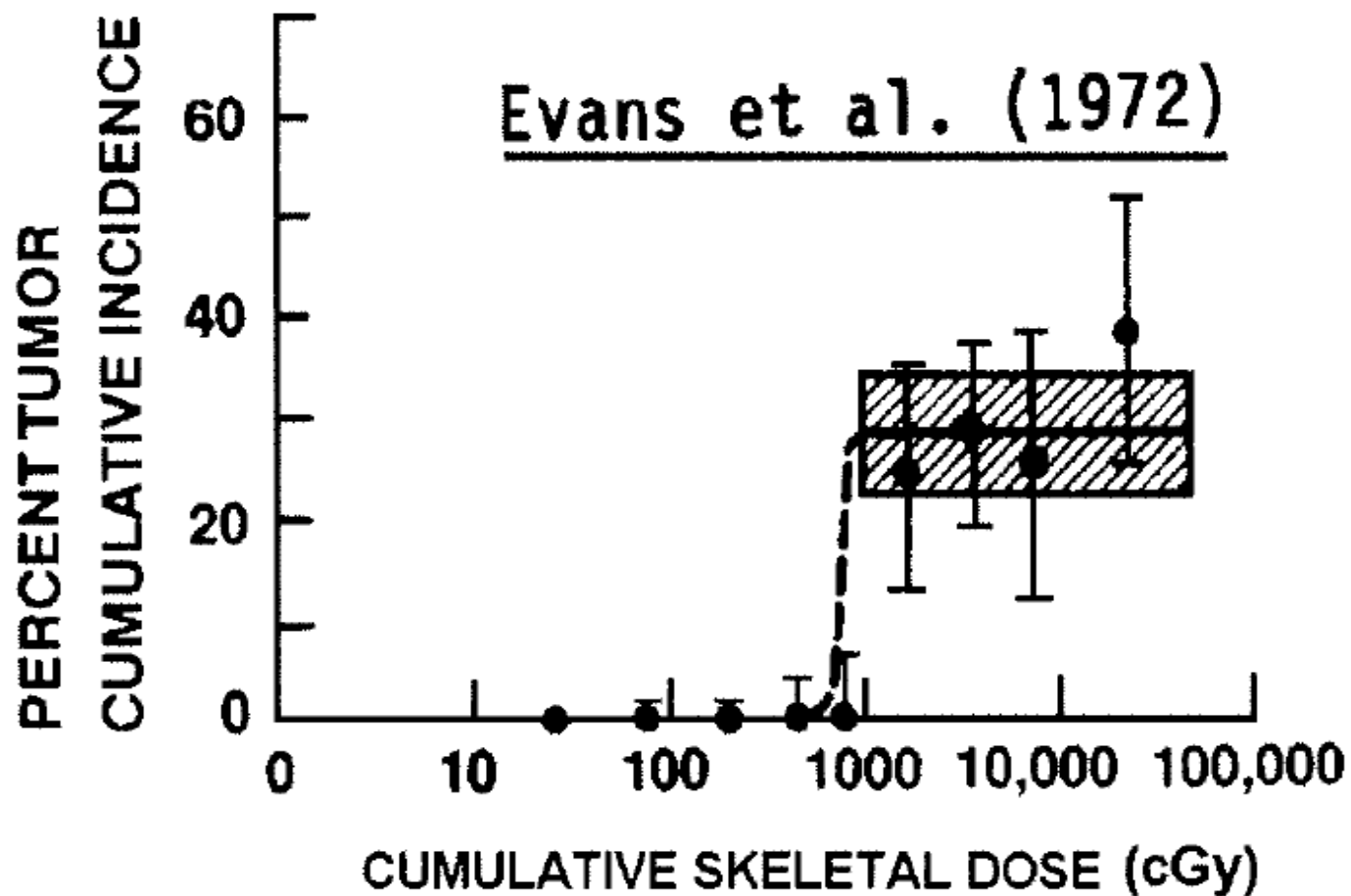


Fig. 11. Cumulative bone sarcoma incidence in people exposed to ^{226}Ra as a function of cumulative dose to the skeleton as reported by Evans et al. (1972).

