Dr. Fuad Ismail
8.50 pg.

Carcinogenesis & other Detrimental Effects of Radiation

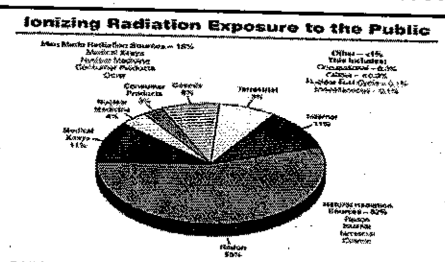
DETRIMENTAL EFFECTS OF RADIATION

- The effect of radiation on health is dependant on the dose and also the organ at risk
- Possible detrimental effects
  - Death
  - Carcinogenesis
  - Hereditary effects
  - Chronic organ damage
  - Non-specific life shortening

RADIATION EXPOSURE

- Natural background radiation comes from cosmic rays and radioactive elements normally present in the soil. This is the major contributor to worldwide radiation exposure.
- Non-medical synthetic radiation
  - occurs as a result of above ground nuclear weapons testing that took place before 1962 as well as occupational and commercial sources.
- Medical radiation
  - Diagnostic x-rays eg CXR, CT
  - Radiation therapy.

NATURAL vs ARTIFICIAL RADIATION



- 80% of our radiation dose comes from background radioactive sources.
  - Internal sources include ^{40}K in the blood

RADIATION AS CARCINOGEN

- Ionizing radiation has been shown to cause cancer
  - in different species of animals and
  - in almost all parts of the body.
- It is a relatively weak carcinogen compared to many chemical agents.
  - Many years may elapse between the radiation exposure and the appearance of cancer.
  - Elapsed time varies between solid tumours and haematological malignancies

MUTATIONS AND CARCINOGENESIS

- DNA in cells damaged by radiation may be repaired and cell survive radiation damage.
  - If repair is imperfect, cell may inherit damaged DNA. These cells are mutated.
  - Further accumulation of DNA damage may lead to cancer formation (carcinogenesis)
  - This is called stochastic effect

STOCHASTIC EFFECTS

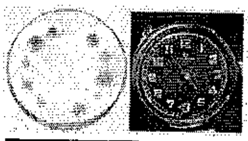
- Characteristics
  - No threshold dose
    - May occur at any radiation dose
  - Probability increases with increasing dose
  - Severity independent of dose
    - Eg cancer induced with 1 Gy same as cancer induced at 10 Gy

EVIDENCE OF RADIATION CARCINOGENESIS

- Skin cancer in early x-ray workers
- Radiologists in early 20th century
- Bone tumours in radium dial painters
- Liver tumours with thorothrast contrast
- Breast cancer with TB fluoroscopy
- Thyroid cancer with irradiation for tinea capitis
- Survivors of atomic bomb and Chernobyl
- Lung cancer in uranium mine workers

Radium dial workers

- Young women worked in factories painting radium on watches



Ingested Radionuclides and sarcomas

- Possible threshold dose around 10Gy

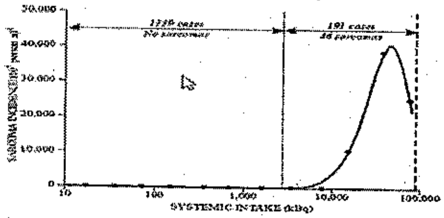


Figure XIX. Bone sarcoma incidence in female radium dial painters [R17].
Systemic intake is kBq ^{226}Ra plus 2.5 × ^{228}Ra activities.

Thyroid cancer in Children post Chenobyl

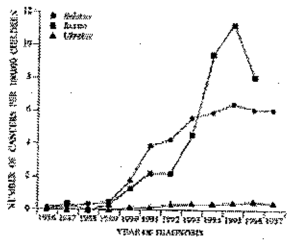


Figure XXV. Thyroid cancer incidence rate in children exposed before the age of 14 years as a result of the Chernobyl accident [I23, K41, T2, T16].

UNSCEAR Report 2010 Annex J

Thyroid cancer post Chenobyl – by age of exposure

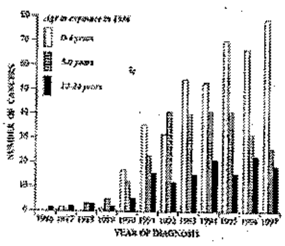


Figure XXVI. Number of diagnosed thyroid cancer cases in Belarus as a result of the Chernobyl accident [K41].

