HPS and ANS Special Session
Low-Dose Issues

Norfolk, Virginia, February 3, 2015

Radiation effects on humans and organism, and reasons for the fear

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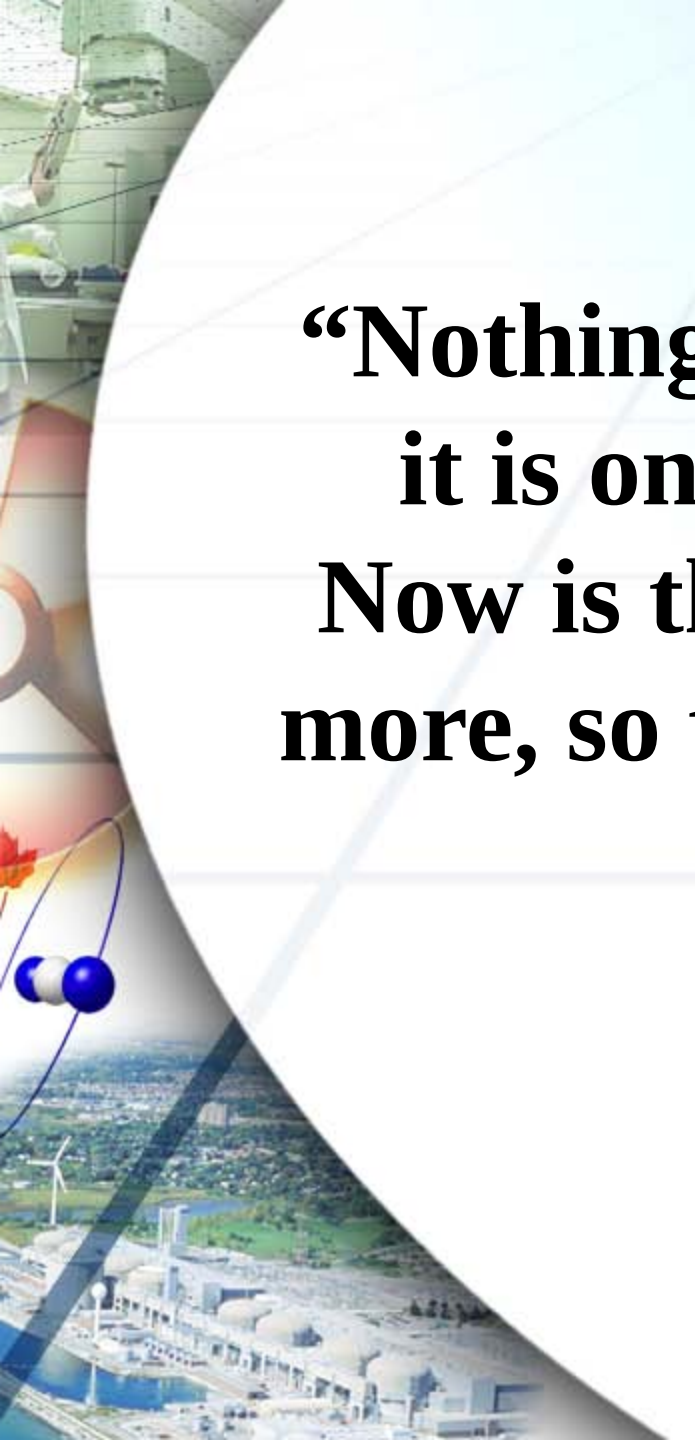
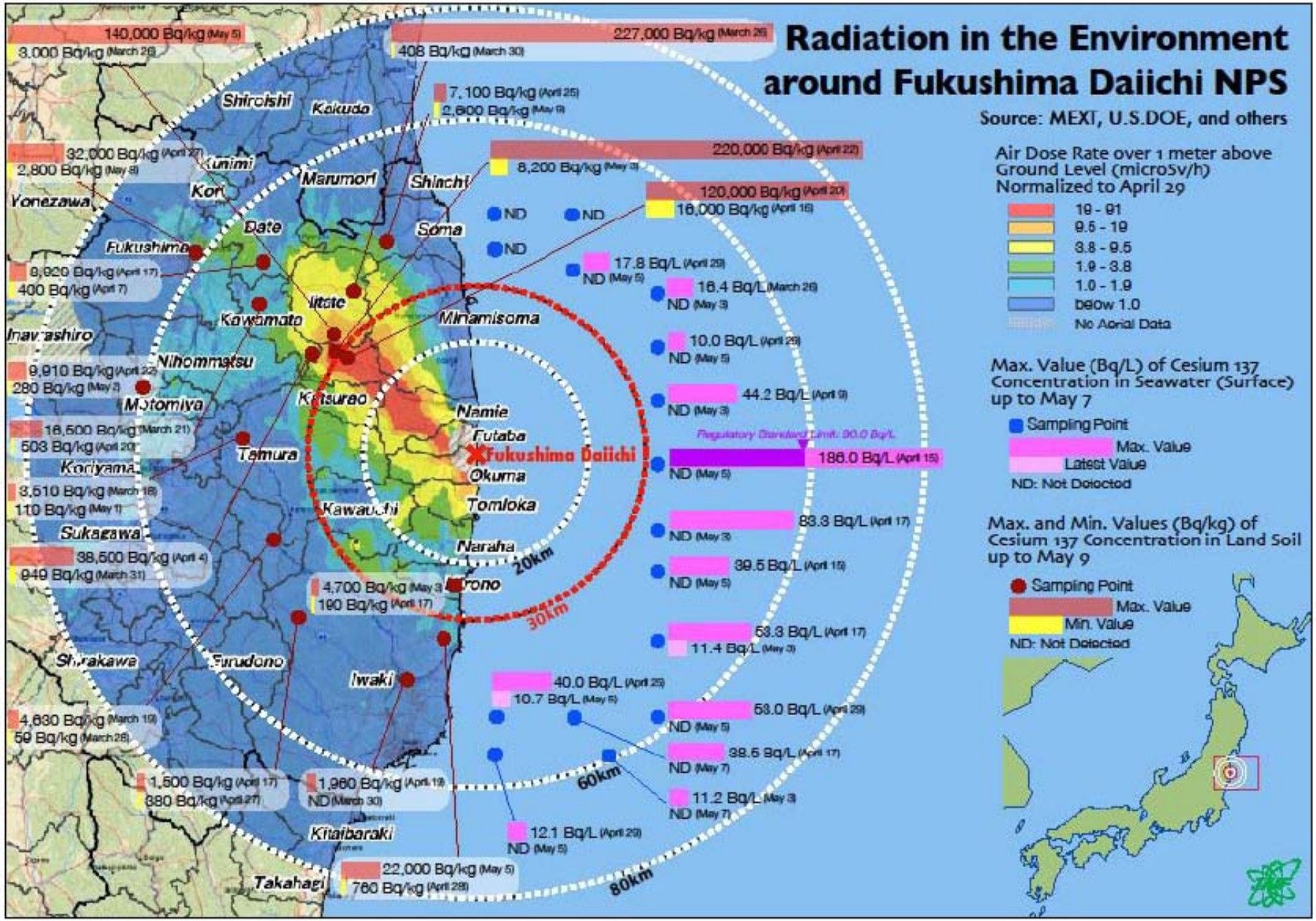


“Nothing in life is to be feared; it is only to be understood. Now is the time to understand more, so that we may fear less.”

Maria Sklodowska Curie

Winner of a second Nobel Prize for
the discovery of polonium and radium

91 µSv/h x 8766 h/y = 798 mSv/y



Main Points

- Fukushima radiation same as natural HBRA
- Evacuation resulted in 1600 premature deaths
- Precautionary action was not “conservative”
- Hiroshima leukemia incidence at 20 mSv is lower than controls. Threshold is at 500 mSv.
- Chronic radiation is beneficial < 700 mGy/year
  Radiation becomes harmful > 700 mGy/year
- LNT theory is invalid, antinuclear ideology
- Revert to 1934 ICRP standard of ‘tolerance dose’ of 0.2 roentgen/day or ~ 700 mGy/year

End regulations based on politicized science

What is the LNT assumption?

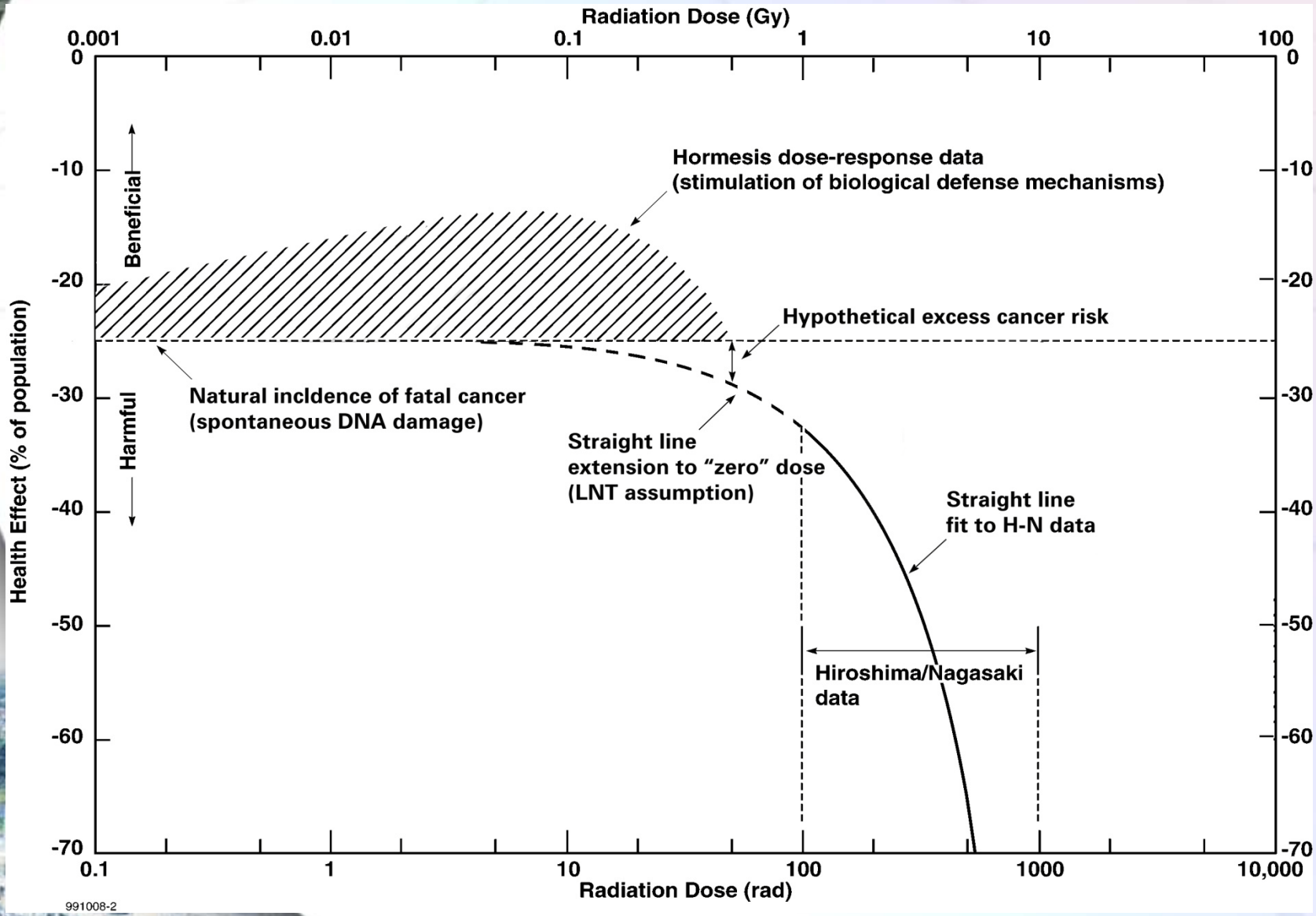
"A history of the ICRP" by R. Clarke and J. Valentin, HPJ 2005

- "Now there were **stochastic effects where probability** of the (genetic) effect, not the severity, is proportional to the size of the dose."
- "The threshold (dose) was rejected."
- "The problem had become one of limiting the probability of harm … estimation of probability of harm and decision on what level of **implied risk** is … unacceptable."
- From germ cells (genetic) ➡ somatic cells (cancers)

Extrapolated LSS cancer mortality linearly to zero dose

People fear radiation-induced cancer from any dose

LNT Assumption (dose on log scale)



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

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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 ^{60}Co 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 μGy 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 μGy. 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.

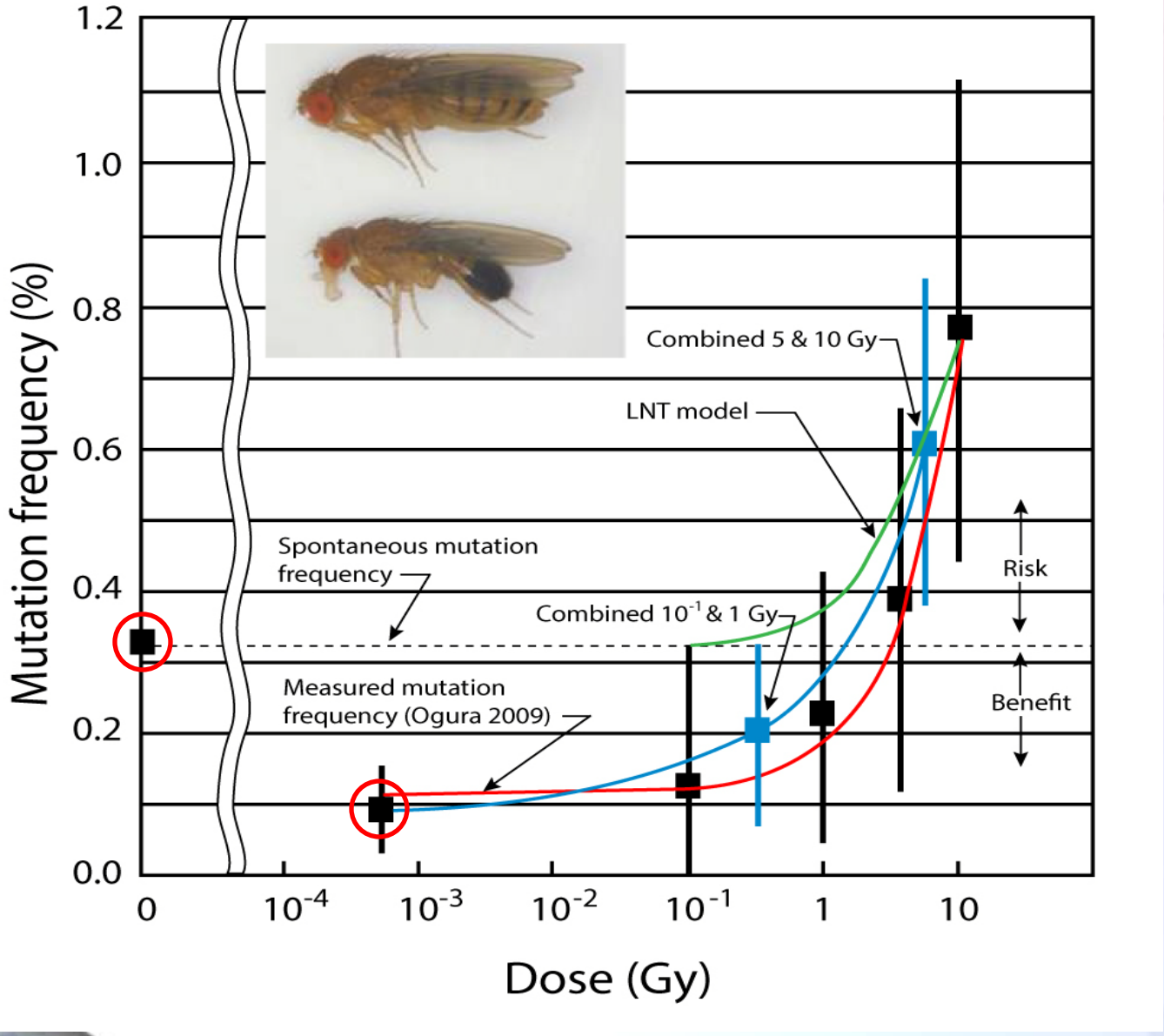
In contrast, we reported previously that in the somatic mutation assay using *Drosophila*, there was a threshold dose at approximately 1 Gy and that a mutation in the DNA repair function decreased the threshold value (*4*). The existence of a threshold, as determined in the sex-linked recessive lethal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

