AAPM 56th Annual Meeting

CE - Therapy

Radiation Biology II

Radiation Biology Principles

Applied to Radiation Protection

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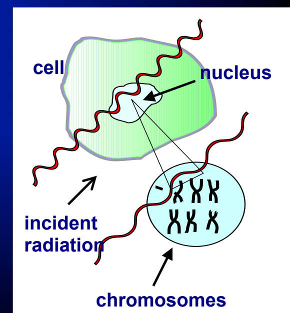
Radiological Physics and Health Services Consultant, Washington DC

Radiation Effects

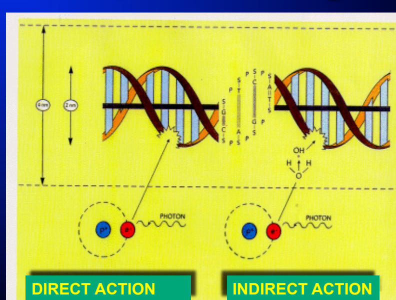
Ionizing radiation interacts at the cellular level:

- ionization
- chemical changes
- biological effects



http://rpop.iaea.org/

Interaction of ionizing radiation with DNA, the critical target



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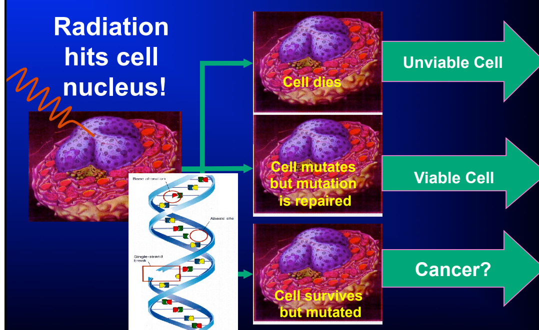
Outcomes after Cell Exposure



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.

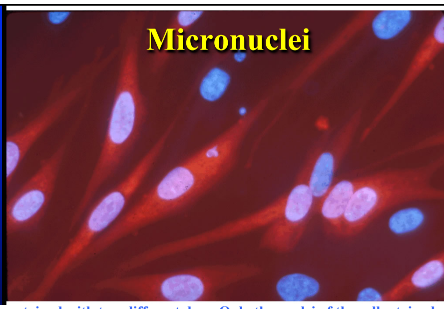
http://lowdose.energy.gov/pdf/Powerpoint_WEBBystander.pdf

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.

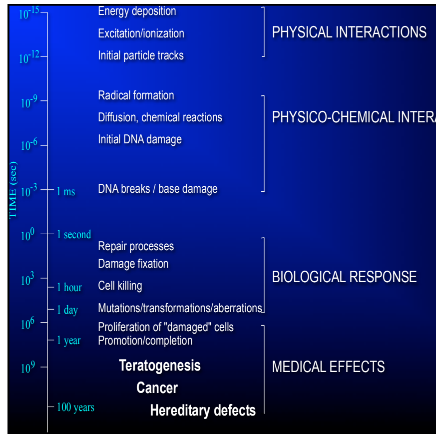
http://lowdose.energy.gov/pdf/Powerpoint_WEBBystander.pdf

Micronuclei



Cells were stained with two different dyes. Only the nuclei of the cells stained with pink dye were hit by alpha particles from a microbeam. The figures show the presence of broken chromosomes in the form of micronuclei (the smaller fragments of pink and blue). These micronuclei are present not only in the pink "hit" cells, but also in the blue non-exposed cells. Such studies provide direct evidence for bystander effects.

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

RBE : radiobiological effectiveness

differs for

- different biological endpoints and
- different tissues or organs

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

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:

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

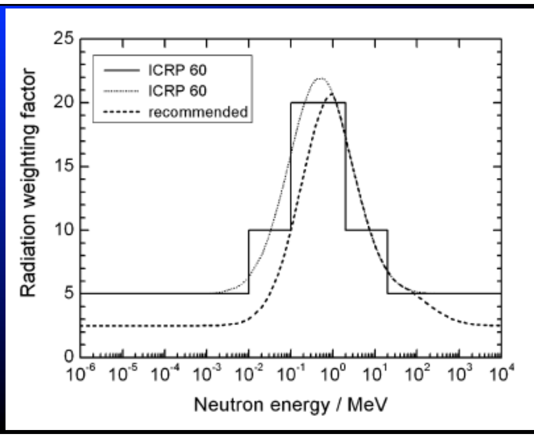
w_R is the radiation weighting factor, which accounts for the detriment caused by different types of radiation relative to photon irradiation

