Living with radioactivity

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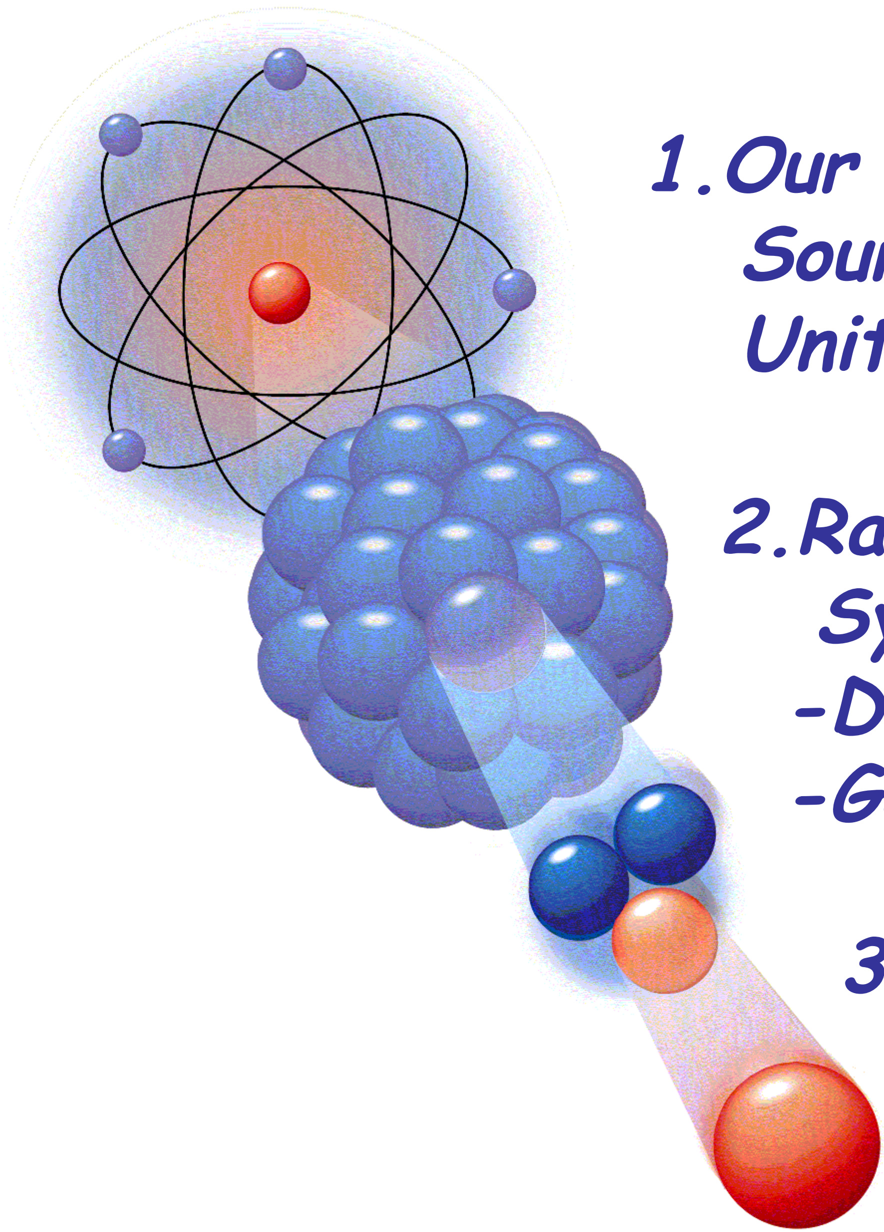


Outline

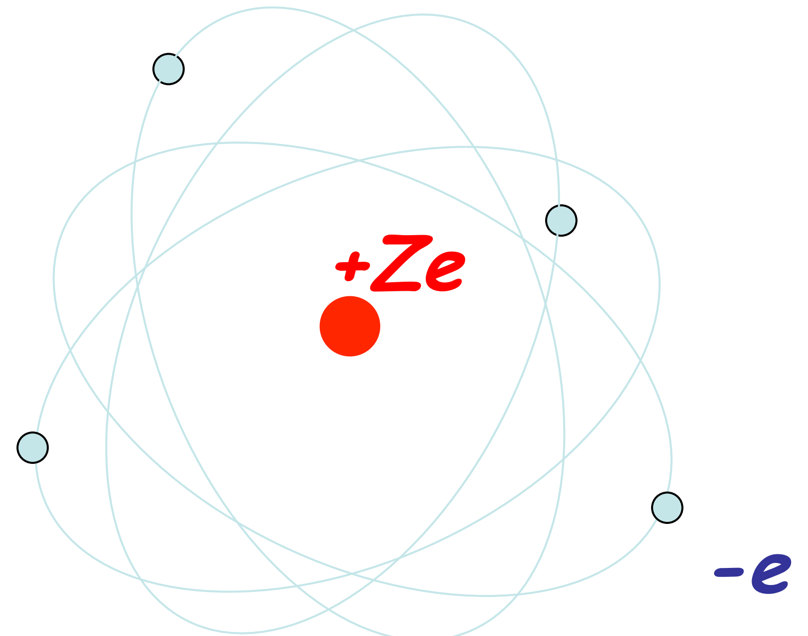
1. Our radioactive World
   Sources of radiation
   Units of rad^n and radioactivity

2. Radiation damage in biological Systems
   -Deterministic Effects
   -Genetic Effects

3. Radiation –Medical Use
   -diagnosis
   -therapy

Ionising and Non-ionising radiation

- Atoms are electrically neutral.



- An atom can lose one or more electrons in various processes.

  Atoms with electrons missing or added are called ions

- We divide radiation into two main categories
  - Ionising radiation
  - Non-ionising radiation

Today we will focus on the effects on health of Ionising radiation

Ionising Radiation

- What types of radiation are Ionising?

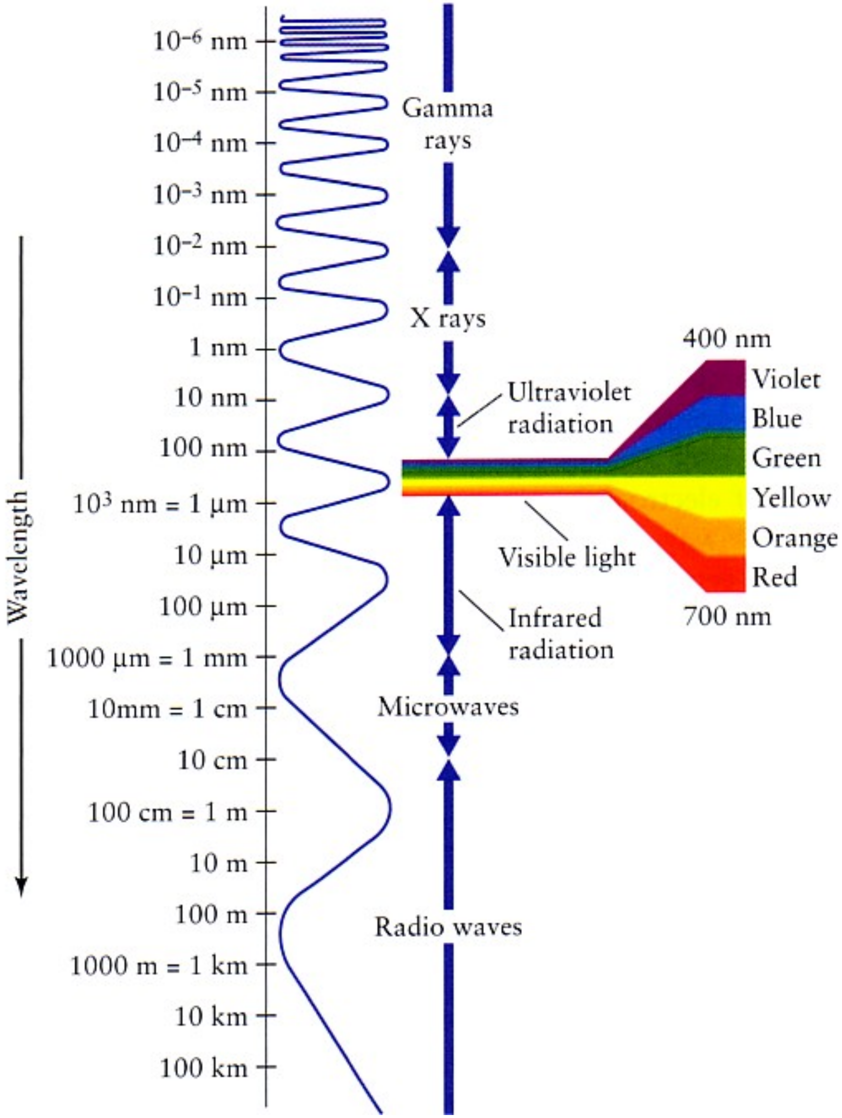
  -Electromagnetic radiation above a certain energy

  -Particles such as protons,electrons,alpha particles, atomic nuclei

- Neutral particles do it indirectly by producing charged particles.

