Review of the Radiobiological Principles of Radiation Protection

Cari Borrás, D.Sc., FAAPM, FACR
Radiological Physics and Health Services Consultant
Washington DC, USA

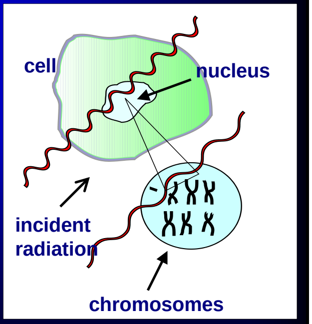
Learning Objectives

1. To understand the radiobiological basis of radiation protection standards.
2. To define the radiation protection magnitudes and units, their values and their practical measurement.
3. To distinguish between stochastic and deterministic effects.

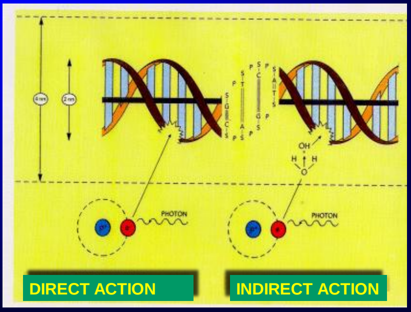
Radiation Effects

Ionizing radiation interacts at the cellular level:

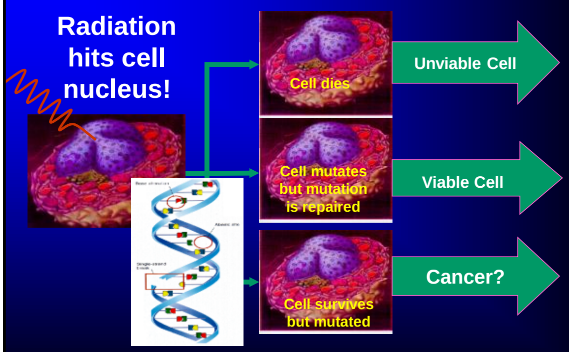
- ionization
- chemical changes
- biological effect



Interaction of ionizing radiation with DNA, the critical target



Outcomes after Cell Exposure



http://rpop.iaea.org/

DNA Damage

There are qualitative and quantitative differences in initial DNA damage caused by radiation

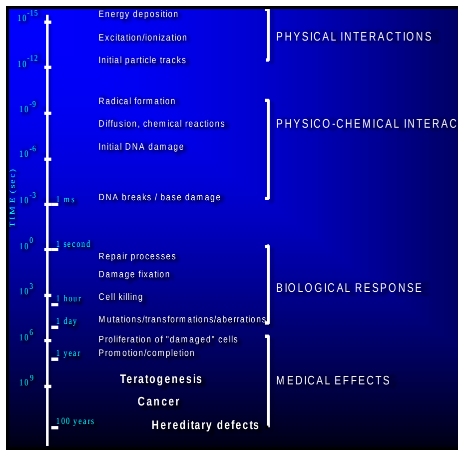
- DNA damage caused by radiation exhibits multiply damaged sites and clustered legions
- Double strand breaks are more common in radiation-induced damage than single strand breaks, which are more common in normal endogenous DNA damage.

http://lowdose.energy.gov/pdf/Powerpoint_WEBBystander.pdf

How does radiation interact with cells?

Past Theory	Present Theories
Hit theory	**Bystander effects**
Radiation causes free radicals to damage only the cell that is "hit" by direct ionization	Radiation causes free radicals to trigger cell-cell communication and cell-matrix communication to cells other than those which are "hit" by the direct ionization.

http://lowdose.energy.gov/pdf/Powerpoint_WEBBystander.pdf



Timing of events leading to radiation effects.

RP Dosimetric Quantities and Units
Tissue Reactions

Dose to Tissue = Absorbed Dose * RBE (Gy)

RBE : radiobiological effectiveness

differs for

- different biological endpoints and
- different tissues or organs

RP Dosimetric Quantities and Units
Stochastic Effects
Evolution of Terminology

ICRP 26 (1977)	ICRP 60 (1991)	ICRP 103 (2007)
*	Equivalent Dose	Equivalent Dose#
Effective Dose Equivalent	Effective Dose	Effective Dose

* No specific term

Radiation Weighted Dose proposed but not accepted

The SI unit is J kg^{-1} and the special name is sievert (Sv)

RP Dosimetric Quantities and Units
Stochastic Effects (Sv)

Equivalent Dose, H_T, in a tissue T:

$$H_T = \Sigma_R \, w_R \; D_{T,R}$$

w_R is the radiation weighting factor, which accounts for the detriment caused by different types of radiation relative to photon irradiation

