REVISION OF RADIATION BIOLOGY
IMPORTANCE OF DOSE-RATE

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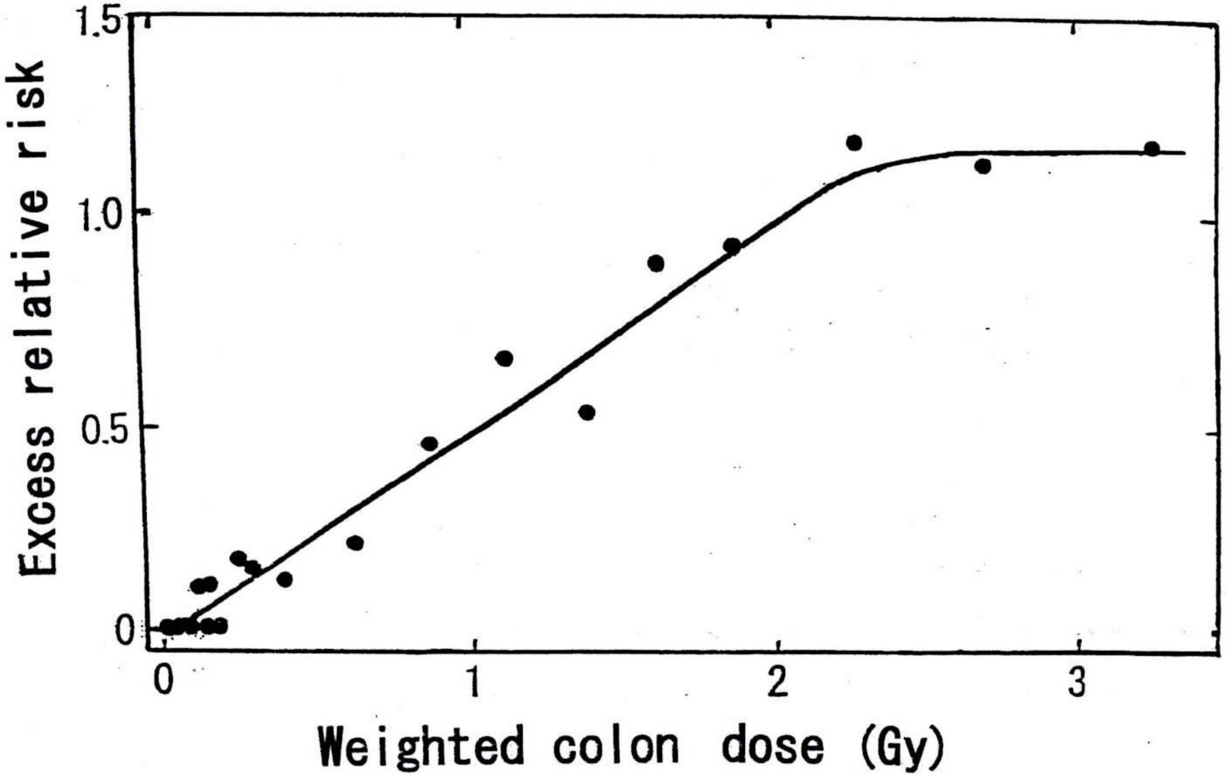
STOCHASTIC EFFECT (Tumorigenesis)



LSS solid cancer incidence , excess relative risk by radiation dose, 1958-1998 [3] [line was redrawn by this author].

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Definition:

Dose-effect relationship is linear with no threshold. Is it correct for tumorigenesis?

Radiobiologists have studied the effect of radiation and also the repair of damaged cells. There should be the repair effect in which the higher repair rate at the lower dose, resulting sigmoidal relationship. There also should be a threshold which is completely reparable dose at a small dose.

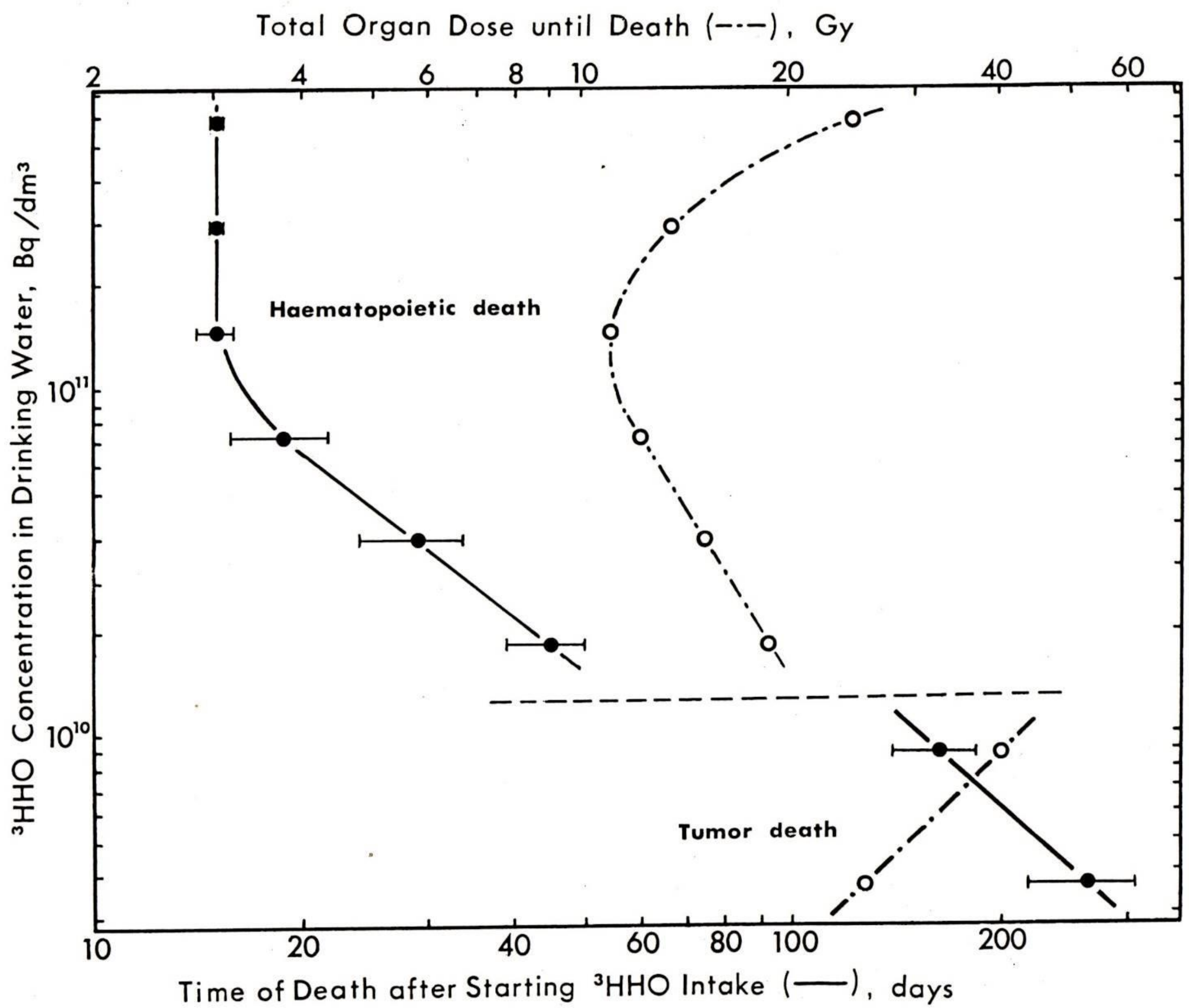
Effect of Tritiated Water

Animal: (C57BL/6N and C3H/He)F_1 female mice at 10 weeks age (24±1 g)

Chamber: Type-2350L (Chiyoda Hoan Yohin Co.)