  For example neutrons can do it by hitting a proton and giving it energy

The Electromagnetic Spectrum



- The figure shows the electromagnetic spectrum over all wavelengths.

- EM radiation exists at all wavelengths and has the same basic properties.In particular they always propagate with velocity v = c in vacuum and can be refracted, reflected, scattered etc

- The various parts of the spectrum are named by the method of production and not by energy or wavelength. For example gamma rays arise from transitions between levels in atomic nuclei.

Some Units we will need!

Unit of Radioactivity:-

One Becquerel (1Bq) =
One radioactive decay per second

Dose and Absorbed Dose (D): is the energy deposited, ΔE_D by ionising radiation to a mass, Δm of matter in a given volume element.

$$\boxed{D = \frac{\Delta E_D}{\Delta m}}$$

The SI unit for absorbed dose is the Gray (Gy) ,

$$\boxed{1\ \text{Gy} = 1\text{Joule} / \text{kg}.}$$

$\boxed{\text{10Gy would constitute a lethal whole body dose in a human.}}$

Equivalent dose (HT)

- The human equivalent dose, ***HT,*** measures the biological damage to a human due to exposure to a particular type of radiation.

- It is defined by ***HT = WR x DT***, where ***T*** represents a specific tissue or part of the body. ***H*** is also called the 'radiation-weighted dose'

- The SI unit for human-equivalent dose is the Sievert (Sv). **1 Sv = 1 gray x WR**

Our World is Radioactive

- There is no escape from Radioactivity!!

- We are constantly bombarded by cosmic rays

- We are constantly irradiated by gamma rays from all the materials around us

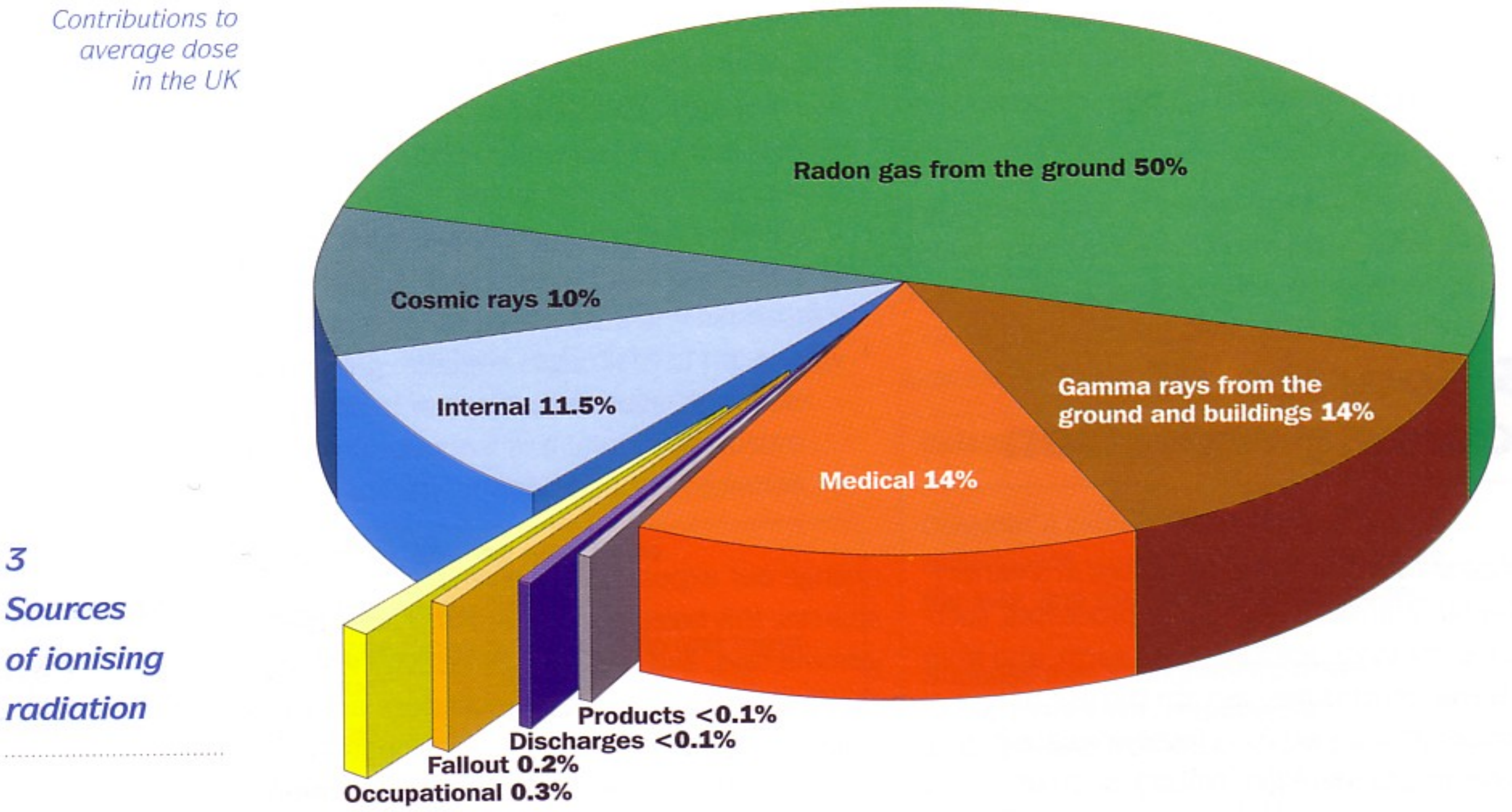
- Everything we eat, drink, breathe, (smoke), is radioactive

- All of us are radioactive and your neighbours here today are all effectively radioactive sources.

Sources of Radiation in our environment

- Cosmic Rays *
- Primordial Radioactivity *
- Natural secondary radioactivity *
- Man-made activity *
- Exposure due to Industrial activity *
- Medical Exposure
- All of these lead or may lead to activity within the body or may be due to activity within the body.

From NRPB-Average Radiation Dose in UK



NRPB is now part of Public Health England

Annual Average Total Effective Dose Equivalent to the U.S. Population

Natural Background, Radon	200 mrems
Cosmic and Terrestrial source	56
Medical and Dental X-Rays	54
Internal Source, ^{40}K	40
Tobacco Smoking	280
Other Consumer Products	10
Total, All Population	640
Total, Non-Smokers	360