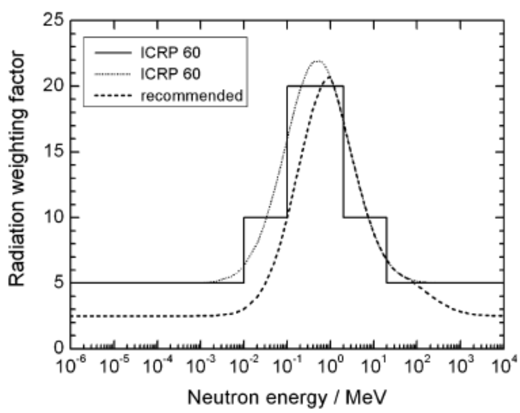
$D_{T,R}$ is the absorbed dose averaged over the tissue T due to radiation R

w_R values are derived from in vivo and in vitro RBE studies

They are independent of dose and dose rate in the low dose region

Radiation Weighting Factors (ICRP 103)

Radiation type and energy range	w_R
Photons	1
Electrons and muons	1
Protons (1991, 2007), pions (2007)	2
Alpha particles, fission fragments, heavy ions	20
Neutrons, energy < 10 keV	Continuous Function
10 keV to 100 keV	
> 100 keV to 2 MeV	
> 2 MeV to 20 MeV	
> 20 MeV	



RP Dosimetric Quantities and Units
Stochastic Effects (Sv)
Effective Dose, E

$$E = \Sigma_T \, w_T \, H_T = \Sigma_T \, \Sigma_R \, w_T \, w_R \, D_{R,T}$$

w_T represents the relative contribution of that tissue or organ to the total detriment resulting from uniform irradiation of the body

$$\Sigma_T \, w_T = 1$$

A uniform dose distribution in the whole body gives an effective dose numerically equal to the radiation-weighted dose in each organ and tissue of the body

Tissue Weighting Factors (ICRP 103)

Tissue	w_T	$\sum w_T$
Bone-marrow (red), Colon, Lung, Stomach, Breast, Remainder Tissues*	0.12	0.72
Gonads	0.08	0.08
Bladder, Oesophagus, Liver, Thyroid	0.04	0.16
Bone surface, Brain, Salivary glands, Skin	0.01	0.04
	Total	1.00

* Remainder Tissues: Adrenals, Extrathoracic region, Gall bladder, Heart, Kidneys, Lymphatic nodes, Muscle, Oral mucosa, Pancreas, Prostate, Small intestine, Spleen, Thymus and Uterus/cervix

RP Dosimetric Quantities and Units
Activity, A

The activity A of an amount of a radionuclide in particular energy state at a given time t is

$$A = dN / dt$$

where d N is the expectation value of the number of spontaneous nuclear transitions from that energy state in the time interval d t

The SI unit of activity is the Becquerel (Bq)

$$1 \text{ Bq} = 1 \text{ s}^{-1}$$

RP Dosimetric Quantities and Units
Stochastic Effects (Sv)

Committed Equivalent Dose

For radionuclides incorporated in the body

$$H_T(\tau) = \int_{t_0}^{t_0+\tau} \dot{H}_T(t)\,dt$$

where τ is the integration time following the intake at time t_0

Committed Effective Dose

$$E(\tau) = \sum_T w_T \cdot H_T(\tau)$$

τ

Adults: 50 y

Children: 70 y

Limitations of Equivalent and Effective Doses

- Are not directly measurable
- Point quantities needed for area monitoring (in a non-isotropic radiation field, effective dose depends on the body's orientation in that field)
- Instruments for radiation monitoring need to be calibrated in terms of a measurable quantity for which calibration standards exist

Operational protection quantities are needed!

RP Operational Quantities - ICRU
Dose Equivalent, H

$$H = Q * D \text{ (Sv)}$$

Where: D = Absorbed Dose

Q = Quality Factor, function of L_∞ (LET)

$$Q(L) = \begin{cases} 1 & \text{for } L < 10 \text{ keV}/\mu\text{m} \\ 0.32\,L - 2.2 & \text{for } 10 \le L \le 100 \text{ keV}/\mu\text{m} \\ 300/\sqrt{L} & \text{for } L > 100 \text{ keV}/\mu\text{m} \end{cases}$$

At a point in tissue:

$$Q = \frac{1}{D}\int_{L=0}^{\infty} Q(L) D_L \, dL$$

Where: D_L is the distribution of D in L for the charged particles contributing to D

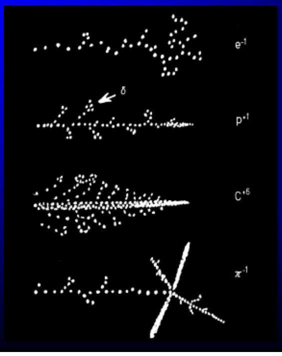
LET: average measure of the rate at which energy is imparted to the absorbing medium per unit distance of track length (keV μm^{-1})

electrons

protons

carbon ions

negative pions



alphas

http://rpop.iaea.org/

C. Borrás D.Sc. Thesis

Task	Operational quantities for	
	area monitoring	individual monitoring
Control of effective dose	ambient dose equivalent $H^*(10)$	personal dose equivalent $H_p(10)$
Control of skin dose	directional dose equivalent $H'(0.07, \Omega)$	personal dose equivalent $H_p(0.07)$