$D_{T,R}$ 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

$H = Q * D$ (Sv)

Where: D = Absorbed Dose

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

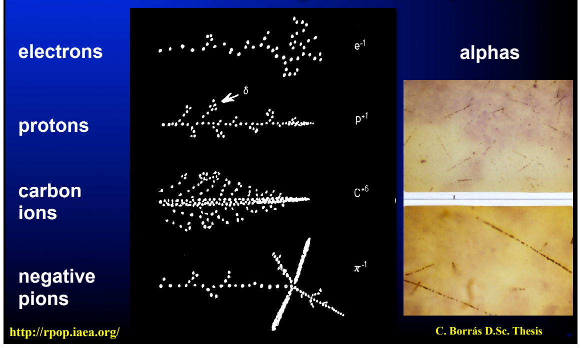
$$Q(L) = \begin{cases} 1 & \text{for } L < 10\ \text{keV}/\mu\text{m} \\ 0.32\,L - 2.2 & \text{for } 10 \le L \le 100\ \text{keV}/\mu\text{m} \\ 300/\sqrt{L} & \text{for } L > 100\ \text{keV}/\mu\text{m} \end{cases}$$

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})



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

$H_p(0.03)$

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

Equivalent dose, H_T, in an organ or tissue T

↓

Effective dose, E

Committed doses, $H_T(\tau)$ and $E(\tau)$

Collective effective dose, S

Operational Quantities

For external exposure

Dose quantities for
area monitoring
individual monitoring

For internal exposure

Activity quantities in combination with biokinetic models and computations

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

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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

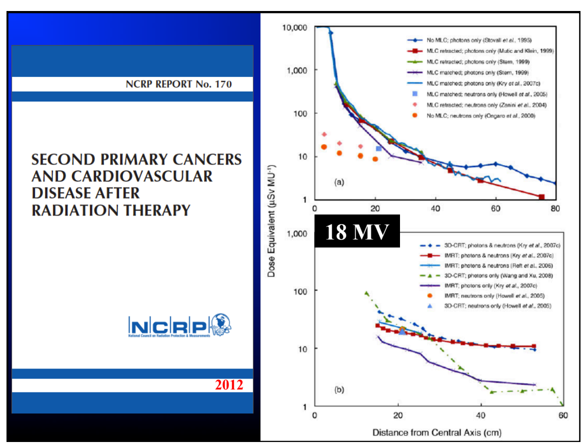
3497 Med. Phys. 37 (7), July 2010 0094-2405/2010/37(7)/3497/4/$30.00 © 2010 Am. Assoc. Phys. Med. 3497

Methods for Determining Organ and Tissue Doses

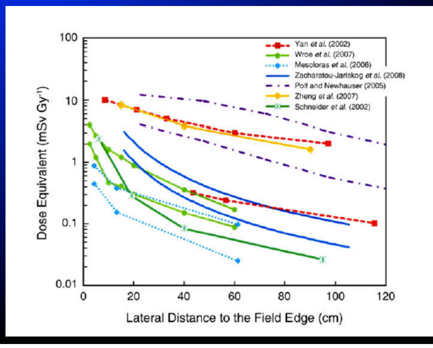
- Measurements in physical phantoms
- Monte Carlo radiation transport calculations

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

Physics in Medicine and Biology > Volume 57 > Number 16

R Kaderka *et al* 2012 *Phys. Med. Biol.* **57** 5059 doi:10.1088/0031-9155/57/16/5059

Out-of-field dose measurements in a water phantom using different radiotherapy modalities

Physics in Medicine and Biology > Volume 59 > Number 8

C La Tessa *et al* 2014 *Phys. Med. Biol.* **59** 2111 doi:10.1088/0031-9155/59/8/2111

Characterization of the secondary neutron field produced during treatment of an anthropomorphic phantom with x-rays, protons and carbon ions