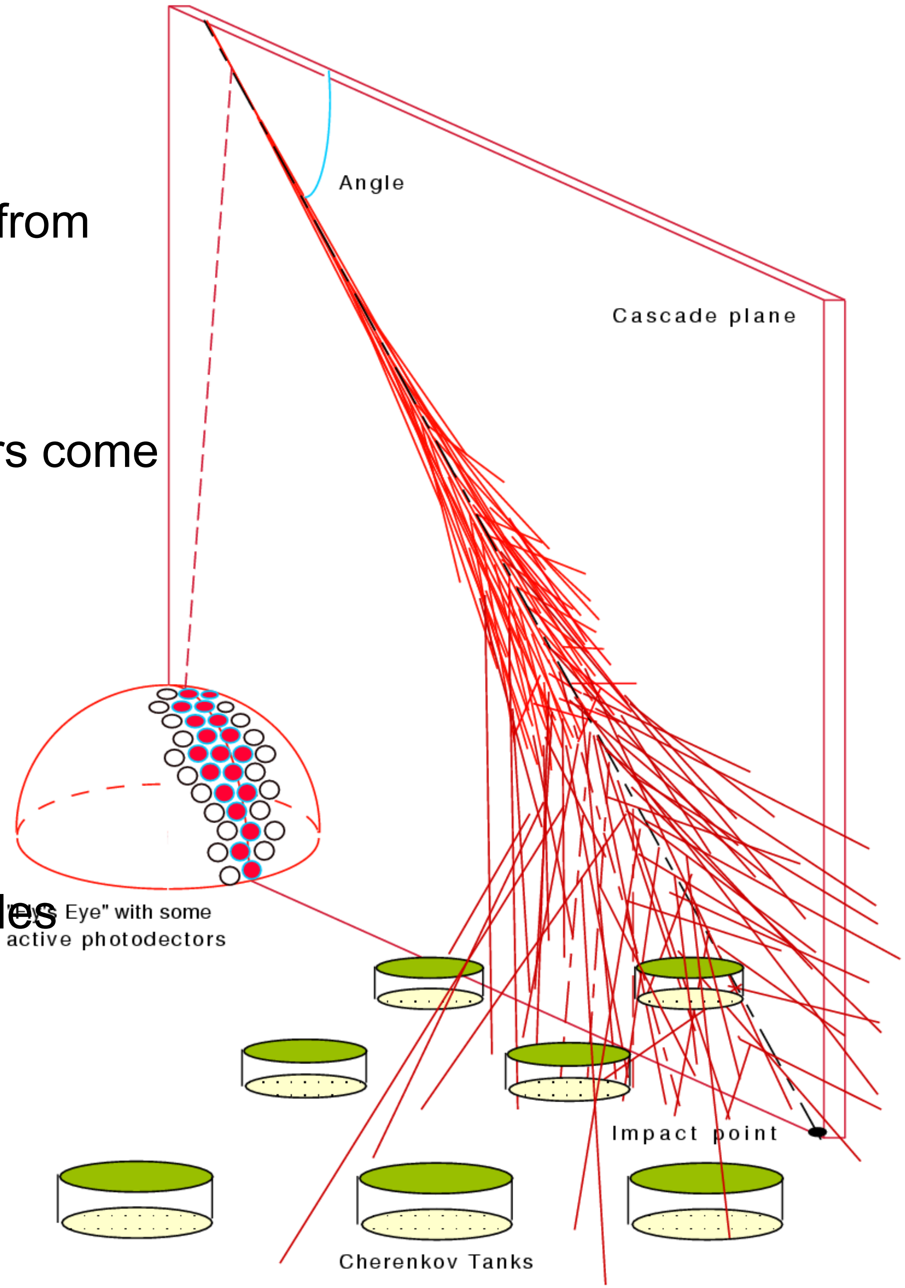
Cosmic Rays

- Earth is constantly bombarded by particles from outside the atmosphere.

  Some have their origins in the Sun but others come from much further away.

- On entering the atmosphere they interact with matter and produce secondary particles, which in turn produce more particles and a “shower” is created

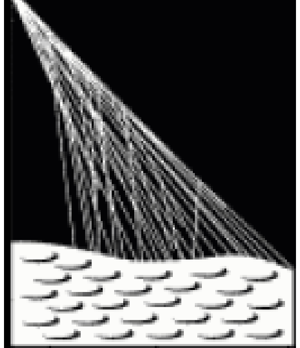
- Most primary cosmic rays are protons but we get atomic nuclei up to Fe and beyond.



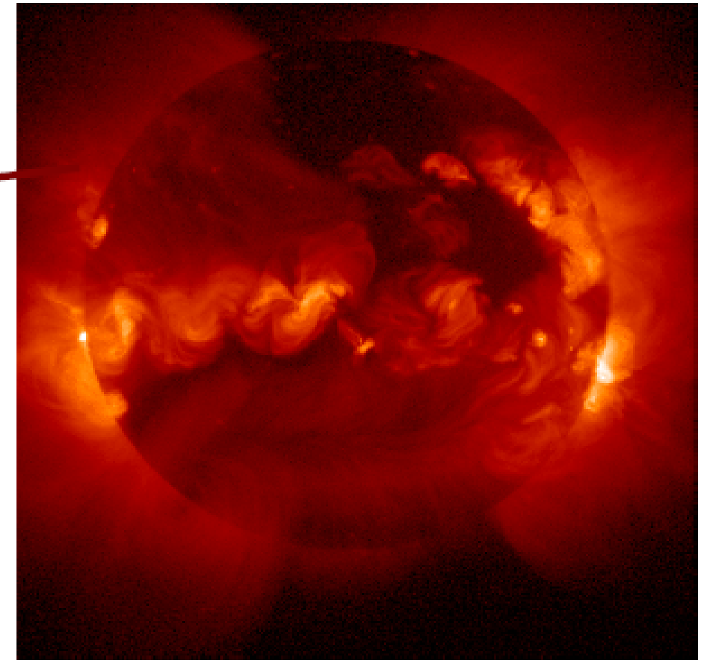
Cosmic rays at High Altitude

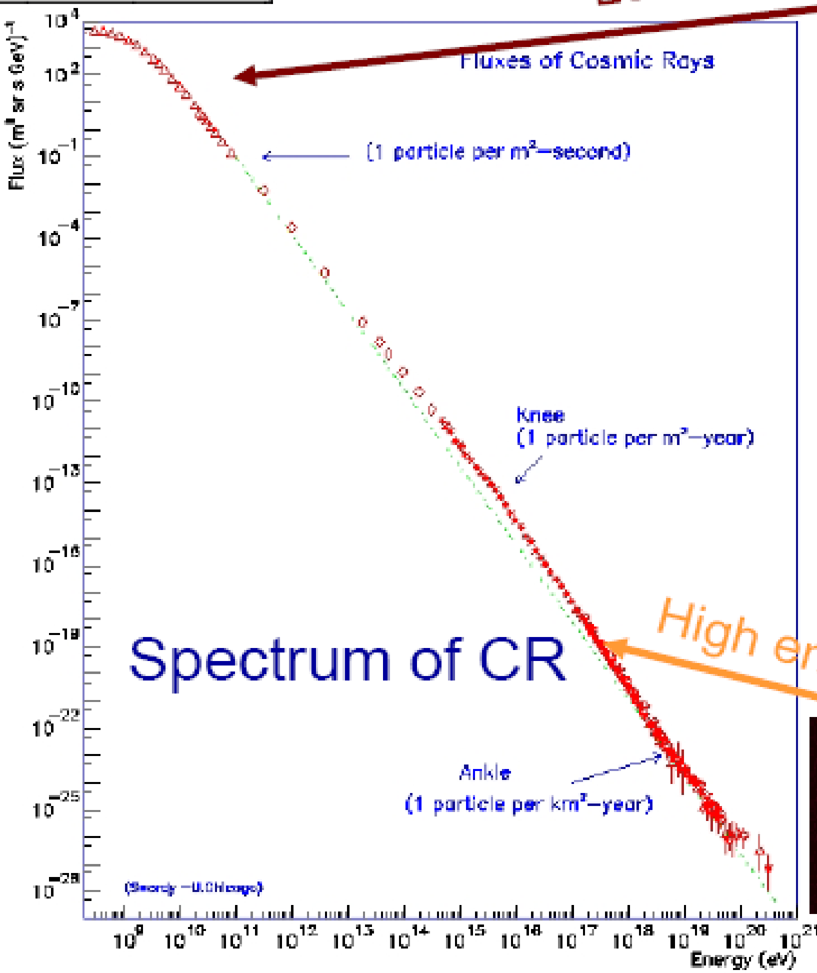
- At sea level atmosphere protects us from most of cosmic radiation.
- On average about 270 μSv dose per annum at sea level due to Cosmic Rays
- This doubles for every 5-6000 feet in altitude. This is how they were discovered by Hess.
- At 36,000 feet – typical TransAtlantic flight – 64 times higher
- Thus 12 return flights to Los Angeles from London gives an extra 350 - 400 μSv dose per annum – cf 2.6 mSv from other natural sources at Sea level.
- Recommended "extra" exposure to public is 1 mSv
- Average exposure in UK is 2.6 mSv