Temperature: 24±2^{o}C Humidity: 50±10%

Daily light cycle: 10 h light and 14 h darkness

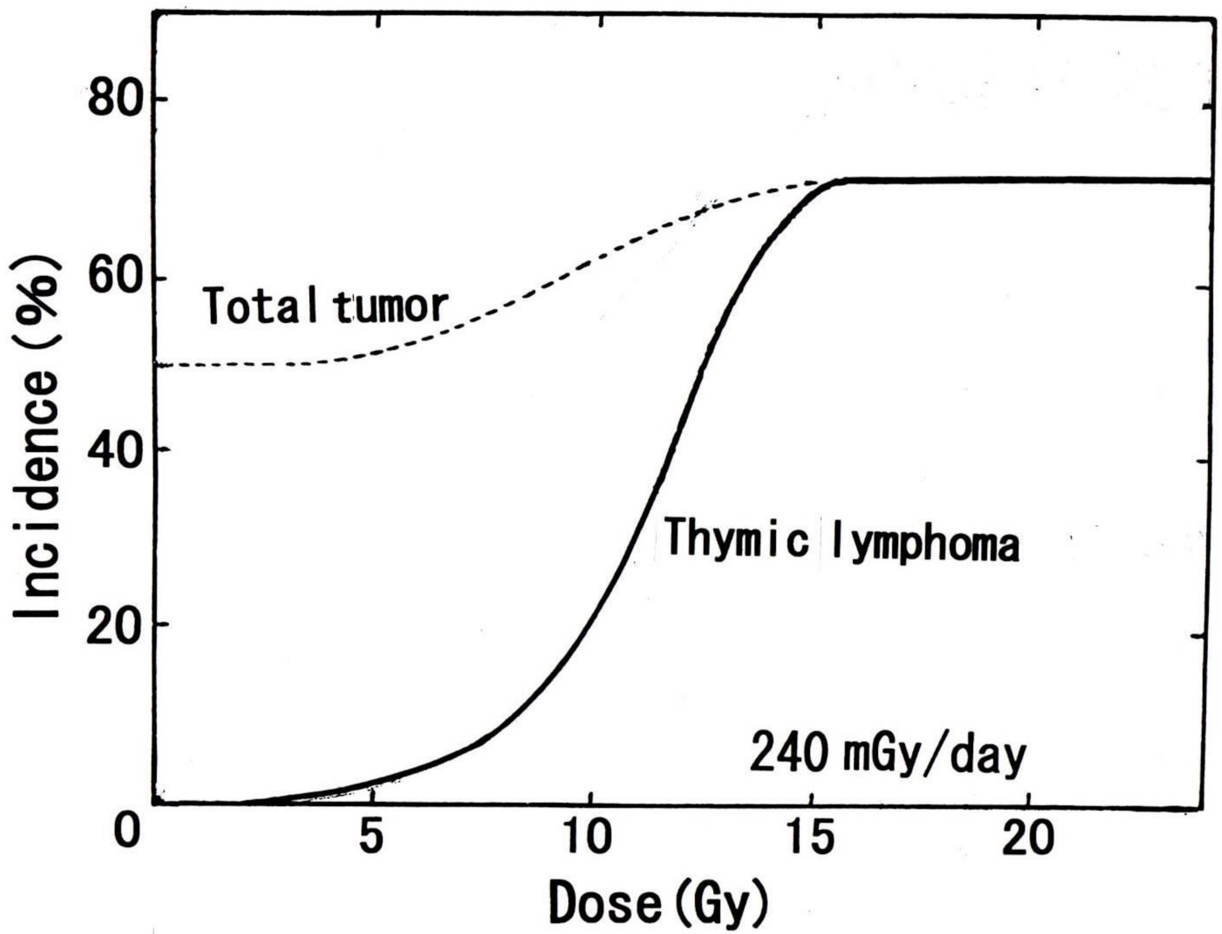


The border line between haematopoietic and tumor death

Table 2. Tumour developments in mice at different doses of HTO at a dose-rate of 240 mGy/day.

Exposure length	Till death	90 days	60 days	30 days	10 days	0 day
Mean cumulative dose (Gy)	39.6	21.6	14.4	7.2	2.4	0
Number of mice used	45	64	62	62	64	120
MST* (day)	165	150	176	515	691	785
Thymic lymphoma (%)	64	70	71	6	2	
Non-thymic lymphoma (%)	11	3	3	32	22	25
Lung tumour (%)		2	2	6	3	4
Fibrosarcoma (%)			2	3	13	8
Ovarian tumour (%)				16	25	5
Liver tumour (%)				3	6	8
Uterus tumour (%)						1
Others (%)					5	5
Multiple tumour-bearing (%)	0	0	0	3	6	5
Tumour-carrying mice (%)	76	75	78	63	70	51

* MST: Mean survival time (days)



Relationship of the incidence of thymic lymphoma with dose by HTO exposure.

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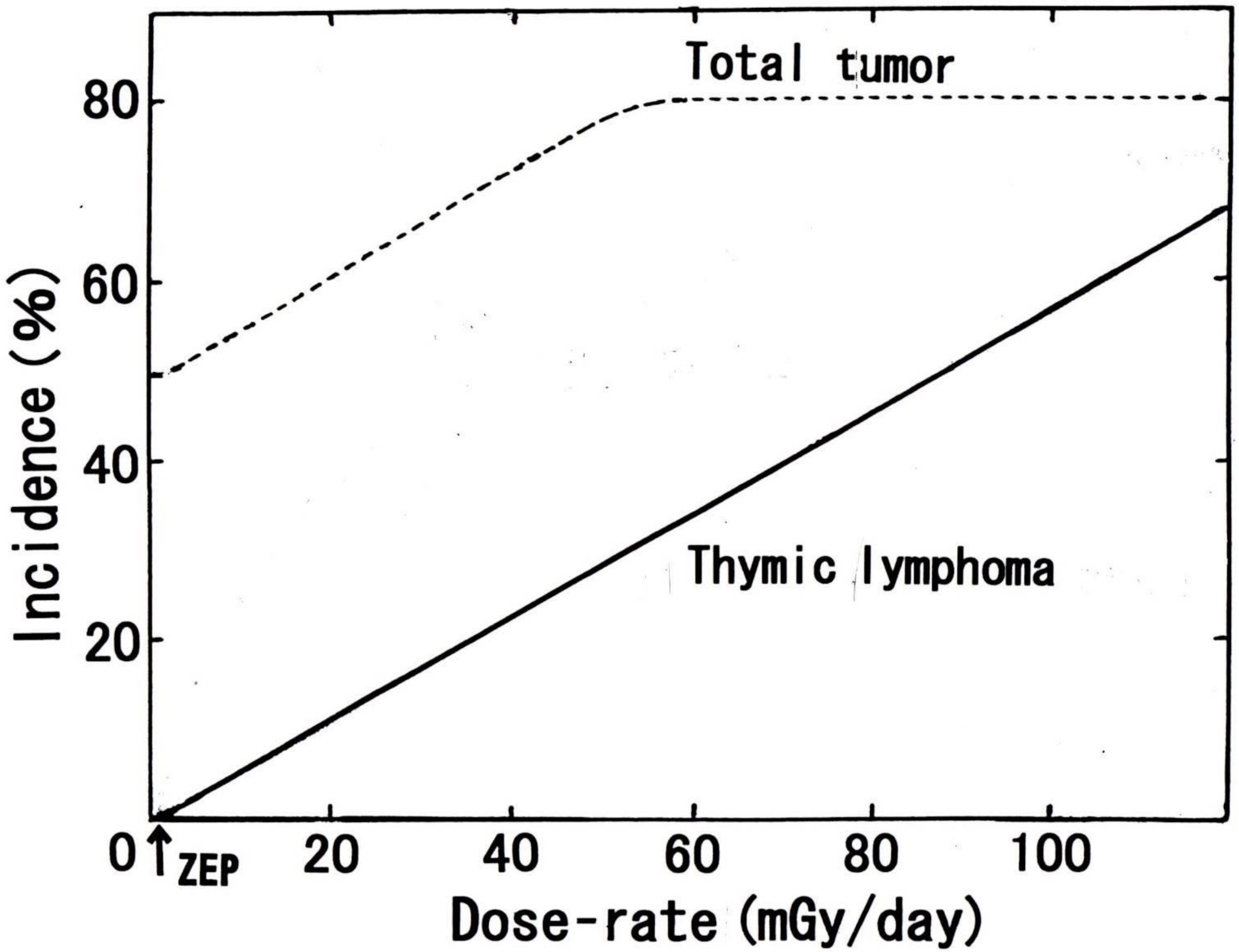
Dose-effect relationship for stochastic effect of tumori-genesis is sigmoidal with a threshold

Table 1. Tumour developments in mice at different dose-rates of HTO.