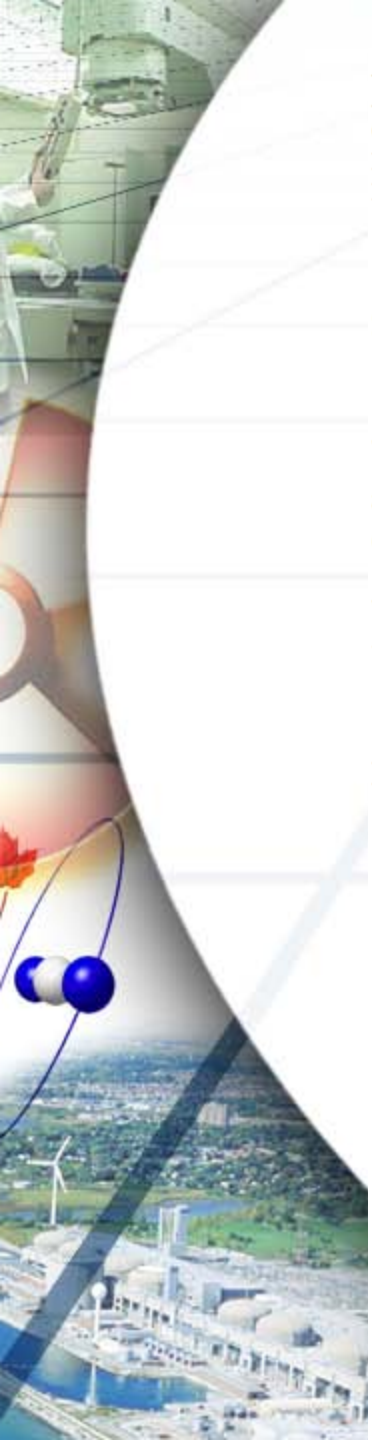
Binomial statistics applied to fruit fly mutation data measured by Ogura et al. 2009

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	2σ/n %	p + 2σ/n %	p – 2σ/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 - fruit flies, 22.4 mGy/h





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International Dose-Response Society

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

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

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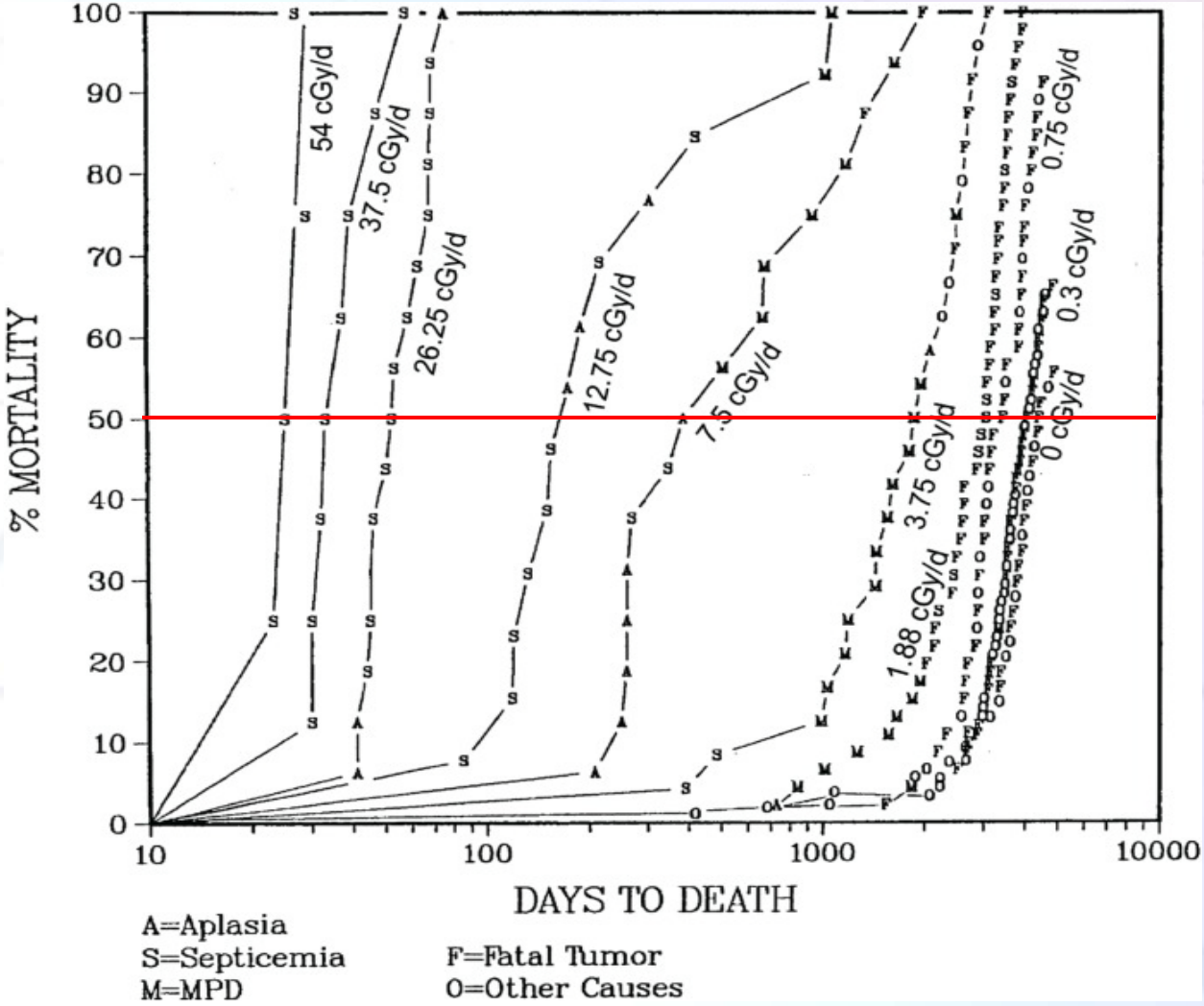
□ Chronic exposure of mammals to low dose-rates of ionizing radiation affects proliferating cell systems as a function of both dose-rate and the total dose accumulated. The lower the dose-rate the higher needs to be the total dose for a deterministic effect, i.e., tissue reaction to appear. Stem cells 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.

Fliedner: blood cell response to chronic radiation

- Review paper in Dose-Response Journal, Dec 2012
- He 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 on mammals is function of dose-rate and total dose
- Blood stem cells are usually very radiosensitive; however, they can tolerate and adapt to chronic radiation---adapt better at lower rate.
- Deliver clones of functioning cells that maintain a lifetime of service
- Beagle dogs at 0.3 rad/day ~ same cancer rate as control dogs
- ICRP standard early 1930s: a tolerance dose of 0.2 r/day or 70 rad/y
- Present-day ICRP recommendations (LNT and ALARA) unjustified

Continuous Co-60 Irradiation of Dogs



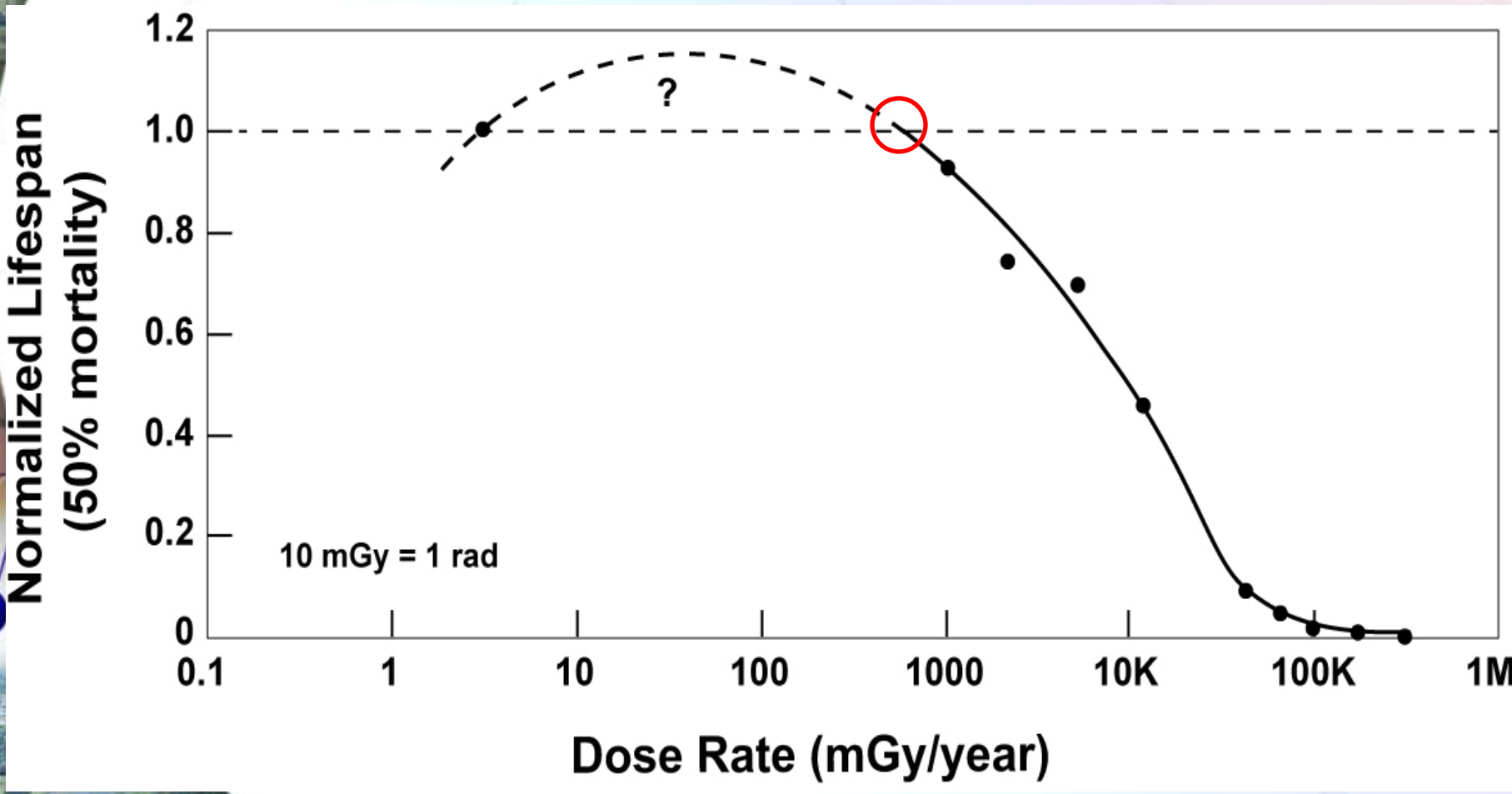
0.3 cGy/d = 1100 mSv/year = 110 rad/year