Cosmic Ray Bombardment



Low energy CR

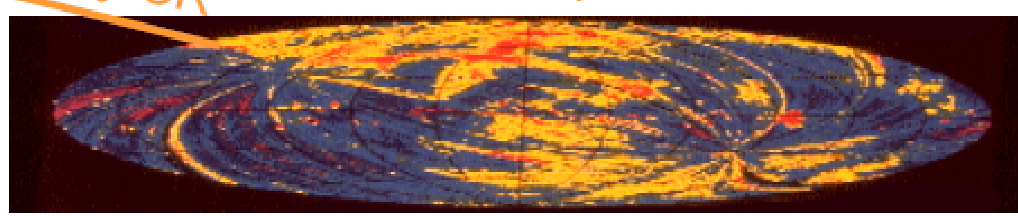




High energy CR

Cosmic Rays origin from:

- solar flares;
- distant supernovae;



Sources of Radiation in our environment

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Radioactivity in our Environment

- We are all constantly subject to irradiation from natural radioactive sources.

- There are three main sources of such radiation.

  a)**Primordial**-around since the creation of the Earth(~4.5 x 10^9 years ago)

  b)**Cosmogenic**-formed by the interaction of Cosmic rays with the Earth and its atmosphere.

  c)Produced or enhanced by **human activity**, e.g fallout from weapons tests.

- Examples:-

  a) ^{235}U or ^{40}K

  b) ^{14}C

  c) The products of fission such as ^{137}Cs in weapons tests

^{14}C Production by Cosmic Rays

- Earth is constantly under bombardment by particles and photons from outer space.

- High energy protons create fast neutrons on interaction with the atmosphere.

- The ^{14}C is then produced in the reaction

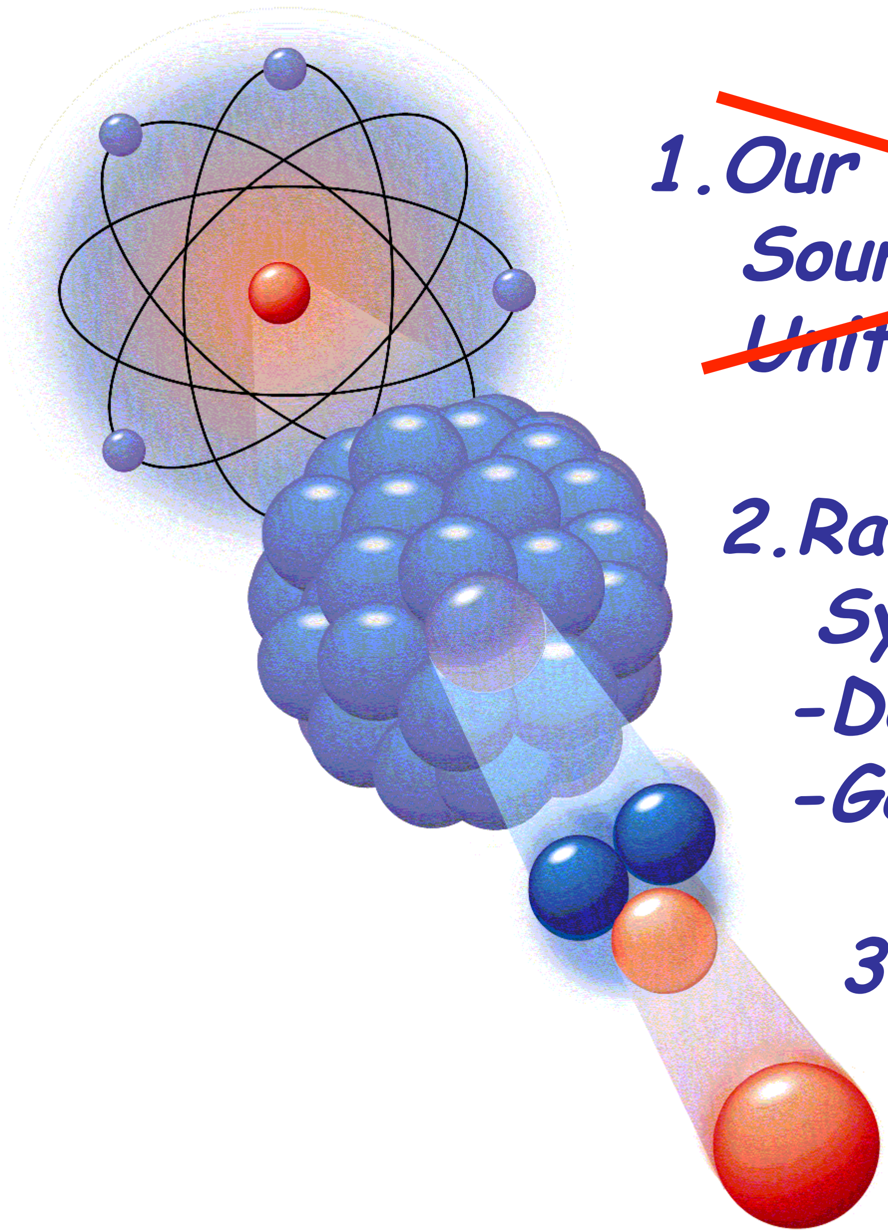
$$n + {}^{14}N \longrightarrow {}^{14}C + p$$

- This radioactive isotope of carbon has a half life of 5730 years. Chemically it is indistinguishable from the natural, stable isotopes of carbon with A = 12 and 13.

- Accordingly it forms carbon dioxide. This mixes with all the carbon dioxide in the atmosphere and becomes part of the carbon in all living things. We inhale it every time we breathe.

- When living things die they no longer acquire new carbon dioxide. The ^{14}C now decays and we can determine how long it is since an object died by measuring the ratio of ^{14}C to the stable isotopes. [Basis of Carbon dating]

- This is just one of a no.of examples of naturally occurring radioactive species which we inhale or ingest and which are a natural part of our bodies.



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   ~~Sources of radiation~~
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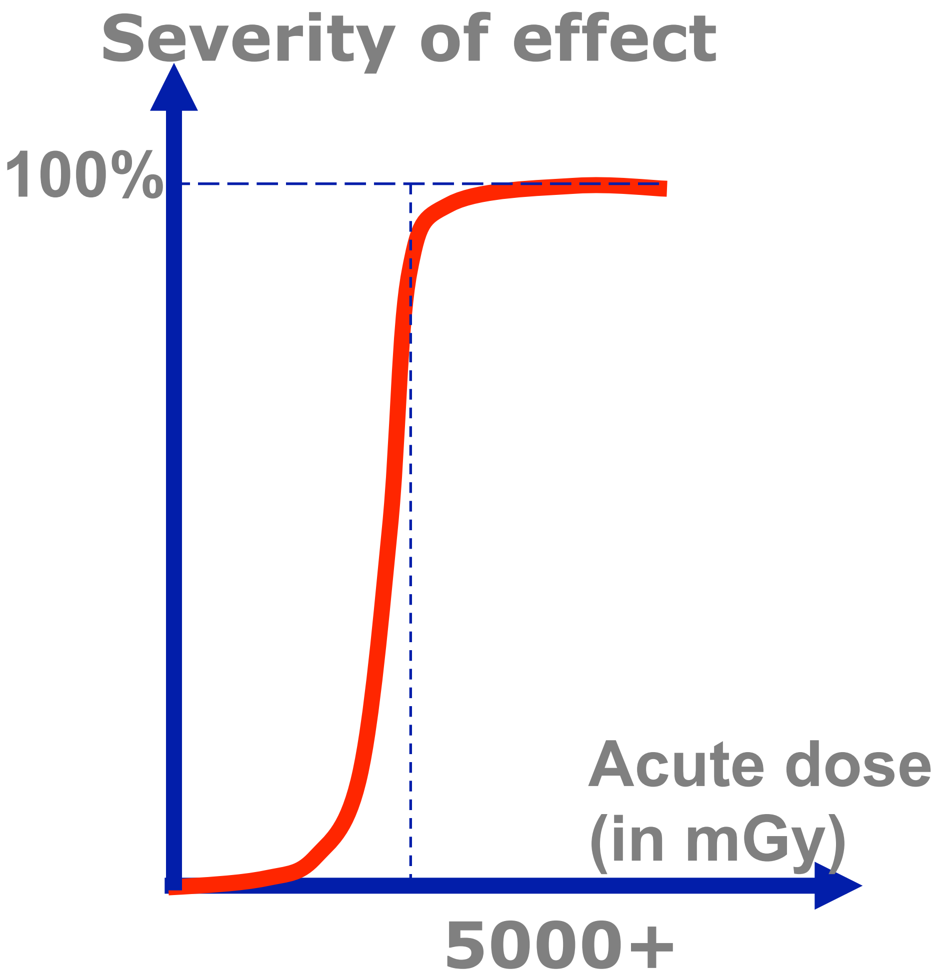
ADVERSE HEALTH EFFECTS OF RADIATION EXPOSURE :

