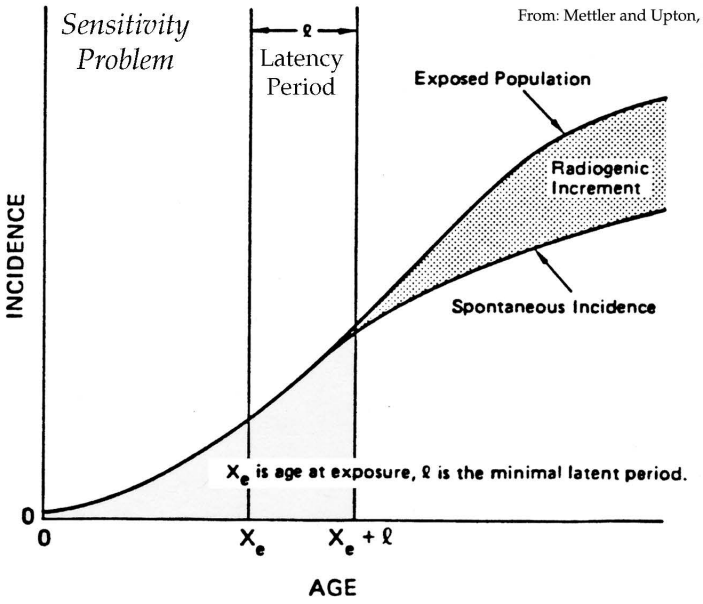
Radiation Carcinogenesis and Risk Assessment

A. Why even study mutagenesis, transformation and carcinogenesis in cells or model organisms when human data is available?

1] Answer: because the human data on radiation carcinogenesis, although obviously the most relevant for human radiation protection purposes, has several, serious limitations

Problem #1 : There are not vast numbers of humans who have been irradiated, meaning that detecting a small excess of cancer cases will be difficult statistically. This situation is made worse by the fact that cancer is quite common "naturally". ("*Data sensitivity issue*")



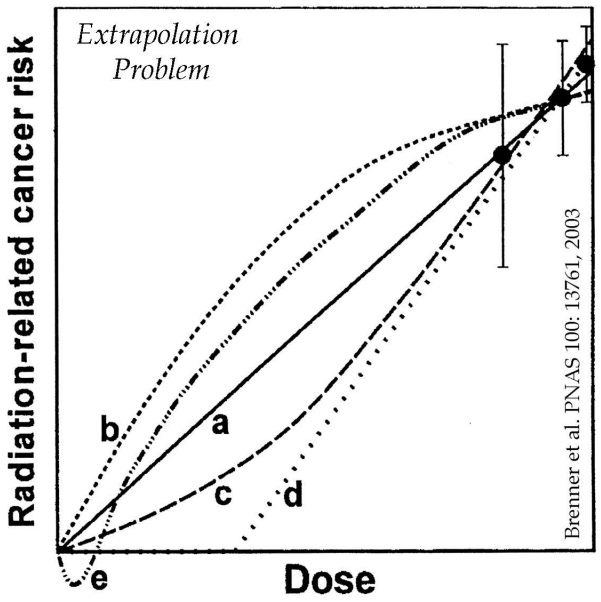
From: Mettler and Upton, *Medical Effects of Ionizing Radiation, 2nd Edition*, 1995

Superimposition of radiogenic effect on spontaneous incidence.

Sample Size Required for Statistical Precision in Obtaining Dose–Response Data on Carcinogenesis

Dose Level	Sample Size
1 Sv	1000
100 mSv	100,000
10 mSv	10,000,000

Problem #2 : Of the human populations that have been irradiated, most have received relatively high doses (more than about 50 cGy...because of bombings and accidents and such), and mostly, these doses have been delivered all at once. Unfortunately, what we really want to know in terms of radiation saftety is what happens when a population is exposed to very small doses over extended periods of time. ("*Data extrapolation issue*")



Schematic representation of different possible extrapolations of measured radiation risks down to very low doses, all of which could, in principle, be consistent with higher-dose epidemiological data. Curve a, linear extrapolation; curve b, downwardly curving (decreasing slope); curve c, upwardly curving (increasing slope); curve d, threshold; curve e, hormetic.

Curve A = linear, no threshold; current standard, and most conservative of the risk estimates

Curve B = supralinear; might be expected if an especially sensitive subpopulation was mixed in with the general population (certainly possible, if not probable)

Curve C = linear-quadratic; plenty of biological precedent for this model, plus it has some vocal supporters

Curve D = threshold; not typically the way a stochastic process would behave, however there could *effectively* be a threshold due to statistical noise at low doses

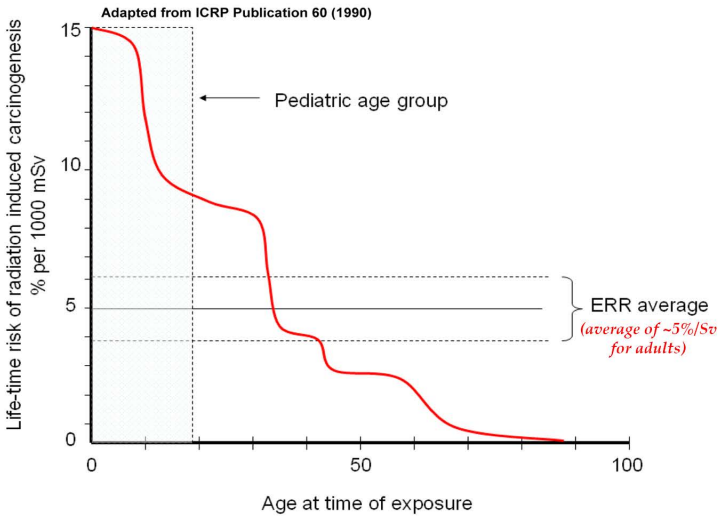
Curve E = hormesis; definitely has some biological precedent, however proponents of the idea that a little radiation is actually good for you are generally considered kooks

Problem #3 : Most radiation-induced cancers take at least years, if not decades, to develop, meaning that there will be no quick answers to what we want to know...plus it will cost tons of money to do the actual studies. ("*Latency period issue*")

Estimates of Mean Latent Periods for Various Tumors Following External Irradiation

Tumor Type	Mean Latent Period (yr)
Brain	27
Salivary glands	20
Pharynx, larynx	24
Thyroid	20
Breast	22
Lung	25
Stomach	14
Sarcomas	12
Colon	26
Bone	10–15
Leukemia	7–10
Skin	24

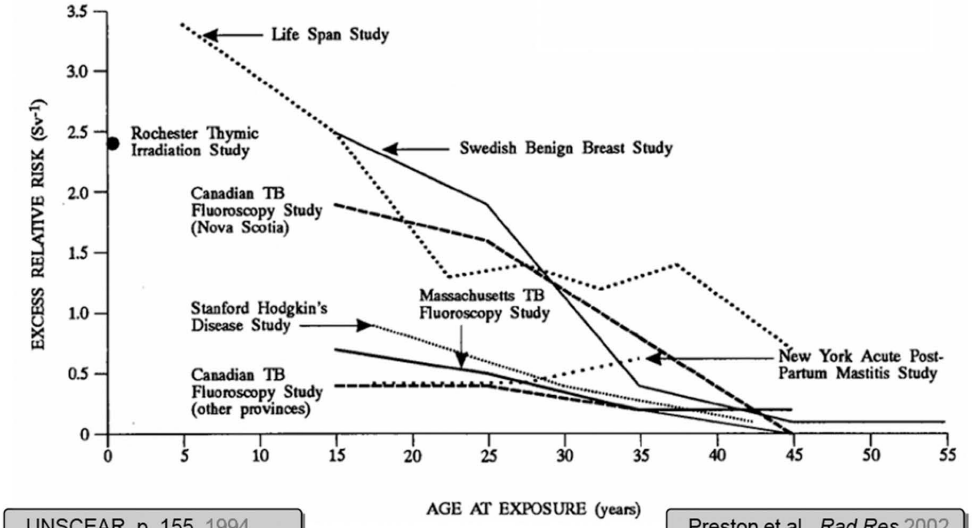
Mettler and Upton, *Medical Effects of Ionizing Radiation*, 3rd Edition, 2008



Predicted city-averaged ERR at 1 Gy as a function of age at exposure and time since exposure.

Further complicating matters is the fact that the latency period is variable and depends on: tumor type induced by radiation (hematological malignancies have shorter latent periods than solid tumors); importantly, ***the age at which the individual was irradiated*** (in general, younger people are both more sensitive to radiation carcinogenesis and for solid tumors at least, show longer latency periods before the tumor is clinically detectable); and ***possibly, the total dose*** (based on radiation-induced tumors in previously-treated radiotherapy patients)

Age at Exposure
Radiation-Induced Breast Cancer Studies

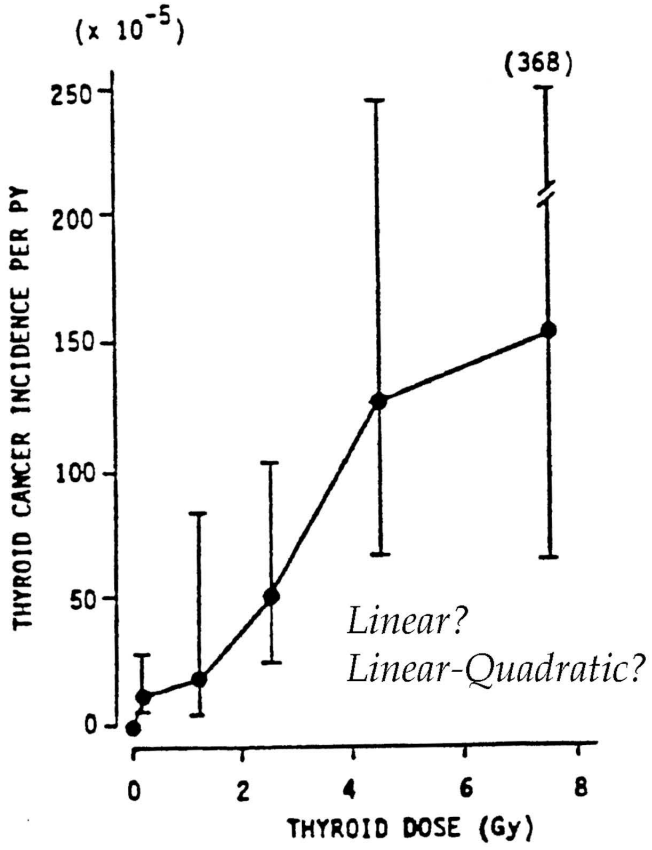


UNSCEAR, p. 155, 1994

Preston et al. *Rad Res* 2002

Problem #4 : Human populations are much more variable in their responses to radiation (and most other things as well) when compared to cells, fruit flies, laboratory rodents, etc., meaning that the data that is obtained will be "scattered", and may be hard to interpret ("*Heterogeneity issue*")

Radiation-induced thyroid cancer in Polynesian Islanders



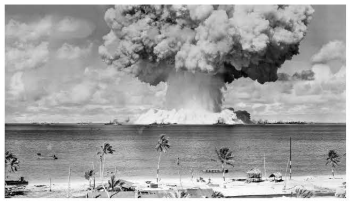
Thyroid cancer incidence per person year (PY) as a function of the radiation dose in the thyroid. Rates adjusted for sex, ethnicity, and interval after irradiation. Error bars represent 90% confidence limits. (From Shore RE, Woodard E, Hildreth N et al: JNCI 74:1177–1184, 1985)

Carcinogenesis in Irradiated Human Populations - usually the latest of all late effects, and the one of most concern for human radiation safety purposes