No significant changes in blood counts

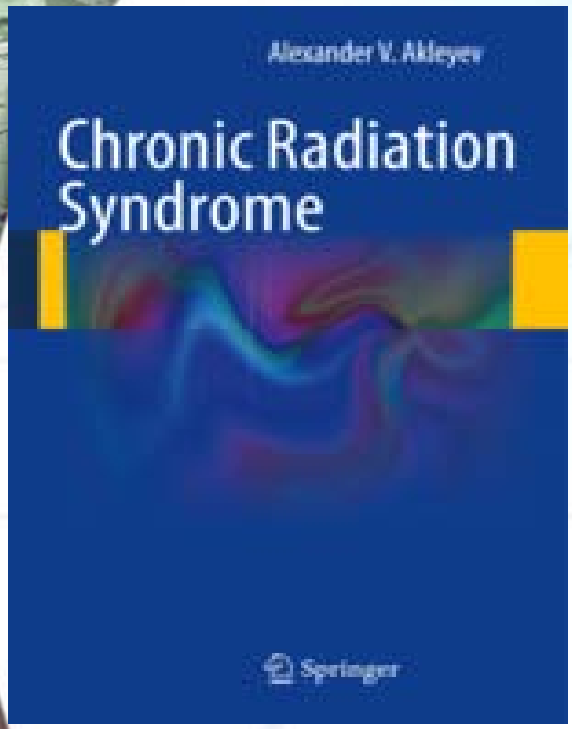
No apparent increase in tumor incidence

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

Lifespan versus Radiation Level



Threshold at ~ 700 mGy per year

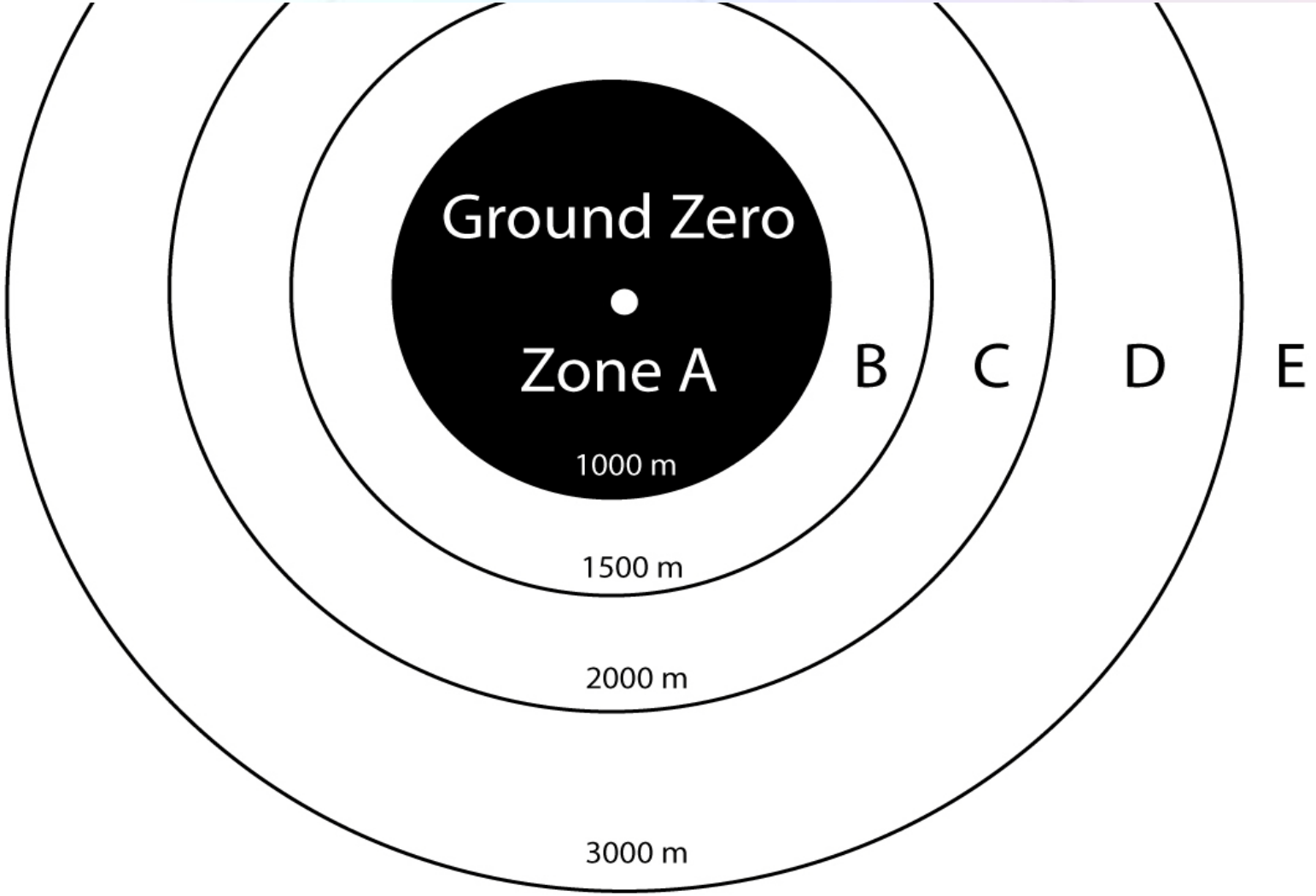


The author describes the chronic radiation syndrome of villagers exposed to radiation from discharges of Mayak nuclear facility into the Techa River in early 1950s. These studies were recognised by United Nations Scientific Committee on Atomic Radiation as an important opportunity for estimating dose-effect relationships for protracted irradiation of humans.

The incidence of mortality from leukemia and cancer estimated for persons with CRS did not exceed those estimated for exposed persons without CRS and Russia as a whole

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

Hiroshima Atomic Bomb Survivor Zones

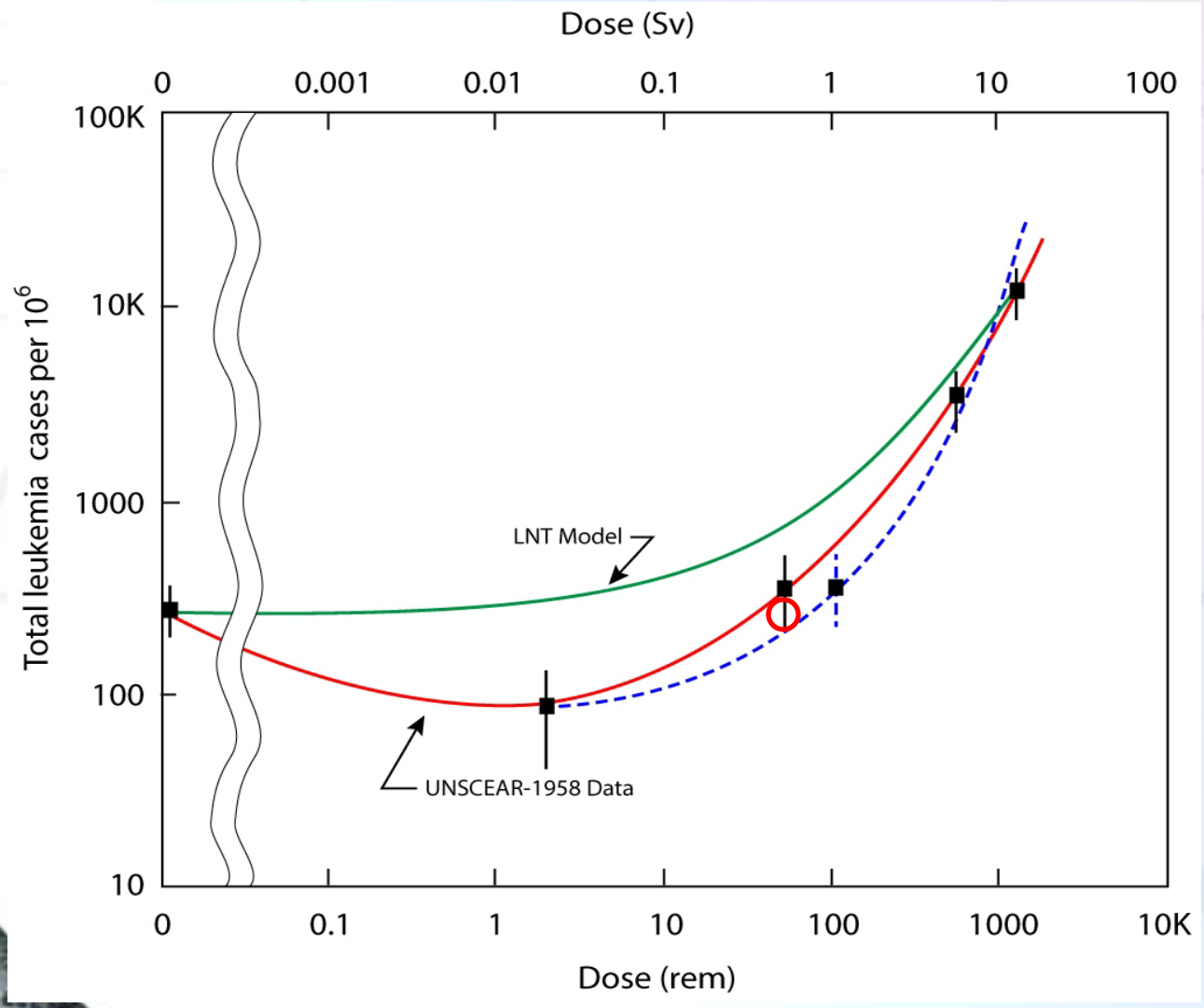


UNSCEAR 1958 Table VII
Leukemia incidence for 1950–57 after exposure at Hiroshima[a]

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 ± 3,143
B	1,000–1,499	500	8,810	33	5.7	3,746 ± 647
C	1,500–1,999	50[c]	20,113	8	2.8	398 ± 139
D	2,000–2,999	2	32,692	3	1.7	92 ± 52
E	over 3,000	0	32,963	9	3.0	273 ± 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 is ~ 50 rem or 500 mSv



***J*-curve, not LNT model**

CARCINOGENESIS FROM INHALED $^{239}PuO_2$ 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 ($^{238}PuO_2$, $^{239}PuO_2$, and $^{239}Pu[NO_3]_4$) 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 $^{239}PuO_2$ dogs compared to controls—with particular focus on the dose-response at relatively low lung doses. A $^{239}PuO_2$ 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 ± 48 Bq (3.5 ± 1.3 nCi), corresponding to 1 Bq g^{-1} lung tissue (0.029 ± 0.001 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) $^{239}PuO_2$, 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 $^{239}PuO_2$. If a threshold for lung cancer incidence exists, it will be observed in the range 15 to 40 cGy.

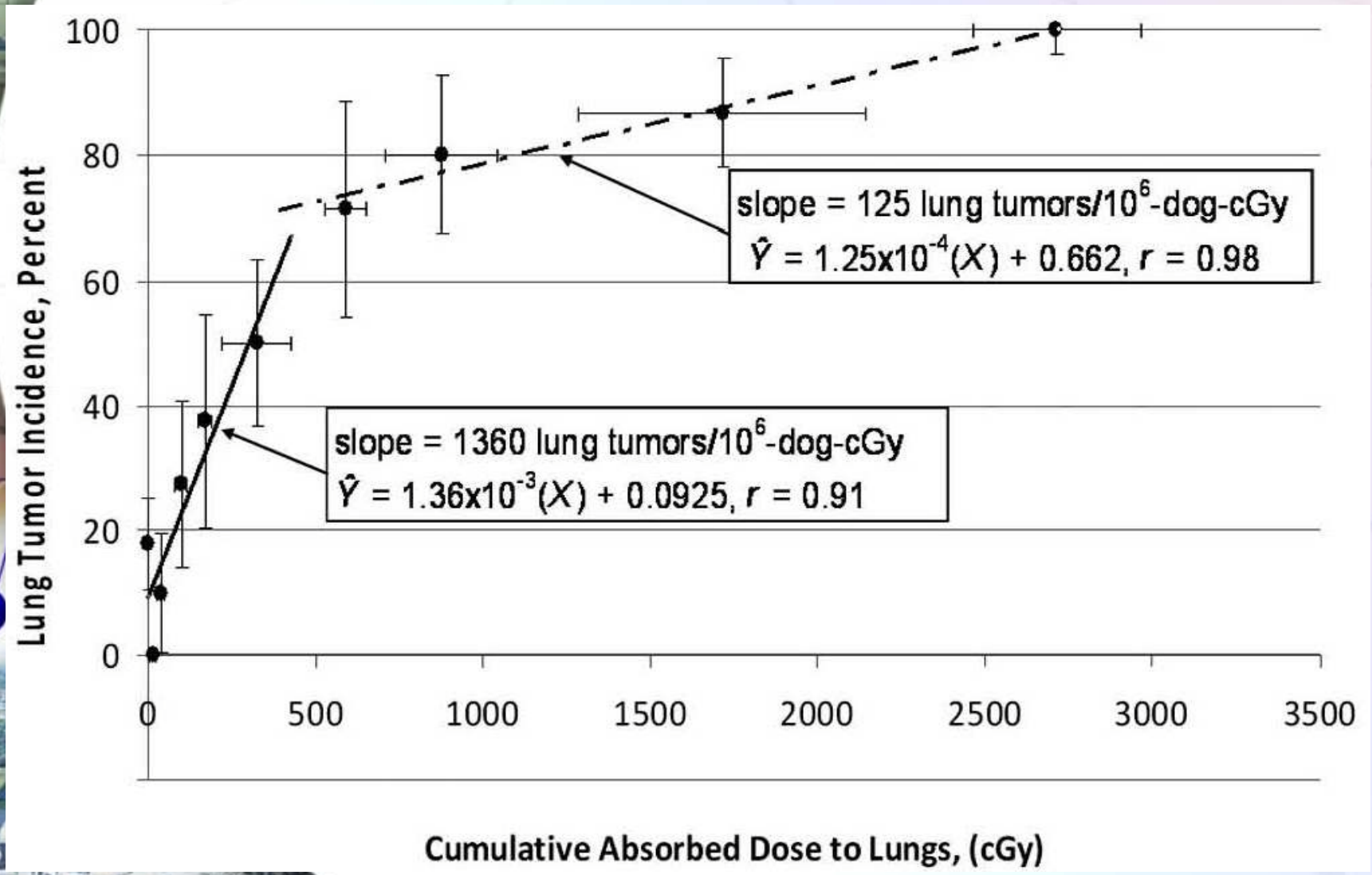
Health Phys. 99(3):357–362; 2010

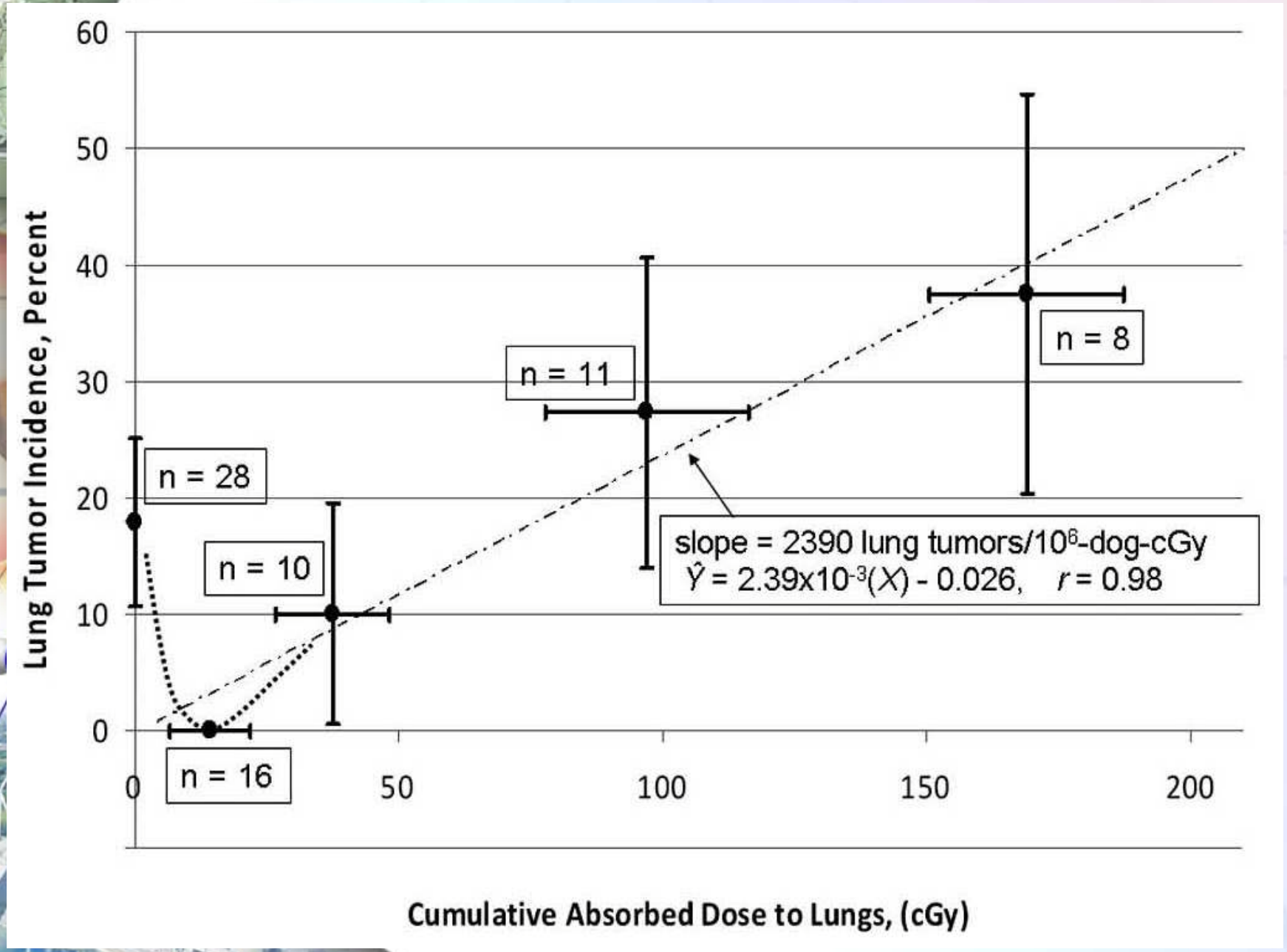
Key words: alpha particles; analysis, risk; dogs; ^{239}Pu