Physics in Medicine and Biology > Volume 57 > Number 19 2012

Estimation of neutron-equivalent dose in organs of patients undergoing radiotherapy by the use of a novel online digital detector

F Sánchez-Doblado[1,2], C Domingo[3], F Gómez[4], B Sánchez-Nieto[5], J L Muñiz[6], M J García-Fusté[3], M R Expósito[2], R Barquero[7], G Hartmann[8], J A Terrón[1], J Pena[4], R Méndez[6], F Gutiérrez[9], F X Guerre[10], J Roselló[11], L Núñez[12], L Brualla-González[11], F Manchado[2], A Lorente[13], E Gallego[13], R Capote[14], D Planes[11], J I Lagares[6], X González-Soto[4], F Sansaloni[6], R Colmenares[15], K Amgarou[3], E Morales[3], R Bedogni[16], J P Cano[2] and F Fernández[17]

THE AIM OF RADIATION PROTECTION

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

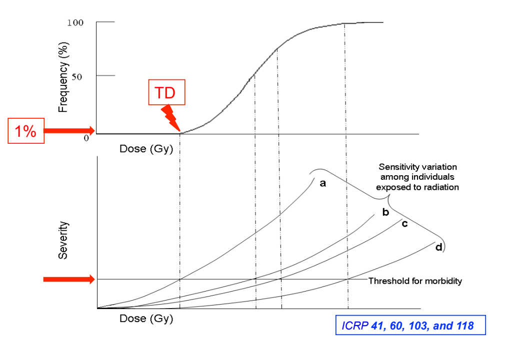
Tissue Harmful (Deterministic) Effects

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.

Threshold dose (TD)

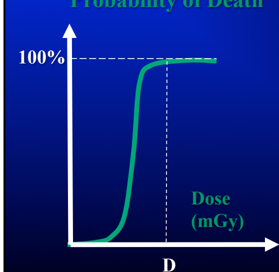


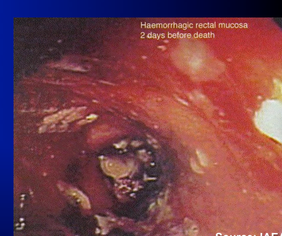
ICRP 41, 60, 103, and 118

ICRP Symposium

J. Hendry 2011

Effects of Cell Death





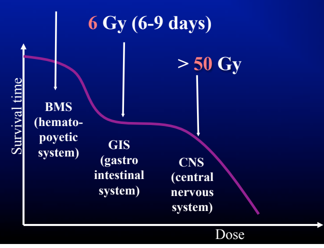
Co-60 Radiotherapy Overexposure Panama 2000-2001

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)

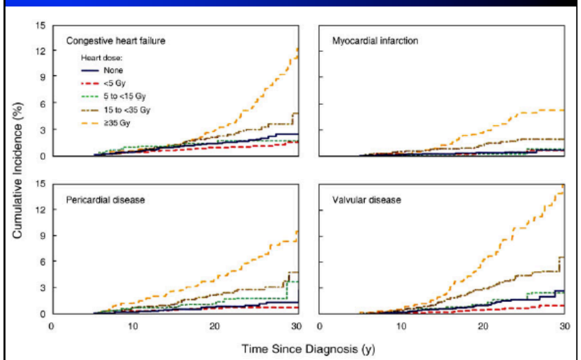
3.3 to 4.5 Gy no medical management

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.

Cardiac Disorders among Childhood Cancer Survivors



NCRP 170

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).

ICRP 118

Irradiation of Gonads

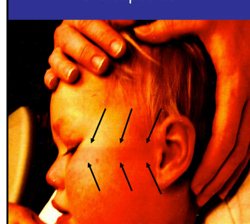
Threshold doses for approximately 1% incidence in morbidity

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

ICRP 118

Skin Injuries

Erythema from accidental CT scan overexposure



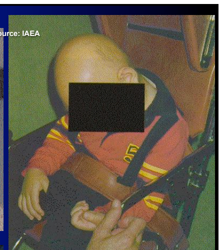
F Mettler 2012 - USA

Figure 1 Clinical case of a 55-year-old male, six months after primary radiochemotherapy due to an advanced squamous cell carcinoma of the hypopharynx. Skin atrophy and soft tissue necrosis were observed 8 weeks after the completion of therapy.