H*(10) and H_P (10) – photons > 12 keV and neutrons

H_P (0.07) – α and β particles and doses to extremities

Ω in RP usually not specified. Instead,

Maximum H'(0.07, Ω) is obtained by rotating meter seeking maximum reading

Assessment of Effective Dose from Individual Monitoring Data

$$E = H_p(10) + \sum_j e_{j,inh}(\tau) \cdot I_{j,inh} + \sum_j e_{j,ing}(\tau) \cdot I_{j,ing}$$

- **H_p (10) personal dose equivalent from external exposure**
- **$e_{j,inh}(\tau)$ is the committed effective dose coefficient for activity intakes by inhalation of radionuclide *j***
- **$I_{j,inh}$ is the activity intake of radionuclide *j* by inhalation**
- **$e_{j,ing}(\tau)$ is the committed effective dose coefficient for activity intakes of radionuclide *j* by ingestion**
- **$I_{j,ing}$ is the activity intake of radionuclide *j* by ingestion**

RP Dosimetric Quantities and Units

Stochastic Effects

Collective Effective Dose, S

(due to Individual Effective Doses E_1 and E_2)

$$S(E_1, E_2, \Delta T) = \int_{E_1}^{E_2} E \frac{dN}{dE} dE$$

- **d *N* / d *E* : number of individuals who experience an effective dose between *E* and *E* + *d E***
- **Δ*T* specifies the time period within which the effective doses are summed**

System of Quantities for Radiological Protection

Absorbed dose, D

Dose Quantities defined in the body	Operational Quantities
Equivalent dose, H_T, in an organ or tissue T ↓ Effective dose, E	**For external exposure** Dose quantities for area monitoring, individual monitoring
Committed doses, $H_T(\tau)$ and $E(\tau)$	**For internal exposure** Activity quantities in combination with biokinetic models and computations
Collective effective dose, S	

RP Dosimetric Quantities and Units

E is calculated averaging gender, age and individual sensitivity

Caveats

Effective Dose should not be used for

- Retrospective dose assessments
- Estimation of specific individual human exposures and risks
- Epidemiological studies without careful consideration of the uncertainties and limitations of the models and values used

RP Dosimetric Quantities and Units

Caveats

Dose to Individuals

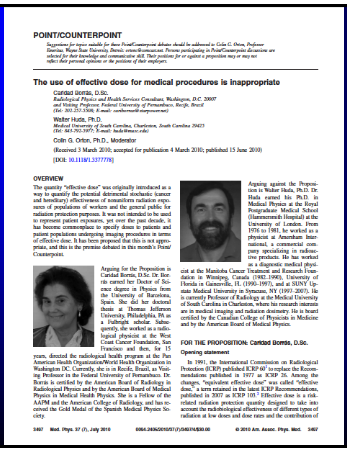
Absorbed doses to organs or tissues should be used with the most appropriate biokinetic parameters, biological effectiveness of the ionizing radiation and risk factor data, taking into consideration the associated uncertainties.

Medical exposures fall in this category!

Effective Dose vs Organ Doses in Medical Exposures

Effective Dose is an adequate parameter to intercompare doses from different radiological techniques

However, to assess individual risks it is necessary to determine organ doses



POINT/COUNTERPOINT

Suggestions for topics suitable for these Point/Counterpoint debates should be addressed to Colin G. Orton, Professor Emeritus, Wayne State University, Detroit: ortonc@comcast.net. Persons participating in Point/Counterpoint discussions are selected for their knowledge and communicative skill. Their positions for or against a proposition may or may not reflect their personal opinions or the positions of their employers.

The use of effective dose for medical procedures is inappropriate

Caridad Borrás, D.Sc.
Radiological Physics and Health Services Consultant, Washington, D.C. 20007 and Visiting Professor, Federal University of Pernambuco, Recife, Brazil (Tel: 202-257-5508; E-mail: cariborras@starpower.net)

Walter Huda, Ph.D.
Medical University of South Carolina, Charleston, South Carolina 29425 (Tel: 843-792-5977; E-mail: huda@musc.edu)

Colin G. Orton, Ph.D., Moderator

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OVERVIEW

The quantity "effective dose" was originally introduced as a way to quantify the potential detrimental stochastic (cancer and hereditary) effectiveness of nonuniform radiation exposures of populations of workers and the general public for radiation protection purposes. It was not intended to be used to represent patient exposures, yet over the past decade, it has become commonplace to specify doses to patients and patient populations undergoing imaging procedures in terms of effective dose. It has been proposed that this is not appropriate, and this is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Caridad Borrás, D.Sc. Dr. Borrás earned her Doctor of Science degree in Physics from the University of Barcelona, Spain. She did her doctoral thesis at Thomas Jefferson University, Philadelphia, PA as a Fulbright scholar. Subsequently, she worked as a radiological physicist at the West Coast Cancer Foundation, San Francisco and then, for 15 years, directed the radiological health program at the Pan American Health Organization/World Health Organization in Washington DC. Currently, she is in Recife, Brazil, as Visiting Professor in the Federal University of Pernambuco. Dr. Borrás is certified by the American Board of Radiology in Radiological Physics and by the American Board of Medical Physics in Medical Health Physics. She is a Fellow of the AAPM and the American College of Radiology, and has received the Gold Medal of the Spanish Medical Physics Society.