- **deterministic effects** or somatic effects(also called tissue reactions) due in large part to the killing/ malfunction of cells following high doses;

- **stochastic effects** (cancer and heritable effects) involving either cancer development in exposed individuals due to mutation of somatic cells or heritable disease in their offspring due to mutation of reproductive (germ) cells.

DETERMINISTIC HEALTH EFFECTS



a. A minimum dose before an effect is observed

b. Magnitude of effect increases with dose

c. Clear, causal relationship between exposure to agent and observed effect

d. Dose threshold is specific to a particular effect

e. Early appearance(days to weeks excluding cataracts)

DETERMINISTIC INJURIES

RADIATION ACCIDENTS WITH FATALITIES

REACTORS

Idaho (USA), Vinca (Yugoslavia), Chernobyl (USSR), Russian submarines

CRITICALITY

Argentina, Japan, Russia, USA

IRRADIATORS

France, Israel, USA, Italy, China, El Salvador, Norway, Belarus,

LOST SOURCES

UK, Mexico, China, Argentina, Algeria, Mexico, Estonia, Georgia, Thailand, Peru, Russia, Brazil, USA, Morocco

MEDICAL

USA, Spain, Costa Rica, Panama, China, France, UK

Stochastic Effects

No threshold

Generally occurs with a single cell

Probability of the effect increases with dose

e.g. Cancer, hereditary effects

Questions: Linear No threshold hypothesis
Individual susceptibility

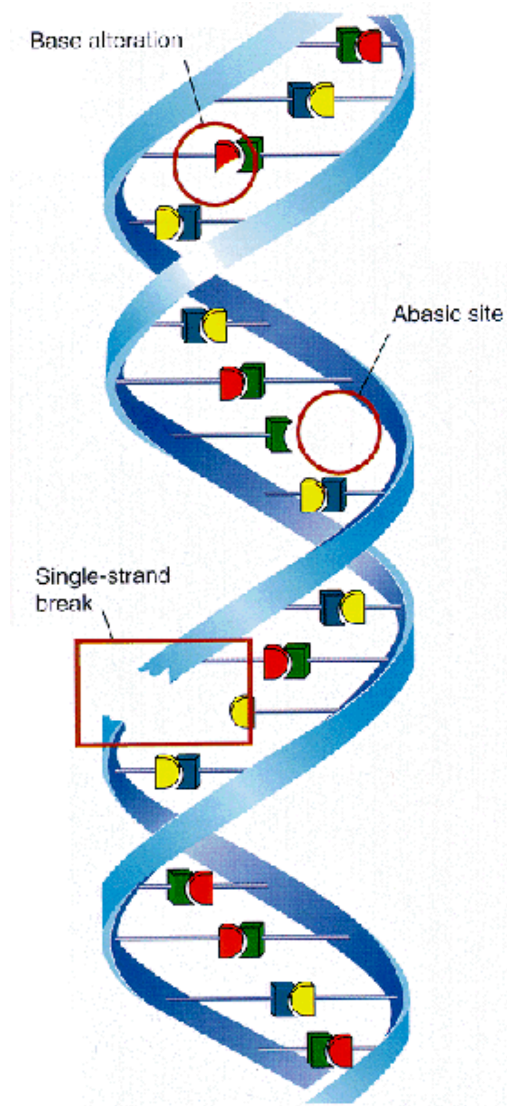
RADIATION-ASSOCIATED CANCER

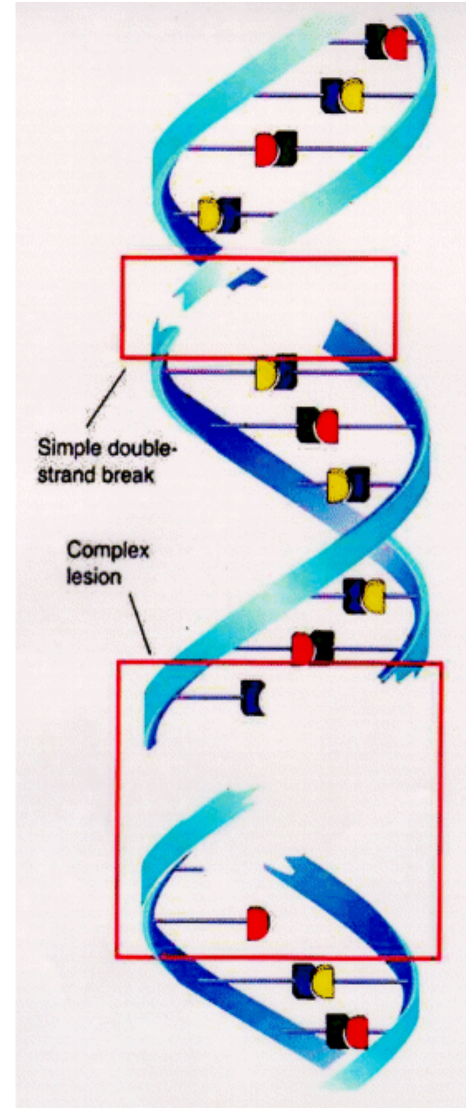
DNA damage recognition/repair; cell cycle effects

Importance of DNA double strand breaks

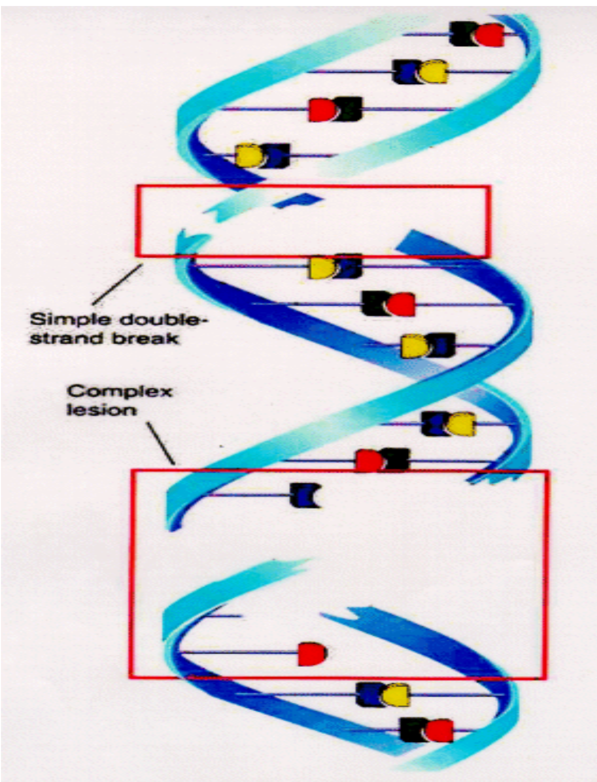
Cancer origins - gene mutation in single cells