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RADIATION CARCINOGENESIS

- Risk varies by :
  - Radiation dose
    - Higher more risk, fractionated less
    - High LET – linear increase with dose
    - Low LET - linear increase with $(dose)^2$
  - Organs at risk
    - Different organs have different risk
      - Bone marrow, breast & thyroid have higher risk
  - Gender
  - Time of exposure

Single vs fractionated RT

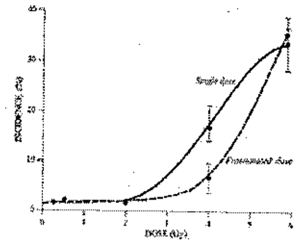

Figure XI. Incidence of thymic lymphoma as a function of dose for single or fractionated x rays [M39].

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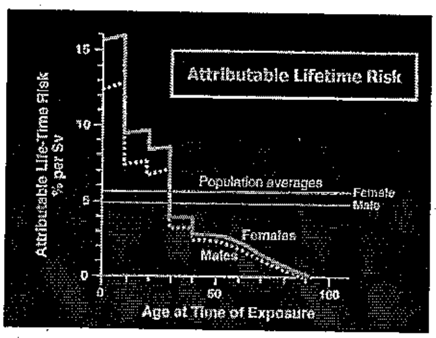
Risk by Gender and Age



Deterministic and stochastic effects

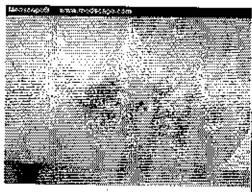


Table 2
Typical effective doses from diagnostic medical examinations using x-rays or isotope scans in the 1990s, and associated broad levels of risk. Data from the UK National Radiological Protection Board

Diagnostic procedure	Effective dose (mSv) (rounded to a value of)	Equivalent period of natural background radiation	Lifetime additional risk of cancer per examination*
Chest x-ray examination Teeth x-ray Arms and legs x-ray Hands and feet x-ray	0.01	A few days	Negligible risk
Skull x-ray Head x-ray Neck x-ray	0.1	A few weeks	Minimal risk: 1 in 1,000,000 to 1 in 100,000
Breast x-ray - mammography Hip x-ray Spine x-ray Abdomen x-ray Pelvis x-ray CT of head Lung nuclear medicine isotope scan Kidney isotope scan	1	A few months to a year	Very low risk: 1 in 100,000 to 1 in 10,000
Kidneys and bladder x-ray (IVU) Stomach x-ray - barium meal Colon x-ray - barium enema CT of abdomen Bone isotope scan	10	A few years	Low risk: 1 in 10,000 to 1 in 1,000

* These very small risk levels are added to the 1 in 3 chance we all have of getting cancer.

- At low and very low radiation doses, statistical and other variation in baseline risk tends to be the dominant source of error in both epidemiological and experimental carcinogenesis studies.
- Estimates of radiation-related risk tend to be highly uncertain both because of a weak signal-to-noise ratio and because it is difficult to recognize or to control for subtle confounding factors.
- Extrapolation of risk estimates based on observations at moderate to high doses continues to be the primary basis for estimation of radiation-related risk at low doses and dose rates.

BIER VII estimates of cancer risk

- At doses of 100 mSv or less, statistical limitations make it difficult to evaluate cancer risk in humans.
- The "linear-no-threshold" (LNT) model
  - The risk would continue in a linear fashion at lower doses without a threshold
  - the smallest dose has the potential to cause a small increase in risk to humans.

Beir VII: Health Risks from Exposure to Low Levels of Ionizing Radiation

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Risk of excess cancers

- Estimated risk of 100 mSv exposure to 100 000 population

	All Solid Cancer		Leukemia	
Excess cases (including non-fatal cases) from exposure to 100 mSv	Males	Females	Males	Females
	800 (400–1600)	1300 (690–2500)	100 (30–300)	70 (20–250)
Number of cases in the absence of exposure	45,500	36,900	830	590
Excess deaths from exposure to 100 mSv	410 (200–830)	610 (300–1200)	70 (20–220)	50 (10–190)
Number of deaths in the absence of exposure	22,100	17,500	710	530

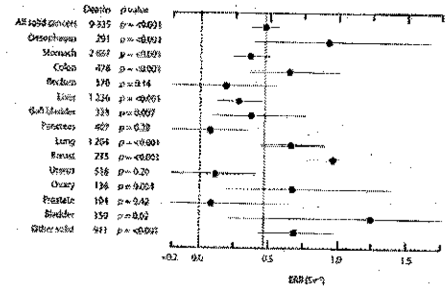
EXCESS CANCERS WITH IRRADIATION

Table 2.5. Distribution of subjects, solid cancers, and estimated radiation-associated, excess solid cancers among 79,901 exposed members of the Life Span Study cohort of Hiroshima-Nagasaki atomic bomb survivors (Pearce and Preston, 2000).