Haubner et al. Radiation Oncology 2012, 7:162

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)	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

ICRP 118

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 52, No. 1, pp. 198–204, 2002
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0360-3016/02/$–see front matter

PII S0360-3016(01)02690-6

BIOLOGY CONTRIBUTION

DETERMINISTIC RATHER THAN STOCHASTIC FACTORS EXPLAIN MOST OF THE VARIATION IN THE EXPRESSION OF SKIN TELANGIECTASIA AFTER RADIOTHERAPY

Akmal Safwat, M.D.,* Søren M. Bentzen, Ph.D., D.Sc.,* Ingela Turesson, M.D.,† and Jolyon H. Hendry, Ph.D., D.Sc.‡

*Group for Biostatistics in Oncology, Gray Laboratory, Northwood, Middlesex, UK; †Radiotherapy Department, Uppsala University Hospital, Uppsala, Sweden; ‡CRC, Experimental Radiation Oncology Group, Paterson Institute for Cancer Research, Manchester, UK

A stochastic (random) component probably related to the random nature of radiation-induced cell killing, possibly in combination with other stochastic processes

A deterministic (patient-related) component probably related to the existence of genetic and epigenetic individual differences in clinical radiosensitivity

Explain 81-90 % of the effects

Eye Injuries

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

ICRP 118

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

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Harmful Tissue Effects

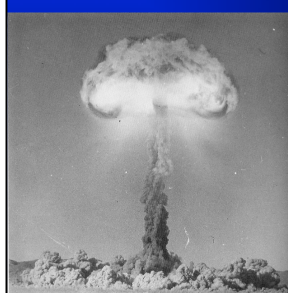
Radiation effects for which generally a threshold level of dose exists above which the severity of the effect is greater for a higher dose.

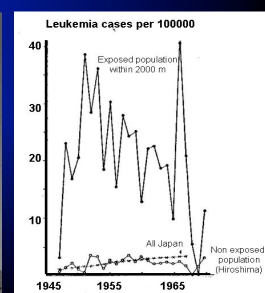
Stochastic Effects

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





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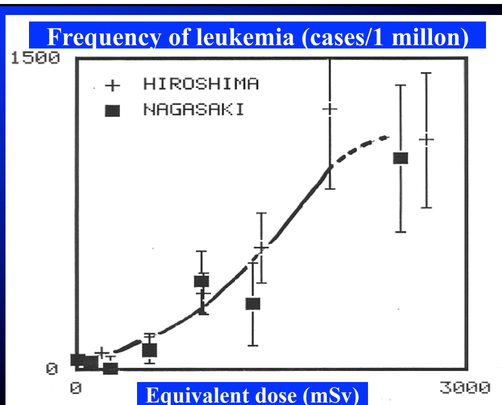
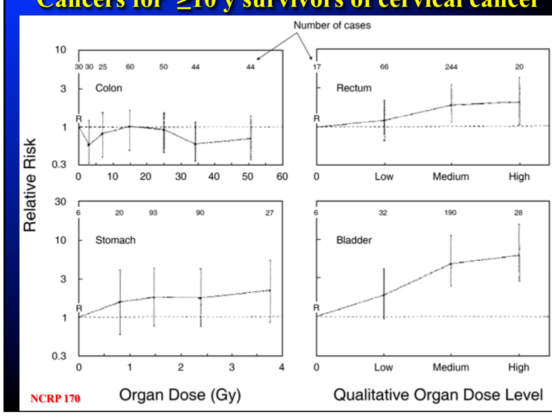


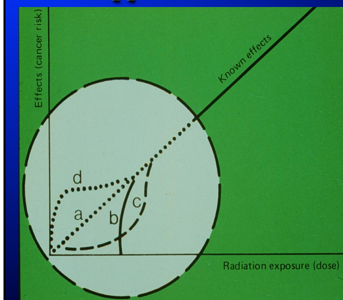
http://rpop.iaea.org/

Cancers for ≥10 y survivors of cervical cancer



NCRP 170

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.