Multi-stage tumorigenesis - role of radiation

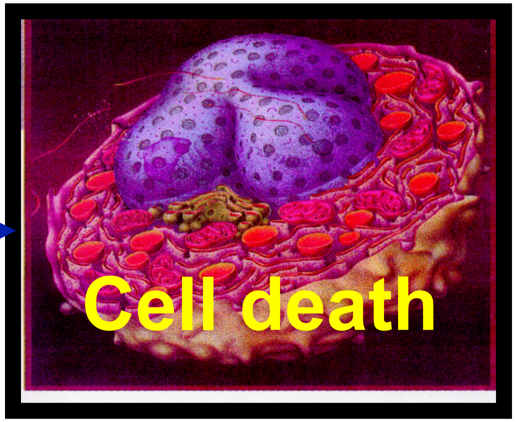




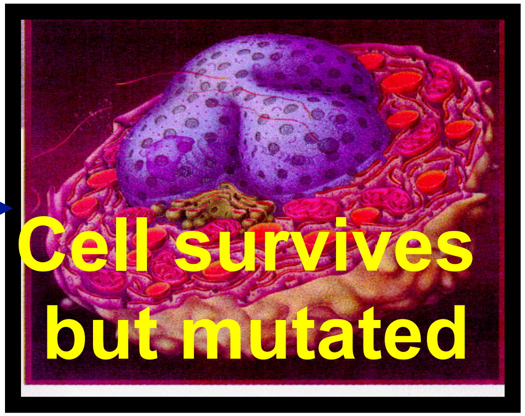
DNA Mutation



Viable Cell



Non-viable Cell



Cancer ?

Genetic Effects

No genetic(or heritable) effects have ever been observed in any human population irradiated at any dose ranging from that due to natural background to that received by survivors of the nuclear bombings at Hiroshima and Nagasaki in Japan.

Sources of Information on Radiation Effects

1. **Survivors of Hiroshima and Nagasaki**
2. **Exposure of Workers**
    - **Medical personnel**
    - **Uranium miners**
    - **Industrial radiographers**
    - **Radium dial painters**
    - **scientists**
3. **Patients who have undergone exposure for diagnosis and therapy**
4. **Workers at nuclear weapons production facilities**
    - **U.S., U.K. and U.S.S.R. particularly at Mayak on the Techa river.**
5. **Exposure of populations to natural background**
    - **This varies by factor of 10**

LIFE SPAN STUDY

Cohort	86,500
Alive in 2000	~35,000

Approximately 10,000 deaths from cancer or leukaemia

Approximate number of radiation-induced cancer deaths

Leukaemia 100 Solid cancers 400

EPIDEMIOLOGY

Substantial information on effects of acute, high dose radiation exposure from Japanese A-bomb survivors and medically-exposed groups

These studies largely form the basis of current radiation risk estimates

However, most interest in radiation protection is on chronic and low doses

Recent review of epidemiological studies by UNSCEAR(2000), ICRP(2006)

Response to Radiation Exposure

1. More is known about the mechanism of radiation effects on molecular, cellular and organ systems than is known for most other environmental stressing agents

   Thus because we know so much about the dose-response relationship we can set levels of exposure for workers and the public which pose much lower risks than we accept in other everyday situations.

2. Observed effects are stochastic or deterministic effects.

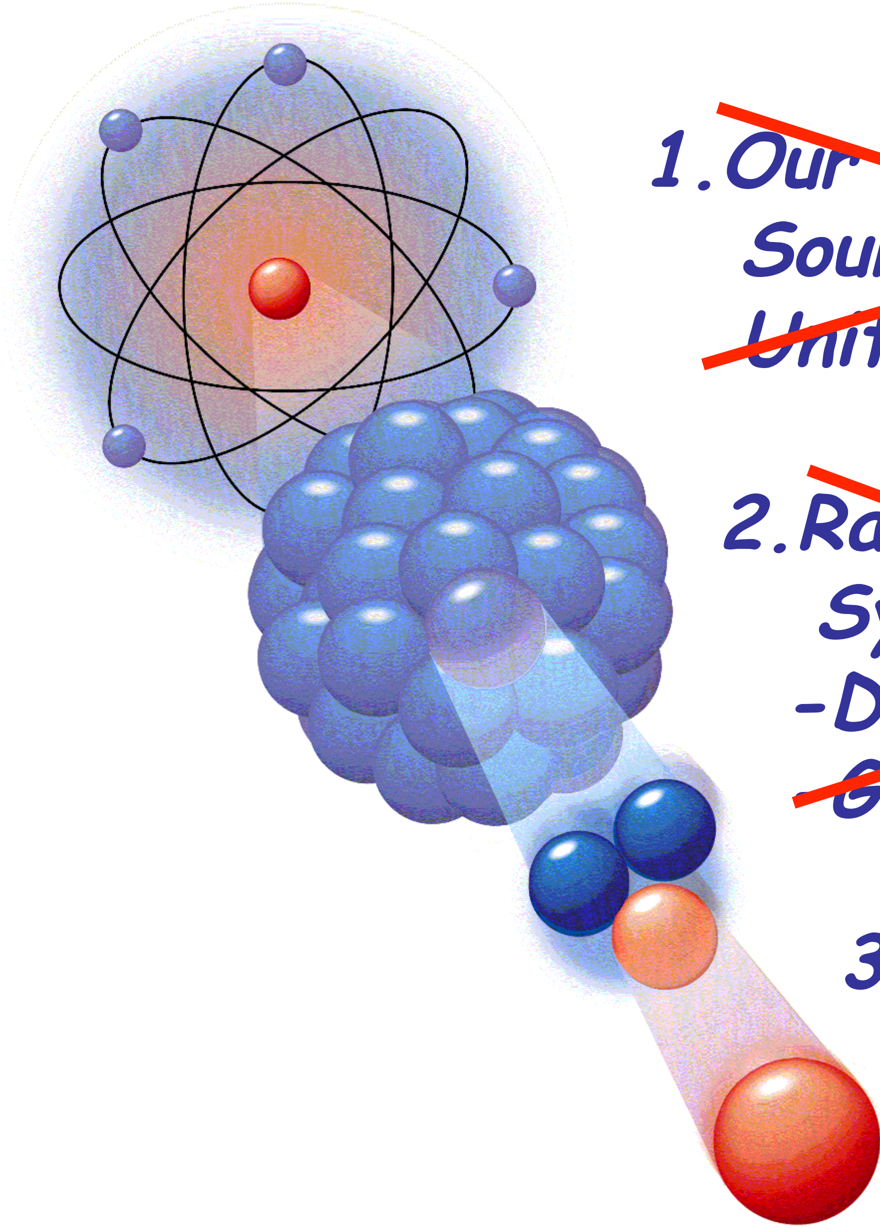
3. Stochastic effects occur randomly and the probability of occurrence rather than severity of effect depends on dose.

ICRP Recommended Annual Dose Limits

Body Part	Occupational	General Public
Whole body (HE)	20mSv	1mSv
Eye lens (HT)	150mSv	15mSv
Skin (HT)	500mSv	50mSv
Hands & Feet (HT)	500mSv	---------

Note these recommended limits EXCLUDE any medical or natural background radiation doses. Remember the annual average exposure of the U.K. population is 2.6mSv.