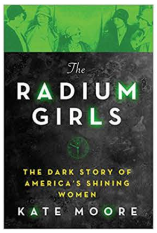
A. Radiation Carcinogenesis: The Human Experience

1. the human populations that have been studied long-term for cancer incidence following exposure to ionizing radiation generally fall into four main categories:

Source of Exposure	Details of Exposure	Cancer Sites and Types
Nuclear Weapons-Related		
Japanese A-bomb survivors *1945*	Prompt radiation from blasts (γ-rays and neutrons), plus fallout (mostly β); up to ~6 Gy total dose	Leukemia and most types of solid tumors
Polynesian Islanders; *1954*	Fallout from US weapons tests (mostly radioiodine)	Thyroid
Diagnostic Imaging Procedures		
Multiple fluoroscopies; in the US and Canada; *1930's – 1950's*	To monitor lung status in TB patients (X-rays); up to several Gy over extended periods	Breast
Thorotrast (nuclear medicine); *1930's – 1950's*	Contrast agent for limb and liver angiography (4-5Gy of α's)	Liver
Imaging of "high-risk" (or not) pregnancies resulting in prenatal exposure; *1940's – 1950's*	Repeat adominal/pelvic diagnostic X-rays	Leukemia in resulting offspring, usually during childhood
Therapeutic Procedures		
Postpartum mastitis; *1940's – 1950's*	X-ray doses (1-6 Gy total) to lactating breasts	Breast
Ankylosing spondylitis; *1930's – 1950's*	Up to 30 Gy X-rays to spine (and bone marrow) for relief of pain and stiffness	Leukemia and a few solid tumors (including thyroid and sarcomas)
Treatment for enlarged thymus or hemangiomas at birth; epilation for treatment of tinea capitis; *1940's – 1950's*	A few Gy of X-rays	Thyroid and a few other tumor types (including sarcomas, gliomas, leukemia and lymphoma)

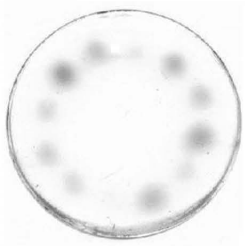


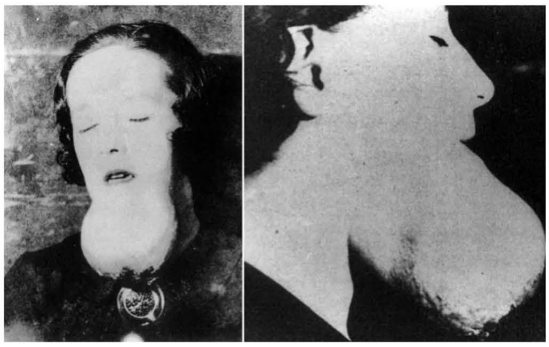
Source of Exposure	Details of Exposure	Cancer Sites and Types
Long-term survivors of radiation therapy; *mostly since the 1970's*	Up to 100 Gy external beam X-rays and/or brachytherapy	Especially leukemia, breast, thyroid and sarcomas, and maybe lung (and a few others too)
Occupation-Related		
Radiology professionals (prior to modern radiation protection standards); *1920's – mid-1950's*	Unknown doses of X-rays protracted over long periods	Leukemia and so-called "non-specific life shortening", most likely a consequence of cancer (so it really isn't "non-specific")
Miners; *up to the present day*	Exposure to uranium, radium and mostly, radon gas deep underground (mostly α-emitters)	Lung
Watch dial painters; *1910's - 1930*	Ingestion of radium-based paints used for luminous watch dials; bone doses as high as 500 Gy from α-emitters	Bone sarcomas, especially of the head and neck
General public living in vicinity of the Chernobyl nuclear power plant at the time of the accident (mostly from Belarus and Ukraine)	Exposed to fallout after the reactor explosion, especially radioactive iodine; other than to the thyroid, exposures above background but otherwise pretty low (worst case: about 1 cGy)	Large excess of thyroid cancer among children living in the immediate area in the decade following the accident; where possible, others being monitored for the appearance of excess solid tumors



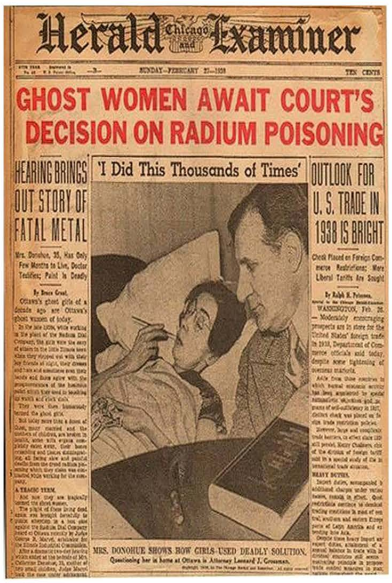
The Sad Story of the Radium Dial Painters

It was not long before the "wonder" of radium was exploited commercially. It was considered trés chic to own a radium-enhanced luminous watch for example. Unfortunately, workers (predominantly women) in the radium dial factories often paid the ultimate price in support of this latest fashion trend...





Front and side views of a dial painter with a radium-induced sarcoma of the chin.
Collection of Ross Mullner



2. some of the general findings of the human radiation carcinogenesis studies:

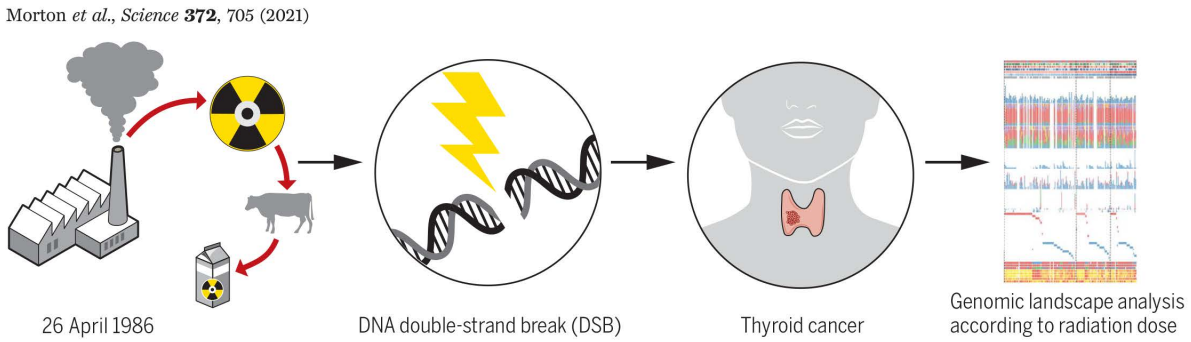
a. **radiation carcinogenesis was found to be a stochastic effect,** i.e., you either get cancer or you don't ("all or nothing" effect), **and that there is apparently no threshold dose** (that is, a dose below which there isn't *some* cancer risk)

b. **the shapes of the dose response curves for the induction of cancer as a function of radiation dose appear to be either linear, linear-quadratic, or sometimes, "bell-shaped"** (the latter mostly observed in animal studies)

c. **for low LET radiation, the risk of carcinogenesis is lower if the dose is fractionated or protracted over time, that is, that there *is* a dose rate effect**

d. **for a given dose, high LET radiation is more carcinogenic than low LET radiation**

Interesting! Genomic profiling of papillary thyroid cancers in Ukrainian and Belarussian children and adolescents who ingested radioiodine after the Chernobyl accident



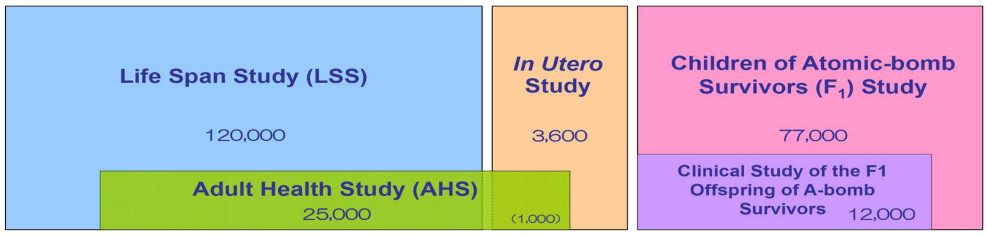
3. Thyroid cancers induced by radiation show some unique genomic signatures not seen in other types of thyroid cancers not caused by radiation exposure, in particular:

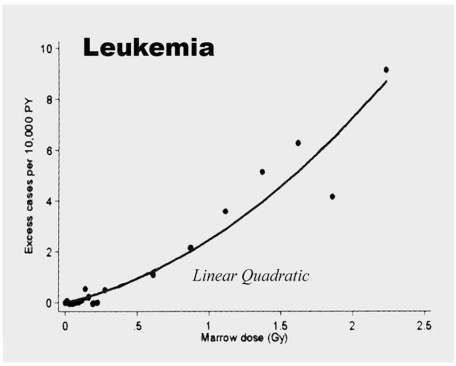
- gene fusions that produced hybrid proteins that acted as oncogenic drivers...most of which were in components of the Ras-Raf-Mek-Erk signaling pathway
- many small deletions in genes that led to structural variant proteins, some impactful and some not
- greater frequency of these changes the higher the estimated thyroid dose and the younger the irradiated individual was

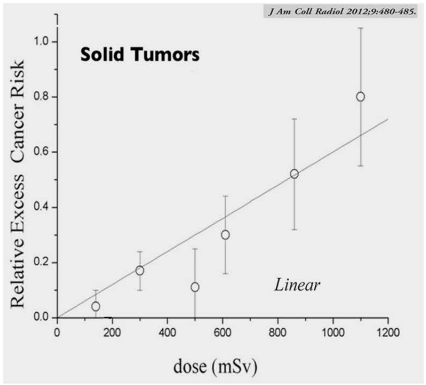
a) **these genomic signatures suggest that the initiating carcinogenic lesion was a double strand break (as opposed to base damage, crosslinks, etc.) that was either misrejoined or left unrepaired...implicating NHEJ as the repair process that failed**

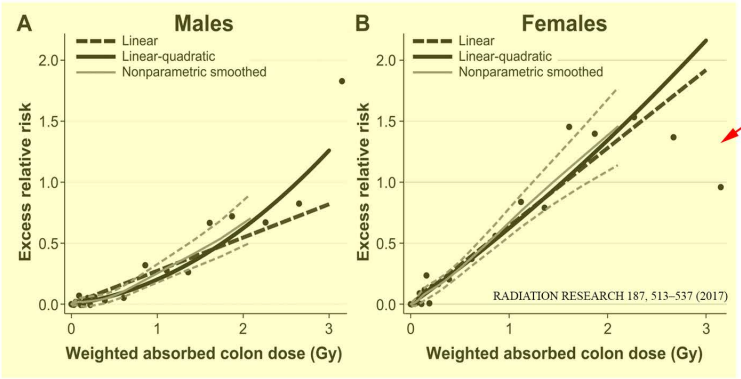
b) **other studies of molecular carcinogenesis like this one further suggest that it's not simply the residual DNA damage that's responsible for tumor initiation and progression, but also that the tissue's micro-environment has changed, which in turn decreases the "fitness" of the surviving cells...making way for mutated cells better able to cope with such conditions to take over**

Tumors in Japanese A-Bomb Survivors









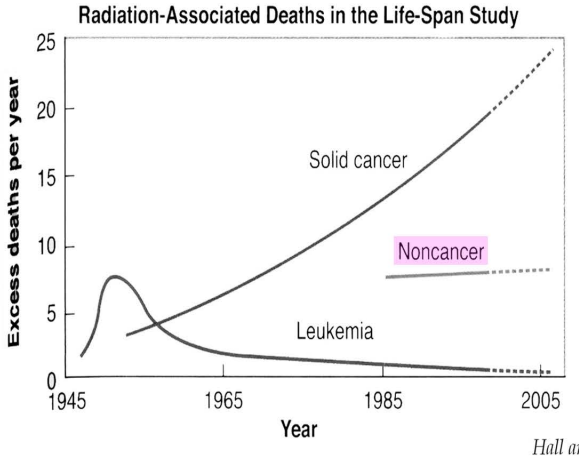
Panels A and B: Solid cancer dose-response functions for males and females (full dose range). Fitted linear (black dashed line) and linear-quadratic (black solid curve) ERRs for all solid cancers using linear and linear-quadratic dose-response functions for males and females.