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 (Stannard 1988). Life-span studies in beagle dogs have provided

PuO_2 in Beagle Dog Lungs




Lung Tumor Incidence, Percent
60
50
40
30
20
10
0
0
50
100
150
200
Cumulative Absorbed Dose to Lungs, (cGy)
n = 28
n = 16
n = 10
n = 11
n = 8
slope = 2390 lung tumors/10⁶-dog-cGy
Ŷ = 2.39x10⁻³(X) - 0.026, r = 0.98

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Radiotoxicity of Inhaled $^{239}PuO_2$ 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]

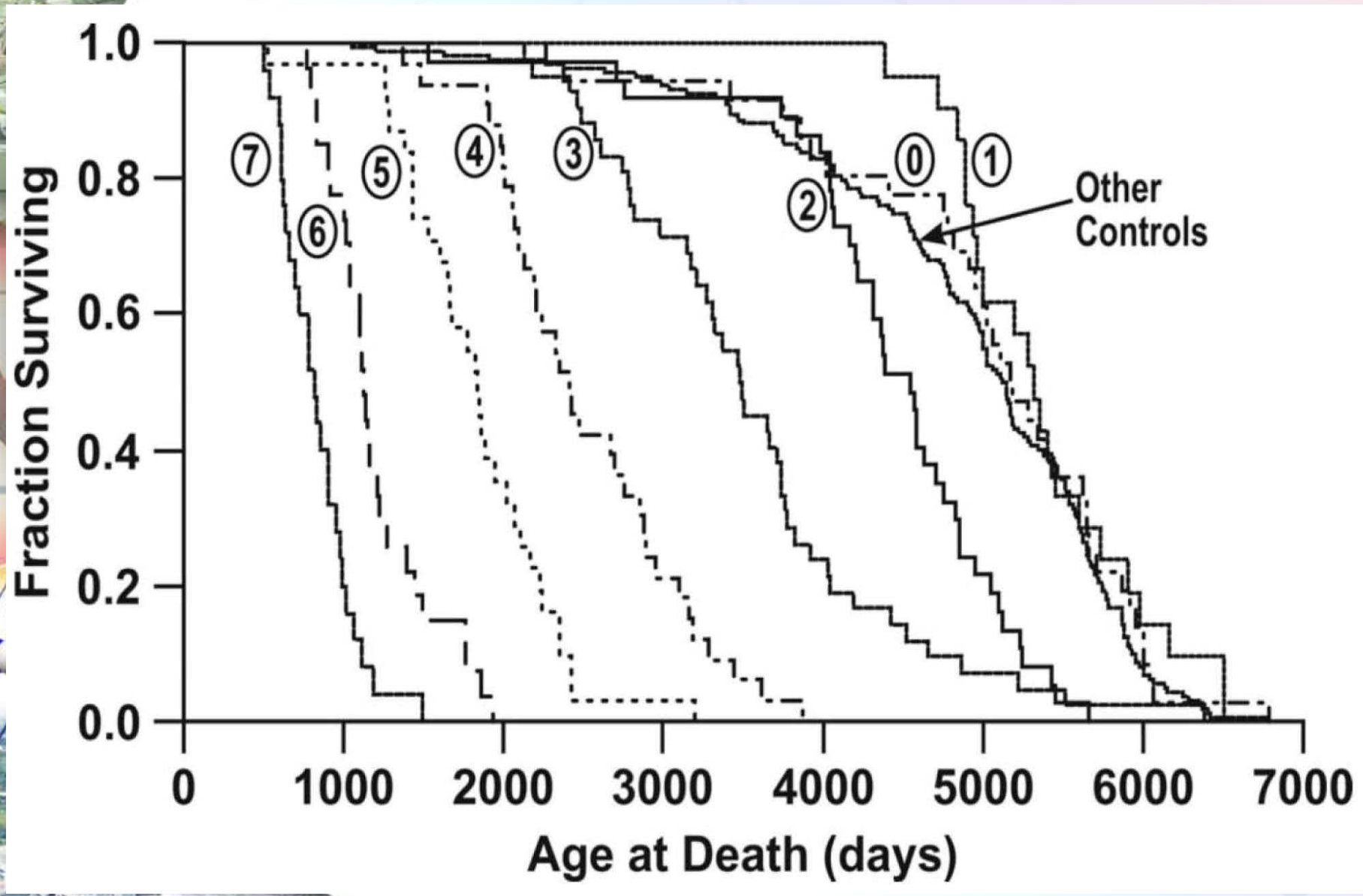
[a] *Lovelace Respiratory Research Institute, Albuquerque, New Mexico 87108; and*[b] *SKS Consulting Services, Siler City, North Carolina 27344*

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 $^{239}PuO_2$ in Dogs. *Radiat. Res.* 170, 736–757 (2008).

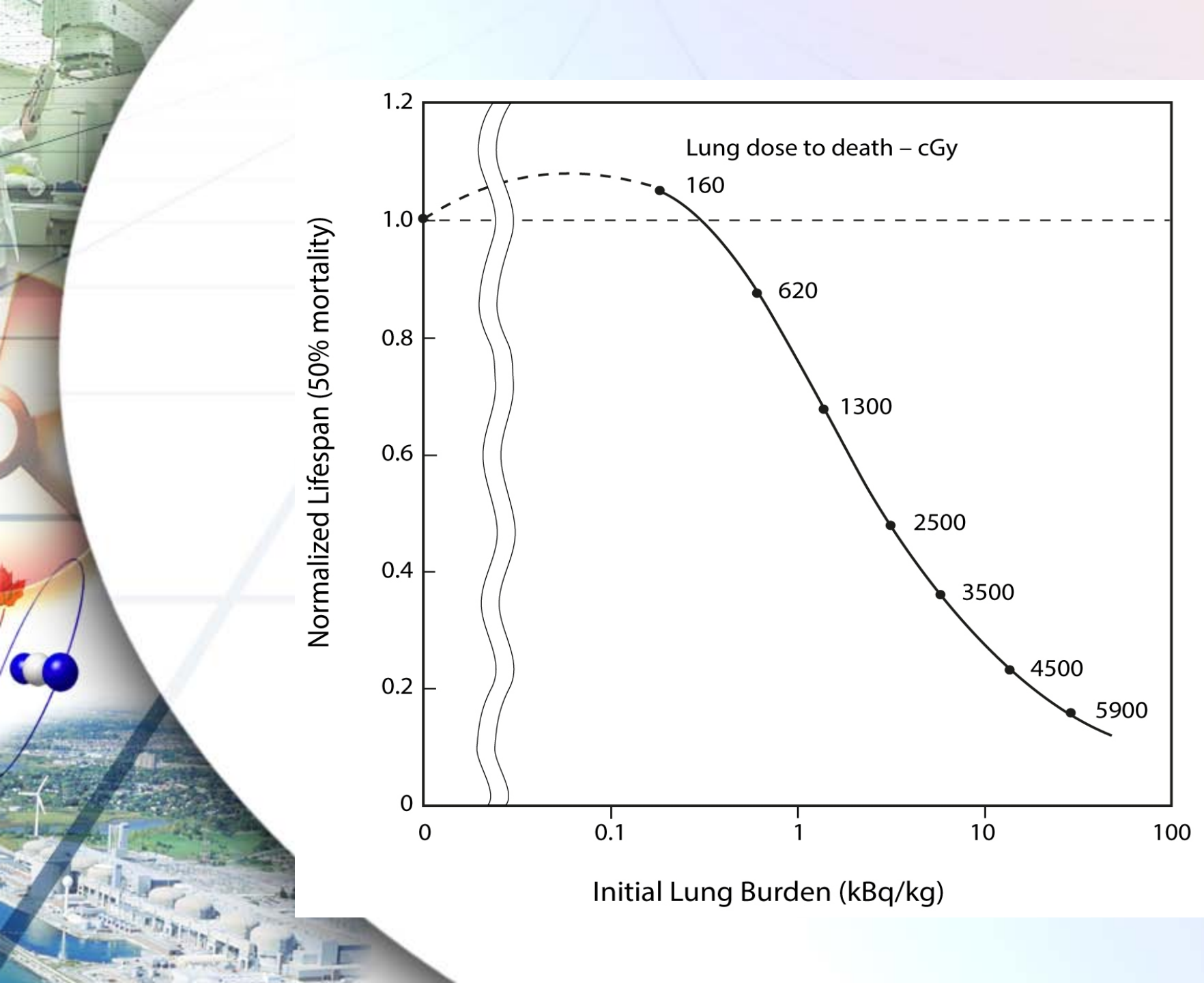
Beagle dogs inhaled graded exposure levels of insoluble plutonium dioxide ($^{239}PuO_2$) aerosols in one of three monodisperse particle sizes at the Lovelace Respiratory Research Institute (LRRI) to study the life-span health effects of different degrees of α-particle dose non-uniformity in the lung. 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

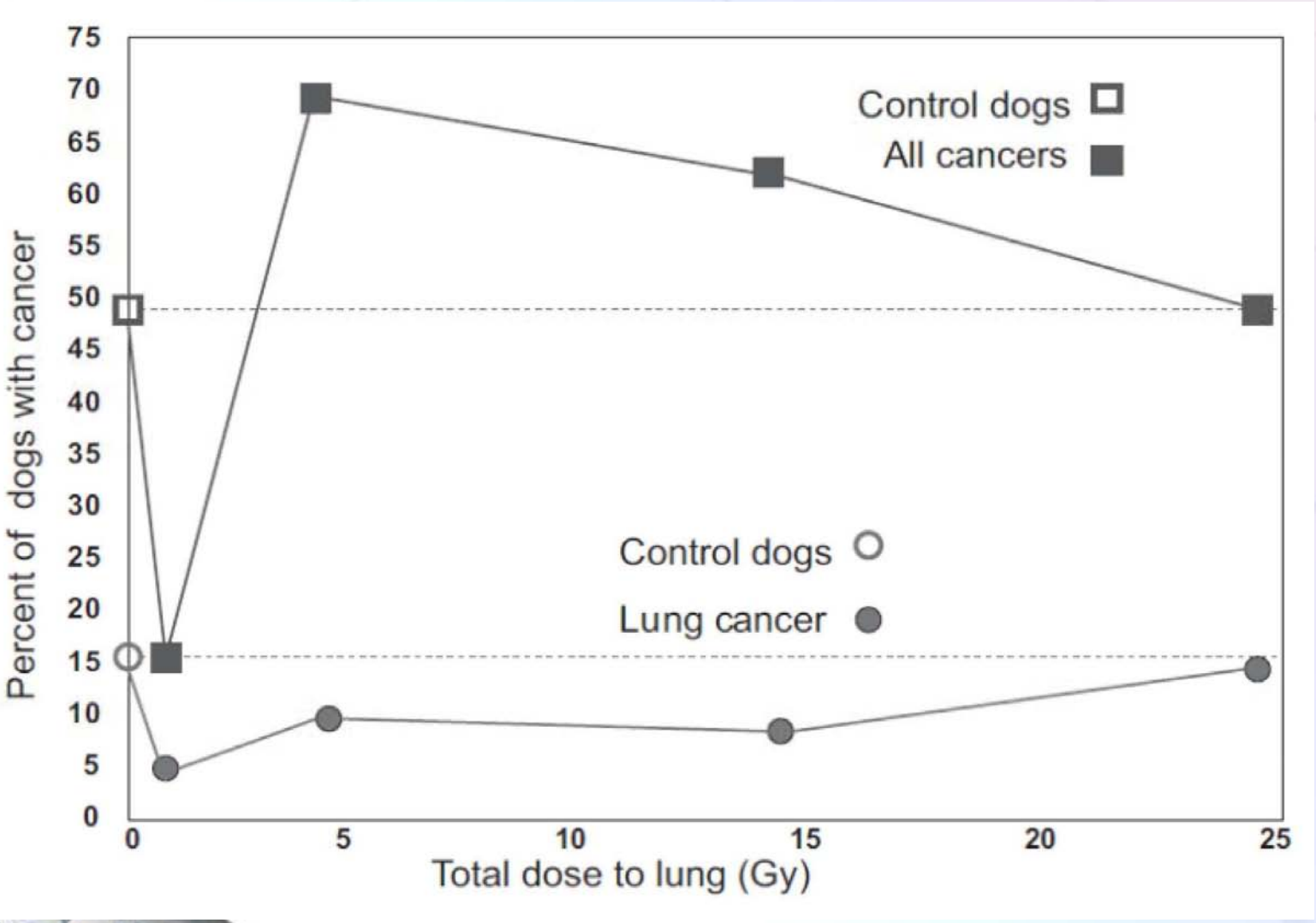

1.0
0.8
0.6
0.4
0.2
0.0
Fraction Surviving
0
1000
2000
3000
4000
5000
6000
7000
Age at Death (days)
⑦
⑥
⑤
④
③
②
⓪
①
Other
Controls

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


Lung dose to death – cGy
160
620
1300
2500
3500
4500
5900
Normalized Lifespan (50% mortality)
Initial Lung Burden (kBq/kg)
1.2
1.0
0.8
0.6
0.4
0.2
0
0
0.1
1
10
100