Estimated colon dose	Number of subjects	Number of solid cancers	Estimated number of radiation-associated excess cancers*
Exposed beyond 3000 m	23,493	3,230	0
<5 mGy, exposed within 3000 m	10,159	1,301	1
5-100 mGy	30,524	4,119	77
100-200 mGy	4,775	739	60
200-500 mGy	5,862	982	164
0.5-1 Gy	3,048	582	177
1-2 Gy	1,570	376	165
>2 Gy	470	126	80

* Fitted values, linear dose response

Types of cancer associated with Radiation

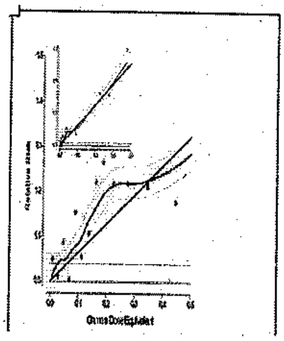


UNSCEAR 2006

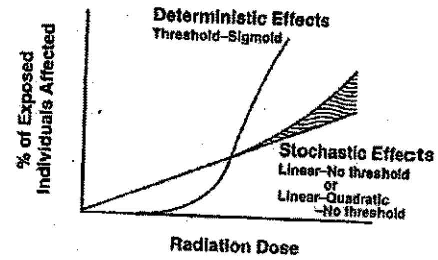
- There is no direct evidence, from either epidemiological or experimental carcinogenesis studies, that radiation exposure at doses on the order of 1 mGy or less is carcinogenic,
- Animal tumor data from experimental carcinogenesis studies tend to support a dose response that, at low doses, is linear with no threshold.

MODEL OF CANCER RISK WITH RADIATION

- Shape of cancer risk may be linear or sigmoidal
- Theoretically no threshold should exist
  - But difficult to prove in real life
- Data is available for doses 0.5 – 5 Gy
  - Extrapolation for very low doses



OTHER MODELS



DOSE-RELATED RADIATION EFFECTS

- Carcinogenesis is a stochastic effect
  - The probability that cancer will result from radiation exposure increases as the dose increases.
  - But not the severity of cancer
- Low-Dose Radiation Exposure
  - A number of studies over the past 20 years have looked at the impact of environmental radiation exposure in the dose range of 10 cGy or less.
  - Careful analysis of this research revealed no significant increase in the incidence of all cancers combined, or of cancers in specific parts of the body.
- Types of Cancer Associated With Ionizing Radiation
  - Leukemia is a major malignancy induced by radaition
    - Leukemias begin appearing as early as 2 years after acute radiation exposure.
  - Other cancers also occur but takes longer to develop (usually at least 10 to 15 years).

DOSE-RELATED RADIATION EFFECTS

- Studies of the survivors of the atomic blasts have demonstrated that high-dose radiation (at least 100cGy) increases the risk of developing several types of cancer.
- For these survivors, the risk of developing leukemia is five and a half times greater than in the general public.
  - Children appear to be twice as sensitive as adults to the leukemia-causing effects of radiation.
  - Unborn children exposed to radiation in the uterus are even more sensitive.
- The risk for developing any type of cancer in those highly exposed to an atomic blast is about 50% higher than the risk in those not exposed.
- Increased risk include : Female breast cancer, lung and myeloma

Estimates of biological effect with different radiation types

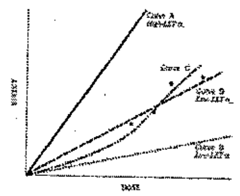


Figure II. Typical dose-effect relationship for low- and high-LET radiations [M18].