Arguing against the Proposition is Walter Huda, Ph.D. Dr. Huda earned his Ph.D. in Medical Physics at the Royal Postgraduate Medical School (Hammersmith Hospital) at the University of London. From 1976 to 1981, he worked as a physicist at Amersham International, a commercial company specializing in radioactive products. He has worked as a diagnostic medical physicist at the Manitoba Cancer Treatment and Research Foundation in Winnipeg, Canada (1982–1990), University of Florida in Gainesville, FL (1990–1997), and at SUNY Upstate Medical University in Syracuse, NY (1997–2007). He is currently Professor of Radiology at the Medical University of South Carolina in Charleston, where his research interests are in medical imaging and radiation dosimetry. He is board certified by the Canadian College of Physicists in Medicine and by the American Board of Medical Physics.

FOR THE PROPOSITION: Caridad Borrás, D.Sc.

Opening statement

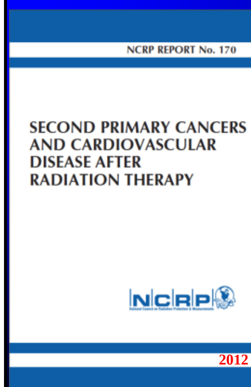
In 1991, the International Commission on Radiological Protection (ICRP) published ICRP 60[1] to replace the Recommendations published in 1977 as ICRP 26. Among the changes, "equivalent effective dose" was called "effective dose," a term retained in the latest ICRP Recommendations, published in 2007 as ICRP 103.[2] Effective dose is a risk-related radiation protection quantity designed to take into account the radiobiological effectiveness of different types of radiation at low doses and dose rates and the contribution of

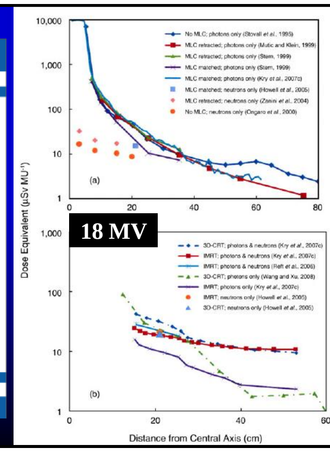
Methods for Determining Organ and Tissue Doses in Medical Imaging (ICRU 74, 2005)

- Measurements in physical phantoms
- Monte Carlo radiation transport calculations
  - Mathematical phantoms
  - Special features of the active bone marrow
  - Voxel phantoms
  - Anthropometric phantoms

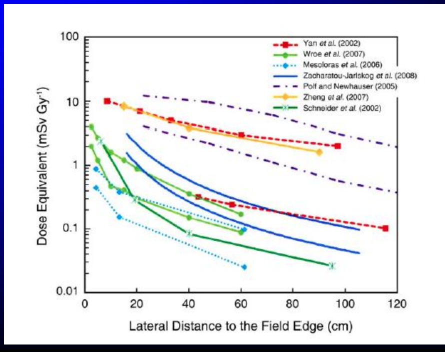
In radiation therapy, the TPS can calculate organ doses

How well?





Neutron Dose Equivalent as a Function of Distance to the Field edge



NCRP 170

THE AIM OF RADIATION PROTECTION

- To prevent (deterministic) harmful tissue effects
- To limit the probability of stochastic effects to levels deemed to be acceptable

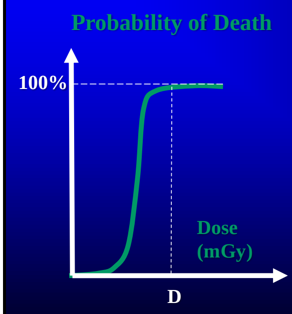
Deterministic Effects

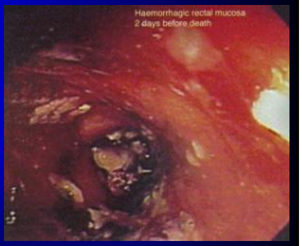
Radiation effects for which generally a threshold level of dose exists above which the severity of the effect is greater for a higher dose.

Stochastic Effects

Radiation effects, generally occurring without a threshold level of dose, whose probability is proportional to the dose and whose severity is independent of the dose.