Nasal radium irradiation

US CDC estimate: up to 2,600,000 children received NRI from 1945-1961 as a standard medical practice to shrink adenoids. Typical Navy protocol: four 10 minute irradiations 2-4 weeks apart. **Contact** gamma dose = **2000 rad** (20 Gy); **1 cm depth** dose = **206 rad** (2 Gy) Beta dose 68 rad (0.7 Gy) from each applicator. Excess lymphoid tissue at Eustachian tube openings tended to prevent pressure equalization, aggravation middle ear problems.



Position of the child patient during treatment

Anesthesia with cocaine precedes introduction of the applicator which is then left in place for twelve minutes on each side
(From Proctor, D.F., *"The Tonsils and Adenoids in Childhood"*, p. 17, Charles C. Thomas, Publisher, 1960)



National Cancer Institute

at the National Institutes of Health

No link to any disease

Reviewed: January 10, 2003

Nasopharyngeal Radium Irradiation (NRI) and Cancer: Fact Sheet

Key Points

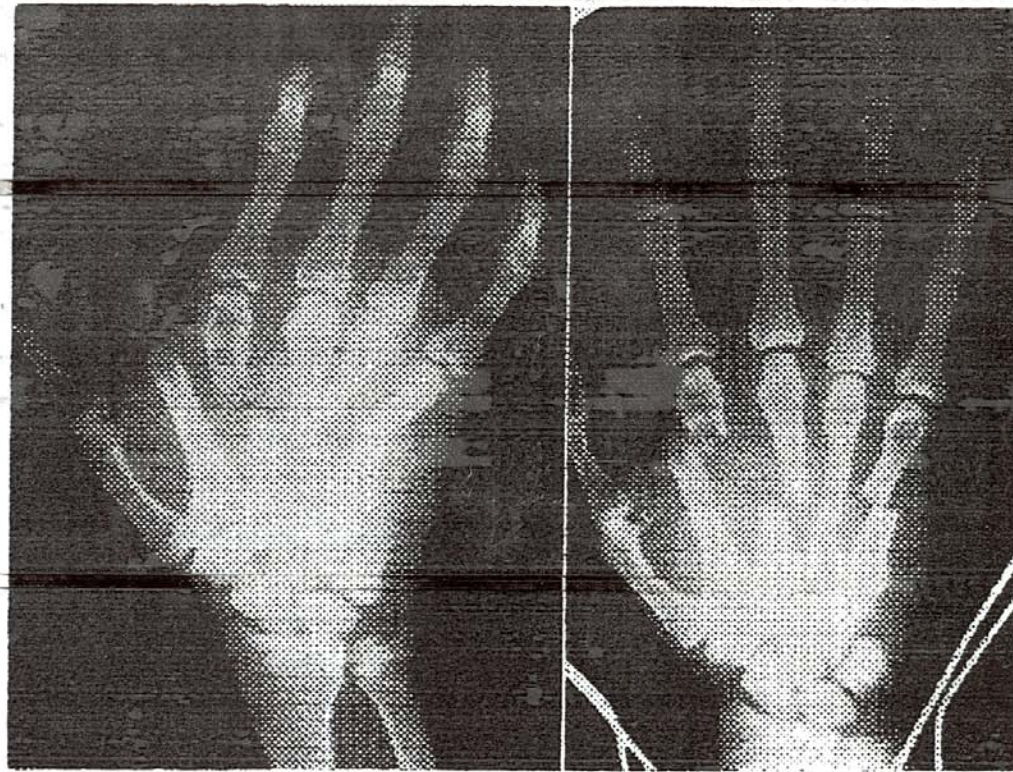
- Nasopharyngeal radium irradiation, (NRI) was widely used from 1940 through 1970 to treat ear dysfunctions in children and military personnel. Use of NRI was stopped when concern arose about possible adverse effects, including cancer.
- The purpose of NRI was to shrink swollen tissue in the nasopharyngeal cavity—the opening behind the nose and mouth. The treatment involved inserting a radioactive compound through the nostril into the nasopharyngeal opening for short periods of time. Some radiation exposure to the salivary, thyroid, and pituitary glands, and to brain tissue also occurred during this process.
- NRI was used in several European countries, Canada, and the United States. In the United States, it is estimated that between 0.5 million and 2.5 million children and at least 8,000 military personnel were treated with NRI.
- Children are considered to be the most vulnerable to radiation-related cancers.
- At this time, worldwide studies have not confirmed a definite link between NRI exposure and any disease.