The Linear-Non-Threshold (LNT) Hypothesis Prevails regardless of New Evidence on:

- Cellular adaptive responses
- The relative abundance of spontaneously arising and low dose-induced DNA damage
- The existence of the post-irradiation cellular phenomena
  - Induced genomic instability
  - Bystander signaling
- Tumor-promoting effects of protracted irradiation
- Immunological phenomena

Dose and Dose-Rate Effectiveness Factor (DDREF)

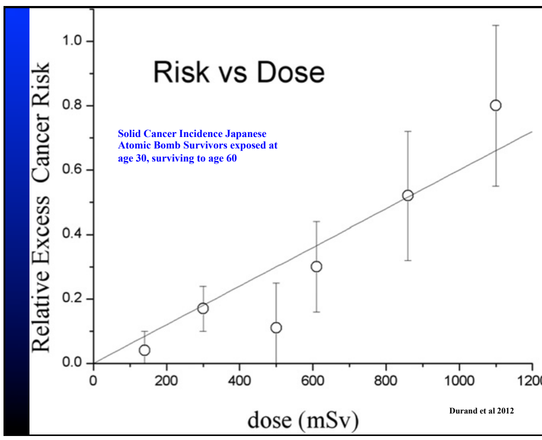
A judged factor that generalizes the usually lower biological effectiveness [per unit of dose] of radiation exposures at low doses* and low dose rates** as compared with exposures at high doses and high dose rates

ICRP is taking a value of 2 for the DDREF

BEIR VII chose a value of 1.5

* 10 mGy

** 5 mGy/min



ICRP Detriment-Adjusted Nominal Risk Coefficient for Cancer (10^{-2} Sv^{-1} – Percent per Sievert)

Exposed Population	ICRP 103 (2007) Cancer Induction	ICRP 60 (1991) Cancer Fatality
Whole	5.5	6.0
Adult	4.1	4.8

TABLE 12D-1 Lifetime Attributable Risk of Cancer Incidence[a]

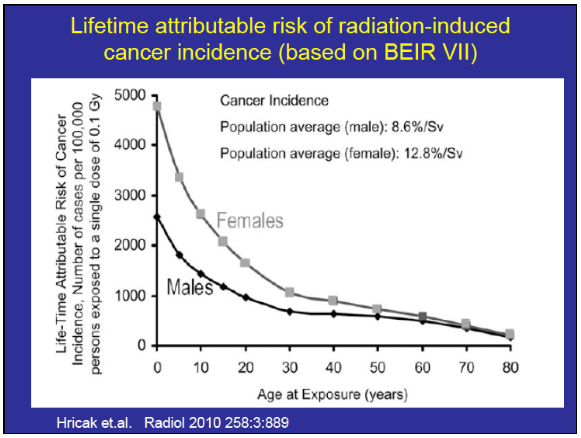
	Age at Exposure (years)										
Cancer Site	0	5	10	15	20	30	40	50	60	70	80
Males											
Stomach	76	65	55	46	40	28	27	25	20	14	7
Colon	336	285	241	204	173	125	122	113	94	65	30
Liver	61	50	43	36	30	22	21	19	14	8	3
Lung	314	261	216	180	149	105	104	101	89	65	34
Prostate	93	80	67	57	48	35	35	33	26	14	5
Bladder	209	177	150	127	108	79	79	76	66	47	23
Other	1123	672	503	394	312	198	172	140	98	57	23
Thyroid	115	76	50	33	21	9	3	1	0.3	0.1	0.0
All solid	2326	1667	1325	1076	881	602	564	507	407	270	126
Leukemia	237	149	120	105	96	84	84	84	82	73	48
All cancers	2563	1816	1445	1182	977	686	648	591	489	343	174
Females											
Stomach	101	85	72	61	52	36	35	32	27	19	11
Colon	220	187	158	134	114	82	79	73	62	45	23
Liver	28	23	20	16	14	10	10	9	7	5	2
Lung	733	608	504	417	346	242	240	230	201	147	77
Breast	1171	914	712	553	429	253	141	70	31	12	4
Uterus	50	42	36	30	26	18	16	13	9	5	2
Ovary	104	87	73	60	50	34	31	25	18	11	5
Bladder	212	180	152	129	109	79	78	74	64	47	24
Other	1339	719	523	409	323	207	181	148	109	68	30
Thyroid	634	419	275	178	113	41	14	4	1	0.3	0.0
All solid	4592	3265	2525	1988	1575	1002	824	678	529	358	177
Leukemia	185	112	86	76	71	63	62	62	57	51	37
All cancers	4777	3377	2611	2064	1646	1065	886	740	586	409	214