The ERRs are given for subjects at attained age of 70 years after exposure at age 30 years.

Emerging Science:

Most recent analysis of Japanese A-bomb survivor data suggests an upward curvature to the curve (for men).

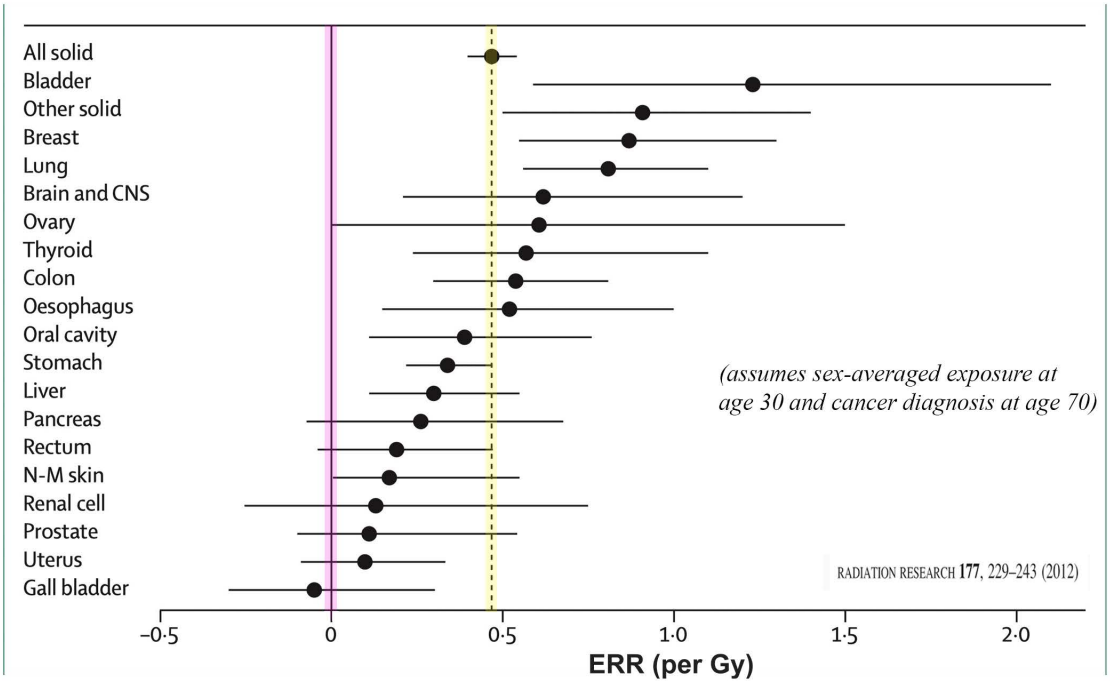
However, it has long been believed that this dose response relationship is strictly linear.



Illustrating the pattern of radiation-associated deaths in the life span study in the A-bomb survivors. Leukemia appeared first, reaching a peak by 5 to 7 years after irradiation, before falling off later. Solid cancers did not appear in excess for several years, but have continued to increase ever since. By about 1990, it was evident that there is also an excess of noncancer deaths, especially stroke and heart disease.

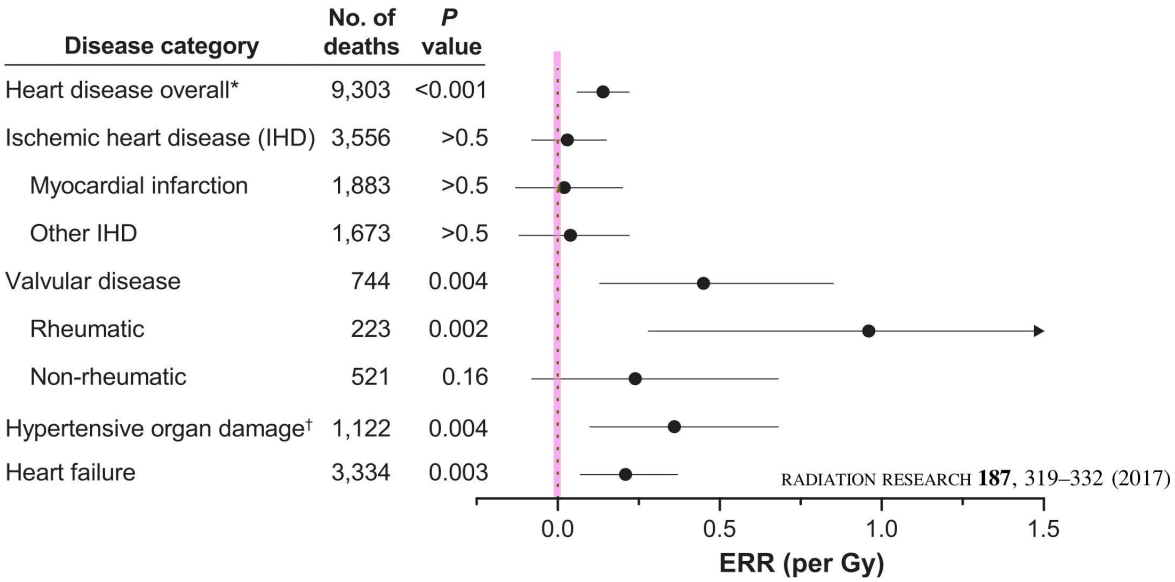
Hall and Giaccia, Radiobiology for the Radiologist, 7th Edition, 2011

Excess relative risk of a radiation-induced solid tumor among Japanese A-bomb survivors (1950-2004)



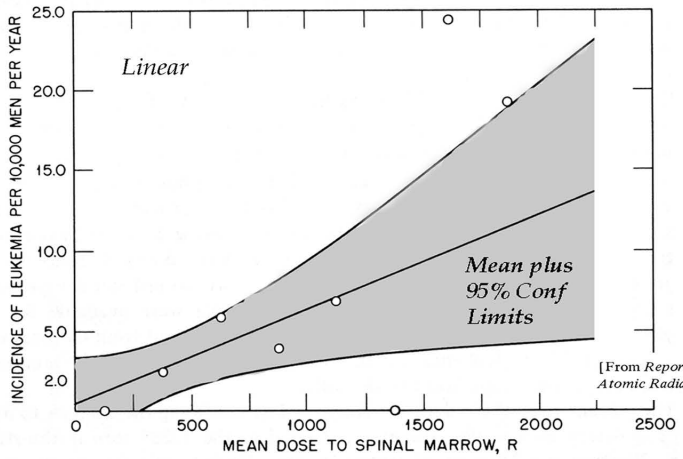
Excess relative risk of radiation-induced heart disease in A-bomb survivors (1950-2008)

(an under-appreciated effect in A-bomb survivors until fairly recently, and similar to what is seen in radiotherapy patients whose hearts were irradiated)



Heart disease subtype-specific excess relative risk per Gy in the Life Span Study, 1950–2008. *Heart disease overall is defined as death from cardiac diseases, not including kidney damage according to the past report †Hypertensive organ damage includes hypertensive renal disease.

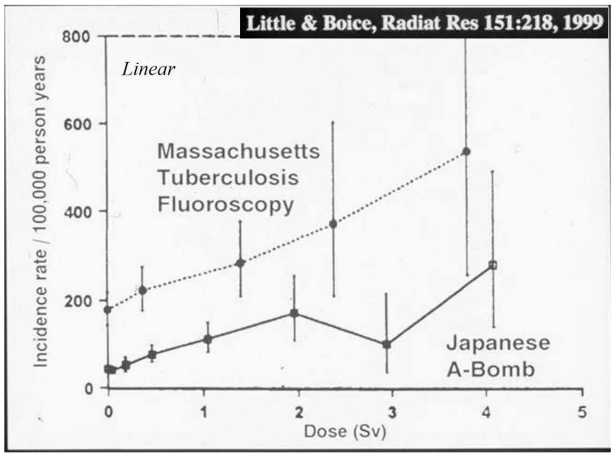
Leukemia in Patients Treated for Ankylosing Spondylitis



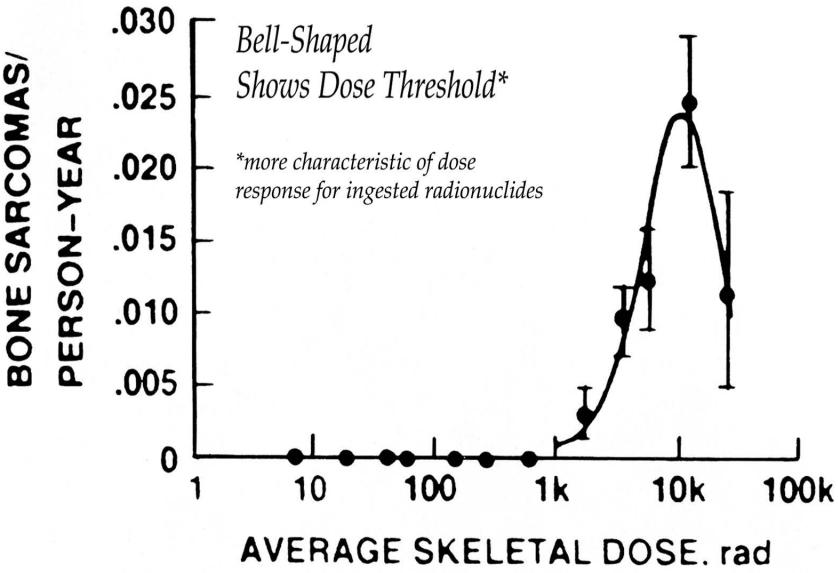
[From *Report of the United Nations Scientific Committee on the Effects of Atomic Radiation*, p. 146, 1962.]

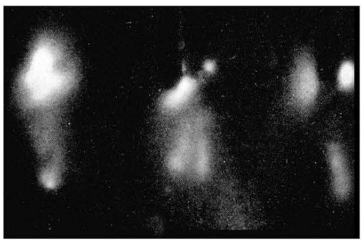
Incidence of leukemia in relation to mean spinal-marrow dose of therapeutic irradiation for ankylosing spondylitis.