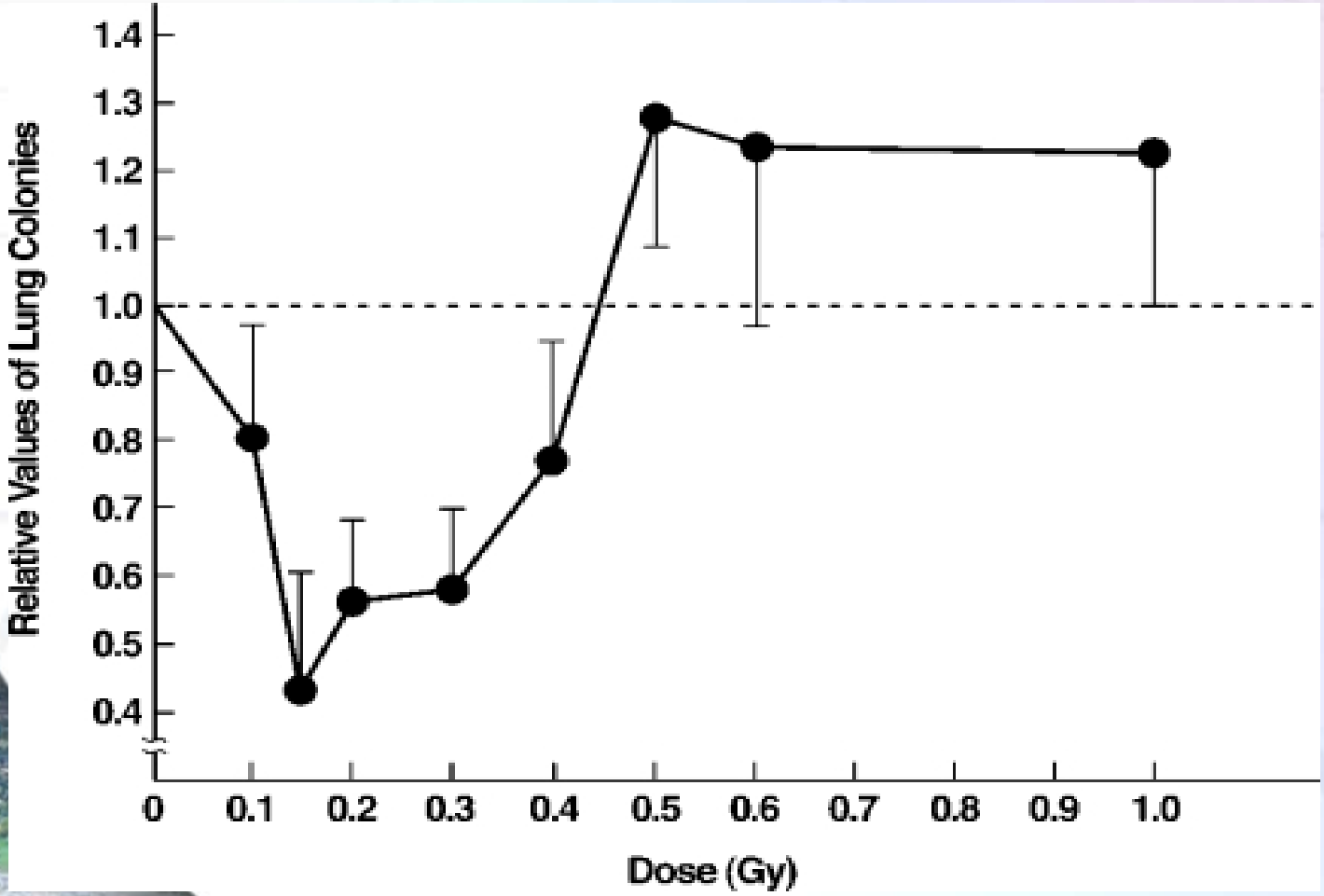
Brooks-2009_Summary of cancer frequency

for inhaled beta-gamma emitting ^{90}Sr, ^{144}Ce, ^{91}Y and ^{90}Y

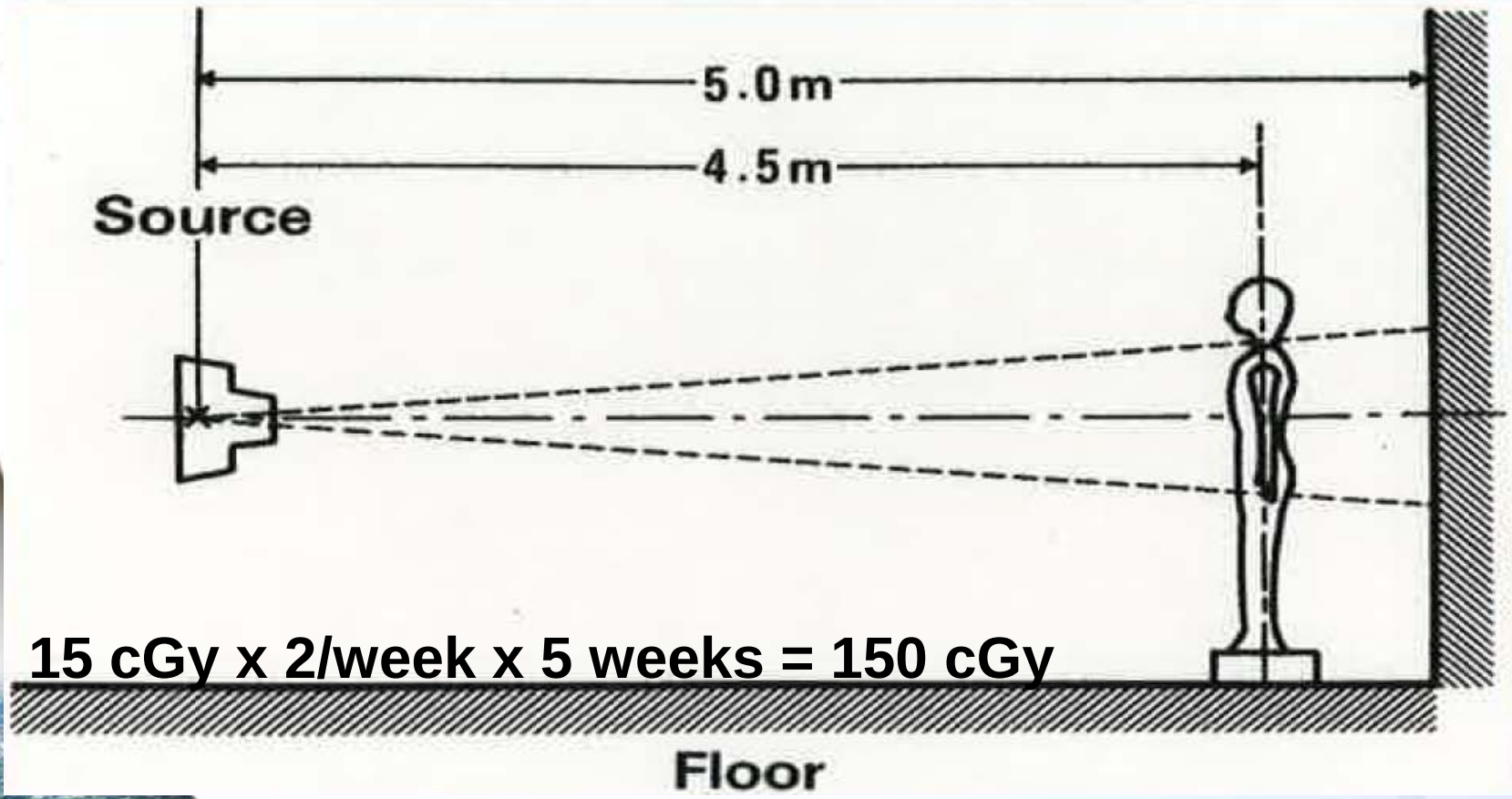


Results of one of Sakamoto's studies:

Spontaneous Lung Metastasis vs. TB Dose

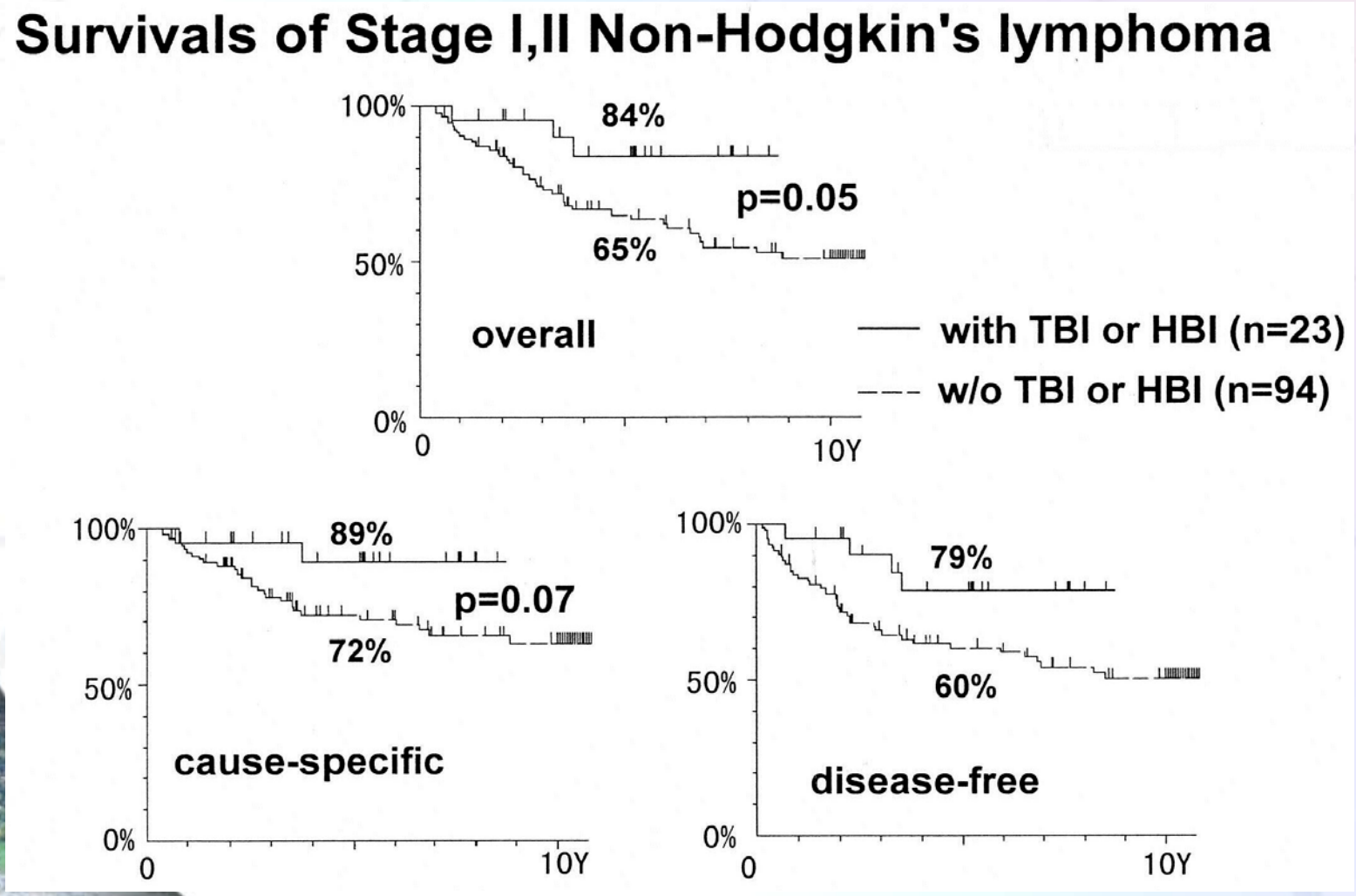


Source – Patient Schema for HB LDR

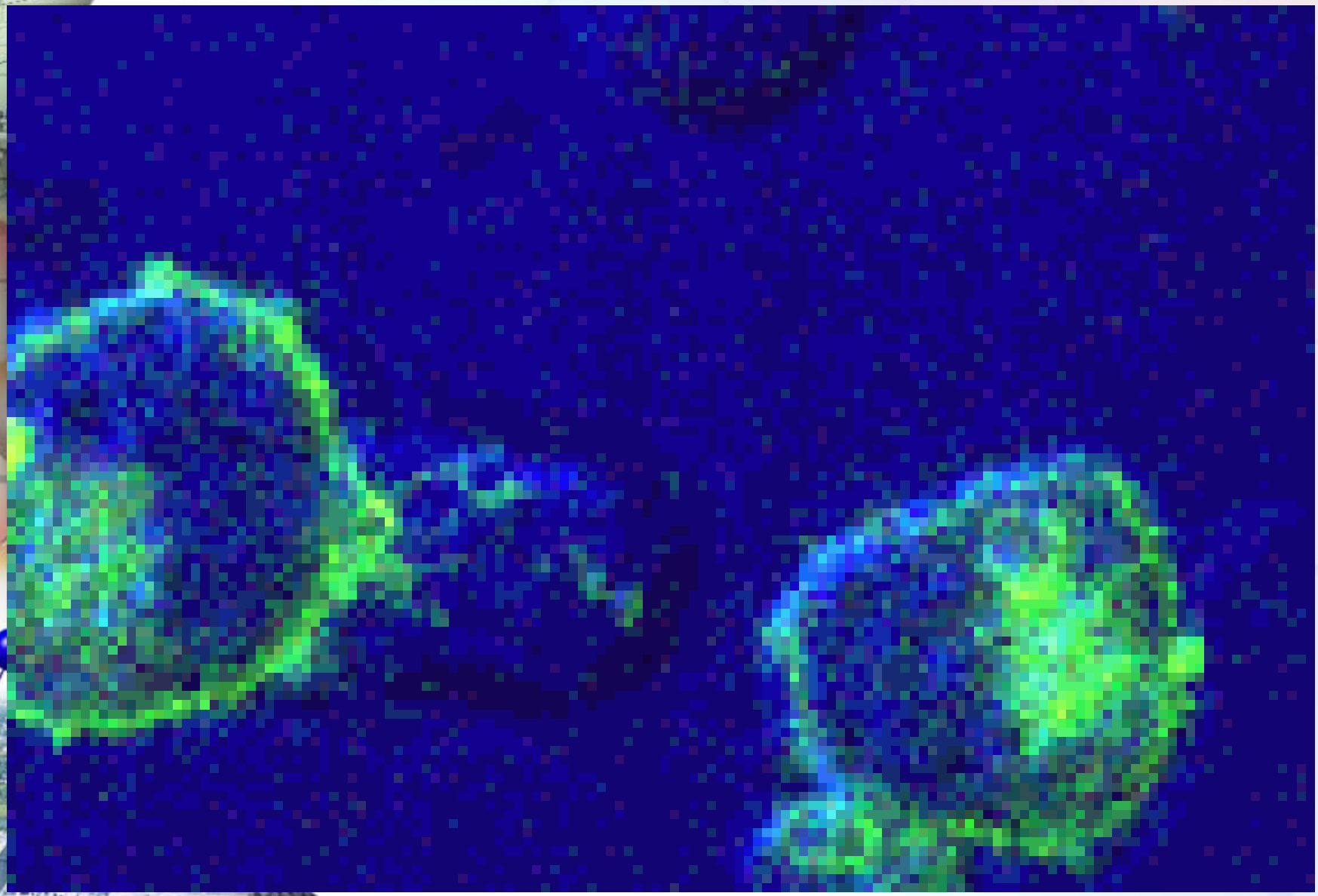


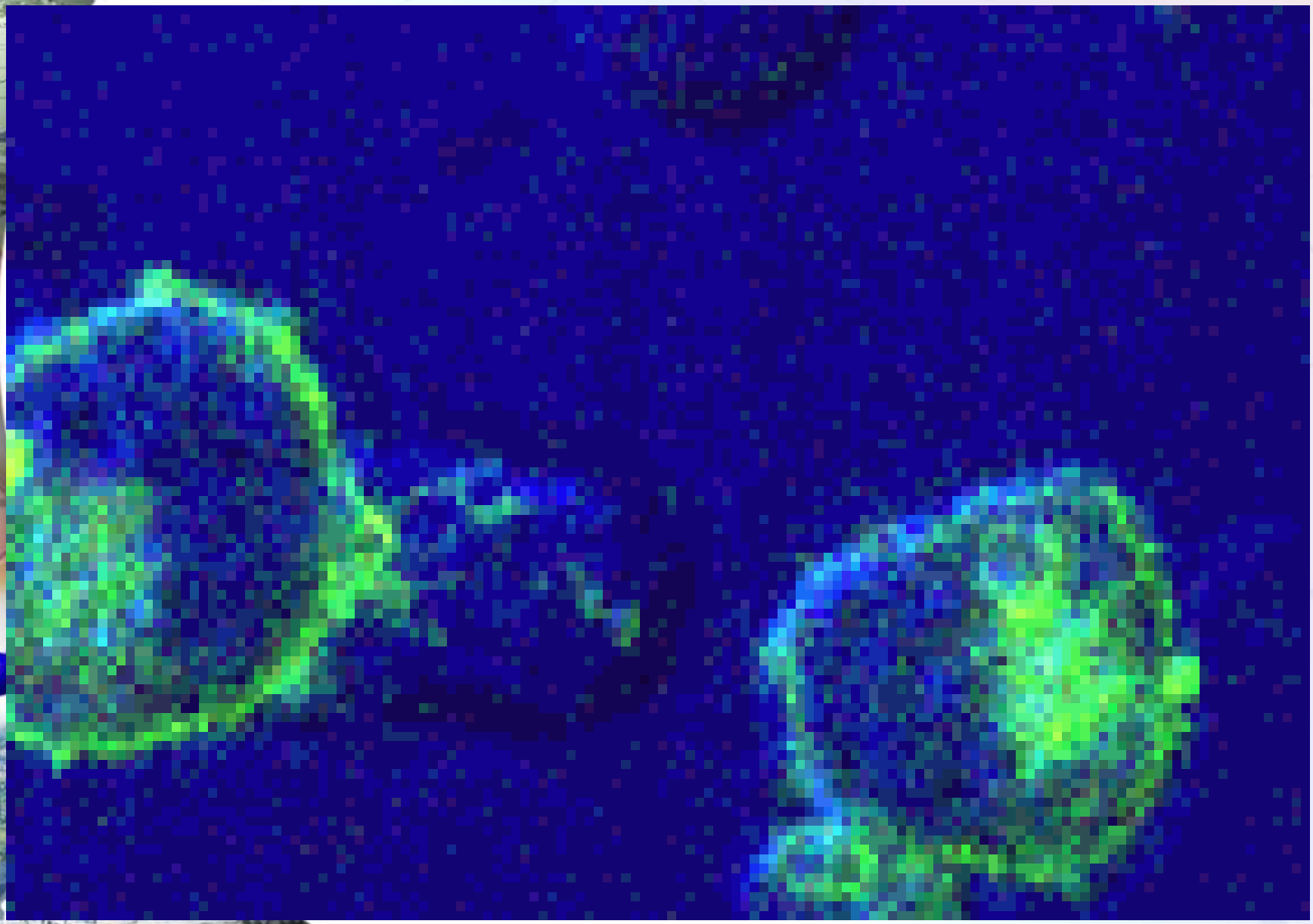
“Observed the total removal of tumors in all regions of the body of a patient with advanced ovarian cancer.”

HBI or TBI for Non-Hodgkin's Lymphoma



Shu-Zheng Liu and Jerry Cuttler at CVH



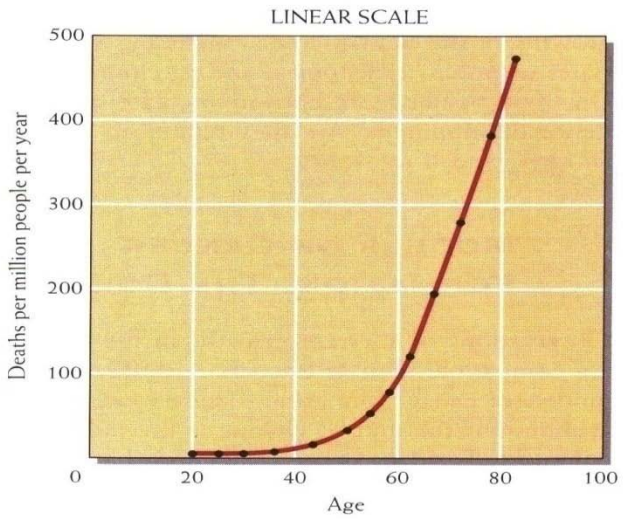


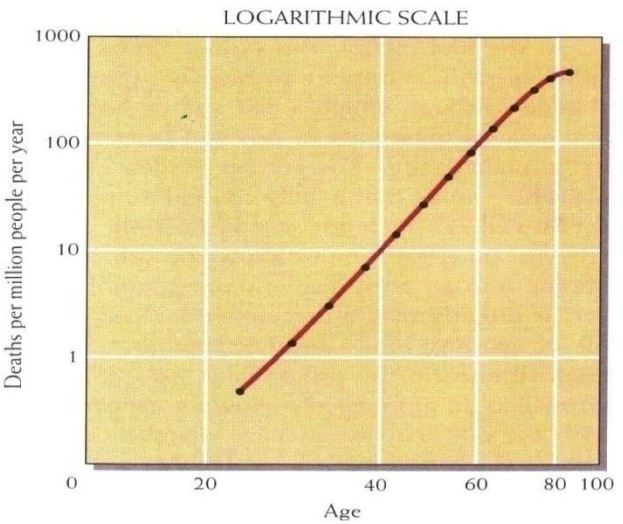
LDR Therapy for Hurthle Cell Carcinoma

HB-LDI Therapy 1500 mGy; 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?

<u>Spontaneous</u> DNA damage? (free radicals, reactive oxygen species, thermal effects)

Other causes …

Protection systems age; immune system becomes weaker

Low radiation doses stimulate protection

Mortality of 1338 British Radiologists 1897-1976

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	0.95	411	541.77	0.76***
		(2) 308.03	1.04		461.14	0.89*
		(3) 327.97	0.97		469.97	0.87**
All neoplasms	62	(1) 49.11	1.26*	72	114.93	0.63***
		(2) 43.07	1.44**		91.07	0.79*
		(3) 35.39	1.75***		68.65	1.05
Other causes	257†	(1) 285.31	0.90*	339†	426.84	0.79***
		(2) 264.96	0.97		370.07	0.92
		(3) 292.58	0.88*		401.32	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.

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

Therapeutic Nuclear Medicine
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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

Contents

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 very high compared with radiation-induced rate:
  - Endogenous DNA single-strand breaks > 10^6 SSBs due to bkgnd radiation
  - Endogenous DNA double-strand breaks > 10^3 DSBs from bkgnd radiation
- Low-dose radiation up-regulates adaptive protection systems
- Static defences act immediately to remove toxins, repair molecules (DNA), remove/replace damaged cells and tissue
- Followed by dynamic defence of up-regulated adaptive systems that may last more than a year and protect against renewed toxic impacts from radiation and non-radiation, endogenous sources
- Adaptive protections have a maximum after 150 mGy acute dose
  - Chronic or repetitive radiation initiates protection at lower level
  - Adaptive protections reduce risks = less cancer, life extension

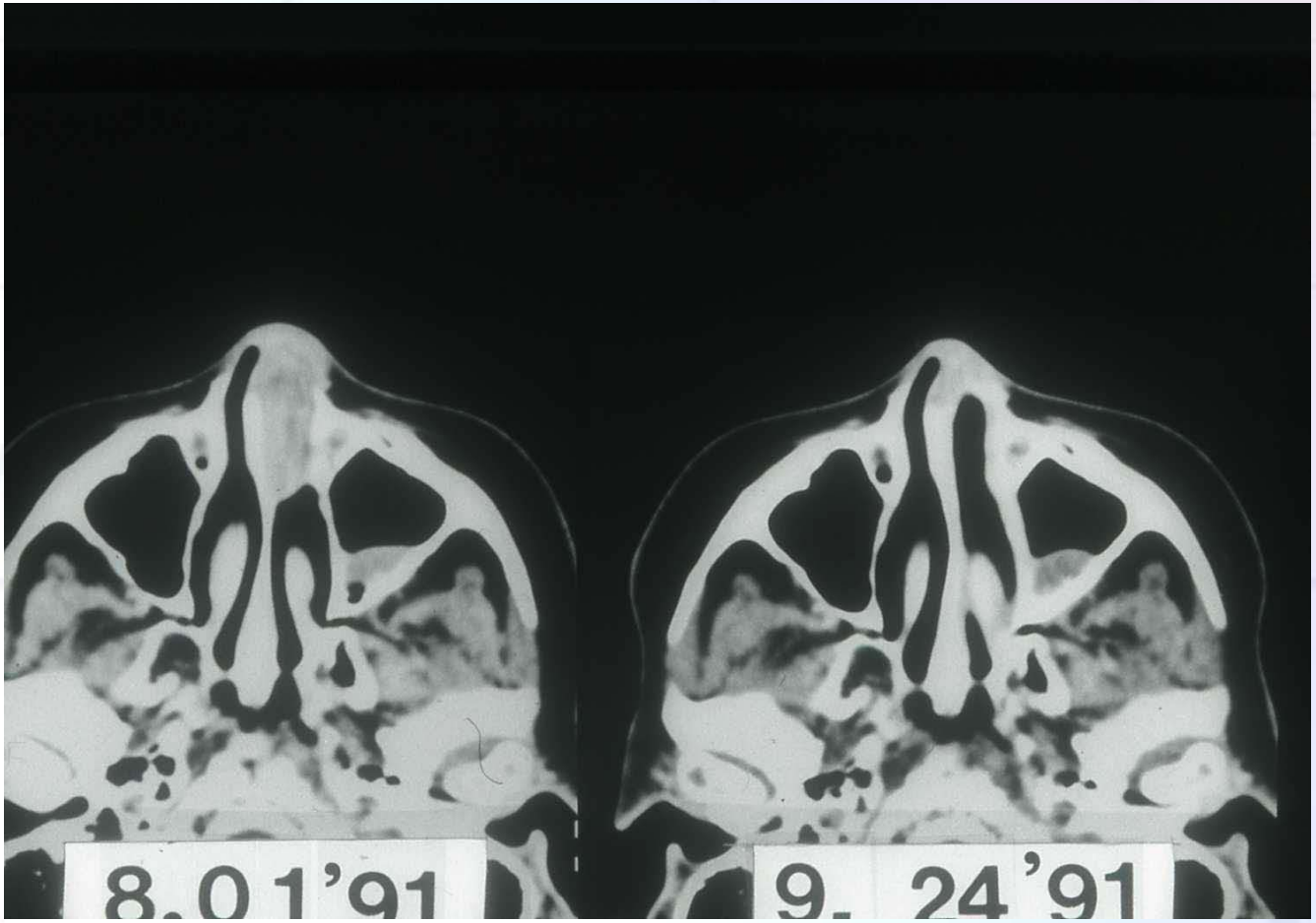
Beneficial Effects of Low Radiation

Medical practitioners used radiation for decades to up-regulate adaptive protection systems:

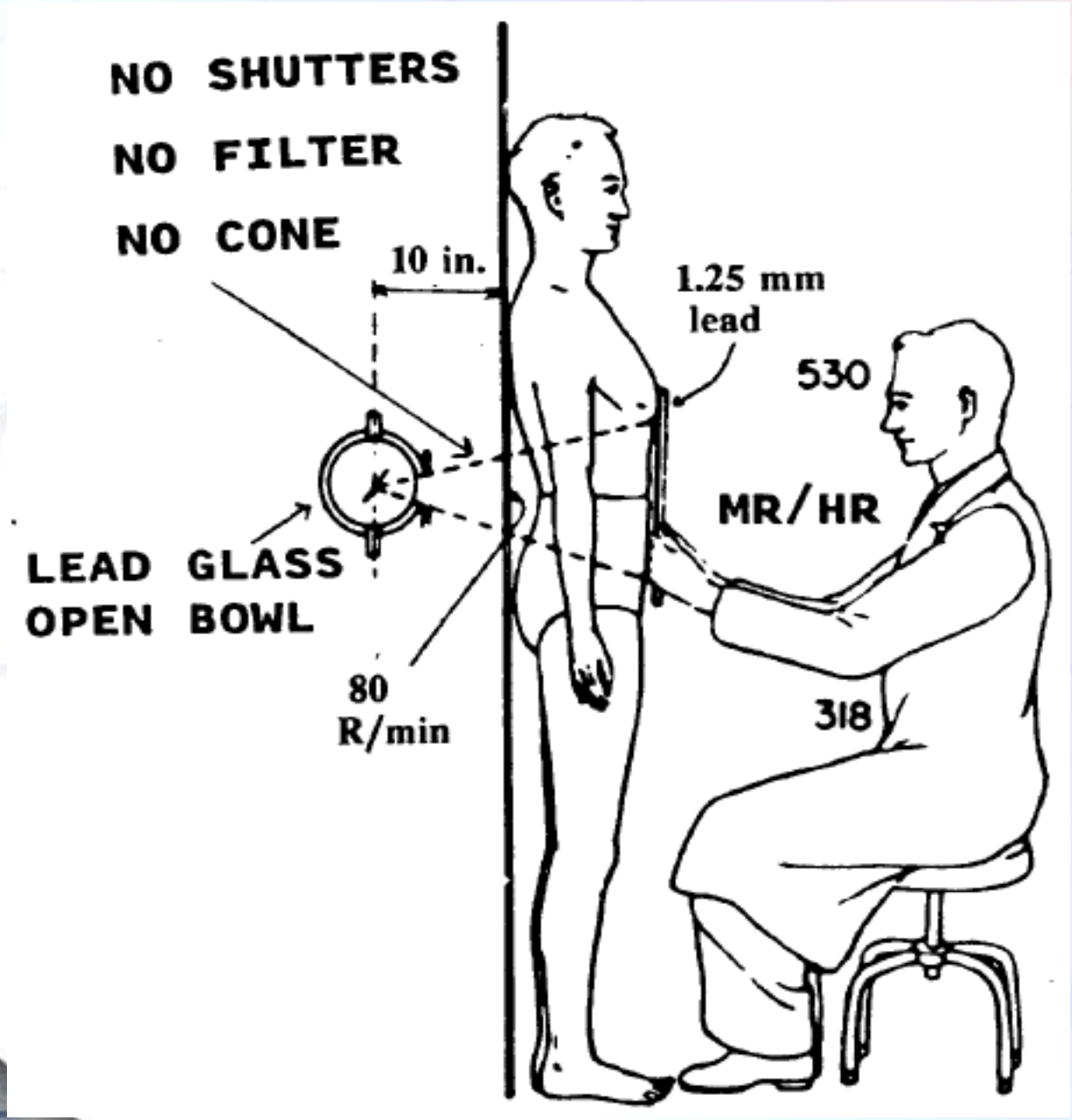
- Eliminate metastases or slow cancer growth
- Accelerate healing of wounds
- Stop infections: gas gangrene, carbuncles and furuncles (boils), sinus, inner ear, etc.
- Treat arthritis, other inflammatory conditions
- Treat swollen lymph glands
- Cure pneumonia, and