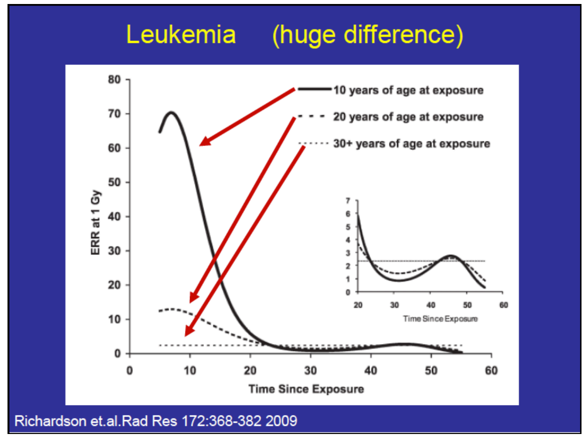
NOTE: Number of cases per 100,000 persons exposed to a single dose of 0.1 Gy.

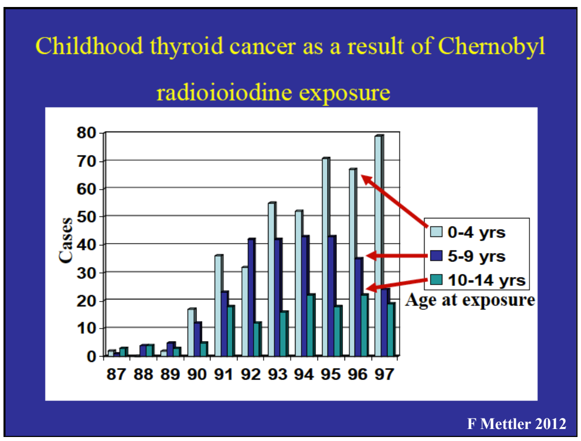
[a]These estimates are obtained as combined estimates based on relative and absolute risk transport and have been adjusted by a DDREF of 1.5, except for leukemia, which is based on a linear-quadratic model.

BEIR VII, 2005

60







Secondary Primary Cancers (SPC)

SPC	Primary cancers	Latency (median)	Risk factors
Breast cancer	HL Bone tumors Soft-tissue sarcomas ALL Brain tumors Wilms' tumors NHL	15 to 20 y	Radiation Female gender
Brain tumors	ALL Brain tumors HL	9 to 10 y	Radiation Younger age ←
Myelodysplastic syndrome/AML	ALL HL Bone tumors	3 to 5 y	Topoisomerase-II inhibitors Alkylating agents
Thyroid cancer	ALL HL Neuroblastoma Soft-tissue sarcoma Bone tumors NHL	13 to 15 y	Radiation Younger age ← Female gender
Soft-tissue sarcomas	Retinoblastoma (heritable) Soft-tissue sarcoma HL Wilms' tumor Bone tumors ALL	10 to 11 y	Radiation Younger age ← Anthracyclines

NCRP 170

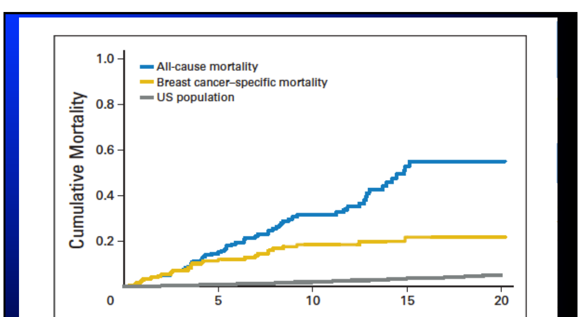
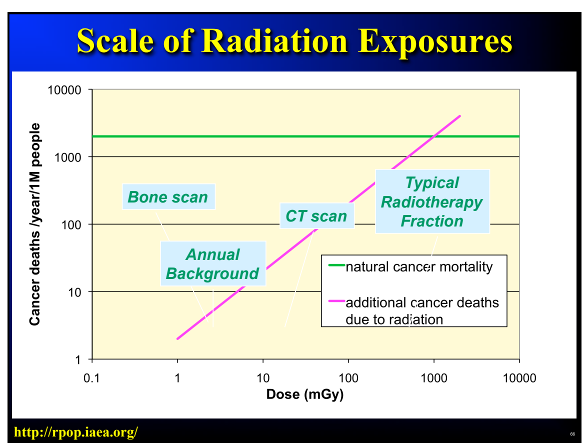
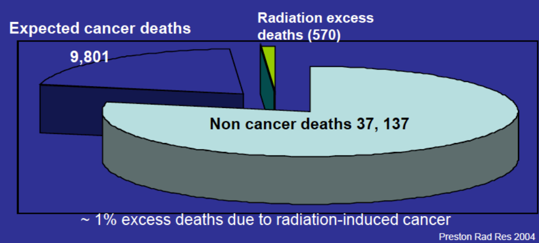