Dose-rate (mGy/day)	240	96	48	24	10	3.6	0.9	0.2	0
Mean cumulative dose (Gy)	39.6	24.6	19.7	11.5	5.9	2.6	0.7	0.2	0
Number of mice used	45	38	60	60	53	56	58	55	120
MST* (day)	165	259	414	481	622	727	804	796	785
Thymic lymphoma (%)	64	58	25	7	6	5			
Non-thymic lymphoma (%)	11	16	28	35	40	20	29	25	25
Ovarian tumour (%)		5	7	13	21	9	3	5	5
Reticular cell sarcoma (%)		5				4	2		
Fibrosarcoma (%)			3	7	11	9	22	9	8
Hardrian gland tumour (%)			3	3	15			4	
Lung tumour (%)			2	5		2	7		4
Skin tumour (%)			2						
Bladder tumour (%)				2					1
Rhabdomyosarcoma (%)				2					
Liver tumour (%)					4	2	17	7	8
Mammary tumour (%)					4				
Pituitary tumour (%)					2		2	2	1
Uterus tumour (%)							2		1
Haemangiosarcoma (%)								2	
Splenic tumour (%)									2
Stomac tumour (%)									1
Multiple tumour-bearing (%)	0	0	0	3	19	4	7	5	5
Tumour-carrying mice (%)	76	84	70	71	84	47	77	49	51

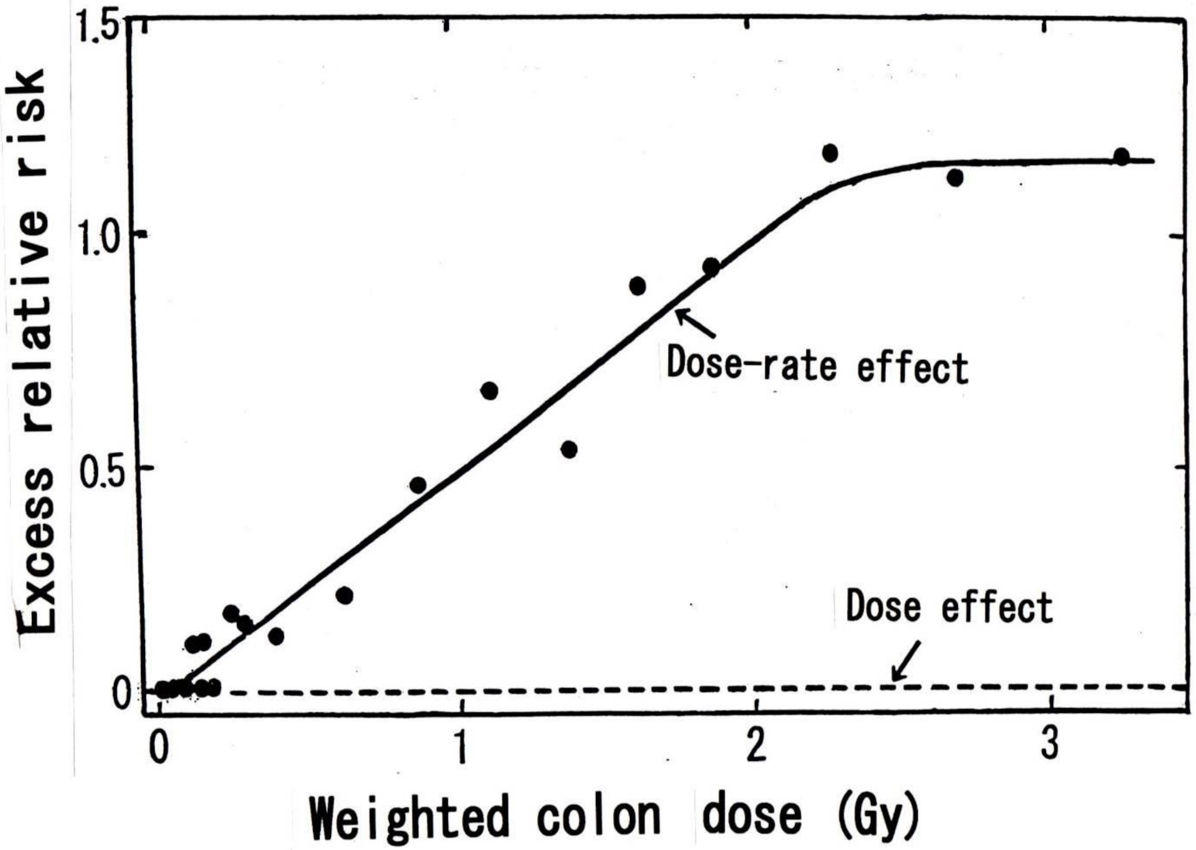
* MST: Mean survival time (days)



Relationship of the incidence of thymic lymphoma with dose-rate by HTO exposure.

Dose rate-effect relationship for tumorigenesis is linear from ZEP. Therefore, the solid tumor incidence by A-bomb exposure should be the result as the dose-rate effect but not the dose.

The dose of A-bomb is dependent on the distance, the dose is also the dose rate because of the same exposure time. The dose effect should be compared at the same dose-rate, which is a basis for radiobiological study.



LSS solid cancer incidence, excess relative risk by radiation dose, 1958-1998 [line was redrawn by this author].

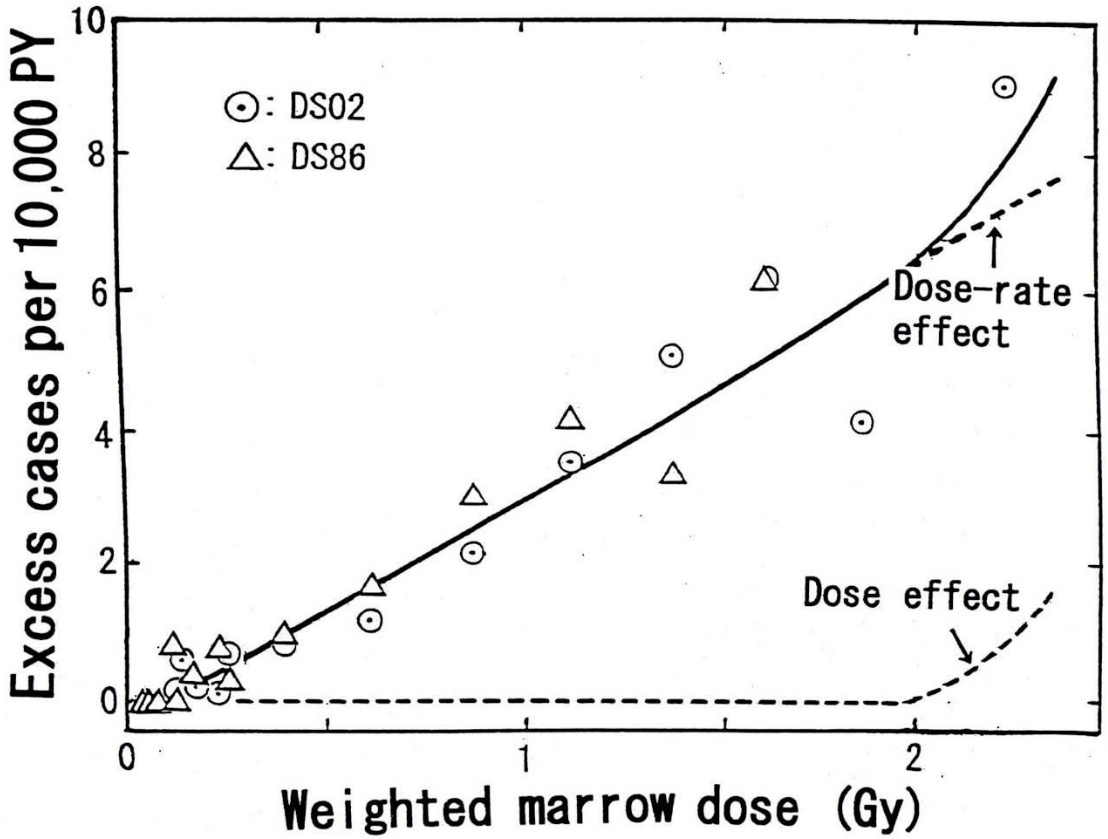


Fig. 9. DS02 and DS86 non-parametric dose responses of leukemia, 1950-2000 (Preston et al. 2007) [line was redrawn by this author]. PY: person-years, in this case the number of excess leukemia per 10,000 persons per year.