Outline



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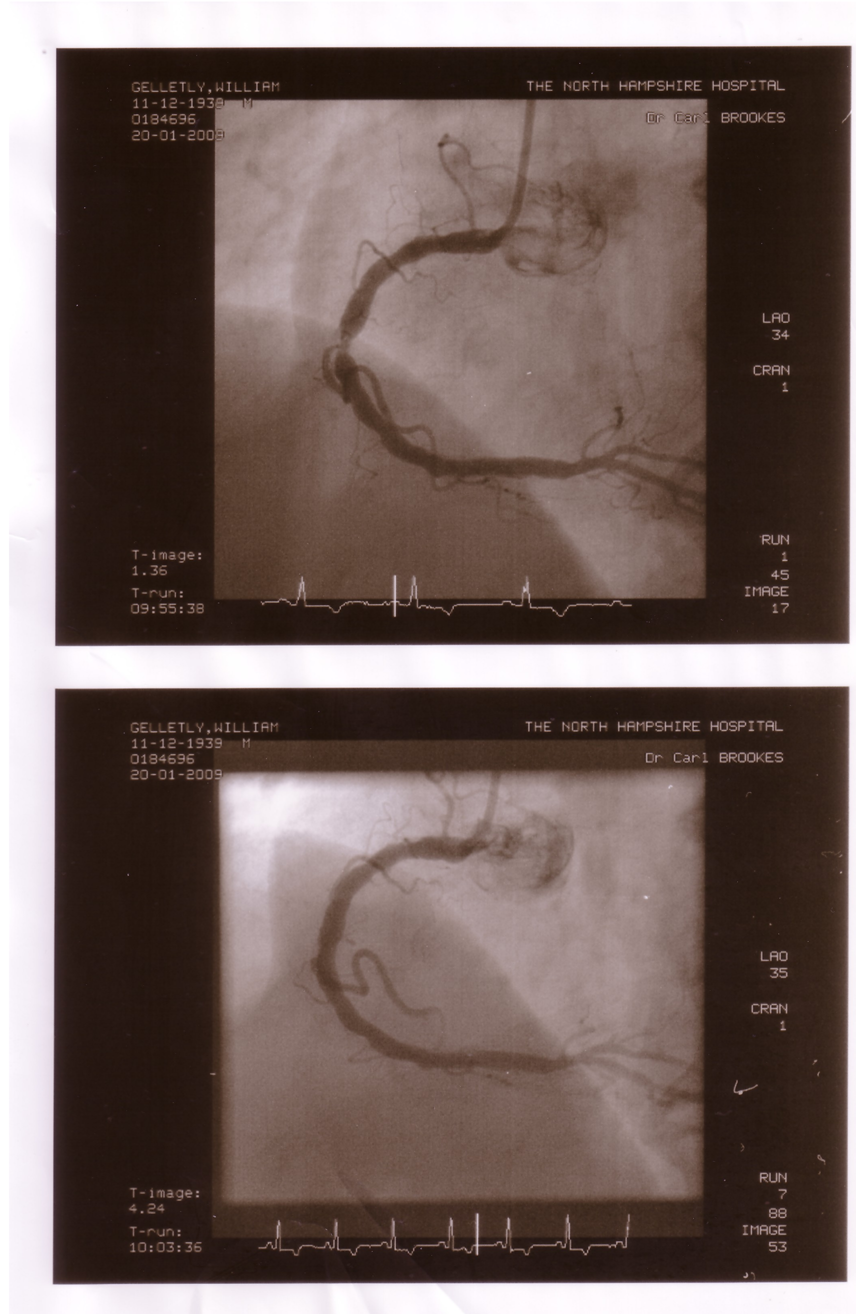
Radiation – A Blessing

Hand with ring



Right Coronary Artery

Cancer

Cancer is characterised by a disorderly proliferation of cells that can invade adjacent tissues and spread via the lymphatic system or blood vessels to other parts of the body.

Radiation interacting with cell molecules

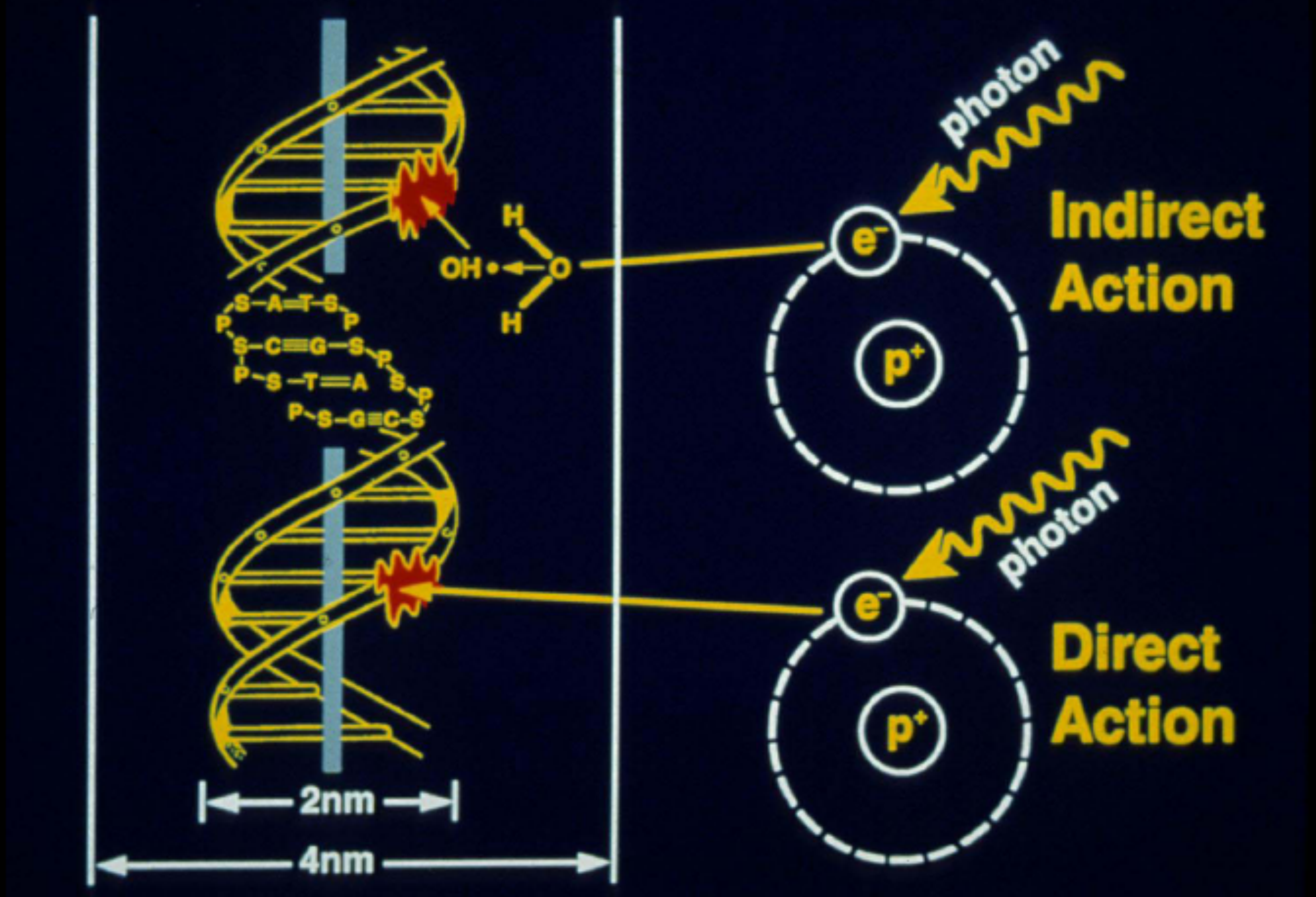
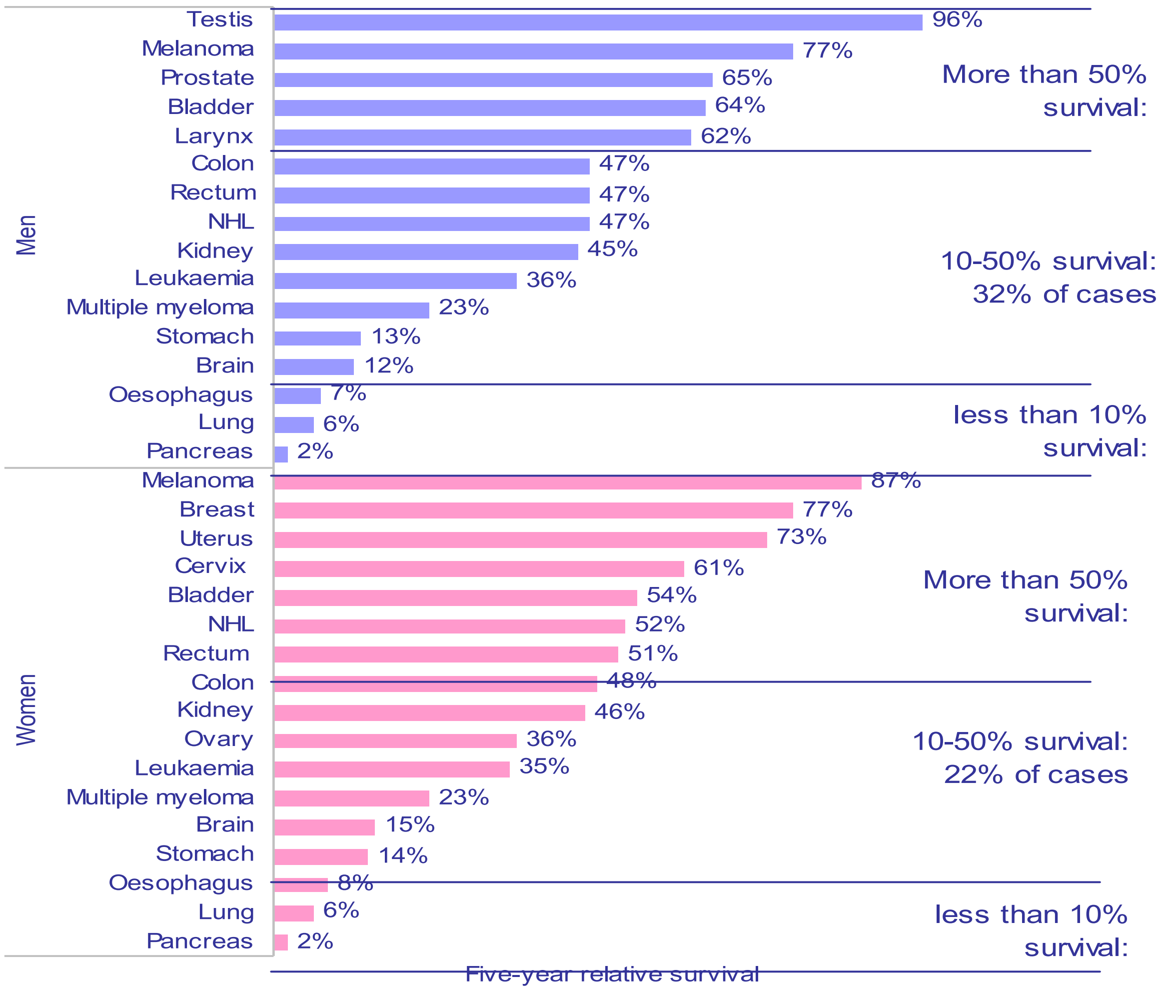