no apparent increases of cancer incidence

Abscopal Effect



Fluoroscopy, circa 1930



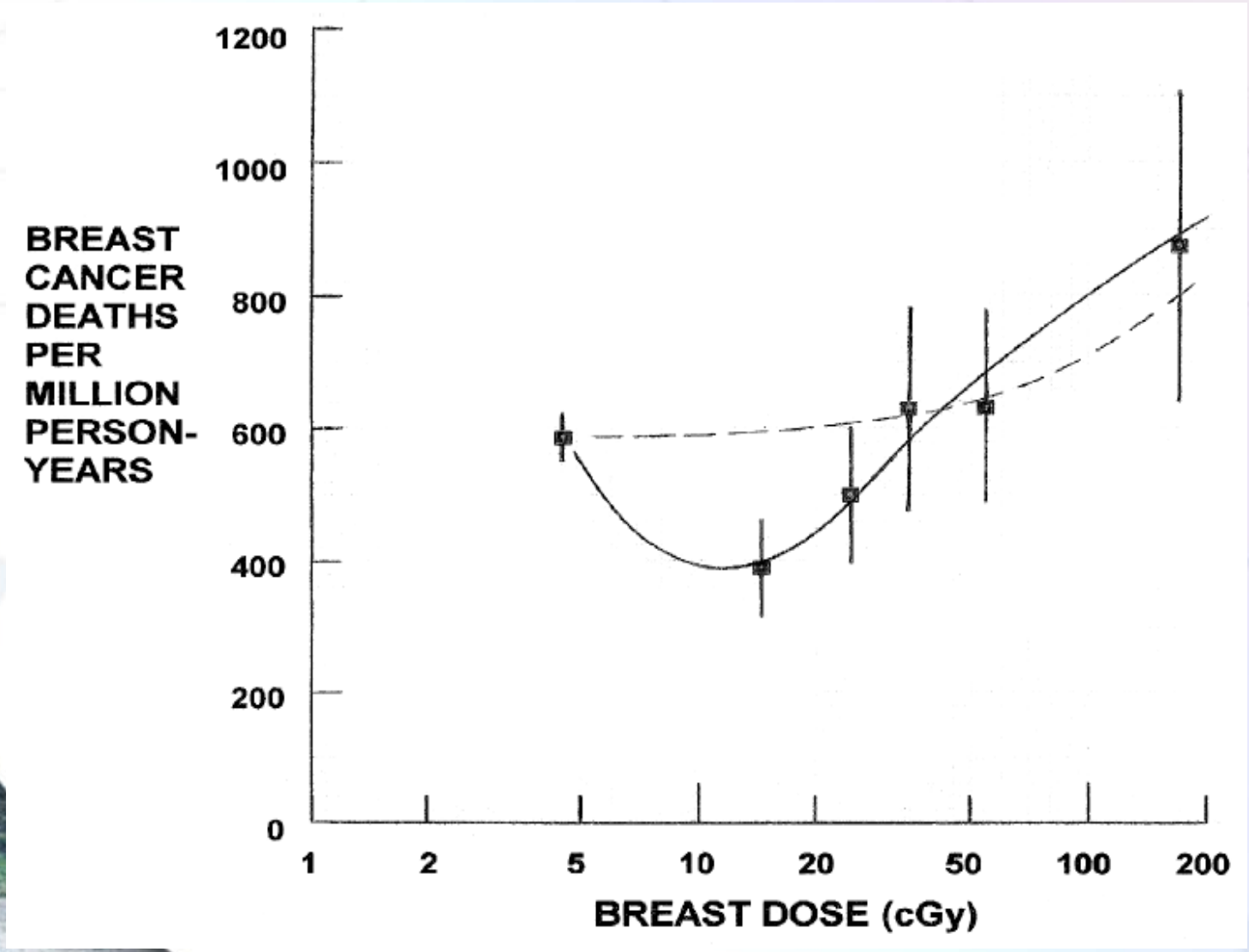
Canadian Breast Cancer Study

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	1709 (11)	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)

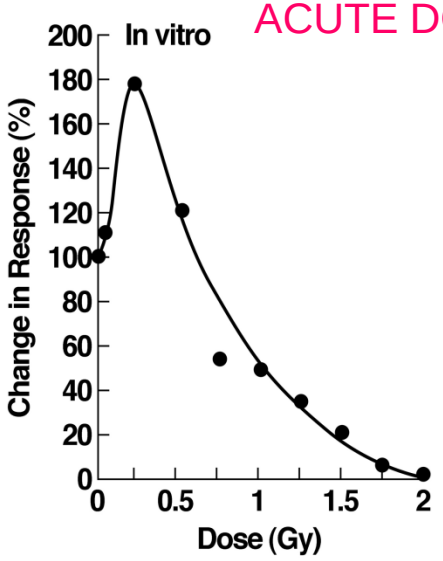
*The number of deaths is shown in parentheses. The calculations exclude the values for 10 years after the first exposure and have been standardized according to age at first exposure (10 to 14, 15 to 24, 25 to 34, and ≥35 years) and time since first exposure (10 to 14, 15 to 24, 25 to 34, and ≥35 years)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

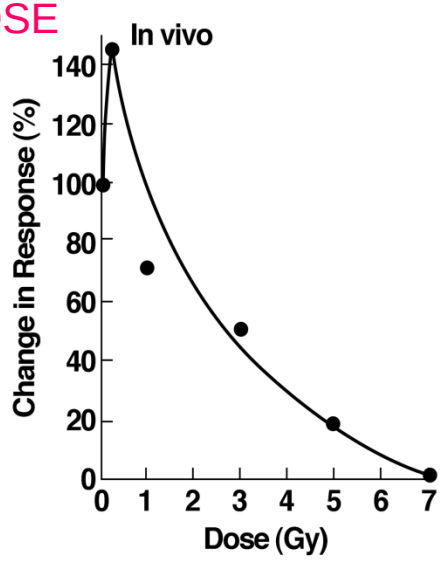
Fluoroscopy of TB Patients



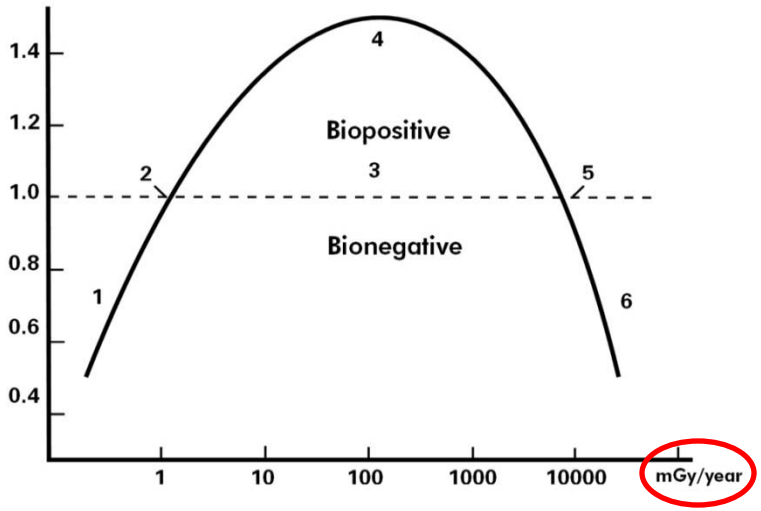
Radiation Hormesis

ACUTE DOSE





CONTINUOUS DOSE



Organisms are stressed: physical, chemical, biological, radiation

Organisms adapt to stress

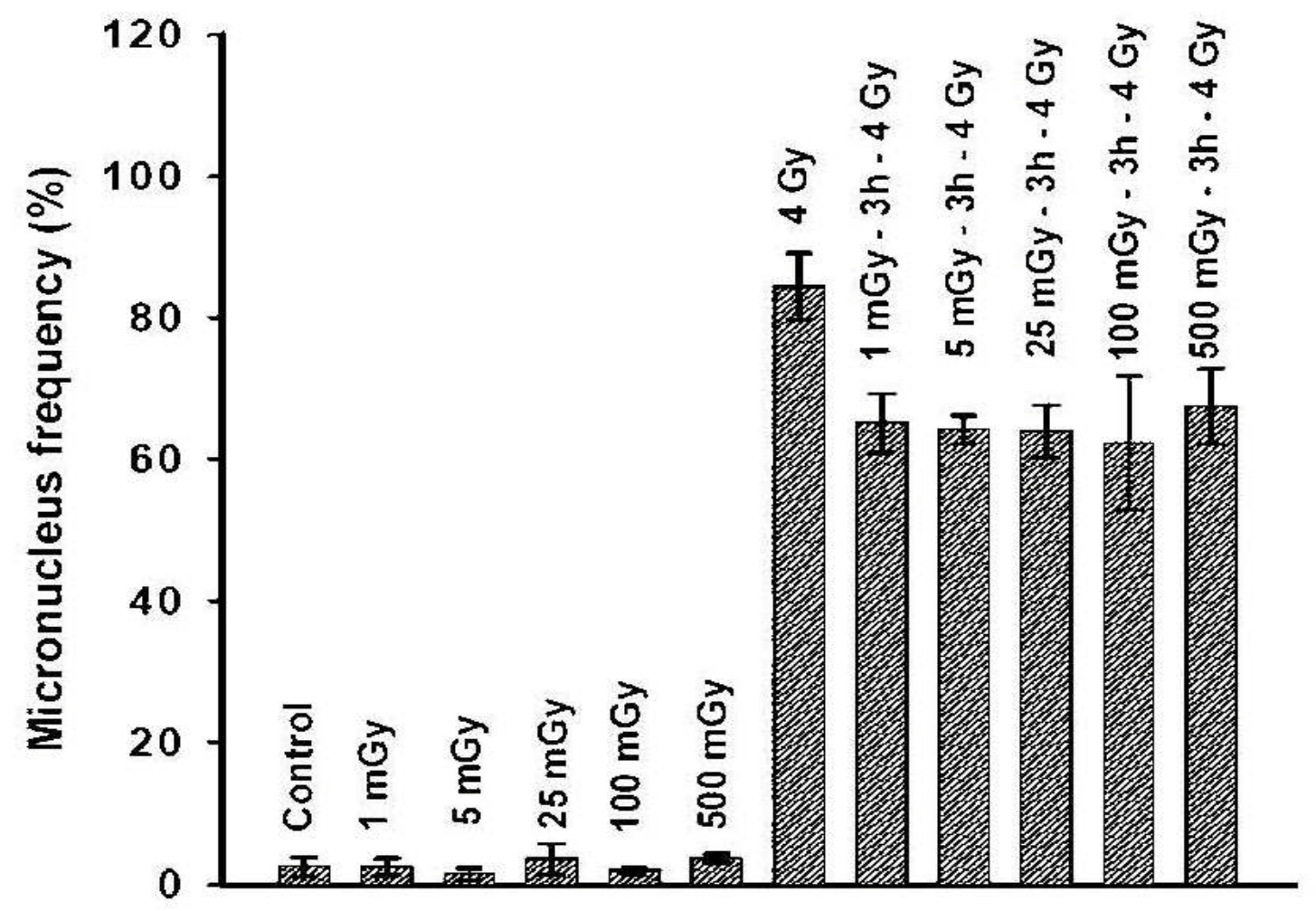
Radiation modulates organism's defenses

Low radiation dose/dose-rate reduces cancer incidence because it stimulates:

- prevention of DNA damage
- repair of DNA damage
- removal of damaged cells and removal of cancer cells

High radiation dose/level has opposite effects

Low radiation dose up-regulates cell repair



4133 Identified Radium Dial Painters in USA

Bone cancer threshold at 10 Gy or 1000 rad of radium alpha radiation

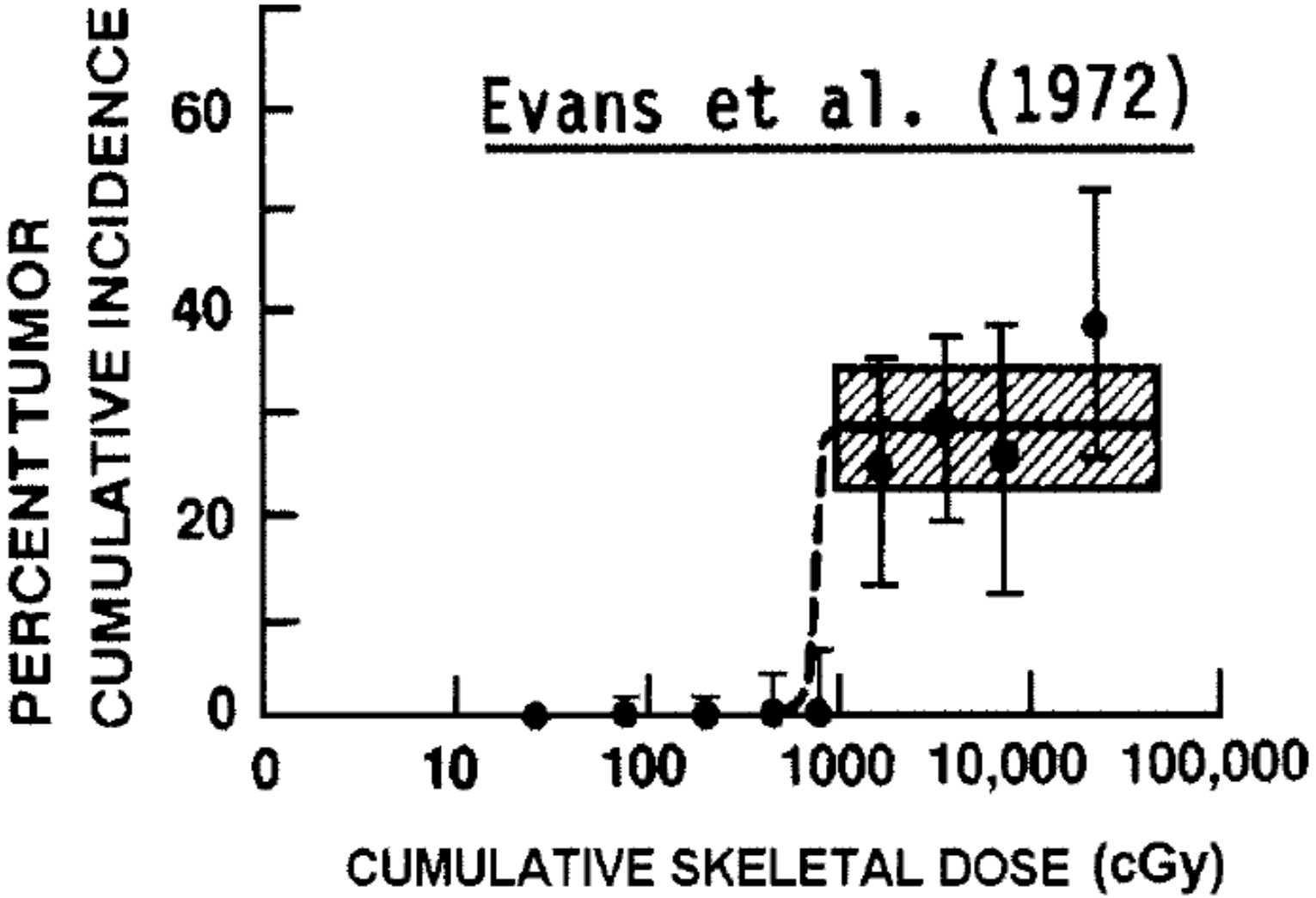
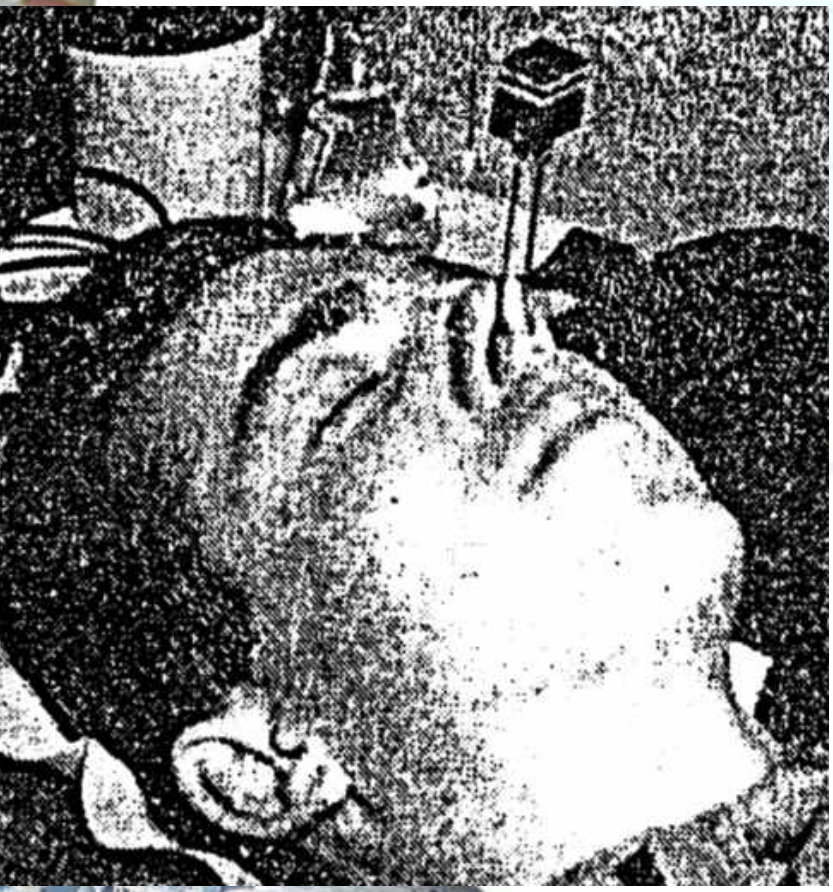