LDR cures gas gangrene infections

430

JAMES F. KELLY AND D. ARNOLD DOWELL

October 1941



Figs. 7-8. Case 1: Severe hand injury, with multiple compound fractures and some gas in tissues (left). Fig. 8 (right) shows same hand a few days after prophylactic x-ray irradiation: no gas in the tissues, no infection, hand on way to complete recovery.

TABLE V: CASES WHICH RECEIVED PROPHYLACTIC IRRADIATION AND HAVE BEEN REPORTED IN THE LITERATURE

Cases Which

those which do not appear until three or four days have elapsed. It is evident from Figure 6 that the second, third, and

Appearance of db/db mice at 90th week of age

Irradiated diabetic mice are healthier and live longer

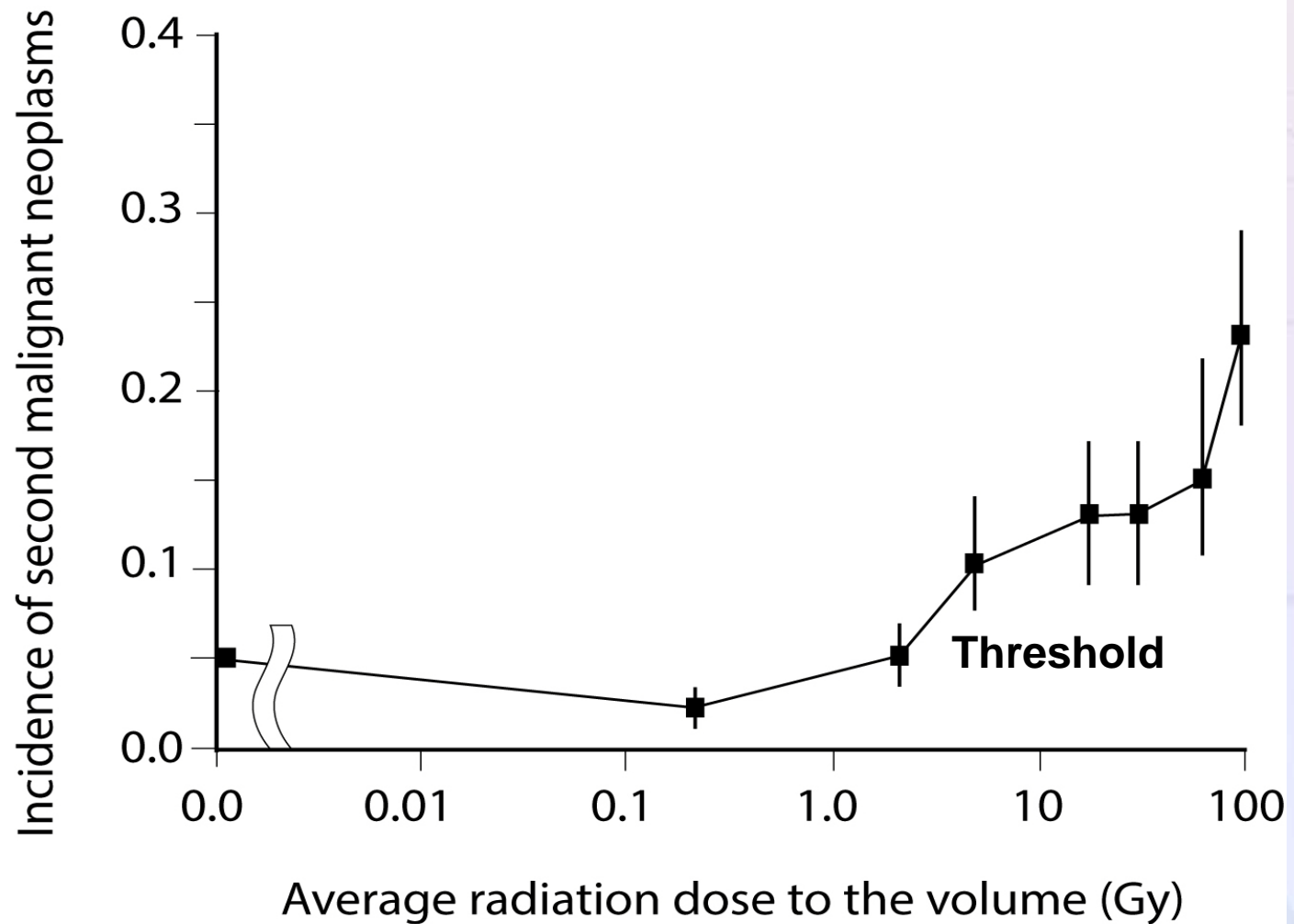


Irradiated Group

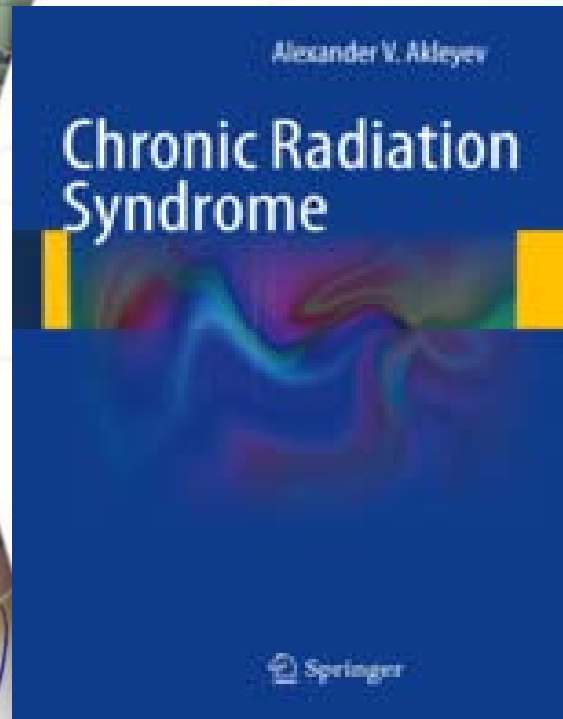


Control Group

Tubiana: 5000 survivors of childhood cancer



Effects of Mayak releases on residents



Residents ingested Mayak radioactive discharges into Techa River, in early 1950s. UNSCEAR recognized this as opportunity to estimate dose–effect of long-term irradiation.

Mortality incidences from leukemia and cancer of CRS people did not exceed cancer incidences for exposed people without CRS and for Russia as a whole

Threshold for CRS is an annual dose of 700 to 1000 mGy

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RADIOBIOLOGY SPECIAL FEATURE: COMMENTARY

What we know and what we don't know about cancer risks associated with radiation doses from radiological imaging

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E-mail: djb3@columbia.edu

ABSTRACT