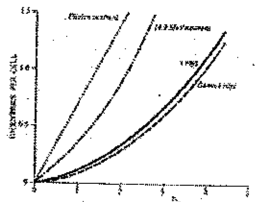
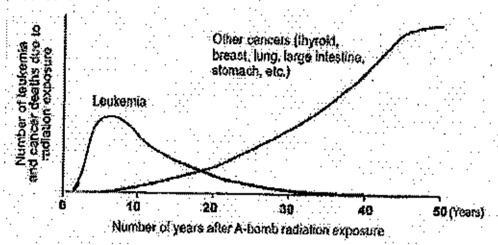


Figure V. Yield of dicentrics in human lymphocytes as a function of dose for some photon and neutron radiations [E6].

UNSCEAR 2008 ANNEX G Biological effects at low radiation doses

Leukaemia and solid cancer risk



RADIATION WEIGHTING FACTOR

TABLE 15.2
Radiation Weighting Factors

Type and Energy Range	Radiation Weighting Factor, W_R
Photons	1
Electrons	1
Protons	2
α-Particles, fission fragments, heavy nuclei	20
Neutrons	A continuous curve is recommended with a maximum of 20 for the most effective neutrons of about 1 MeV

Based on International Commission on Radiological Protection: Relative biological effectiveness (RBE), quality factor (Q), and radiation weighting factor (W_R). ICRP Publication 92. Oxford, UK, Elsevier Science Ltd, 2004.

- As different forms of radiation have different carcinogenic potential, a radiation weighting factor is applied

ORGAN SENSITIVITY TO RADIATION CARCINOGENESIS

- Organs differ in their sensitivity to radiation.
  - The thyroid gland and bone marrow are most sensitive
  - kidney, bladder, and ovary are least sensitive.
- Evidence that ionizing radiation causes cancer comes from studies of
  - atomic bomb survivors in Japan,
  - persons exposed to large amounts of x-rays,
  - occupational exposures,
    - workers with lung exposure to alpha radiation.
    - Radium dial workers
- These studies, however, generally involved relatively high-dose exposure - greater than 10 centigray.
  - Therefore, the risk estimates for lower doses of radiation have to be estimated from the high-dose data, and may not be accurate.

TISSUE WEIGHTING FACTOR

- Due to differing sensitivity of tissues to radiation carcinogenesis, a tissue weighting factor is also applied.

Table 4-2. Tissue Weighting Factors

Tissue or Organ	Tissue Weighting Factor, WT
Gonads	0.20
Bone Marrow (red)	0.12
Colon	0.12
Lung	0.12
Stomach	0.12
Bladder	0.05
Breast	0.05
Liver	0.05
Esophagus	0.05
Thyroid	0.05
Skin	0.01
Bone Surface	0.01
Remainder*	0.05

Cucinotta FA & Durante M : Risk of Radiation Carcinogenesis

IS RADIATION RISKIER THAN OTHER COMMON ACTIVITIES

- Another way of looking at risk, is to look at the Relative Risk of 1 in a million chances of dying of activities common to our society.
- Smoking 1.4 cigarettes (lung cancer)
- Eating 40 tablespoons of peanut butter
- Spending 2 days in New York City (air pollution)
- Driving 40 miles in a car (accident)
- Flying 2500 miles in a jet (accident)
- Canoeing for 6 minutes
- Receiving 10 mrem of radiation (cancer)

RISK LEVELS OF VARIOUS ACTIVITIES

Table 6-4 Risk of Dying from Various Activities

Activity	Cause of Death	Risk of Death (per million per year)
Smoking one pack of cigarettes per day	All causes	3500
Canoeing for 20 hours	Drowning	200
Traveling 1500 miles by car	Accident	40
Fishing	Drowning	10
Eating	Choking	8
Traveling 5000 miles by airplane	Accident	5
Having a chest X-ray	Cancer (radiation induced)	1
Living near a nuclear power plant	Cancer (radiation induced)	< 0.1

Based on data from J. B. Little in *Holland-Frei Cancer Medicine*, 5th ed. (R. C. Bast et al., eds., Lewiston, NY: Decker, 2000), Chapter 14, Table 14.3.