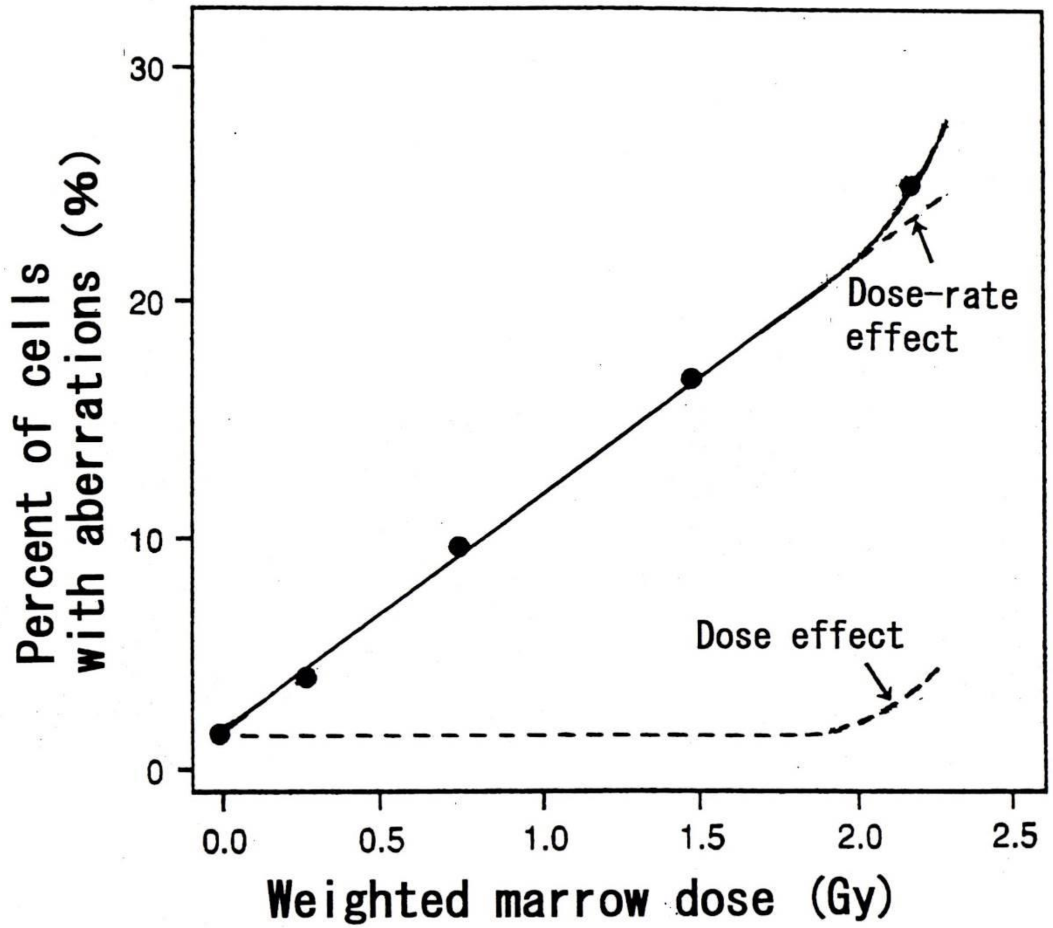


Fig. 10 Relationships between the fraction of cells with chromosome aberrations and the radiation dose to AHS survivors exposed in typical Japanese houses (RERF 2013) [line was redrawn by this author].

Dose effect appears from 2 Gy (2 Sv).

No data at more than 2.5 Gy suggests the haematopoietic death in the case of A-bomb radiation exposure.

Dependency on dose-rate for haematopoietic death

A-Bomb	Text Book	THO
2.5 Gy	5 Gy	10-20 Gy
A few sec.	A few min.	14-40 d.

STOCHASTIC EFFECT

(Life Shortening)

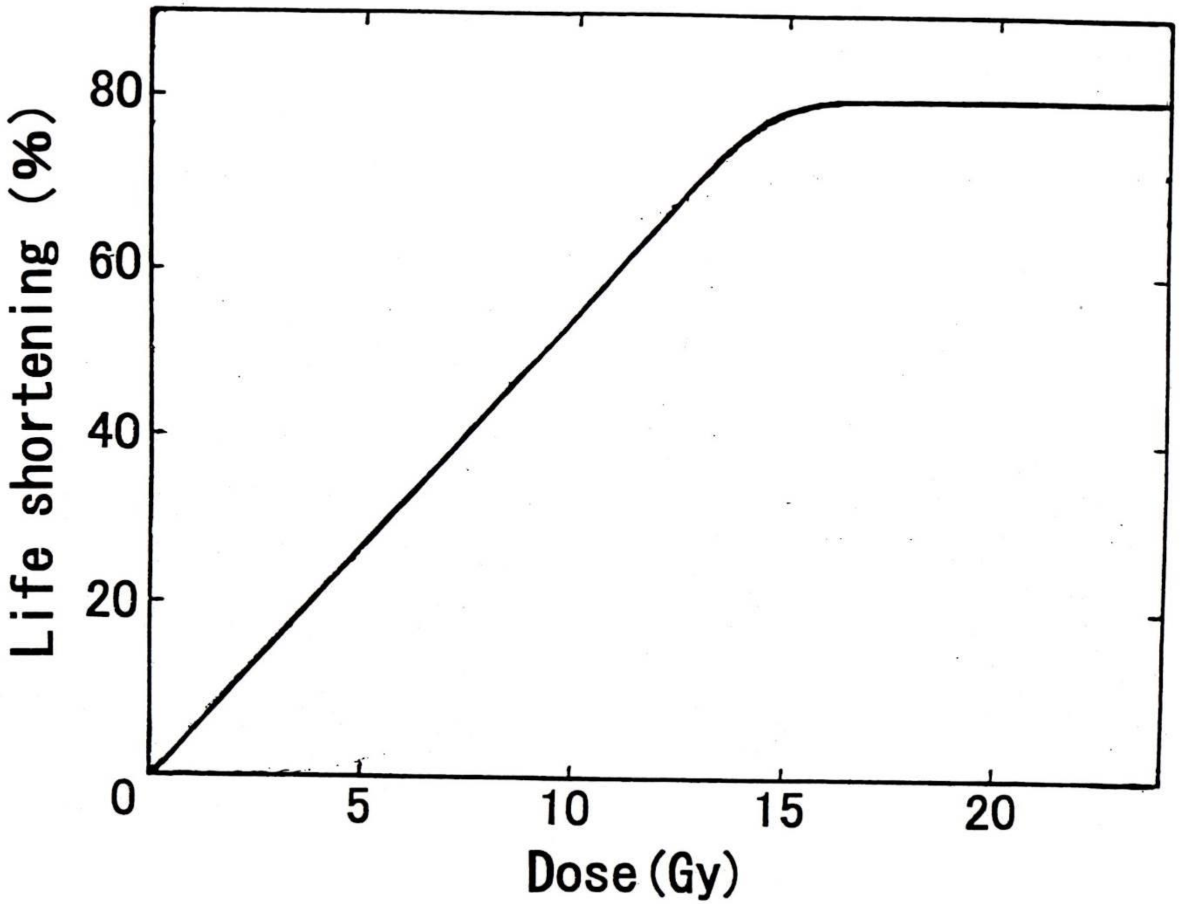


Fig. 7. Relationship of the life shortening with the dose by HTO exposure (dose-rate: 240 mGy/d).