Quantifying radiation-induced cancer risks associated with radiological examinations is not easy, which has resulted in much controversy. We can clarify the situation by distinguishing between higher dose examinations, such as CT, positron emission tomography-CT or fluoroscopically guided interventions, and lower dose "conventional" X-ray examinations. For higher dose examinations, the epidemiological data, from atomic bomb survivors exposed to low doses and from direct epidemiological studies of paediatric CT, are reasonably consistent, suggesting that we do have a reasonable quantitative understanding of the individual risks: in summary, very small but unlikely to be zero. For lower dose examinations, we have very little data, and the situation is much less certain, however, the collective dose from these lower dose examinations is comparatively unimportant from a public health perspective.

Conclusions

- Social concern about nuclear energy “safety” is caused by policy link of *human-made* radiation to a risk of cancer
- Radiation scare of 1950s, to stop atom-bombs, continues
- Authorities are ignoring beneficial effects of low doses
- Will threshold model for radiation protection bring social acceptance of nuclear energy and radiation diagnostics?
- The British radiologist study showed 1934 ICRP “tolerance dose” of 500 mGy/year is adequate for radiation protection

Recommendations

- Scientific societies should organize events to discuss radiation health benefits
- Regulatory bodies and health organizations should examine the data and use The Scientific Method
- Use a dose-response model that is based on data
- Stop calculating radiation-induced cancer risk
- Develop/implement public communication programs
- Learn 3 lessons from Chernobyl and Fukushima:
 - Severe accidents result in *low* radiation dose-rate levels
 - Long-term evacuations are not appropriate when no risk
 - Emergency precautionary actions cause stress and deaths

**Raise radiation level threshold for evacuation
from 20 to 700 mGy/year (2 to 70 rad/year)**