COMPARING RISKS

- The following is a comparison of the risks of some medical exams and is based on the following information:
- Cigarette Smoking - 50,000 lung cancer deaths each year per 50 million smokers consuming 20 cigarettes a day, or one death per 7.3 million cigarettes smoked or 1.37 x 10-7 deaths per cigarette
- Highway Driving - 56,000 deaths each year per 100 million drivers, each covering 10,000 miles or one death per 18 million miles driving, or 5.6 x 10-8 deaths per mile driven
- Radiation Induced Fatal Cancer - 4% per Sv (100 rem) for exposure to low doses and dose rates

RADIATION DOSES FOR RADIOGRAPHS

Effective Doses for Common Diagnostic Procedures (United States)

	ESAK, mGy	Entrance Skin Exposure, mR	Effective Dose, mSv (mrem)	
			Male	Female
Chest (PA)	0.18	20	0.03 (3)	0.03 (3)
Chest (lateral)	0.57	65	0.05 (5)	0.08 (8)
Skull (AP)	2.9	330	0.04 (4)	0.04 (4)
Skull (lateral)	1.5	165	0.02 (2)	0.02 (2)
C-spine (AP)	1.3	150	0.05 (5)	0.05 (5)
C-spine (lateral)	0.88	100	0.02 (2)	0.02 (2)
T-spine (AP)	2.5	280	0.27 (27)	0.54 (54)
T-spine (lateral)	6.0	680	0.25 (25)	0.27 (27)
L-spine (AP)	5.6	640	0.40 (40)	0.78 (78)
L-spine (lateral)	20	2300	0.53 (53)	0.84 (84)
Abdomen (AP)	5.3	600	0.37 (37)	0.73 (73)

Entrance skin exposure values taken from Wagner LK: Radiation Bioeffects and Management Test and Syllabus. Reston, VA, American College of Radiology, 1991.
Effective doses calculated by Dr. Keith A. Schueler using Rosenstein M: Handbook of Selected Tissue Doses for Projections Common in Diagnostic Radiology. Rockville, MD, US Department of Health and Human Services, Public Health Service, Food and Drug Administration Publication 89-8031, 1988 for organ doses and ICRP weighting factors.

RADIATION DOSES FOR RADIOGRAPHS

Effective Doses from Computed Tomography in the United Kingdom

Examination	Mean Effective Dose, mSv* United Kingdom, 1989	Mean Effective Dose, mSv* Wales, 1994
Routine head	1.8	1.6
Posterior fossa	0.9	1.2
Pituitary	0.6	0.9
Internal auditory meatus	0.4	1.0
Facial bones	0.7	0.3
Orbits	0.6	0.8
Cervical spine	2.6	1.5
Thoracic spine	4.9	2.4
Lumbar spine	3.3	3.3
Chest	7.8	9.7
High-resolution lung	—	1.9
Abdomen	7.6	12.0
Liver	7.2	10.3
Pancreas	4.8	7.4
Kidneys	6.3	9.1
Pelvis	7.1	9.8

*Multiply by 100 to convert mSv to mrem.
Adapted from Shrimpton PC, Wall BF, Hart D. Diagnostic medical exposures in the U.K. Appl Radiat Isot 50:261–269, 1999, with permission.

HOW DOES DIFFERENT BACKGROUND RADIATION DOSE AFFECT CANCER RISK

- The citizens of Colorado are exposed to background radiation of some 180 mrem per year; the figure for Massachusetts is only 102 mrem/year.
  - If the linear non-threshold model is correct, we would expect to find a higher incidence of cancer in Colorado than in Massachusetts.
- If radiation is detrimental, we would expect more cancers in Colorado.
  - If radiation is protective, then less cancers in Colorado
- In 1999, when adjusted for the age of the population, the incidence of cancer averaged 16% higher in Massachusetts than in Colorado.
- Some other parts of the world have background radiation levels much higher than in Colorado.
  - Ramsar, Iran, the inhabitants are exposed to an annual dose of background radiation of as much as 13,000 mrem per year — over 70 times that in Colorado. Nevertheless, the inhabitants of Ramsar are just as healthy as control populations exposed to far lower levels of radiation.

CALCULATING EXCESS CANCERS

- If the risk of cancer is 4% per Sv (100 rem)
- The population of the U.S. in 2004 was about 294 million.
- so anything that increases the annual exposure of the U.S. population by as little as 1 mrem per year would cause an additional 294 cases of cancer.

  (294 x 106 persons) (1 mrem) = 294 cancers
  1 x 106 person mrem/cancer
- But consider:
  - The current death rate in the U.S. is about 0.008; that is,
  - ~2.4 million people die each year (294 x 106 x 0.008)
  - 23-24% of these deaths are caused by cancer, so the number of cancer deaths each year exceeds 550,000
- How can we possible detect an increase of 294 faced with these large numbers?

Does Higher Background radiation Equate to higher risk of cancer?