Dose-effect relationship for stochastic effect of life-shortening is linear with no threshold at higher dose-rate than ZEP.

Why is there no repair?

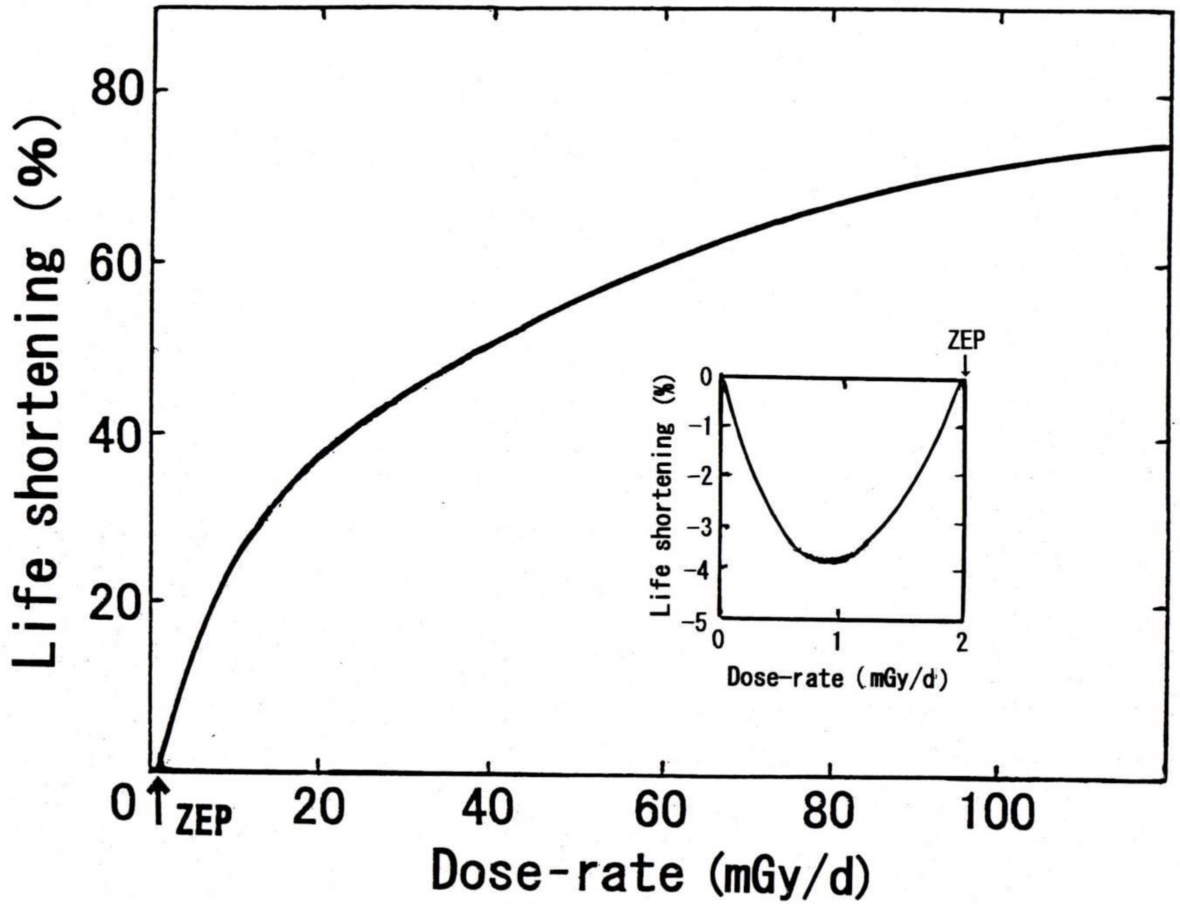


Fig. 6. Relationship of the life shortening with the dose-rate by HTO exposure. ZEP: zero equivalent point.

Dose rate-effect relationship for stochastic effect of life-shortening is parabolic at higher dose-rate than ZEP.

Why is it parabolic?

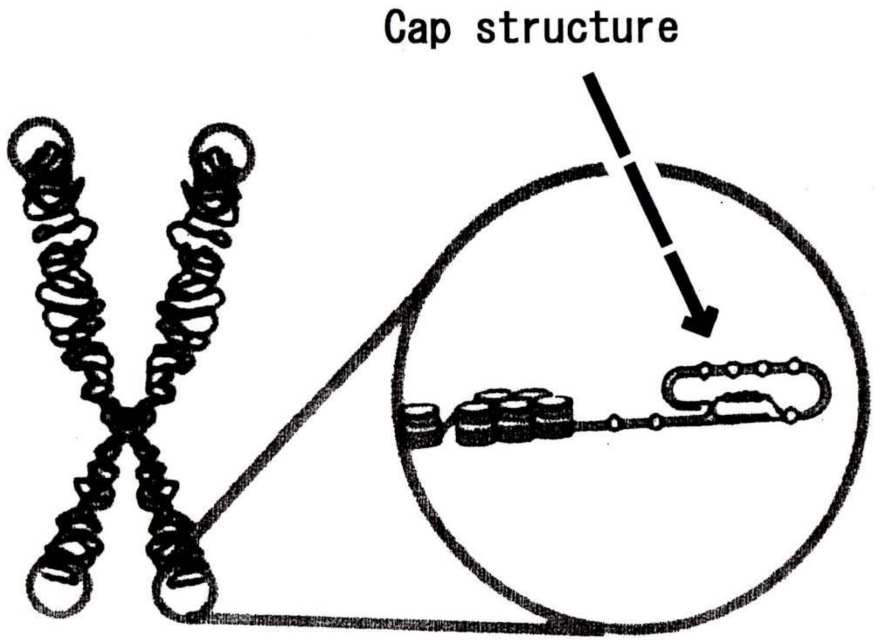


Fig. 11. Cap structure of the life span related gene (teromea [center part in cap structure]).

No repair would be caused by no action of repair enzyme. Parabolic relationship would be caused by overlapped attack with radicals in the cap structure.

BIOLOGICAL HALF-LIFE

RI	Organ	Physical Half Life	Biological Half Life	Effective Half Life
H-3	Whole Body	12 y	12 d	12 d
C-14	Whole Body	5700 y	40 d	40 d
P-32	Bone	14 d	1155 d	14 d
Fe-59	Spleen	45 d	600 d	42 d
Sr-90	Bone	29 y	50 y	18 y
I-131	Thyroid	8 d	138 d	8 d
Cs-137	Muscle	30 y	70 d	70 d
Ra-226	Bone	1600 y	45 y	44 y

$$\frac{1}{\text{Effective Half Life}} = \frac{1}{\text{Physical Half Life}} + \frac{1}{\text{Biological Half Life}}$$