Radiation-induced breast cancer among A-bomb survivors and TB patients receiving multiple fluoroscopies



Bone Tumors in Radium Dial Painters



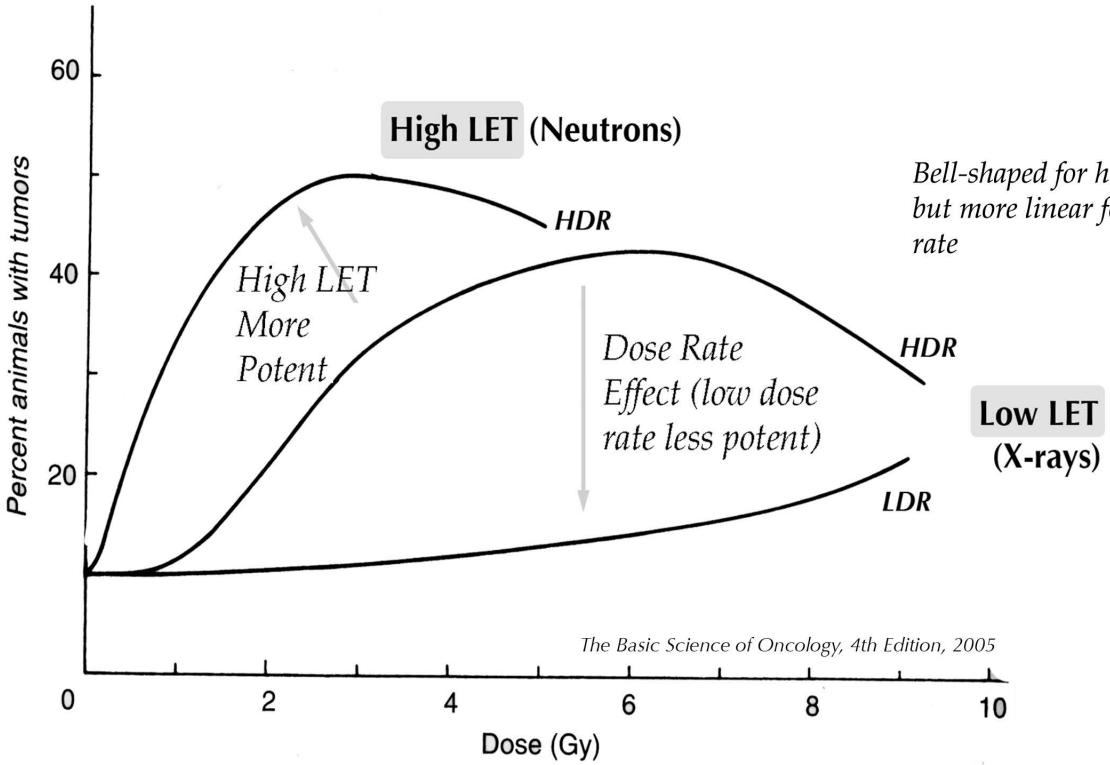


So who needs an X-ray machine for a dental study?

Teeth from radium dial painters expose X-ray film all by themselves!

From BEIR IV: Report of the National Academy of Sciences. Washington, D.C., National Academy Press, 1988

Radiation carcinogenesis in mice as a function of LET or dose rate



Bell-shaped for high dose rate, but more linear for low dose rate

Schematic diagram of induction of a specific tumor type in mice exposed to various doses of ionizing radiation given to the whole body based on a review of a number of different in vivo results.

4. Special Cases of Radiation Carcinogenesis

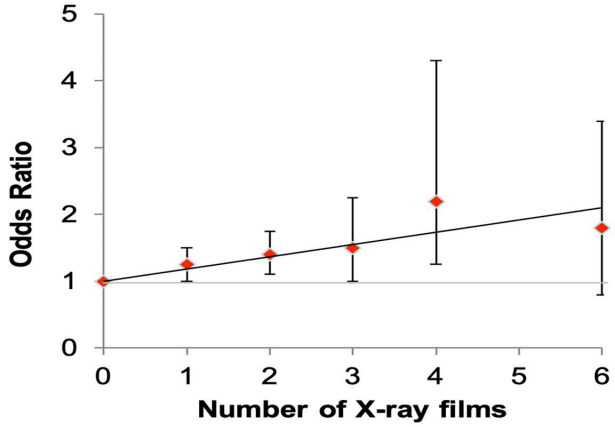
a) ***Prenatal Irradiation*** - elevated cancer risk?

1] the **Oxford Survey of Childhood Cancers**, a retrospective, case-controlled epidemiological study originally published in the 1950's by Stewart and Kneale, demonstrated a clear association between childhood leukemia risk and prenatal exposure to *diagnostic* X-rays

Childhood Cancer and Irradiation In Utero

Number of children with leukemia or cancer before age 10 years	7649
Number x-rayed in utero	1141
Number of matched controls	7649
Number of controls irradiated in utero	774
Number of films	1 to 5
Fetal dose per film	0.46 to 0.2 rad (4.6 to 2 mGy)
Relative cancer risk estimate, assuming radiation to be the causative agent	1.52

Stewart A and Kneale, G. Lancet *1*: 1185-1188, 1970



The relative risk of childhood cancer after radiation exposure during pregnancy. (Reproduced from Doll and Wakeford, 1997.)

2] other large studies have backed up these findings (see: Harvey *et al.*, N Engl J Med *312*: 541-545, 1985; and Doll and Wakeford, Br J Radiol *70*: 130-139, 1997)

3] in contrast, a-bomb survivors receiving comparable effective doses did not show an excess of *childhood* cancers, but did show an excess later in life (i.e., at older ages when the spontaneous cancer incidence increases)

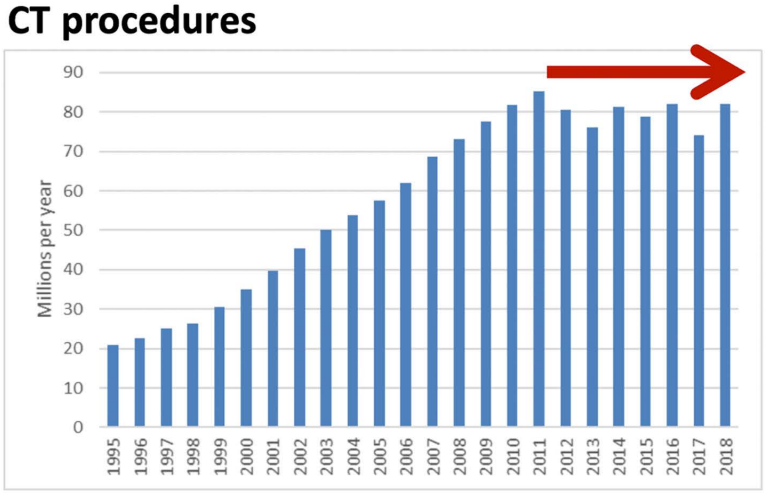
Therefore, in order to err on the side of caution, even in the absence of proof of causation, for human radiation protection purposes, we do assume that embryos and fetuses are more sensitive to radiation carcinogenesis – either in childhood or later in life – by a factor of about 1.5-2.0.

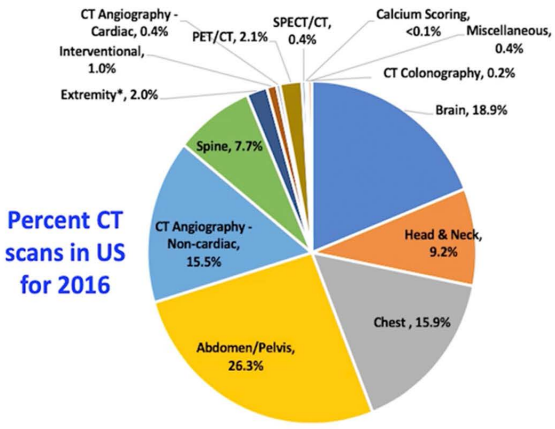
b) ***Imaging Procedures Employing Ionizing Radiation*** - elevated cancer risk?

1] *because the radiation doses are orders of magnitude lower for diagnostic scans than for radiation therapy, the risk of causing a malignancy will also be much, much lower…but NOT zero, because there is always some risk*

2] *however, there are many, many more diagnostic scans performed per year than radiation therapy treatments, so with a very large number of patients, even a very small risk might manifest itself;* also remember that many individuals will get more than one scan during the course of a procedure

3] one warning: **the use of CT scanning in particular (which gives a higher dose than other diagnostic procedures relatively speaking) has increased dramatically over the past 40 years, especially in the pediatric population**





a. **based on cancer risk estimates for the a-bomb survivors, there was a very small but significant excess relative risk measurable at 34 mSv, *although in practice, most assume that the lowest dose that causes a measurable increase in cancers is 100 mSv***

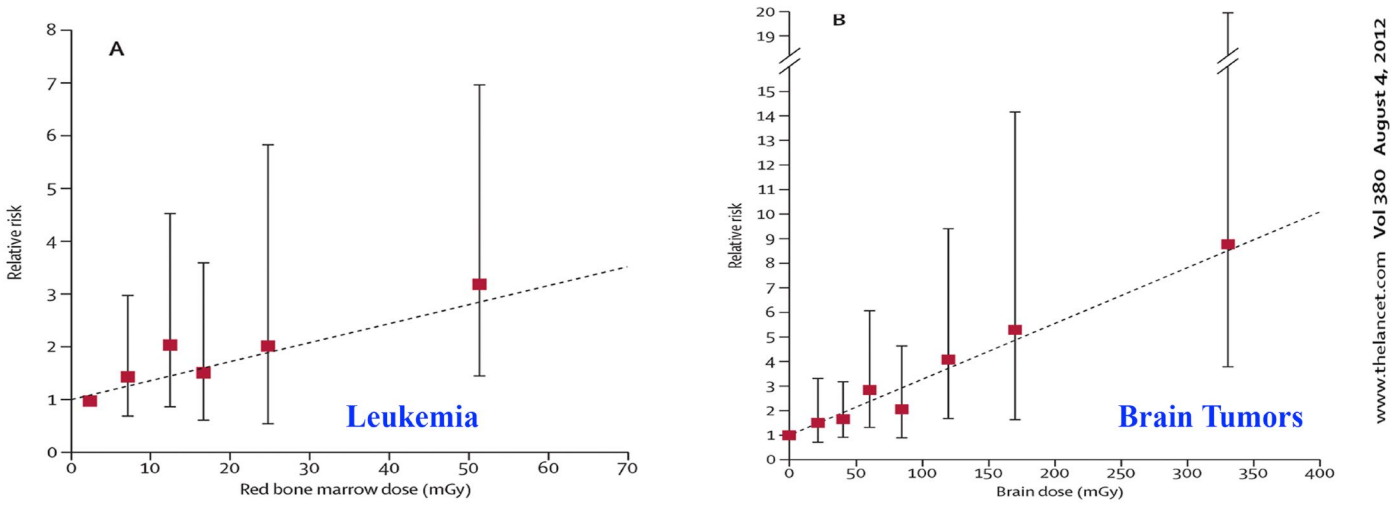
1. *doses in this range can be delivered during CT scanning, especially in the pediatric population*

b. **since young children are more sensitive to radiation carcinogenesis, and since they also should have the longest remaining lifespans to develop such malignancies, many radiobiologists feel that the use of pediatric CT scanning should not be allowed to continue to proliferate indefinitely, and certainly should not be used unnecessarily...**

...or at minimum, that the machine amperage should be turned down some in order to reduce the doses delivered

A useful statistic to bear in mind:

Every 10,000 CT scans, on average, will produce one excess case of:



Relative risk of leukaemia and brain tumours in relation to estimated radiation doses to the red bone marrow and brain from CT scans
(A) Leukaemia and (B) brain tumours. Dotted line is the fitted linear dose-response model (excess relative risk per mGy). Bars show 95% CIs.