Fig. 11. Cumulative bone sarcoma incidence in people exposed to ^{226}Ra as a function of cumulative dose to the skeleton as reported by Evans et al. (1972).

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)

http://www.cancer.gov/cancertopics/factsheet/Risk/nasopharyngeal-radium

National Cancer Institute
at the National Institutes of Health

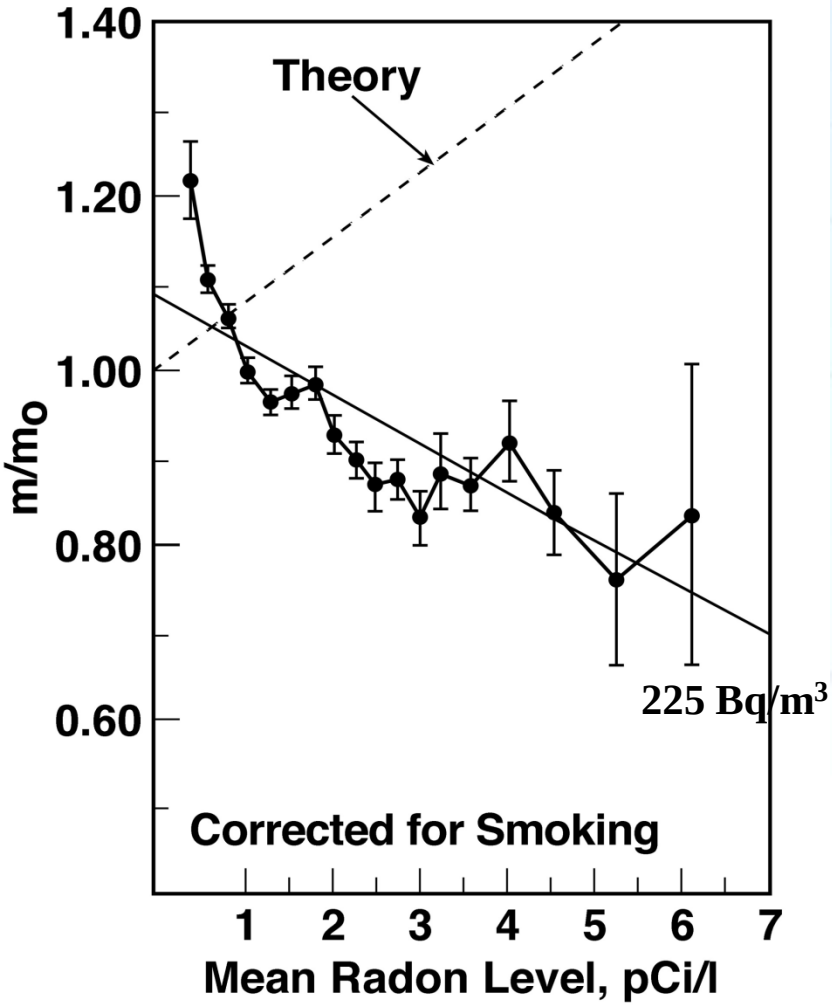
Reviewed: January 10, 2003

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.

Radon Exposure Study Disproves the LNT Hypothesis



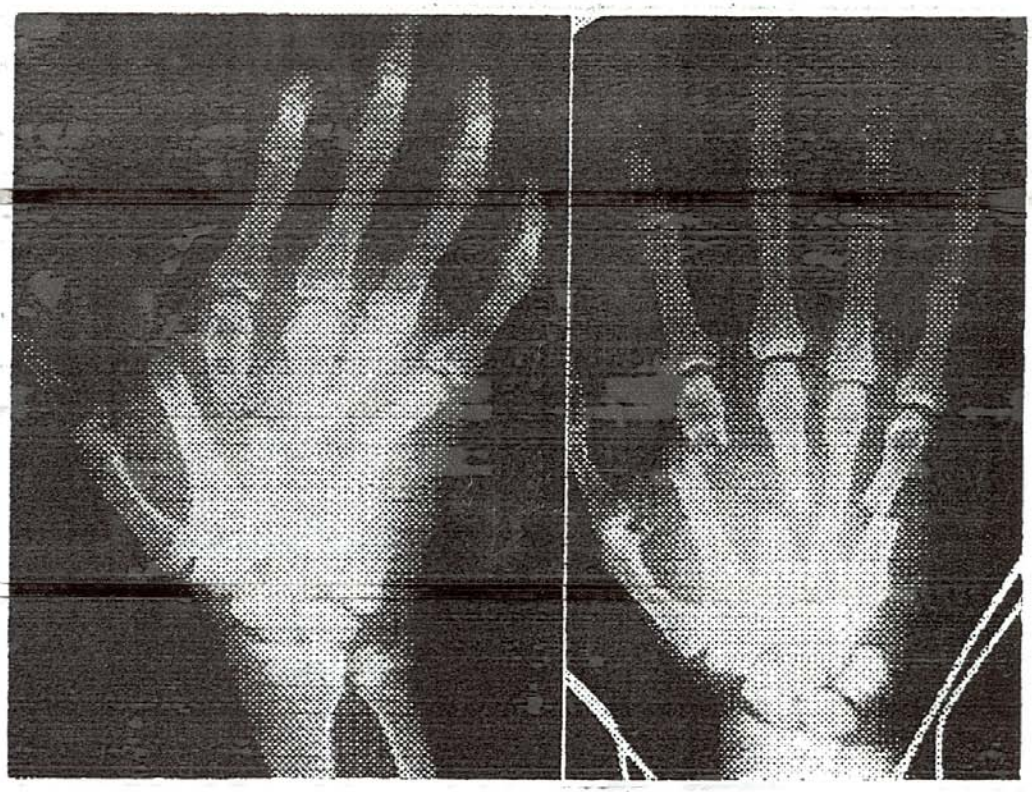
Greatest natural radiation exposure is radon gas from uranium activity

Cohen tested the LNT model, as used, and clearly disproved it; lung cancer mortality *lower* where radon *higher*

Lung cancer *higher* where radon is *lower* than the average of 1.7 pCi/L

Instead of discarding LNT assumption, objection raised (ecological study). This is not relevant to testing model

Authorities still accept LNT assumption



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

Henry Kaplan was the first one to use a linear accelerator at Stanford Hospital in San Francisco in 1957. The patient was a boy (Gordon Isaacs) that was suffering from a tumor in his eye (retinoblastoma). The treatment saved the child's sight and he lived the rest of his life with his vision intact.

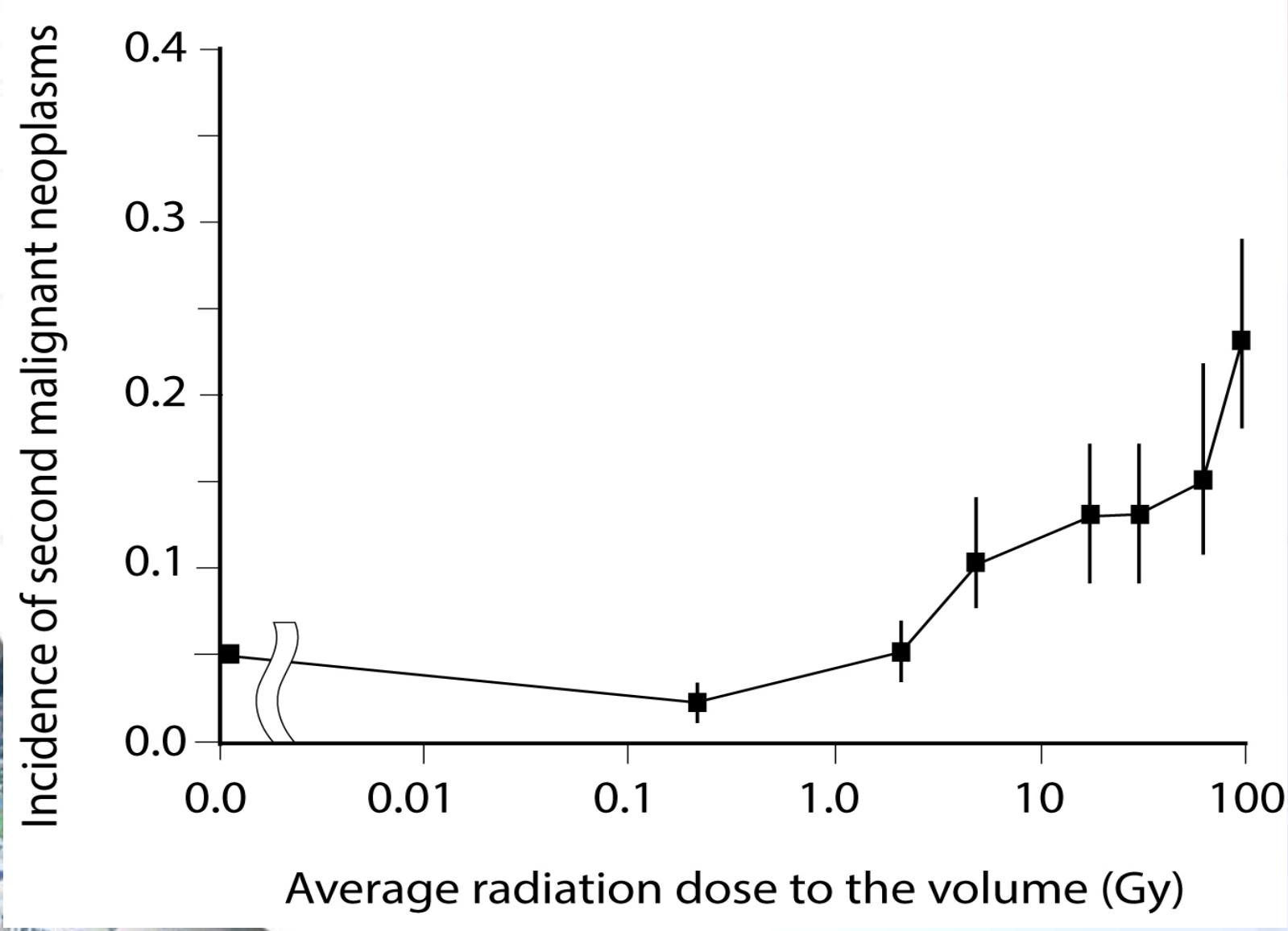
Below is a picture taken during the treatment.

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

Irradiated Group

Control Group

Tubiana: 5000 survivors of childhood cancer



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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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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.

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-

Calabrese on NAS BEAR failing to assess LNT prior to recommending its use by US regulators

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 support

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-

Is low radiation a cancer risk? No!

- Spontaneous (natural) DNA damage[1] occurs at very high rate > 1000 x background radiation DNA damage[1] rate
- Organisms have very powerful protection systems against all cell and tissue damage (internal and external)
- Low radiation up-regulates protections → less cancer
- High radiation impairs protection → more damage, harm

---

[1] double-strand breaks

Repeat these points over and over and over again

Conclusions

- Social concern about nuclear safety caused by ideological link of human-made radiation to a risk of cancer, via LNT
- Radiation scare in 1950s to stop atomic-bombs continues
- Radiation protection ignoring evidence of beneficial effects
- Threshold model for radiation protection will bring social acceptance of nuclear energy and radiation diagnostics.
- British radiologist study (1897-1954) showed “tolerance dose” of 0.2 roentgen/day or 700 mGy/year is effective and more than adequate for radiation protection

Human Data

Threshold for Acute Radiation Exposure

- UNSCEAR 1958, Table VII shows a dose threshold at 500 mSv (50 rem) for leukemia incidence in study of 96,000 Hiroshima atomic bomb survivors

Threshold for Chronic Radiation Exposure

- 1981 Study of British Radiologists (1897 - 1954)
- Tolerance dose of 0.2 roentgen/day ≈ 700 mGy/year
- Lauriston Taylor speech at 1980 IRPA Congress: "No one has been identifiably injured by radiation while working within the first numerical standards set by the NCRP and the ICRP in 1934."

Recommendations

- Scientific societies should organize events to discuss radiation health benefits and risks
- Urge regulatory bodies and health organizations to use Scientific Method instead of LNT “target theory”
- Change to a dose-response concept based on data
- Stop calculating nuclear safety cancer risk with LNT
- Develop public communication programs
- Learn 3 lessons from Chernobyl and Fukushima:
  - Severe accidents result in low radiation dose levels
  - Long-term evacuations are not appropriate when risk low
  - Precautionary actions cause severe stress and early deaths

Raise radiation level threshold for evacuation from 20 to 700 mSv/year (2 to 70 rem/year)

What do you do when an entire industry has no political constituency?

- Nuclear energy has no constituency, and that is very dangerous in a democracy
- Public fear of nuclear radiation has to be eliminated or nuclear will be phased out
- The authorities will have to communicate factual information about the health effects of nuclear radiation