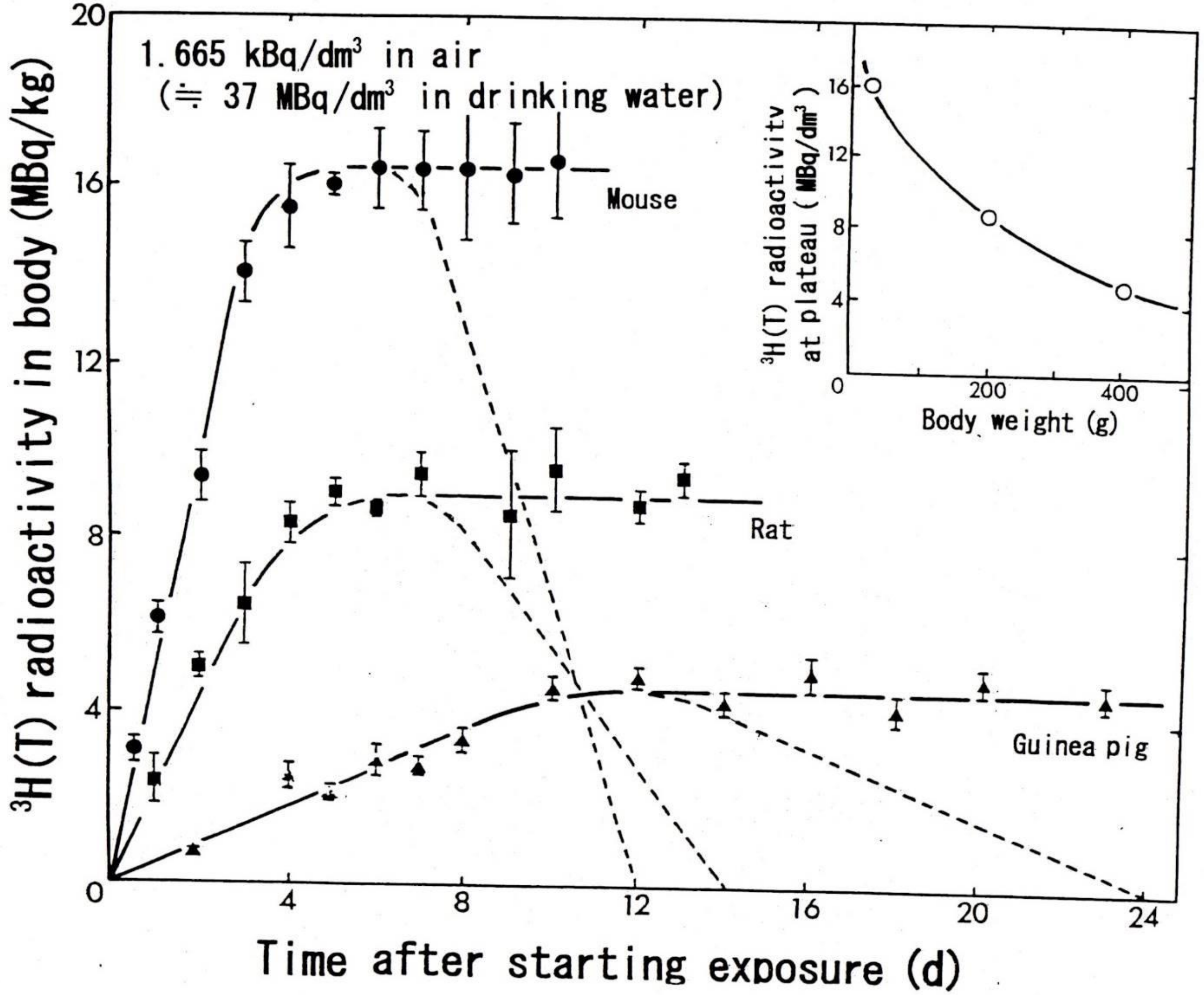


Fig. 1. Change of specific radioactivity in body after starting administration of HTO vapor and HTO drinking water (dotted line: decrease of radioactivity after removing of HTO).

Analysis of Cs-137 in human body (Takesita et al. 1966)

Sample	Examined Number	Cs-137
Food	16	0.9±0.4 Bq/day/person
Urine(Male)	4	1.2±0.4 Bq/day/person
Urine(Female before birth)	8	1.0±0.2 Bq/day/person
Urine(Female after birth)	40	0.9±0.4 Bq/day/person

If the biological half-life (70days) of Cs-137 is correct, not only Cs-137 but also K-40 contained in food could be piled up with limitless in the body. But “take in” and “take out” are comparable.

Definition of “Biological Half-Life” should be reconsidered.

RADIATION WEIGHTING FACTOR (RBE)

LET and Radiation Weighting Factor (W_R)

Radiation	LET (eV/μm)	W_R
X-ray, γ-ray, β-ray	lower than 3.5	1
Newtron (lower than 1MeV)	3.5-7.0	2.5
Newtron (1MeV-50MeV)	7.0-23	5.0
Newtron (higher than 50MeV)	higher than 23	2.5
Proton	higher than 8	2
α-ray, Heavy nucleus, Nuclear fission fragment	63-175	20

Definition:

Radiation weighting factor (W_R) or RBE is the larger constant when LET is the larger.

Is W_R constant? No, it is not constant. It should be variable depending on dose-rate.

At the higher dose-rate, W_R should be the smaller. Because when ionizing density/volume by low LET radiation becomes the higher, the effect comes to be the nearer to that of high LET radiation.

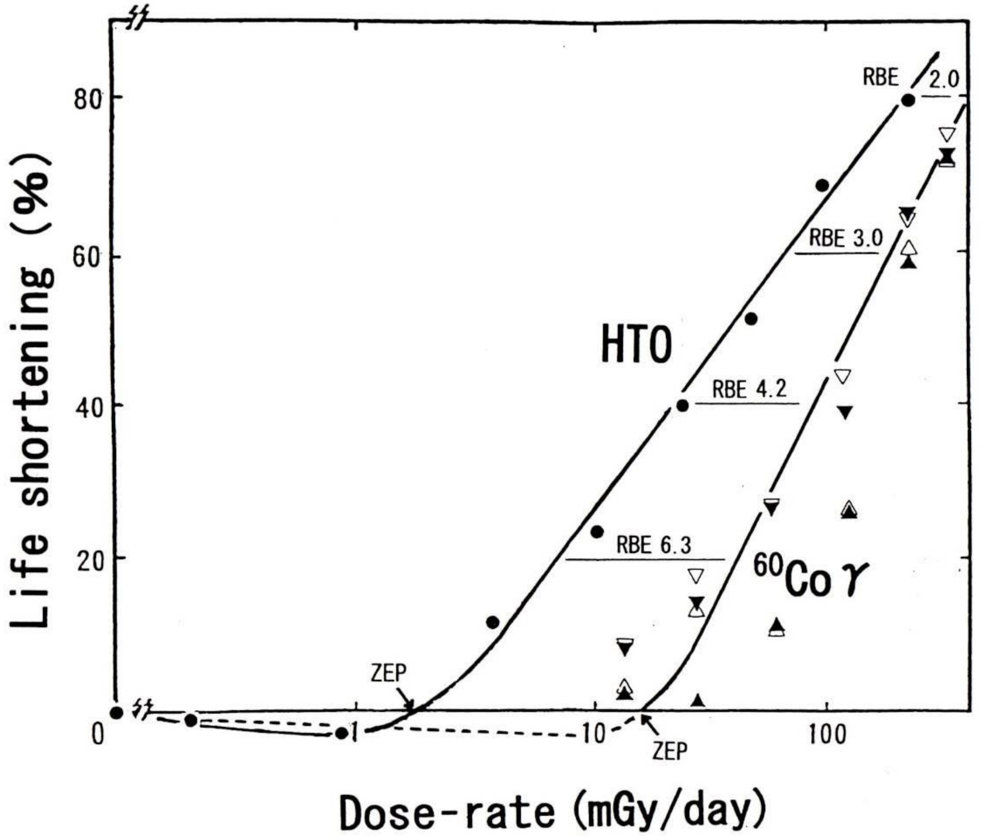


Fig. 12. Relationship of life shortening with dose-rate of HTO for (C57BL/6N x C3H/He)F_1 mice [●] compared with ^{60}Co γ -ray irradiation of various mouse strains: LAF_1 [○] [4-5] and A/Jax [▲]; BALB/c [▼]; C57BL/6N [△]; BCF_1 [▽] [6].

Why is the effect of HTO larger than that of γ-rays?