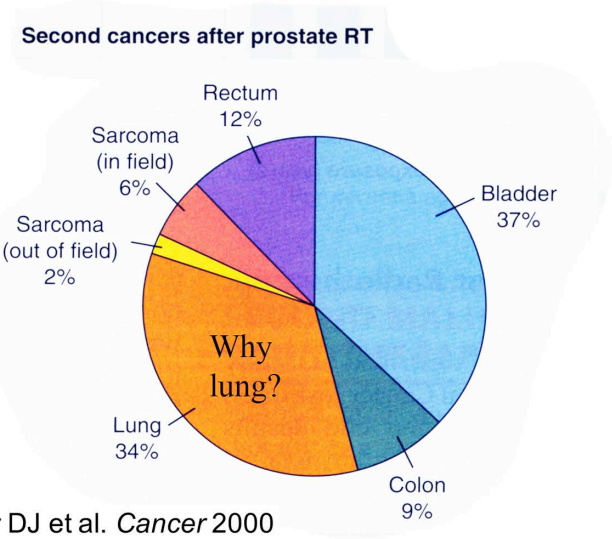
c) ***Second Malignancies in Long-Term Cancer Survivors Who Received Radiotherapy*** - a growing problem, as more and more patients survive their original cancer

1] *an increasing number of epidemiological studies of long-term cancer survivors do show an elevated risk of getting a different type of cancer in or near a previously-irradiated treatment field (receiving 40 Gy or more total dose)*; the most common types of second malignancies seem to be:

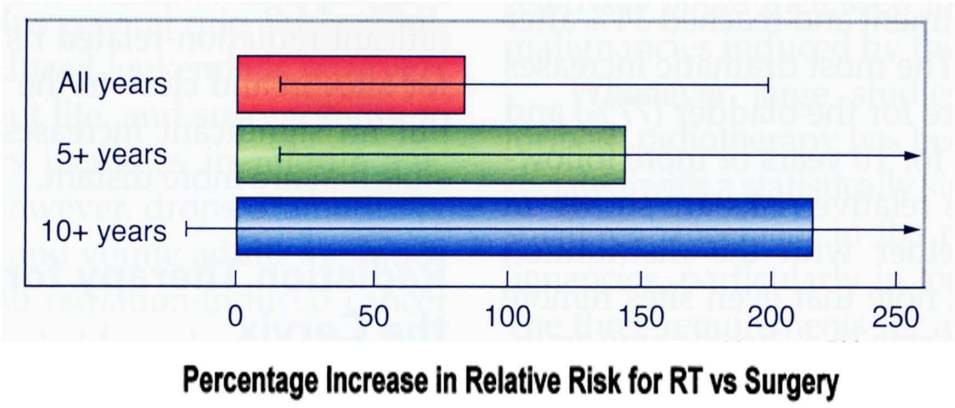
leukemia
thyroid cancer
breast cancer
soft tissue sarcoma
lymphoma
lung cancer

Prostate Cancer Survivors

- Brenner et al compared relative risk for secondary cancers among men who underwent RT (51, 584) vs. surgery (n = 70, 539) for prostate cancer
- No evidence for an increase in leukemia
- *Significant increase in risk for second solid tumors (34% increase after 10+ y)*
- Largest risk was for bladder at 10+ y past diagnosis



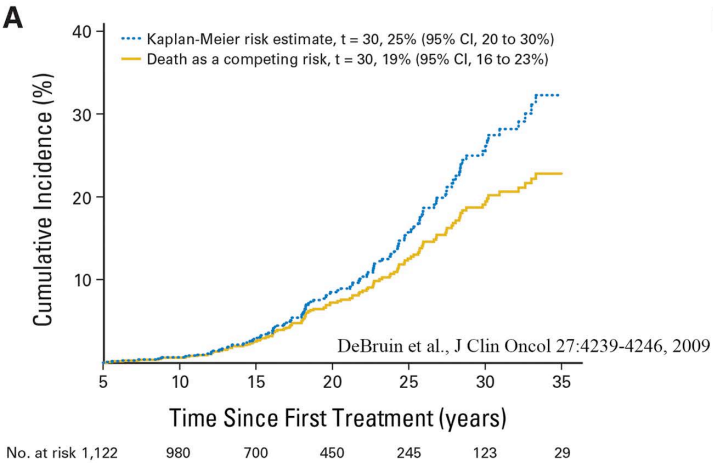
Brenner DJ et al. *Cancer* 2000

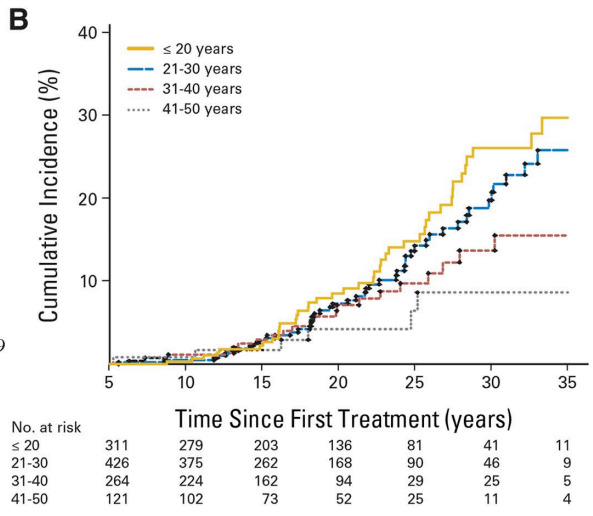


Percentage Increase in Relative Risk for RT vs Surgery

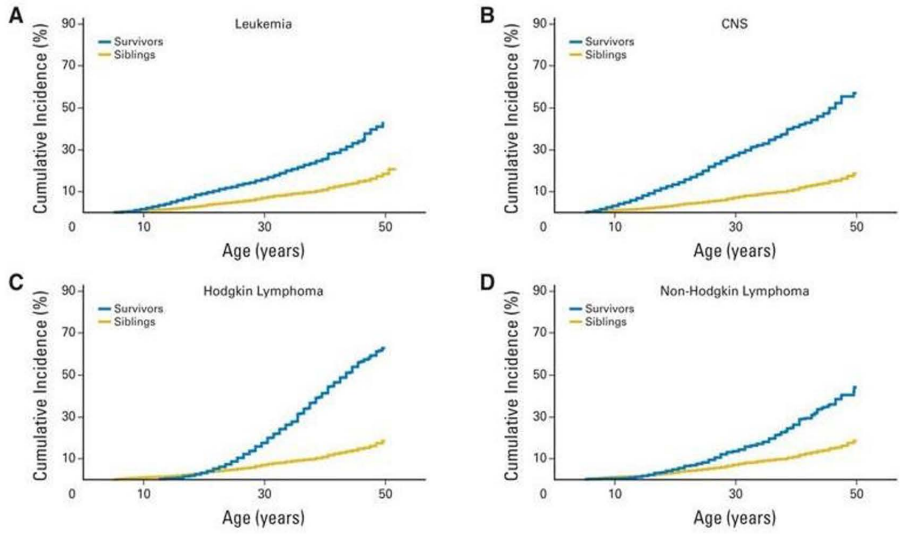
The risk of a radiation-induced sarcoma in or near the original treatment field is increased by over a factor of two at 10 years after treatment.

Hodgkin's Disease Survivors





Cumulative incidence of breast cancer (DCIS and invasive combined) after prior treatment for Hodgkin lymphoma.
Panel A: Incidence as a function of time since completion of Hodgkin's treatment (with death as a competing risk).
Panel B: Incidence as a function of time since completion of Hodgkin's treatment, grouped by age at time of treament.

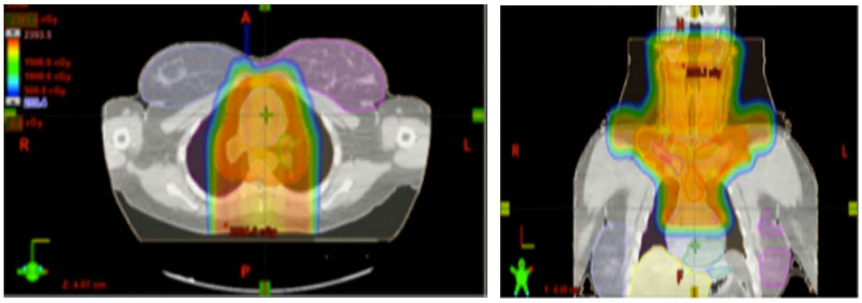


Cumulative incidence of severe, disabling, life-threatening, or fatal late effects by primary childhood cancer diagnosis. (A) Leukemia, (B) CNS tumors, (C) Hodgkin lymphoma, (D) Non-Hodgkin lymphoma.

Incidence of comparable effects also shown for (non-treated) siblings.

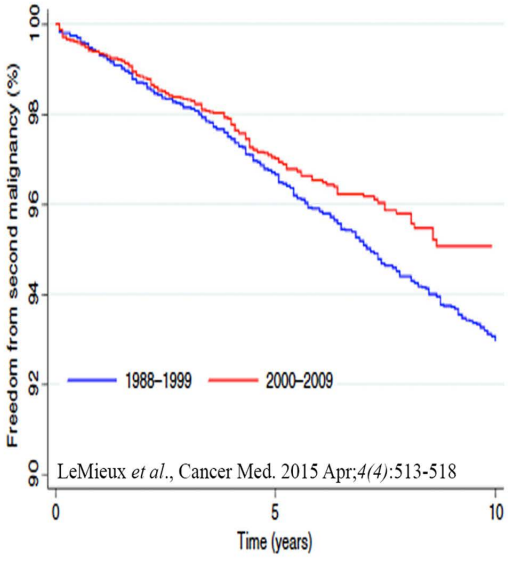
J Clin Oncol 2014;*32(12)*:1218-1227.

Will these radiation-induced second cancers continue to increase over time? After all, the conformality of our treatments has greatly improved over the last 30 years, meaning less and less normal tissue is now in the radiation field compared to the past...



Today, radiotherapy for Hodgkin lymphoma spares a lot more breast tissue, and lung, and heart, than it used to back in the 1970's and 80's. (And it is the women who were treated then as children/adolescents who are currently showing the highest rates of second cancers.)

Answer: Given the long latency periods involved, it's still hard to tell, although there is *some* evidence the problem may be abating



Freedom from second malignancy (FFSM). FFSM in patients diagnosed in 1988–1999 versus 2000–2009.

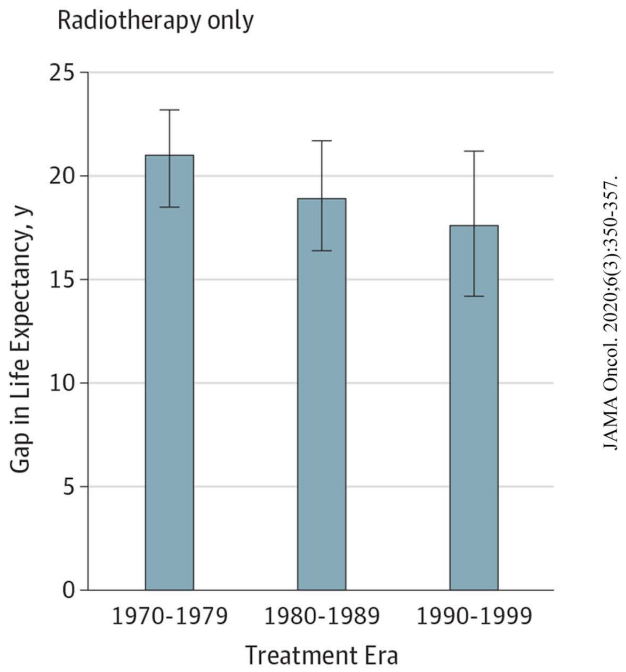
Second malignancy characteristics by year-group of diagnosis.

	1988–1999 (*n* = 3463)	2000–2009 (*n* = 5344)
Second malignancies (*n*)	376 (10.9%)	147 (2.8%)
Secondary tumor location (selected sites)	*n* (%)	*n* (%)
Breast	77 (21%)	15 (10%)
Lung	61 (16%)	17 (12%)
Prostate	26 (7%)	17 (12%)

This recent study seems to show fewer second cancers in radiotherapy patients treated between 2000 and 2009, than between 1988 and 1999 (particularly for breast cancer).

Another - if indirect - piece of evidence that late effects of childhood cancer treatment (second cancers and heart disease in particular) have decreased a bit over time as radiation therapy techniques have improved

Projected Gap in Life Expectancy Among Childhood Cancer Survivors



JAMA Oncol. 2020;6(3):350-357.

Projected gaps in life expectancy compared to the general population for survivors of childhood cancer who had received radiotherapy alone, as a function of decade when treated.