- Study in India
- The coastal belt of Kerala, India, is known for high background radiation (HBR) from thorium containing monazite sand.
- Median outdoor radiation levels > 4 mGy y1 and, in certain locations on the coast, as high as 70 mGy y1.
- HBR has been shown to increase the frequency of chromosome aberrations in lymphocytes
- A cohort of all 385,103 residents in was established in the 1990's to evaluate health effects of HBR

Nair RR et al Health Phys. 96(1):55–66; 2009

Does Higher Background radiation Equate to higher risk of cancer?

- Based on radiation level measurements, a radiation subcohort consisting of 173,067 residents was chosen.
- Cancer incidence in this subcohort aged 30–84 y (*N* 69,958) was analyzed.
- Cumulative radiation dose for each individual was estimated based on outdoor and indoor dosimetry.
- Following for 10.5 years on average = 736,586 person-years of observation.
- 1,379 cancer cases including 30 cases of leukemia were identified by the end of 2005.

Nair RR et al Health Phys. 96(1):55– 66; 2009

Does Higher Background radiation Equate to higher risk of cancer?

- The excess relative risk of cancer excluding leukemia was estimated to be 0.13 Gy-1 (95% CI: 0.58, 0.46).
- In site-specific analysis, no cancer site was significantly related to cumulative radiation dose.
- Leukemia was not significantly related to HBR, either.
- Our cancer incidence study, together with
- reported cancer mortality studies in the HBR area of Yangjiang, China, suggests it is unlikely that estimates of risk at low doses are substantially greater than currently believed.

Nair RR et al Health Phys. 96(1):55– 66; 2009

Kerala Study

Table 4. Risk of all cancers excluding leukemia according to cumulative radiation dose, lagged by 10 y, estimated for each individual.*

	Cumulative radiation dose (mGy)					
	0–49	50–99	100–199	200–499	500+	*P* value for trend
Mean dose (mGy)	36	74	141	283	638	
SD	6	9	17	49	119	
Total						
Case	282	321	363	213	23	
Person-y	211,905	222,091	206,337	83,836	6,255	
RR	1	0.97	1.02	0.93	0.95	
95% CI	Reference	0.83–1.14	0.87–1.19	0.77–1.13	0.60–1.49	>0.5
Male						
Case	149	196	254	153	13	
Person-y	90,622	100,359	97,088	41,540	3,223	
RR	1	0.97	0.97	0.98	0.81	
95% CI	Reference	0.79–1.20	0.78–1.20	0.76–1.26	0.45–1.46	>0.5
Female						
Case	133	175	209	70	9	
Person-y	121,346	127,733	109,249	42,296	3,032	
RR	1	0.95	1.08	0.86	1.25	
95% CI	Reference	0.75–1.20	0.85–1.37	0.63–1.16	0.62–2.49	>0.5
Cases with pathological diagnosis						
Case	202	264	348	134	17	
Person-y	211,965	223,091	206,337	83,836	6,355	
RR	1	1.07	1.16	0.93	1.23	
95% CI	Reference	0.89–1.29	0.96–1.39	0.73–1.17	0.72–2.01	>0.5

Nair RR et al Health Phys. 96(1):55– 66; 2009

Kerala Study

Table 3. Risk of all cancers excluding leukemia according to household dose rate.*

	Environmental radiation dose (mGy y^{-1})					
	0–0.9	1–1.9	2–4.9	5–9.9	10+	*P* value for trend
Mean dose (mGy)	0.8	1.5	3.2	6.8	14.1	
SD	0.1	0.2	0.6	1.0	4.2	
Attained age						
Total						
Case	175	416	512	180	64	
Person-y	99,328	235,851	279,133	98,792	32,391	
RR	1	0.92	0.89	0.88	0.91	
95% CI	Reference	0.77–1.10	0.75–1.07	0.71–1.10	0.68–1.22	0.307
30–49						
Case	33	83	95	33	12	
Person-y	41,259	110,993	133,055	47,891	15,621	
RR	1	0.91	0.87	0.83	0.88	
95% CI	Reference	0.61–1.32	0.55–1.31	0.51–1.35	0.45–1.72	>0.5
50–69						
Case	95	223	286	101	37	
Person-y	35,633	92,706	112,634	39,212	12,531	
RR	1	0.92	0.91	0.92	1.02	
95% CI	Reference	0.71–1.17	0.71–1.15	0.69–1.23	0.65–1.51	>0.5
70+						
Case	47	110	131	46	15	
Person-y	11,176	26,152	32,593	11,659	4,242	
RR	1	0.95	0.88	0.84	0.74	
95% CI	Reference	0.67–1.36	0.62–1.25	0.54–1.29	0.40–1.34	0.213