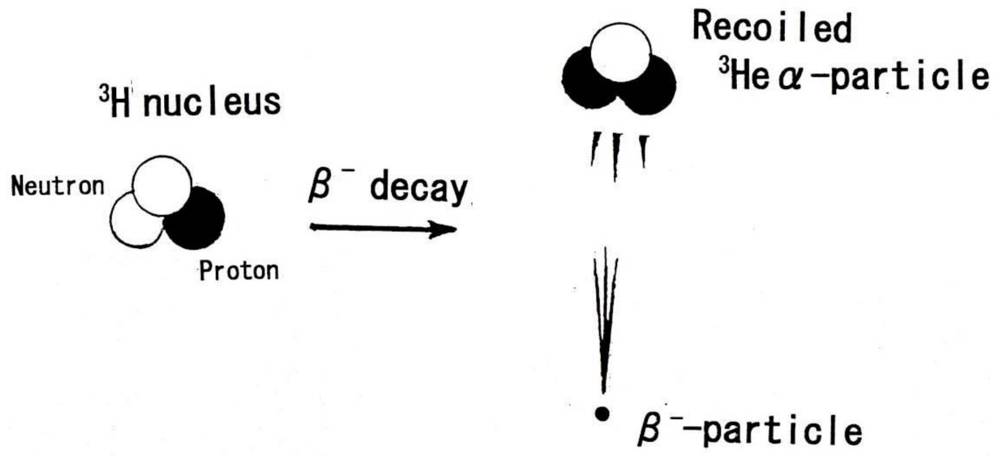


Fig. 12. Hypothesis of ^{3}He recoil α-ray by ^{3}H β⁻-decay.

Equivalent Dose

Equivalent Dose = Absorption Dose x $\underline{W_R}$

↑

Dose-rate dependent

∴ Equivalent Dose: Dose-rate dependent

"Dose-Rate" description should be added.

EFFECTIVE DOSE

Effective Dose (ICRP 2017) [Tumorigenic risk dose]

= Equivalent Dose x W_T(Tissue weighting factor)

↑

A-bomb dose-rate

∴ Effective Dose ≠ "Dose"

Essentially, the effective dose should be not for tumorigenesis and should be the dose which gives the same level damage for all kind of tissues or organ cells, and “Dose-Rate” description should be added.

Radiation Weighting Factor (RBE):

A at X/sec

Equivalent dose:

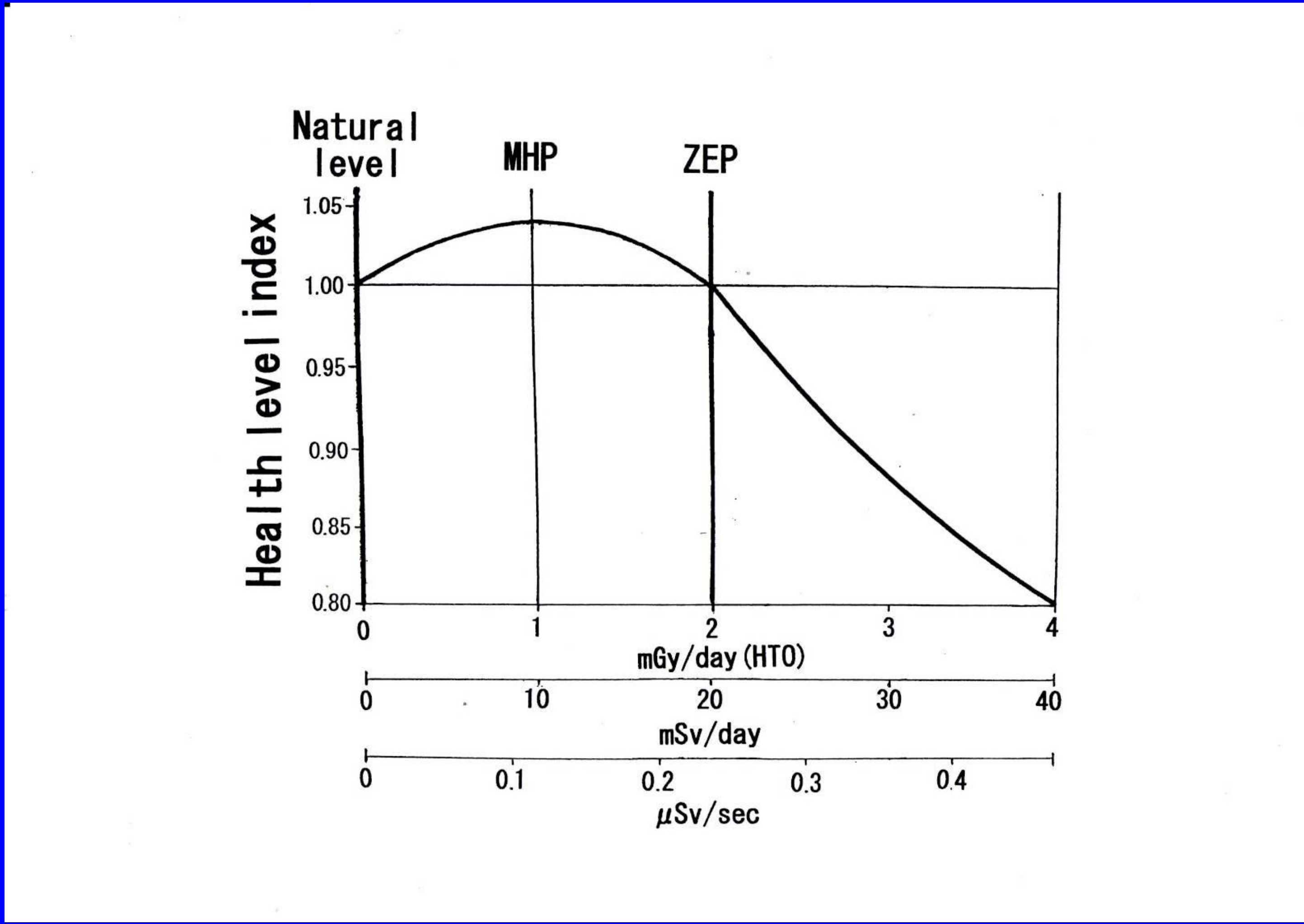
B Sv at X/sec

Effective dose:

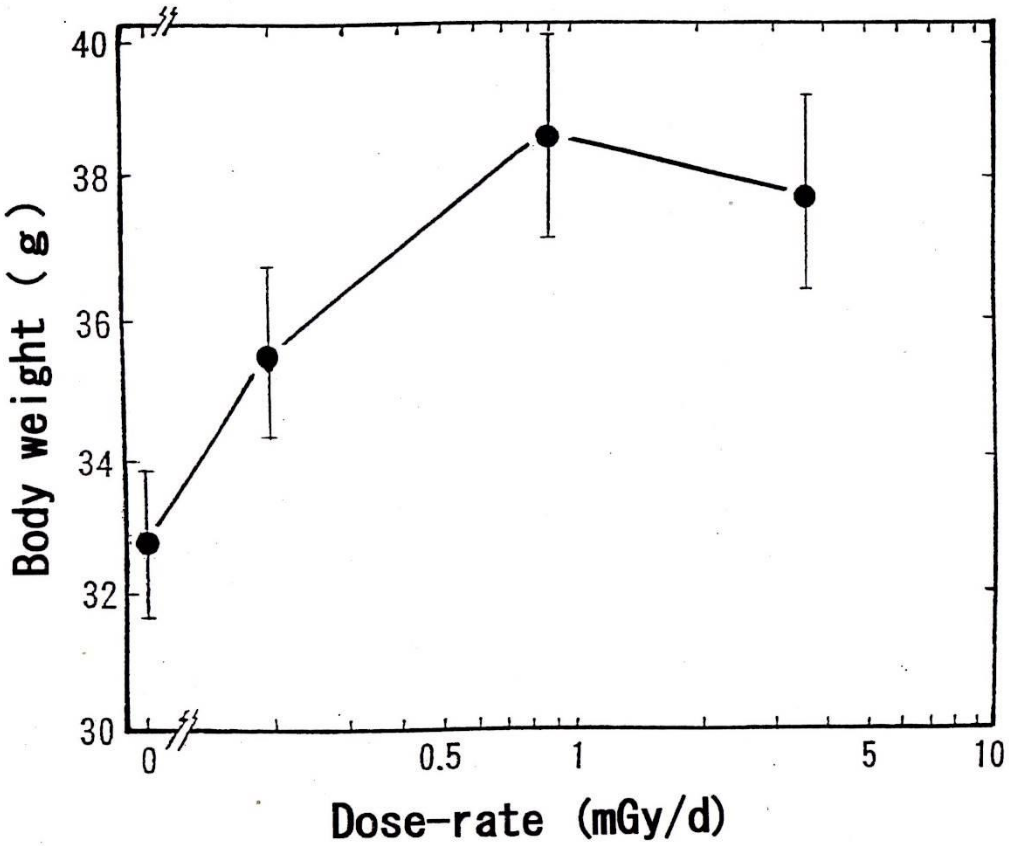
C Sv at X/sec

X = Dose

HORMESIS AND MEDICAL DIAGNOST RADIATION



Hormesis is observed at the dose-rate (0~ZEP), which is evidence of health increase effect (life span, body weight, and moving activity). Reason can be explained by activation of cell metabolic system with direct energy transfer of radiation at very small dose.