Effects of Cell Death





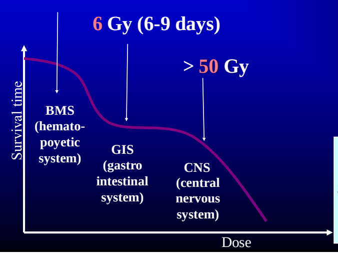
Co-60 Radiotherapy
Overexposure
Panama 2000-2001

Radiation Syndromes

(Whole Body Exposures)

Acute

Threshold: 0.5 Gy (3-7 days)
Death: 1 Gy, 2-3 Gy with medical care



Chronic

Annual radiation exposures exceeding 0.7 - 1.0 Gy and cumulative doses > 2-3 Gy over 2-3 years

$LD_{50/60}$ (Acute)

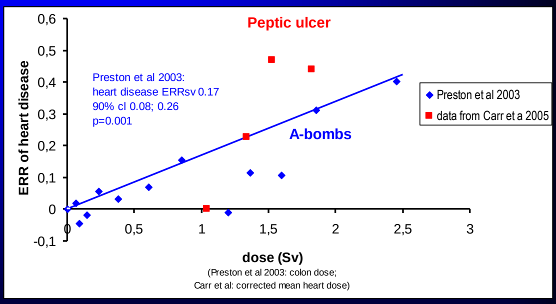
3.3 to 4.5 Gy no medical management

6 to 7 Gy with medical management

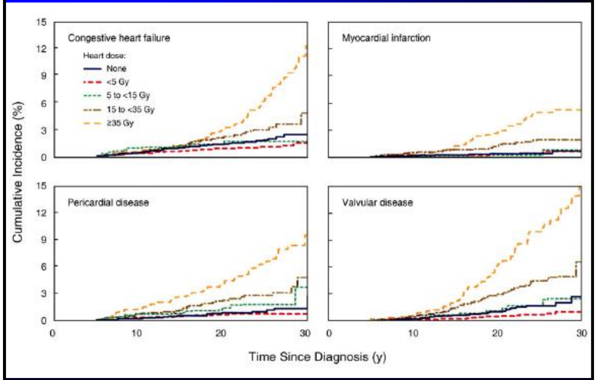
Radiation-induced Cardiovascular Disease

- **Radiotherapy** – well documented side effect of irradiation for breast cancer, Hodgkin's disease, peptic ulcers & others.
- **A-bomb data** – statistically significant dose-related incidence.
- **Chernobyl** – some evidence in the Russian study on emergency workers for a dose-related increase

Excess Relative Risk of Heart Disease



Cardiac Disorders among Childhood Cancer Survivors



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From current evidence, a judgement can be made of a threshold acute dose of about 0.5 Gy (or 500 mSv) for both cardiovascular disease and cerebrovascular disease. On that basis, 0.5 Gy may lead to approximately 1% of exposed individuals developing the disease in question, more than 10 years after exposure. This is in addition to the high natural incidence (circulatory diseases account for 30-50% of all deaths in most developed countries).

Draft ICRP on Tissue Effects. http://www.icrp.org/page.asp?id=116

Irradiation of Gonads

Threshold doses for approximately 1% incidence in morbidity

Effect	Organ/tissue	Time to develop effect	Acute exposure (Gy)	Highly fractionated (2 Gy per fraction) or equivalent protracted exposures (Gy)	Annual (chronic) dose rate for many years (Gy y^{-1})
Temporary sterility	Testes	3-9 weeks	~0.1	NA	0.4
Permanent sterility	Testes	3 weeks	~6	<6	2.0
Permanent sterility	Ovaries	< 1week	~3	6.0	>0.2

Draft ICRP on Tissue Effects. http://www.icrp.org/page.asp?id=116

Skin Injuries

Industrial Irradiator Accident
El Salvador, 1989

Multiple Coronary Angiography & Angioplasty Procedures
USA, 1991 →

Spain, 1998

Hair Loss

Co-60 Overexposure
Costa Rica 1996
→

CT Brain Perfusions, USA 2011
←

Threshold doses for approximately 1% incidence in morbidity

Effect	Organ/tissue	Time to develop effect	Acute exposure (Gy)	[b]Highly fractionated (2 Gy per fraction) or equivalent protracted exposures (Gy)	Annual (chronic) dose rate for many years ($Gy\ y^{-1}$)
Main phase of skin reddening	Skin (large areas)	1-4 weeks	<3-6	30	NA
Skin burns	Skin (large areas)	2-3 weeks	5-10	35	NA
Temporary hair loss	Skin	2-3 weeks	~4	NA	NA
Late atrophy	Skin (large areas)	> 1 year	10	40	NA
Telangiectasia @ 5 years	Skin (large areas)	> 1 year	10	40	NA

Draft ICRP on Tissue Effects. http://www.icrp.org/page.asp?id=116

Eye Injuries

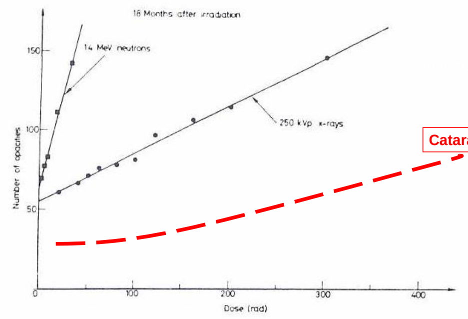


FIG. 7. Number of lens opacities in mice as a function of dose after exposure to X rays and 14 MeV neutrons 18 months after irradiation.