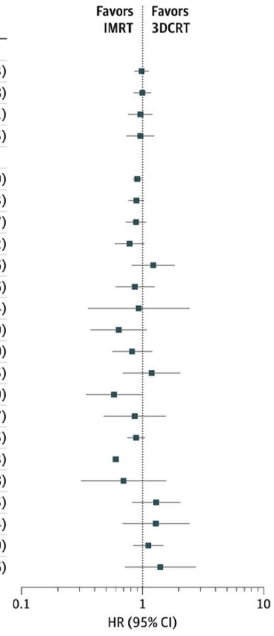
What about the advent of IMRT? Has it led to a *decrease* in second cancers? Or an *increase*?

1. when IMRT was first introduced, there was concern that there'd be an increased risk of radiation carcinogenesis because of the higher integral dose to the whole body

Association Between Radiotherapy Type and Second Primary Cancers Among Male Prostate Cancer Survivors in the Linked SEER-Medicare Cohort

JAMA Oncol. doi:10.1001/jamaoncol.2023.1638

Second cancer type	Events, (IMRT/3DCRT)	HR (95% CI)
Hematologic cancers		
All hematological cancers	603/504	0.98 (0.86-1.13)
All lymphoid cancers	392/333	1.00 (0.84-1.18)
All myeloid cancers	211/171	0.96 (0.76-1.21)
AML/MDS	162/124	0.96 (0.73-1.25)
Solid cancers		
All solid cancers	1306/1382	0.91 (0.83-0.99)
Sites likely in-field tumors	410/456	0.89 (0.77-1.03)
Bladder	237/276	0.88 (0.73-1.07)
Colon	114/124	0.77 (0.58-1.02)
Anorectum	59/56	1.23 (0.82-1.86)
Kidney and renal pelvis	68/70	0.87 (0.60-1.26)
Other urinary cancers	<11/12	0.93 (0.36-2.44)
Stomach	27/45	0.64 (0.37-1.09)
Pancreas	60/74	0.82 (0.56-1.20)
Liver	39/27	1.19 (0.69-2.05)
Esophagus	30/37	0.58 (0.34-0.99)
Other GI cancers	26/29	0.87 (0.48-1.57)
Lung	345/333	0.88 (0.75-1.05)
Larynx	21/29	0.60 (0.32-1.13)
Thyroid	11/20	0.70 (0.31-1.58)
Oral cavity/pharynx	54/41	1.30 (0.82-2.05)
Soft tissue sarcoma	29/20	1.29 (0.69-2.44)
Melanoma	113/124	1.12 (0.84-1.49)
CNS	22/20	1.40 (0.71-2.76)

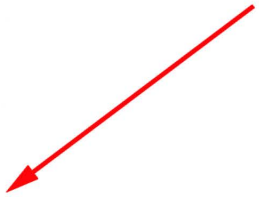


This study of second malignancies after prostate cancer radiotherapy suggests otherwise, i.e., *that the use of IMRT did not increase second cancer risks in a variety off tissues/organs compared to 3D-CRT.*

All things considered though, a second cancer caused by prior radiotherapy is NOT a huge problem overall, although it does vary by site and it's a bigger issue if the prior radiotherapy was during childhood or adolescence

Estimated number of excess second solid cancers attributable to radiotherapy of first cancer sites

First cancer site	Observed second cancers	Excess number	Percentage (%) attributable to radiotherapy
Brain	314	28	9
Testes	628	150	24
Prostate	11,292	1131	10
Lung	2,395	152	6
Head and neck	7,166	375	5
Breast	12,450	660	5
All	42,294	3266	8



What about reducing the number of medical imaging procedures (or the dose per procedure) as another means of reducing the risk of radiation carcinogenesis?

Trends in medical imaging radiation exposure from 2006 to 2016

	2006		2016	
	No. of procedures	Avg. individual effective dose	No. of procedures	Avg. individual effective dose
Radiography	281 million	0.3 mSv	275 million	0.22 mSv
CT	62 million	1.46 mSv	74 million	1.37 mSv
Nuclear medicine	17 million	0.73 mSv	13.5 million	0.32 mSv
Noncardiac interventional fluoroscopy	12 million	0.2 mSv	4 million	0.12 mSv
Cardiac interventional fluoroscopy	4.6 million	0.23 mSv	4.1 million	0.13 mSv

There has been progress in reducing the number of imaging procedures per year (and therefore, the annual individual effective dose) between 2006 and 2016. However, the number of CT scans - the worst offenders - did not drop overall over that time period, but did drop from an all-time high of ~85M/year in the early 2010s. (The effective dose from CT scanning did drop a little though.)

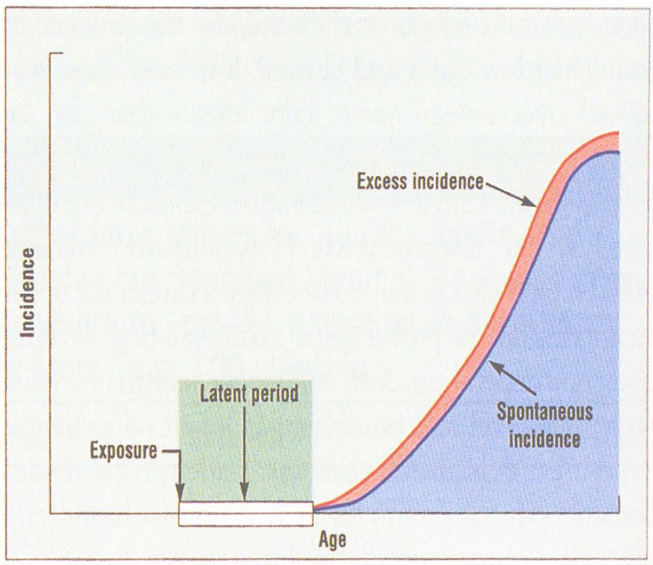
C. How Radiation Carcinogenesis Data are Turned into Risk Estimates for Radiation Protection Purposes

1. to use the human data for the purposes of numerical risk estimation, it is first necessary to use a risk model to fit it (main reason being that the data is not all that robust to start with)

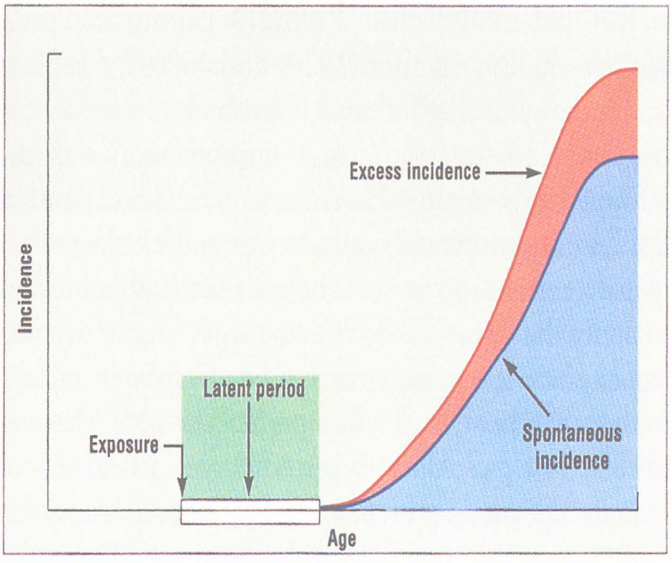
a) at present, there are two models used, the ***absolute risk model (seems to work best for radiation-induced leukemias)*** and the ***relative risk model (favored for solid tumor induction by radiation)***

The absolute risk model assumes that the radiation induces a discrete "crop" of excess cancers that, after the appropriate latency period are ADDED to the natural incidence of that type of cancer. Then, once all the excess cases are manifest, the incidence of that type of cancer returns to its spontaneous levels.

Radiation-induced leukemia incidence for the Japanese A-bomb survivors seems to follow the absolute risk model.



ABSOLUTE RISK MODEL



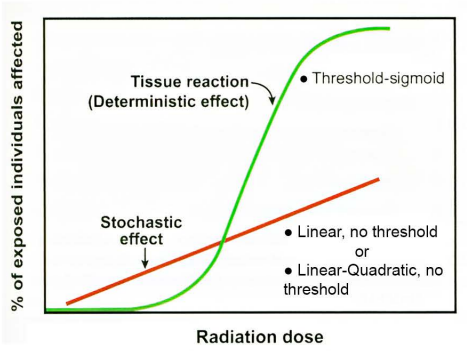
RELATIVE RISK MODEL

The relative risk model assumes that radiation causes a *multiplicative* increase in the natural cancer incidence, meaning that most of the radiation-induced cancers will manifest when the spontaneous ones do, that is, in older age.

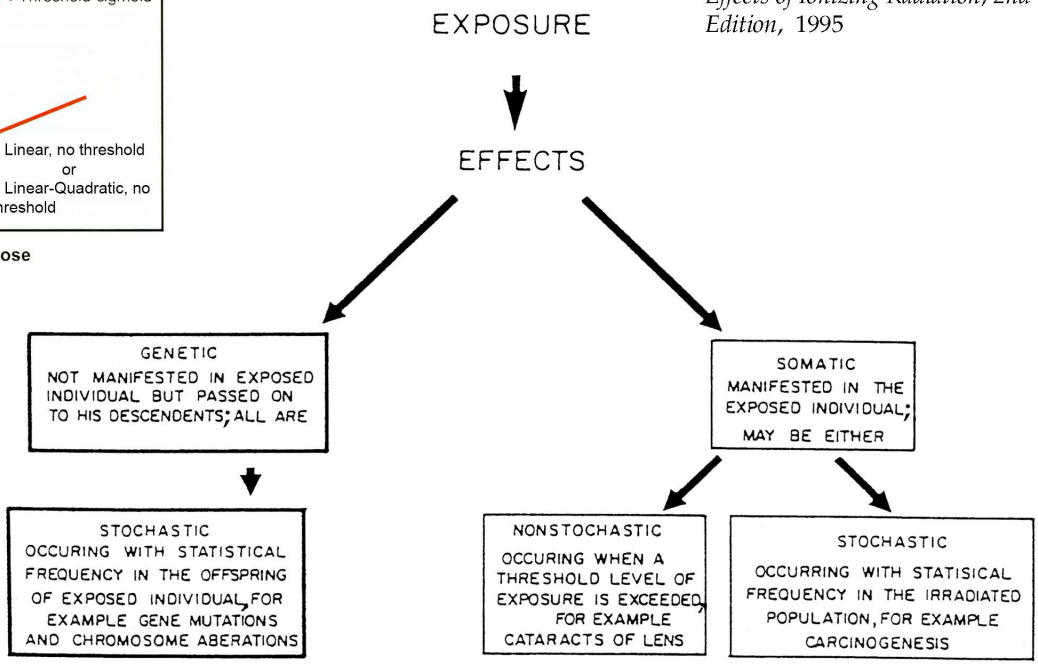
Solid tumor data for the Japanese A-bomb survivors seem to seem to follow the relative risk model (more or less - see below). This explains why, 70 years after the fact, that epidemiological studies of the Japanese survivors are still ongoing.

Radiation Protection Standards - how all the negative biological consequences of exposure to ionizing radiation are redefined in terms of numerical risk estimates and maximum permissible doses

1. **What are the radiation-induced effects that we want to protect ourselves from?**
   a. answer: *both the possible genetic and somatic consequences of exposure to ionizing radiation*



From: Mettler and Upton. *Medical Effects of Ionizing Radiation, 2nd Edition*, 1995



1) **"genetic effects" occur in the descendants of the individual who received the exposure, and are stochastic in nature (example: mutagenesis, carcinogenesis)**

2) **"somatic effects" occur in the exposed individual, and may be stochastic (example: carcinogenesis) or non-stochastic (example: cataracts) in nature**

b. *stochastic vs. non-stochastic: what's the difference????*

1) **stochastic effects are "all or nothing", and occur with a certain statistical frequency in an irradiated population**

2) **non-stochastic (deterministic) effects are now called "tissue reactions", and only occur once a threshold level of exposure is exceeded, and will vary in severity depending on dose**

Who is in charge of evaluating the scientific data, formulating the radiation exposure standards, and enforcing radiation safety compliance in the workplace?