SUMMARY

- Radiotherapy causes acute and late side-effects
- Acute effects are deterministic, dependant on dose/fractionation and site
- Late effects include mutagenesis and carcinogenesis which are stochastic effects
- The actual risk of carcinogenesis with low level radiation is difficult to determine as data is extrapolated from exposure at higher doses

RADIOTHERAPY IN PREGNANCY

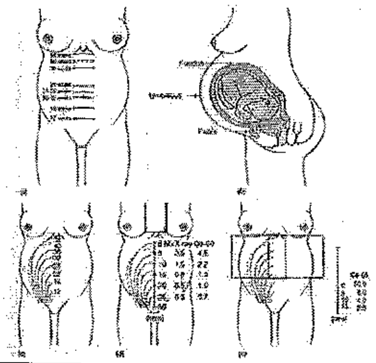
RADIOTHERAPY IN PREGNANCY

- Treatment of choice for certain tumours eg NPC, is radiotherapy
  - Not treating maybe detrimental to mother and fetus
- Radiotherapy treatment must be continuous
  - Interruptions may be worse than starting later.
  - Change in tumour kinetics
- Addition of chemotherapy
  - Improves local control in head & neck cancers
  - May improve survival

RISKS OF RADIATION TO FETUS

- Depends on
  - Dose to fetus
    - Area irradiated
    - Dose given
    - Shielding
  - Fetal age

DISTANCE FROM TREATMENT SITE



RISK VS DOSE

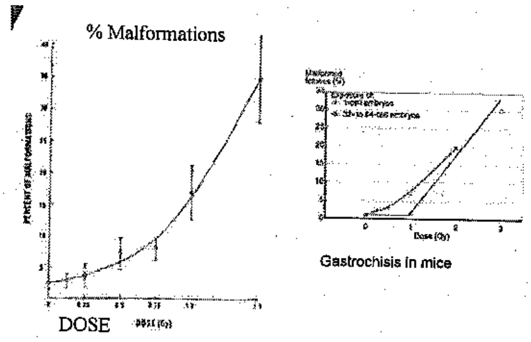
TABLE VI. Summary of risk as function of dose

Dose (Gy)	Risk
<0.05	Little risk of damage
0.05–0.10	Risk uncertain
0.10–0.50	Significant risk of damage during first trimester
>0.50	High risk of damage during all trimester

ICRU recommendations

- Termination of pregnancy at fetal doses of less than 100 mGy (10,000 mrad) is **NOT** justified based upon radiation risk
- At fetal doses between 100 and 500 mGy, decisions should be based upon individual circumstances
- At fetal doses in excess of 500 mGy, there can be significant fetal damage, the magnitude and type of which is a function of dose and stage of pregnancy

RISK VS DOSE (2)



DETRIMENT TO FETUS

- Spontaneous abortion
- Organ malformation
- Genital / skeletal malformation
- Mental retardation
- Microcephaly
- Cataract
- Sterility
- Carcinogenesis

Gross Anomalies Caused by Irradiation During Organogenesis in Mice

Exencephaly Evisceration Normal Anencephaly

(5 live fetuses, 4 resorbed fetuses)

POST-CHERNOBYL

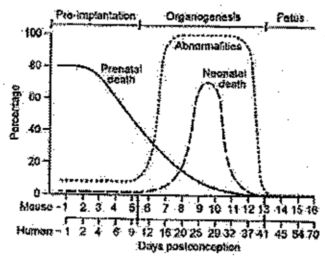
RISK BY GESTATION AGE

- Three periods of risk
  - Fertilisation to implantation
  - Organogenesis
  - Fetal development

PRE-IMPLANTATION

- 0 – 9 days
- Risk is absolute
  - All or nothing
  - May lead to death of embryo
  - Malformations rare
  - No growth delay
- LD_{50} in mice is 0.5 Gy