Di Paola, Bianchi, Baarli: Rad Res 73, 340 (1978)

Increased Risk of Cortical and Posterior Subcapsular Cataract Formation

- Reanalysis of Atomic Bomb Survivors
- A Cohort Of Patients With Chronic Exposure to Low-dose-rate Radiation
- From Cobalt-60 Contaminated Steel in their Residences
- Studies of Children Exposed to Low Doses from the Chernobyl (Ukraine) Accident
- Chernobyl Clean-up Workers
- Commercial Airline Pilots
- Space Astronauts

Threshold doses for approximately 1% incidence in morbidity

Effect	Organ/tissue	Time to develop effect	Acute exposure (Gy)	Highly fractionated (2 Gy per fraction) or equivalent protracted exposures (Gy)	Annual (chronic) dose rate for many years (Gy y^{-1})
Cataract (visual impairment)	Eye	>20 years	~0.5	~0.5	~0.5 divided by years duration

Draft ICRP on Tissue Effects. http://www.icrp.org/page.asp?id=116

Dose Limits – ICRP 1991, 2007

For occupational exposure of workers over the age of 18 years

- An effective dose of 20 mSv per year averaged over five consecutive years (100 mSv in 5 years), and of 50 mSv in any single year;
- An equivalent dose to the lens of the eye of 150 mSv in a year;
- An equivalent dose to the extremities (hands and feet) or the skin of 500 mSv in a year

For apprentices (16-18 years of age)

- effective dose of 6mSv in a year.

Dose Limits – ICRP 2011

For occupational exposure of workers over the age of 18 years

- An effective dose of 20 mSv per year averaged over five consecutive years (100 mSv in 5 years), and of 50 mSv in any single year;
- An equivalent dose to the lens of the eye of 20 mSv in a year;
- An equivalent dose to the extremities (hands and feet) or the skin of 500 mSv in a year

For apprentices (16-18 years of age)

- effective dose of 6mSv in a year.

Harmful Tissue Effects

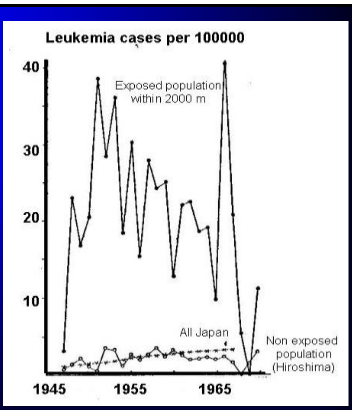
Radiation effects for which generally a threshold level of dose exists above which the severity of the effect is greater for a higher dose.

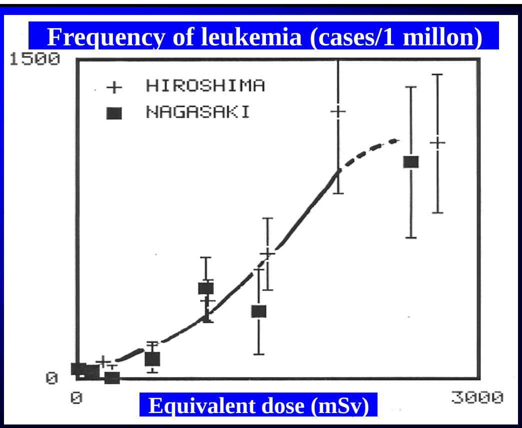
Stochastic Effects

Radiation effects, generally occurring without a threshold level of dose, whose probability is proportional to the dose and whose severity is independent of the dose.

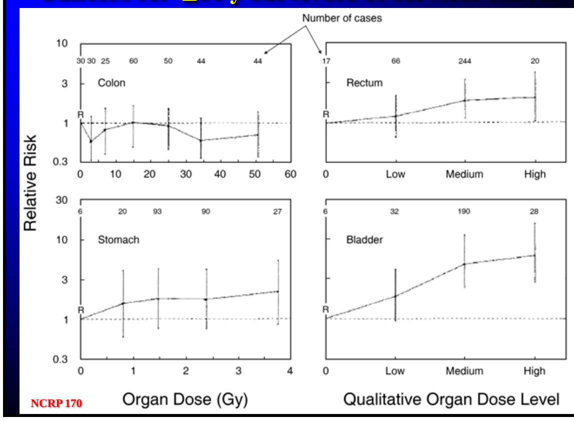
Cancer **Heritable Effects**

Stochastic Effects of Ionizing Radiation





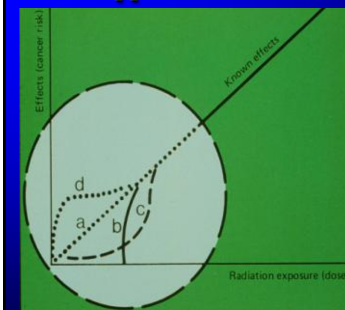
Cancers for ≥10 y survivors of cervical cancer



NCRP 170

53

What happens at the low-dose end of the graph?