Answer: A veritable alphabet soup of different committees, agencies and organizations!

• Evaluates the current scientific data on radiation effects

Biological Effects of Ionizing Radiations (BEIR) Committee - made up of senior radiation scientists appointed by the National Academy of Sciences; they meet every 5-7 years and make recommendations about whether the safety standards need to change or not *(International equivalent: UNSCEAR)*

- Formulates the language of radiation safety and establishes exposure limits for radiation workers and the general public

National Council on Radiological Protection and Measurement (NCRP) - made up of senior radiation safety experts and administrators appointed by Congress, who review the BEIR Committee findings and come up with the radiation safety standards accordingly *(International equivalent: ICRP)*

- Enforcers of NCRP regulations - can vary or overlap depending on the situation

Environmental Protection Agency (EPA) - mainly concerned with radioactive materials (radon, radionuclides, radiation sources, etc.) released into the environment

Nuclear Regulatory Commission (NRC) - enforces radiation safety standards at nuclear power plants and experimental reactors, but **also is in charge of radioactive materials used medically and in research**

Food and Drug Administration (FDA) - along with food and drugs, **also has regulatory oversight of "medical devices", including those that generate radiation (equipment) and/or facilitate its delivery (software, etc.)**

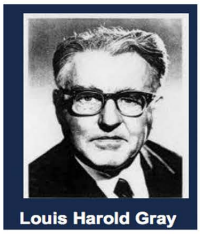
Occupational Safety and Health Administration (OSHA) - mainly involved with employee safety in the workplace, sometimes including radiation safety

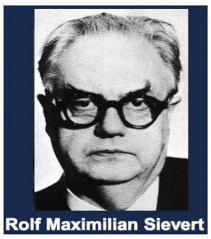
Department of Energy (DOE) - enforces radiation safety standards at national laboratories and military installations

Department of Transportation (DOT) - concerned with the safety of inter- and intra-state transport of hazardous materials, including radioactive ones

Department of Homeland Security (DHS) - concerned with reducing the likelihood of domestic terrorism, including that involving the use of radioactive materials (cesium-137 in particular)

Radiation Protection Terminology


Louis Harold Gray


Rolf Maximilian Sievert

Absorbed dose vs Equivalent dose

the absorbed dose is the energy imparted by ionizing radiation per unit mass of irradiated material; the current unit is the Gray (Gy)

the dose equivalent is the quantity used for radiation protection purposes, that corrects the absorbed dose by a factor related to the biological potency of the type of radiation (low vs. high LET); the current unit of dose equivalent is the Sievert (Sv)

1] the correction factor that converts absorbed dose to dose equivalent is called the *radiation weighting factor* (W_R) :

Equivalent dose (**Sv**) = Radiation weighting factor w_R × Absorbed dose (**Gy**)

Type of radiation	Radiation weighting factor w_R
γ-rays, X-rays, β-particles	**1**
Proton beams	**2**
α-particles, heavy ions	**20**
Neutron beams	**2.5～21**

Equivalent Dose vs. Effective Dose

a} even knowing the equivalent dose is not enough to fully describe the biological effects of exposure to radiation, reason being that certain tissues are more or less sensitive to radiation effects, and that this needs to be taken into account as well (especially in the case of whole-body irradiation where all tissues are affected, or in the case of ingested radioactive materials that spread all over the body)

b] therefore, a new term is needed: **the effective dose, which is the dose equivalent corrected by another factor (the *tissue weighting factor,* W_T) that corrects for the risk to particular tissues**

Effective dose (Sv) = Σ (Tissue weighting factor w_T × Equivalent dose)

Tissue	Tissue weighting factor w_T
Red bone marrow, colon, lungs, stomach, breasts	**0.12**
Gonad	**0.08**
Bladder, esophagus, liver, thyroid	**0.04**
Bone surface, brain, salivary gland, skin	**0.01**
Total of the remaining tissues	**0.12**

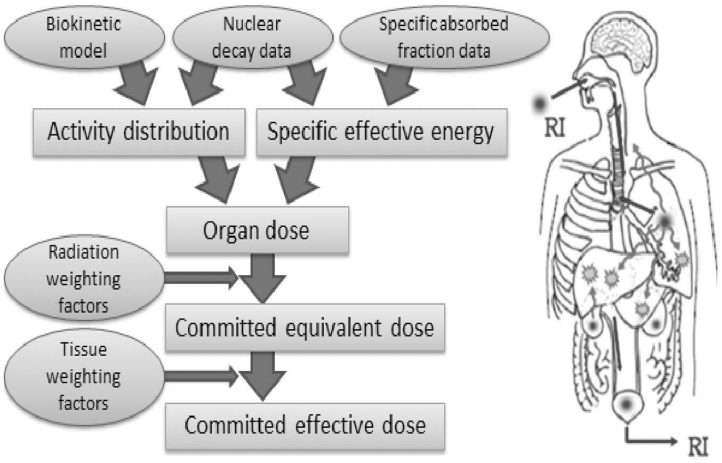
Source: 2007 Recommendations of the ICRP

c] **the effective dose is also expressed in units of Sv**, and in order to estimate the total risk to an individual receiving whole-body irradiation, you'd need to add up the effective doses for all the tissues in the body

Effective Dose vs. Committed Dose

The term committed dose (or committed dose equivalent is used for the special case where the exposure comes from radionuclides that have been ***ingested***, i.e., they are "committed" to irradiate the individual for as long as their physical and biological half-lives permit. The appropriate unit is Sievert.

Unless otherwise indicated,this committed time period is assumed to be 50 years, that is, the average working lifetime of an adult



Collective Dose

the collective dose (or collective or committed dose equivalent) refers to the case where a population, rather than an individual is irradiated, and that the total estimate of risk has to be summed up for all the irradiated individuals in that population; units = person-sievert or man-rem

Summary of Quantities and Units Used in Radiation Protection

Quantity	Definition	Unit	
		New	Old
Absorbed dose	Energy per unit mass	Gray	Rad
For individuals			
Equivalent dose (Radiation weighted dose)	Average dose × radiation weighting factor	Sievert	Rem
Effective dose	Sum of equivalent doses to organs and tissues exposed, each multiplied by the appropriate tissue weighting factor	Sievert	Rem
Committed equivalent dose	Equivalent dose integrated over 50 years (relevant to incorporaated radionuclides)	Sievert	Rem
Committed effective dose	Effective dose integrated over 50 years (relevant to incorporated radionuclides)	Sievert	Rem
For populations			
Collective effective dose	Product of the average effective dose and the number of individuals exposed	Person-sievert	Man-rem
Collective committed effective dose	Integration of the collective dose over 50 years (relevant to incorporated radionuclides)	Person-sievert	Man-rem

From: Hall and Giaccia, *Radiobiology for the Radiologist, 6th Edition*, 2006

Overriding Principles of Radiation Protection

1. just because there are specific annual exposure limits for radiation workers and the general population, this doesn't mean that an individual should "shoot for" that exposure each year!

2. instead **there are overriding principles of radiation protection that should be followed above and beyond the upper limits dictated by the rules and regulations**

a] **ALARA, "As Low as Reasonably Achievable":**

a) most of the time, *the ALARA rule can be implemented by: keeping the* ***time*** *of exposure to radiation as short as possible; keeping the* ***distance*** *between the source of radiation and the exposed individual as large as possible; and inserting* ***shielding*** *material between the source of radiation and the exposed individual*

b] **GSD, "Genetically Significant Dose":**

1) *the dose of radiation to the gonads weighted for the age and sex distribution in those members of an irradiated population expected to have offspring; measured in Sieverts*; pretty much the same idea as "effective dose", except specific to the gonads

Annual genetically significant dose (GSD) in the U.S. population

Source	Contributions to GSD in mrems (mSv)
Natural sources	
Radon	10 (0.1)
Other	90 (0.9)
Medical	
Diagnostic x-rays	20–30 (0.2–0.3)
Nuclear medicine	2 (0.02)
Consumer products	5 (0.05)
Occupational	~0.6 (0.006)
Nuclear fuel cycle	<0.05 (0.0005)
Miscellaneous environmental sources	<0.1 (0.001)
Total	~132 (1.32)

NCRP report No. 93, 1987

c] **NIRL, "Negligible Individual Risk Level":**

2) *the NIRL is defined as "the radiation dose below which the risks of undesirable health effects are considered negligible, and that no efforts to monitor, alert, or reduce radiation exposure are required" (currently estimated to be about* 0.01 mSv per year)

Current US Radiation Protection Risk Estimates and Exposure Limits

a) **today's radiation protection standards are designed to keep the risks of stochastic and non-stochastic radiation effects to members of the whole population no greater than the comparable annual risk of a fatal accident in other, so-called "safe" industries (estimated at about 2 fatalities/10,000 workers or 2 x 10^{-4})**

these calculations are based on the assumption that the dose response for radiation effects is linear, with no threshold dose; this is a consevative approach, and probably overestimates the risk in some situations

Risk Estimates for a Radiation-Induced, FATAL Cancer

Risks of Cancer Lethality by Radiation

"Infrequent Exposure" — applies to accidental or medically-necessary exposures

applies to day-to-day low-level exposure (like occupational) — "Frequent Exposure"

	High Dose High Dose Rate	Low Dose Low Dose Rate
Working population	8×10^{-2} per Sv	4×10^{-2} per Sv
Whole population (includes children and the elderly)	10×10^{-2} per Sv	5×10^{-2} per Sv

International Commission on Radiological Protection: Recommendations. *Annals of the ICRP Publication 60*, Oxford, England, Pergamon Press, 1990

Summary of Recommended Annual Radiation Dose Limits: National versus International Regulatory Agencies

	NCRP	ICRP (If Different)
Occupational Exposure:		
Stochastic effects: effective dose limits		
Cumulative	10 mSv × age	20 mSv/y averaged over 5 years
Annual	50 mSv/y	50 mSv/y
Deterministic effects: dose equivalent limits for tissues and organs (annual):		
Lens of eye (*New as of 2017*)	50 mGy/y*	20 mSv/y averaged over 5 years
Skin, hands, and feet	500 mGy/y	500 mSv/y
Embryo/Fetus Exposure:		
Effective dose limit after pregnancy declared	0.5 mSv/month	Total of 1 mSv to abdomen surface

*For tissue reactions, the unit preferred by the NCRP is "mGy" rather than "mSv"

Summary of Recommended Annual Radiation Dose Limits: National versus International Regulatory Agencies

	NCRP	ICRP (If Different)
Public Exposure (annual):		
Effective dose limit, continuous or frequent exposure	1 mSv/y	No distinction between frequent and infrequent—1 mSv/y
Effective dose limit, infrequent exposure	5 mSv/y	
Dose equivalent limits; lens of the eye	15 mGy/y	2 mSv/y
Skin and extremities	50 mGy/y	50 mSv/y
Education and Training Exposure (annual):		
Effective dose limit	1 mSv/y	No statement
Dose equivalent limit for lens of eye	15 mGy/y	No statement
Skin and extremities	50 mGy/y	No statement
Negligible Individual Dose (annual):	0.01 mSv/y	No statement

Based on National Council on Radiation Protection and Measurements: *Recommendations on Limits for Exposure to Ionizing Radiation.* NCRP Report No. 116. Bethesda, MD; 1993; and International Commission on Radiation Protection: *Recommendations of the ICRP.* ICRP Publication 103. New York, NY: Pergamon Press; 2007.