Body weight of mice plotted against the dose-rate of HTO, measured at 630 days after start of HTO intake.

At the present the permissible dose is 1 mSv/y.

However, 10 mSv/day is the most healthy dose-rate according to animal experiments.

At least, 1 mSv/d is rather useful dose for health.

Risk of Medical Diagnostic Radiation

Exposure Dose of Medical Diagnostic Radiation
in Japan (mSv)

Examination	Exposure Dose	Examination	Exposure Dose
Chestgraphy		Vertebra	
Direct	0. 057 (0. 14)	Breast	1. 45 (1. 8)
Indirect	0. 053 (0. 65)	Middle	0. 65 (1. 4)
Perspective	1. 14 (1. 08)	Neck	0. 26 (0. 27)
Pervis	0. 053 (0. 83)	Cervix	0. 09 (0. 07)
Abdomen	0. 24 (0. 53)	Gallbladder	0. 88 (2. 3)
Intestine		Urinary tract	2. 47 (3. 7)
Upper	3. 33 (3. 6)	Breast	
Lower	2. 68 (6. 4)	Mass exm.	-- (0. 07)
CT (Bo d y)	4. 6-13. 3 (13. 3)	Crinic exam.	-- (0. 21)
Vascular		Dental	
Brain	-- (2. 0)	Single	0. 26 (0. 27)
Heart	2. 68 (6. 4)	Panorama	0. 26 (0. 27)

( ): Country of health care level 1

The exposure time is very short for almost medical diagnostic radiations which are much higher than ZEP dose rate, 20mSv/day = 0.24 μSv/sec.

All kinds of medical diagnostic radiation are risky for tumori-genesis and life-shortening.

IN ADDITION

“Radioactivity” has been mistranslated as “Radioability” in Japan.

We, Japanese radiation specialists must call the correct name of the radioactivity “Hosha-Kassei” instead of “Hoshano (Radioability)”.

SUMMARY

1. Stochastic effect

    Tumorigenesis: Sigmodal dose effect and linear dose-rate effect

    Life shortening: Linear dose effect and parabolic dose-rate effect

2. A-bomb effect: Dose-rate effect ≺ 2Sv, Dose effect ≻2Sv
3. Biological half –life: Exponential decrease having to reconsider
4. Radiation weighting factor (RBE):

    Not constant and dose-rate dependent

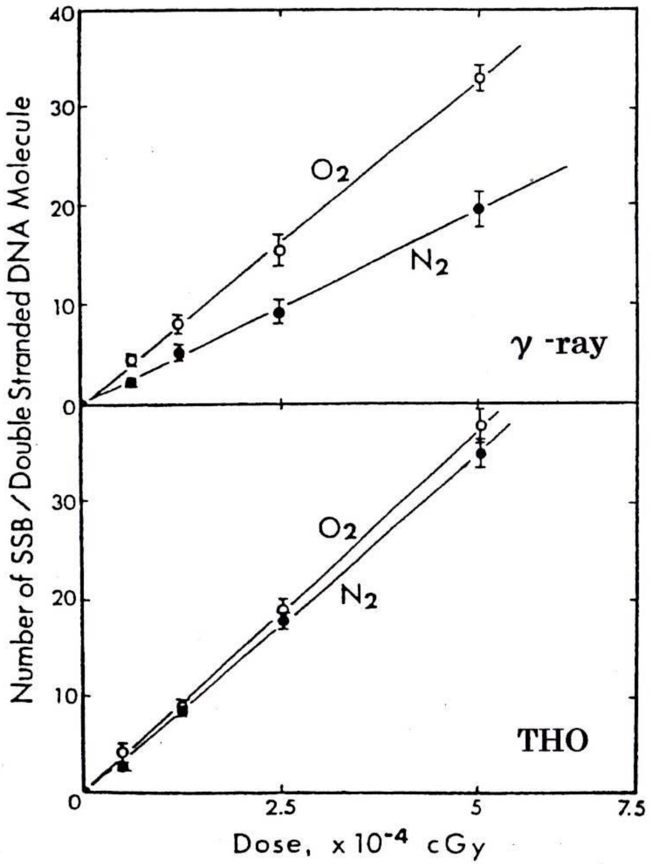
5. Effective dose: No meaning, definition change is necessary
6. Hormesis and medical diagnostic radiation

    Hormesis: Dose-rate but not dose (MHP = 0.12 μSv/sec)

    Medical diagnostic radiation: Risky (≫ZEP 0.24 μSv/sec)

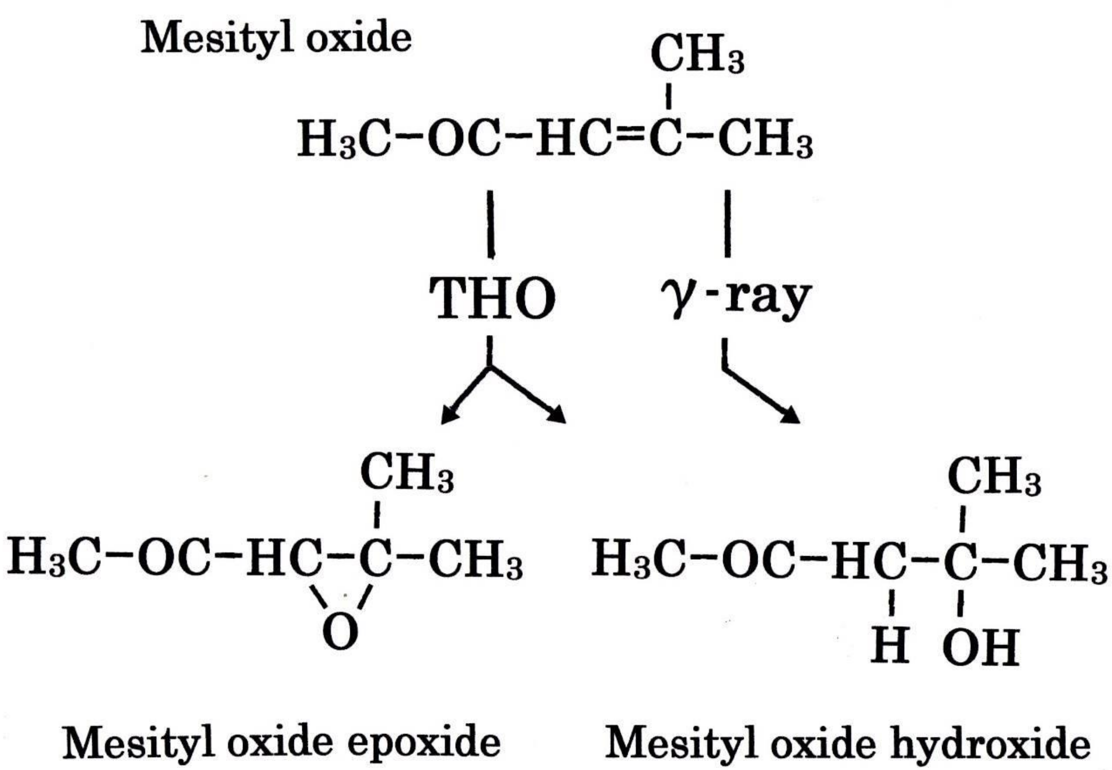
ADDENDUM 1

No oxygen effect in THO (Yamamoto 1984)



ADDENDUM 2

Verification of nascent oxygen formation in tritiated water (Yamamoto 1984)



ADDENDUM 3

The higher rate of activation at the higher LET proposed by this author (Yamamoto 2012)