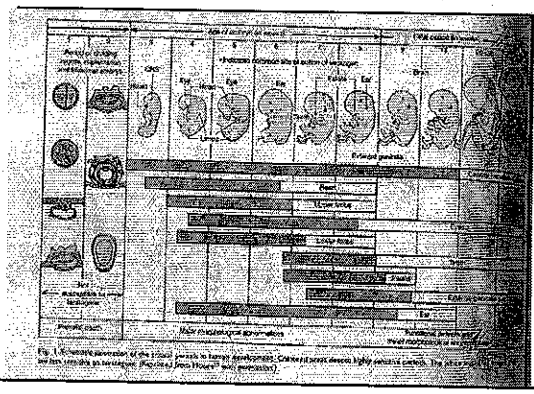
TIME-LINE OF RADIATION RISK



ORGANOGENESIS

- 9 – 60 Days
- Effects
  - Intra-uterine death
  - Malformations
  - Neonatal and post-natal death
- High risk period for malformations
  - Many different cell lineages undergoing growth and transformation
    - Each tissue have different periods of maximal radiation sensitivity
    - Doses as low as 5cGy can lead to severe malformation

RISKS BY GESTATION PERIOD



FETAL PERIOD

- 61 days to birth
- Effects
  - CNS (mental retardation
  - Growth retardation
  - Sterility
  - Cataracts
  - Carcinogenesis
  - Non-specific life shortening
- Frequency and severity of malformations smaller
  - Reducing risk with increasing gestational age
    - Number of cells is greater

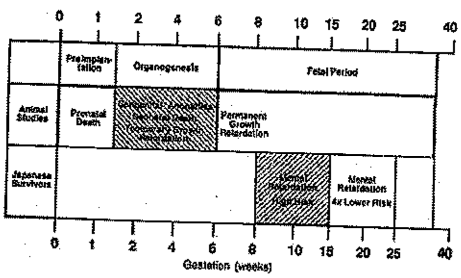
SUMMARY

TABLE V. Risk associated with irradiation during fetal development (After Brent, Ref. 29).

	Preimplantation	Organogenesis	Early fetal	Mid-fetal	Late fetal
Postconception time, days	0 to 8	9 to 50	51 to 105	106 to 175	>175
Postconception time, weeks	1	2 to 7	8 to 15	16 to 25	>25
Effects					
Lethality	+++	+	+	–	–
Gross malformations	–	+++	+	–	–
Growth retardation	–	+++	++	+	–
Mental retardation	–	–	+++	+	+
Sterility	–	+	++	+	–
Cataracts	–	+	+	+	+
Other neuropathology	–	+++	+	+	+
Malignant disease	–	+	+	+	+

– No observed effect.
\+ Demonstrated effect.
++ Readily apparent effect.
+++ Occurs in high incidence.

Radiation in Man and Animal: Gestation, Death and Anomalies



Note: Different Reproductive Strategies!!!

Minimum Dose to Cause Effects in Embryos and Fetus

TABLE 12.2. *Minimum Doses at Which Effects on the Embryo and Fetus Have Been Observed*

Animal data	
Oocyte killing (primates)	50% lethal dose at 5 rads (0.5 Gy)
Central nervous system damage (mouse)	Threshold at 10 rads (0.1 Gy)
Brain damage and behavioral damage (rat)	Threshold at 6 rads (0.06 Gy)
Human data	
Small head circumference	Air kerma 10–19 rads (0.1 to 0.19 Gy) Fetal dose 6 rads (0.06 Gy)
Summary	
Readily measurable damage caused by doses below 10 rads (0.1 Gy) (acute exposure) delivered at sensitive stages	

Summarized from Committee on the Biological Effects of Ionizing Radiation: The Effects on Populations of Exposure to Low Levels of Ionizing Radiation. Washington, DC, National Academy of Sciences, 1980.

Risk to fetus

- Naturally-occurring genetic (i.e., hereditary) diseases arise as a result of alterations (mutations) occurring in the genetic material (DNA) contained in the germ cells (sperm and eggs) and are heritable (i.e., they can be transmitted to the offspring and subsequent generations).
- Studies of 30,000 children of exposed A-bomb survivors show a lack of significant adverse genetic effects.

CONCLUSION

- No fixed policy regarding chemotherapy or radiotherapy in pregnancy
  - Treatment "individualised"
- Consider risk to fetus and probability of cancer cure
  - Estimate dose to fetus by monitoring dose to abdomen
- Theoretically safe to irradiate supra-diafragmatic area beyond 26 weeks
  - Versus rate of spontaneous malformation.

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- ICRP pub. 86 Clinical consequences of accidents in radiotherapy
- ICRP supporting guidance No.2
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