Lots of Ways of Expressing Risk

Activities Estimated to Increase Risk of Death by One Chance in a Million

Activity	Cause of Death
Smoking 1 cigarette	Cancer, heart disease
Drinking half liter of wine	Cirrhosis of the liver
Spending 1 hr in a coal mine	Black lung disease
Spending 3 hr in a coal mine	Accident
Living 2 days in New York or Boston	Air pollution
Rock climbing for 1.5 min	Accident
Traveling 6 min by canoe	Accident
Traveling 10 miles by bicycle	Accident
Traveling 30–60 miles by car	Accident
Flying 1000 miles by jet	Accident
Flying 6000 miles by jet	Cancer caused by cosmic radiation
Living 2 mo in Denver	Cancer caused by cosmic radiation
Living 2 mo in an average city	Cancer caused by natural radioactivity
Being a man age 60 for 20 min	Illness
One chest x-ray taken in a good hospital	Cancer caused by radiation
Living 2 mo with a cigarette smoker	Cancer, heart disease
Eating 40 tsp of peanut butter	Liver cancer caused by aflatoxin B
Drinking Miami drinking water for 1 yr	Cancer caused by chloroform
Drinking 30 cans (12 oz) of diet soda	Cancer caused by saccharin
Living 5 yr at site boundary of a typical nuclear power plant in the open	Cancer caused by radiation
Drinking 1000 soft drinks from recently banned (24 oz) plastic bottles	Cancer from acrylonitrile monomer
Living 20 yr near PVC plant	Cancer caused from vinyl chloride (1976 standard)
Living 150 yr within 20 miles of a nuclear power plant	Cancer caused by radiation
Eating 100 charcoal-broiled steaks	Cancer from benzopyrene
Risk of accident by living within 5 miles of a nuclear reactor for 50 yr	Cancer caused by radiation

From Pochin E: Why be quantitative about radiation risk estimates? NCRP Annual Meeting. Crystal City, MD: NCRP, 1978; Cohen EL, Lee IS: A catalog of risks. Health Phys 1979;36:707–722; Wilson R: Analyzing the daily risks of life. Technol Rev 1979;81(4):40.

Average Reduction in Lifespan (Days)

Occupation	For 1 yr of Working Life	For 35 yrs of Working Life
Deep sea fishing	32	923
Coal mining	3.6	103
Oil refinery	2.6	74
Railways	2.2	63
Construction	2.1	62
Industry (average value)	0.5	13.5
Occupational exposure to radiation at the annual limit of 50 mSv (5 rem)	1.3	32
Occupational exposure to radiation at 5mSv (0.5 rem)	0.1	3

Annual Risk of Dying from Various Activities

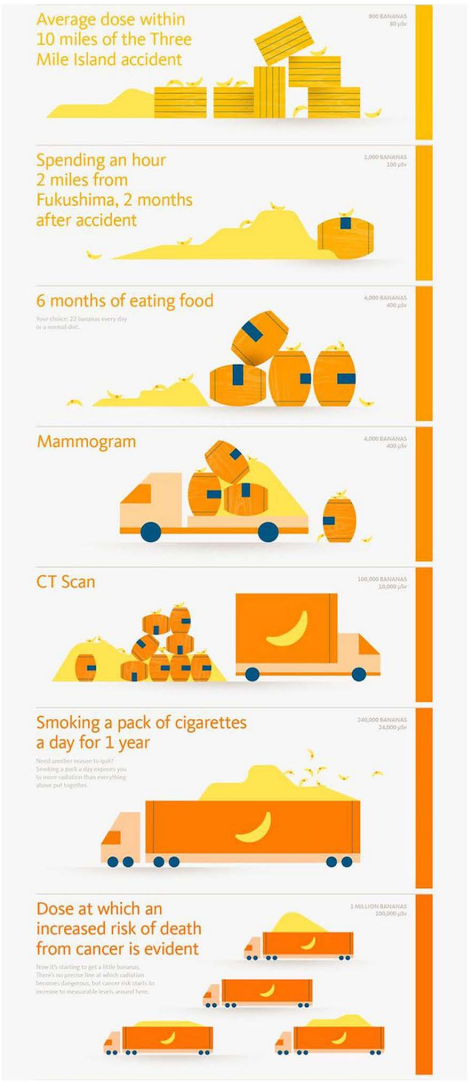
Risk Comparisons: Annual Risk of Dying in the U.S. per Million Persons at Risk	
Cause Deaths	**Death per 1,000,000/year**
Heart disease	2800
All cancers	2050
Parachutist	2000
Fire fighter; Hang glider	800
Lung cancer	590
Pneumonia	320
Diabetes; Police officer	230
Motor vehicle accidents; Breast cancer	160
Homicide	80
Falls	50
Foodborne bacteria	36
Accidental poisoning (drugs and medication)	30
Fires and burns; Drowning	15
Tuberculosis; Firearms	5
Choking, inhalation or ingestion of foreign object/food	4
Electric current; Railway	2
Airline crash (one trip)	0.6
Floods	0.4
Lightning; Insect bite or sting	0.2
Hit by falling aircraft	0.06
Hurricane	0.04
Sources: 1997 US Statistical Abstract; National Safety Council (1995), *Accident Facts;* Crouch & Wilson (1982), *Risk/Benefit Analysis.*	

Comparison of the Risks of Some Medical Exams

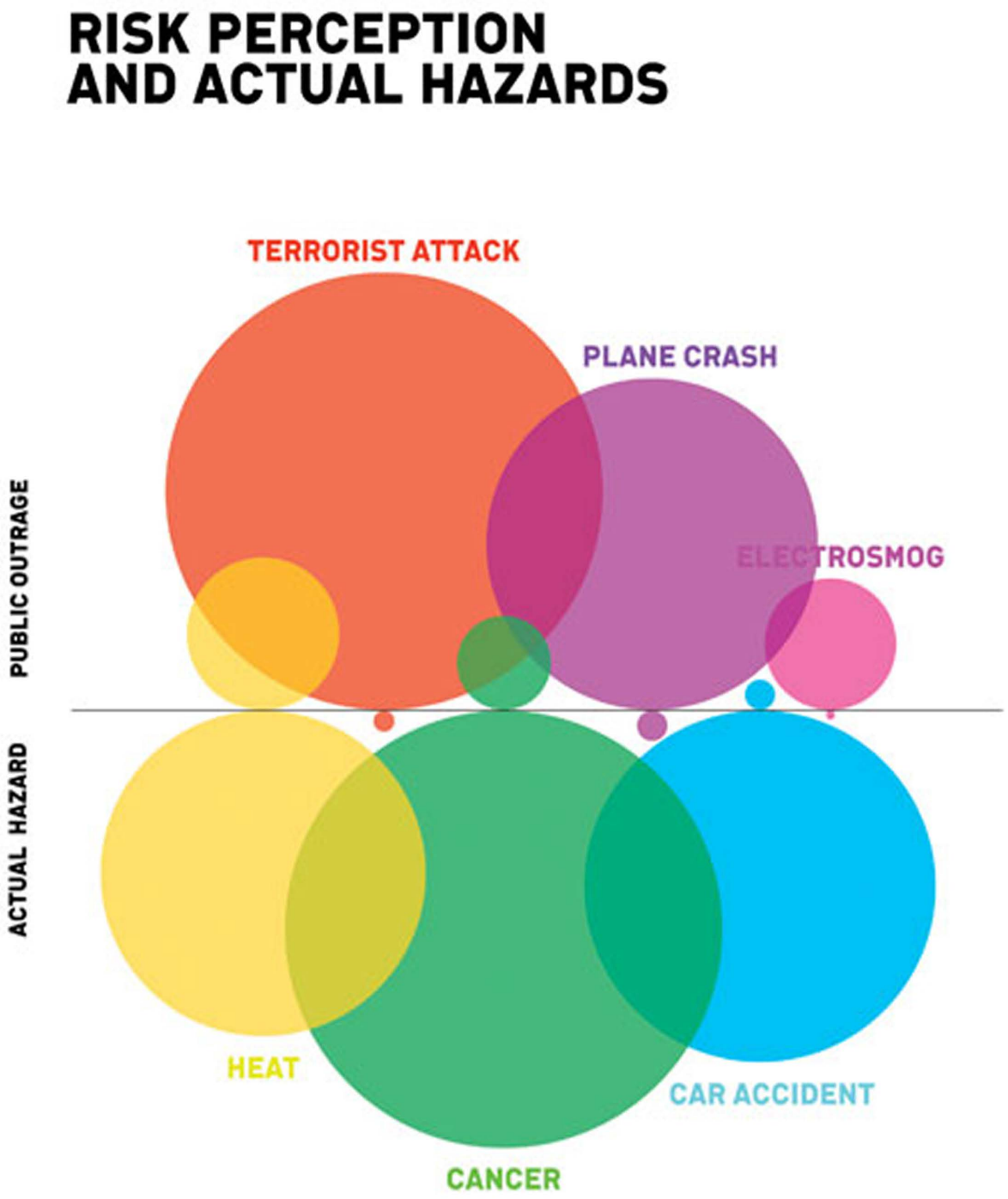
Radiation Dose to Adults From Common Imaging Examinations

Procedure		Approximate effective radiation dose	Comparable to natural background radiation for	Equivalent to Number of Cigarettes Smoked	Equivalent to Number of Highway Miles Driven
ABDOMINAL REGION	Computed Tomography (CT) — Abdomen and Pelvis	10 mSv	3 years	2219	5429
	Computed Tomography (CT) — Abdomen and Pelvis, repeated with and without contrast material	20 mSv	7 years		
	Computed Tomography (CT) — Colonography	6 mSv	2 years		
	Intravenous Pyelogram (IVP)	3 mSv	1 year	1226	3000
	Radiography (X-ray) — Lower GI Tract	8 mSv	3 years		
	Radiography (X-ray) — Upper GI Tract	6 mSv	2 years		
BONE	Radiography (X-ray) — Spine	1.5 mSv	6 months	292	714
	Radiography (X-ray) — Extremity	0.001 mSv	3 hours		
CENTRAL NERVOUS SYSTEM	Computed Tomography (CT) — Head	2 mSv	8 months	526	1286
	Computed Tomography (CT) — Head, repeated with and without contrast material	4 mSv	16 months		
	Computed Tomography (CT) — Spine	6 mSv	2 years		
CHEST	Computed Tomography (CT) — Chest	7 mSv	2 years	2277	5571
	Computed Tomography (CT) — Lung Cancer Screening	1.5 mSv	6 months		
	Radiography — Chest	0.1 mSv	10 days	12	29
DENTAL	Intraoral X-ray	0.005 mSv	1 day		
HEART	Coronary Computed Tomography Angiography (CTA)	12 mSv	4 years		
	Cardiac CT for Calcium Scoring	3 mSv	1 year		
MEN'S IMAGING	Bone Densitometry (DEXA)	0.001 mSv	3 hours		
NUCLEAR MEDICINE	Positron Emission Tomography — Computed Tomography (PET/CT)	25 mSv	8 years		
WOMEN'S IMAGING	Bone Densitometry (DEXA)	0.001 mSv	3 hours		
	Mammography	0.4 mSv	7 weeks	29	71

Plus there's always "Dose Expressed in Banana Equivalents"



Let's face it, we're all really bad at assessing risk!



S. Shertrich, "Devices that Alter Perception", UbiComp 2008 Workshop, London

"Electrosmog" = the accumulation of different electromagnetic influences in a single area, such as from cell phones and cell towers, wifi networks, power lines, utility meters, TVs, radios, microwave ovens, etc.