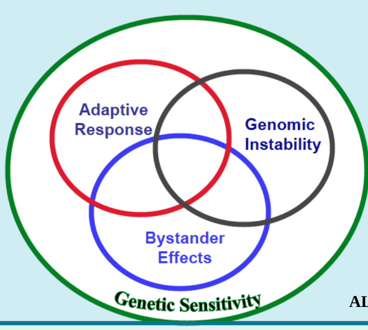


a) Linear extrapolation
b) Threshold dose
c) Lower risk per dose for low doses
d) Higher risk per dose for for low doses

For radiation protection purposes, ICRP has chosen a), acknowledging that below 100 mSv or 0.1 Gy no deleterious effects have been detected in humans.

54

Biological Responses Induced by Low Doses of Radiation



AL Brooks 2012

Dose and Dose-Rate Effectiveness Factor (DDREF)

A judged factor that generalizes the usually lower biological effectiveness [per unit of dose] of radiation exposures at low doses and low dose rates as compared with exposures at high doses and high dose rates)

ICRP is taking a value of 2 for the DDREF

BEIR VII chose a value of 1.5

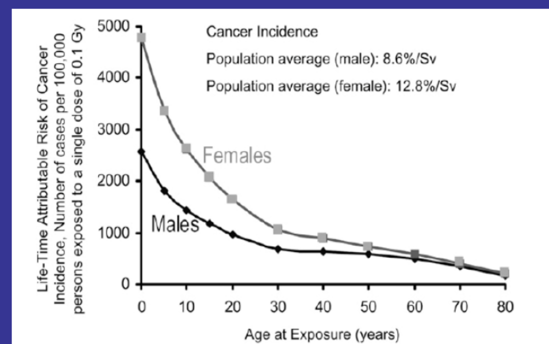
56

ICRP Detriment-Adjusted Nominal Risk Coefficient for Cancer Induction (ICRP 103, 2007)

(10^{-2} Sv^{-1} – Percent per Sievert)

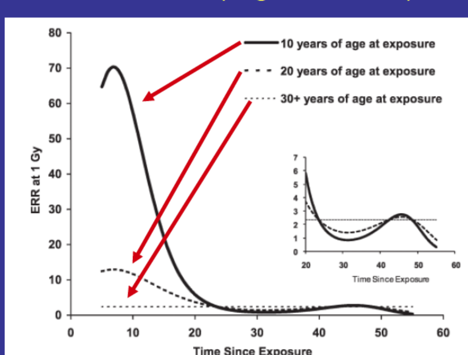
Exposed Population	Cancer Induction
Whole	5.5
Adult	4.1

Lifetime attributable risk of radiation-induced cancer incidence (based on BEIR VII)



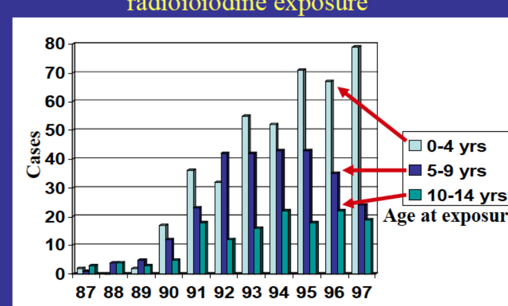
Hricak et.al. Radiol 2010 258:3:889

Leukemia (huge difference)

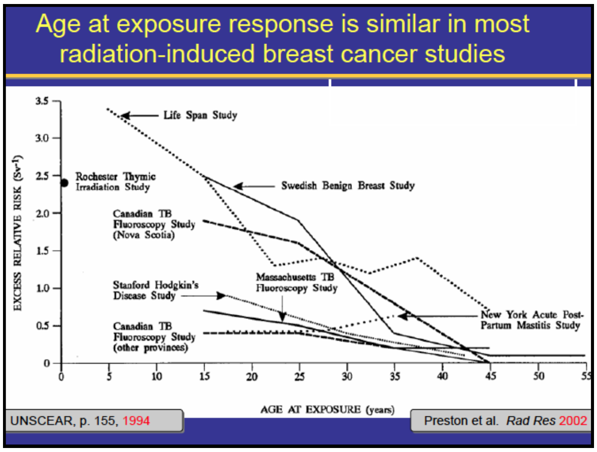


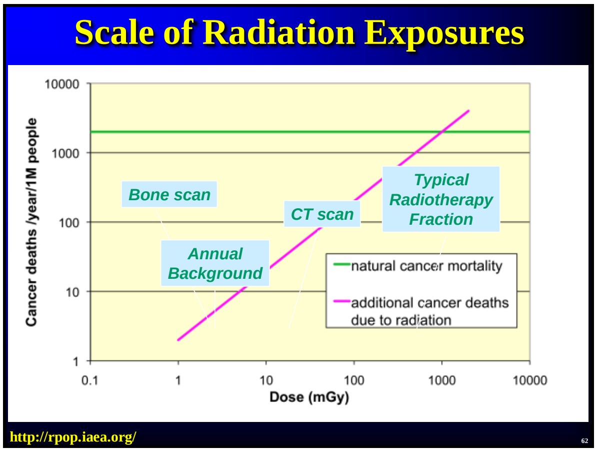
Richardson et.al.Rad Res 172:368-382 2009