Fig 3. Death after breast cancer among childhood cancer survivors treated with chest irradiation. All-cause and breast cancer–specific mortality after breast cancer after chest radiotherapy for childhood cancer compared with expected mortality, age and year standardized to US population. Moskowitz et al 2014



Causes of Death in Atomic Bomb Survivors (2001)

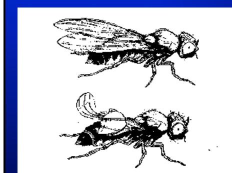


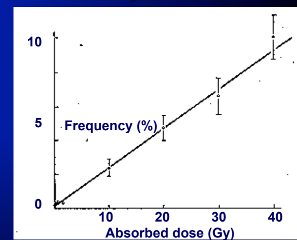
~ 1% excess deaths due to radiation-induced cancer

Preston Rad Res 2004

Genetic (Heritable) Effects

Fruit Fly Experiments - YES





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 changes.

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

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

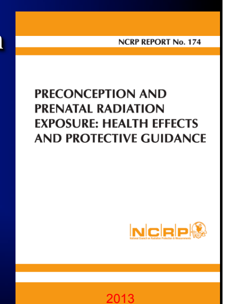
Exposed Population	Cancer Induction	Heritable Effects
Whole	5.5	0.2
Adult	4.1	0.1

HERITABLE EFFECTS

should not be confused with

EFFECTS FOLLOWING IRRADIATION IN UTERO

some of which are deterministic; some, stochastic



IRRADIATION *IN UTERO*

NCRP 174 (2013)

End Point	Period	Dose Threshold	Normal incidence in live-born
Death	Pre-Implantation	100 mGy	---
Malformations	Major Organogenesis	300 mGy	1 in 17
Severe Mental Retardations	8 - 15 Weeks* Post-Conception	500 mGy	1 in 200
Cancer Risk	In Utero Exposure	None	1 in 1000

*IQ reduction as high as 30 per Gy

Typical Radiotherapy Doses (cGy) to Gonads, Uterus and Pituitary

Tumor treated	Age (y) at radiotherapy	Regions treated	Tumor dose range	Gonadal dose range[a] Males	Gonadal dose range[a] Females	Uterine dose range	Pituitary dose range
Cranio-spinal tumors	7	Brain	4,500–5,500	2–7	3–13	3–13	4,500–5,500
Leukemia	4	Brain only or Brain + Spine	1,800–2,500	1–84	2–2,000	2–2,400	1,800–2,500
Hodgkin's Disease	15	Chest and abdomen	3,500–4,500	13–54	73–175	56–142	73–171
		Chest/Abdomen/ Pelvis	3,500–4,500	250–500	300–4,500	300–4,500	73–171
Wilms (Kidney)	4	Abdomen	1,500–2,500	18–67	139–330	85–230	4–22
Neuroblastoma	2	Chest	1,200–2,500	2–21	4–35	4–34	12–80
		Abdomen	1,200–2,500	7–54	28–125	22–120	3–25
Osteosarcoma	15	Limb	5,500	115–200	16–55	20–55	1–4

[a] The above doses have not been reduced to account for special gonadal shielding, which may have been used for some treatments that would otherwise deliver a high dose to the gonads. In general, special shielding reduces doses to 10% of those shown.

JD Boice et al, 2003