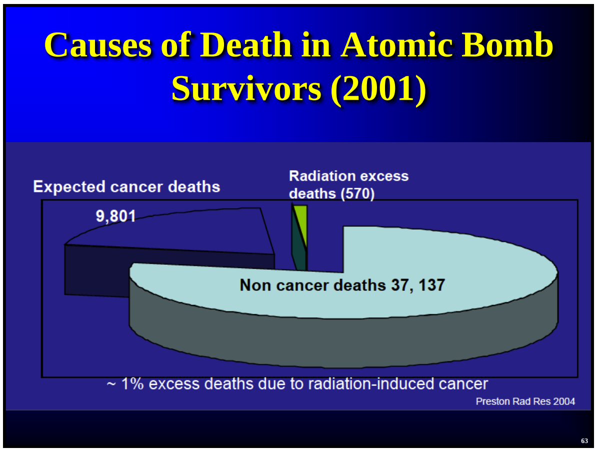
Childhood thyroid cancer as a result of Chernobyl radioioiodine exposure

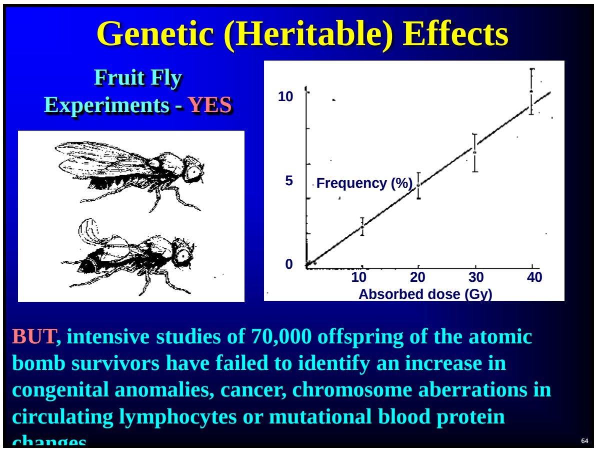


F Mettler 2012


Age at exposure response is similar in most radiation-induced breast cancer studies
EXCESS RELATIVE RISK (Sv⁻¹)
Life Span Study
Rochester Thymic Irradiation Study
Swedish Benign Breast Study
Canadian TB Fluoroscopy Study (Nova Scotia)
Massachusetts TB Fluoroscopy Study
Stanford Hodgkin's Disease Study
Canadian TB Fluoroscopy Study (other provinces)
New York Acute Post-Partum Mastitis Study
AGE AT EXPOSURE (years)
UNSCEAR, p. 155, 1994
Preston et al. Rad Res 2002


Scale of Radiation Exposures
Cancer deaths /year/1M people
Dose (mGy)
Bone scan
CT scan
Typical Radiotherapy Fraction
Annual Background
natural cancer mortality
additional cancer deaths due to radiation
http://rpop.iaea.org/
62


Causes of Death in Atomic Bomb Survivors (2001)
Expected cancer deaths
9,801
Radiation excess deaths (570)
Non cancer deaths 37, 137
~ 1% excess deaths due to radiation-induced cancer
Preston Rad Res 2004
63


Genetic (Heritable) Effects
Fruit Fly Experiments - YES
Frequency (%)
Absorbed dose (Gy)
BUT, intensive studies of 70,000 offspring of the atomic bomb survivors have failed to identify an increase in congenital anomalies, cancer, chromosome aberrations in circulating lymphocytes or mutational blood protein
64

ICRP Detriment-Adjusted Nominal Risk Coefficient for Cancer and Heritable Effects (ICRP 103, 2007)

(10^{-2} Sv^{-1} – Percent per Sievert)

Exposed Population	Cancer Induction	Heritable Effects
Whole	5.5	0.2
Adult	4.1	0.1

HERITABLE EFFECTS

should not be confused with

EFFECTS FOLLOWING IRRADIATION IN UTERO

some of which are deterministic; some, stochastic

IRRADIATION *IN UTERO* ICRP 103 (2007)

End Point	Period	Dose Threshold	Normal incidence in live-born
Death	Pre-Implantation	100 mGy	---
Malformations	Major Organogenesis	100 mGy	1 in 17
Severe Mental Retardations	8 - 15 Weeks Post-Conception	300 mGy	1 in 200
Cancer Risk	In Utero Exposure	None*	1 in 1000

* Lifetime cancer risk ~ 3 times that of the population as whole

Principles of Radiation Protection

General	*Medical Exposure*
Justification of Practices	
benefit to the exposed individuals or to society to outweigh the radiation detriment?	benefits and risks of available alternative techniques that do not involve ionizing radiation?
Dose Limitation	
for occupational and public exposure	not applicable to medical exposure
Optimization of Protection	
ALARA	dose minimum necessary to achieve the required diagnostic or therapeutic objective