Table 5.1: Risk of being diagnosed with cancer by age 65 and over a lifetime, England and Wales, 1997

	% of cohort that develop cancer					
	Males			Females		
	by age 65	over lifetime	lifetime risk	by age 65	over lifetime	lifetime risk
Bladder	0.7	3.3	1 in 30	0.2	1.3	1 in 79
Brain and CNS	0.4	0.7	1 in 147	0.3	0.5	1 in 207
Breast	…	…	…	5.6	10.9	1 in 9
Cervix	…	…	…	0.6	0.9	1 in 116
Kidney	0.4	1.1	1 in 89	0.2	0.6	1 in 162
Large bowel	1.4	5.7	1 in 18	1.1	4.9	1 in 20
Leukaemia	0.4	1.0	1 in 95	0.3	0.8	1 in 127
Lung	1.7	8.0	1 in 13	1.0	4.3	1 in 23
Melanoma	0.4	0.7	1 in 147	0.5	0.9	1 in 117
Multiple myeloma	0.1	0.6	1 in 177	0.1	0.5	1 in 204
Non-Hodgkin lymphoma	0.6	1.4	1 in 69	0.4	1.2	1 in 83
Oesophagus	0.4	1.3	1 in 75	0.2	1.1	1 in 95
Ovary	…	…	…	0.9	2.1	1 in 48
Pancreas	0.3	1.0	1 in 96	0.2	1.1	1 in 95
Prostate	0.9	7.3	1 in 14	…	…	…
Stomach	0.5	2.3	1 in 44	0.2	1.2	1 in 86
Uterus	…	…	…	0.6	1.4	1 in 73

Five year age standardised relative survival (%), adults diagnosed 1996-1999, (England & Wales by sex and site)



Treatment of Cancer

1. Surgery to excise or resection a tumour

2. Chemotherapy

3. Radiation treatment

Treatment is highly individual. It depends on the organ Involved, the nature of the tumour, its size, its location relative to other organs etc. All of these factors will Influence the oncologist in deciding what treatment to propose. The treatment may be any combination of 1-3.

Some issues of Importance in Treatment using radiation

1. ***Hypoxia – tumours may outgrow their blood supply and they run out of Oxygen, which is highly radiosensitive.***

2. ***High LET (Linear Energy Transfer) – the higher the density of ionisation the greater the fraction of damage to the DNA/Cell is due to direct rather than indirect action.***

3. ***Side scatter – The way in which photons scatter means that there is much more sideways scattering than in the case of hadron beams. This exposes the normal tissue to a greater risk of secondary malignancy.***

4. ***Number 3 is particularly important if tumour is close to another organ sensitive to radiation. This is particularly bad for children – roughly speaking 30% experience a 2nd. Malignancy after five years.***

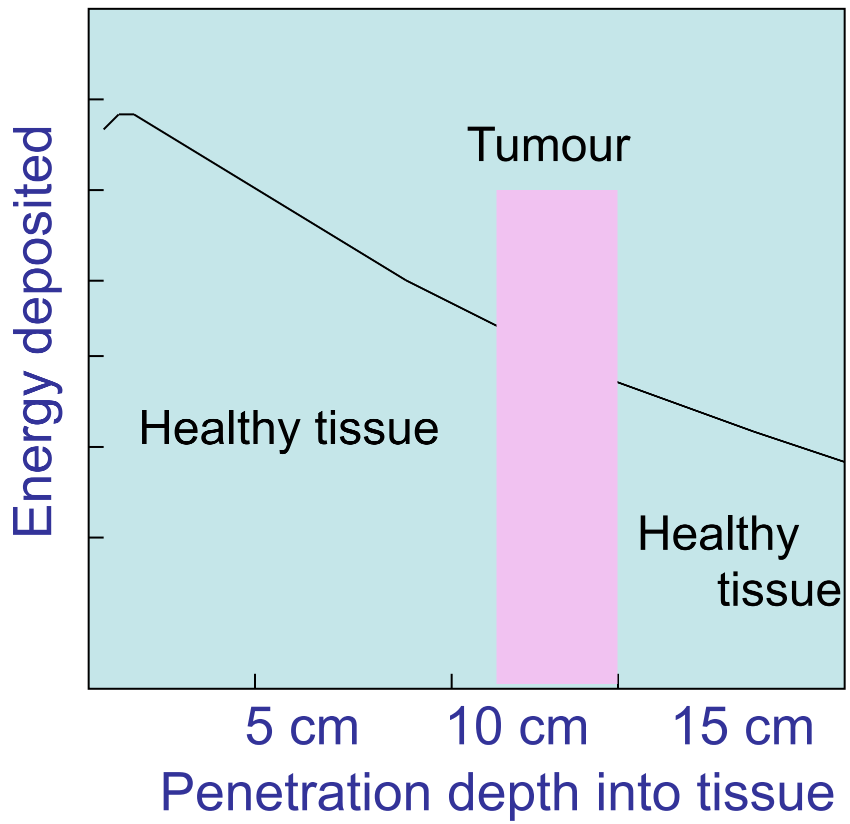
Forms of Radiation Treatment

1. Brachytherapy – A sealed source is placed close to the tumour. This maximises the dose to the tumour and minimises radiation to normal tissue further away. Good for cervix, prostate, breast etc

2. Unsealed sources – taken by infusion or ingestion. Usually chosen so that the radioisotope is selectively absorbed by the affected organ. Examples – ^{131}I which selectively goes to the thyroid or ^{153}Sm lexidoman which goes to damaged bone and spares normal bone. Advantage is that it is highly focussed on organ concerned but technique is limited to a few situations.

3. External beam – either of photons or hadrons. In former case the source of photons can be a large ^{60}Co source or bremsstrahlung from an electron beam produced by an electron linear accelerator. By far the most commonly used hadron beams are proton and carbon beams although other beams have been used in the past. Typically cyclotrons are used to produce the proton beams and the carbon beams are produced in a synchrotron.

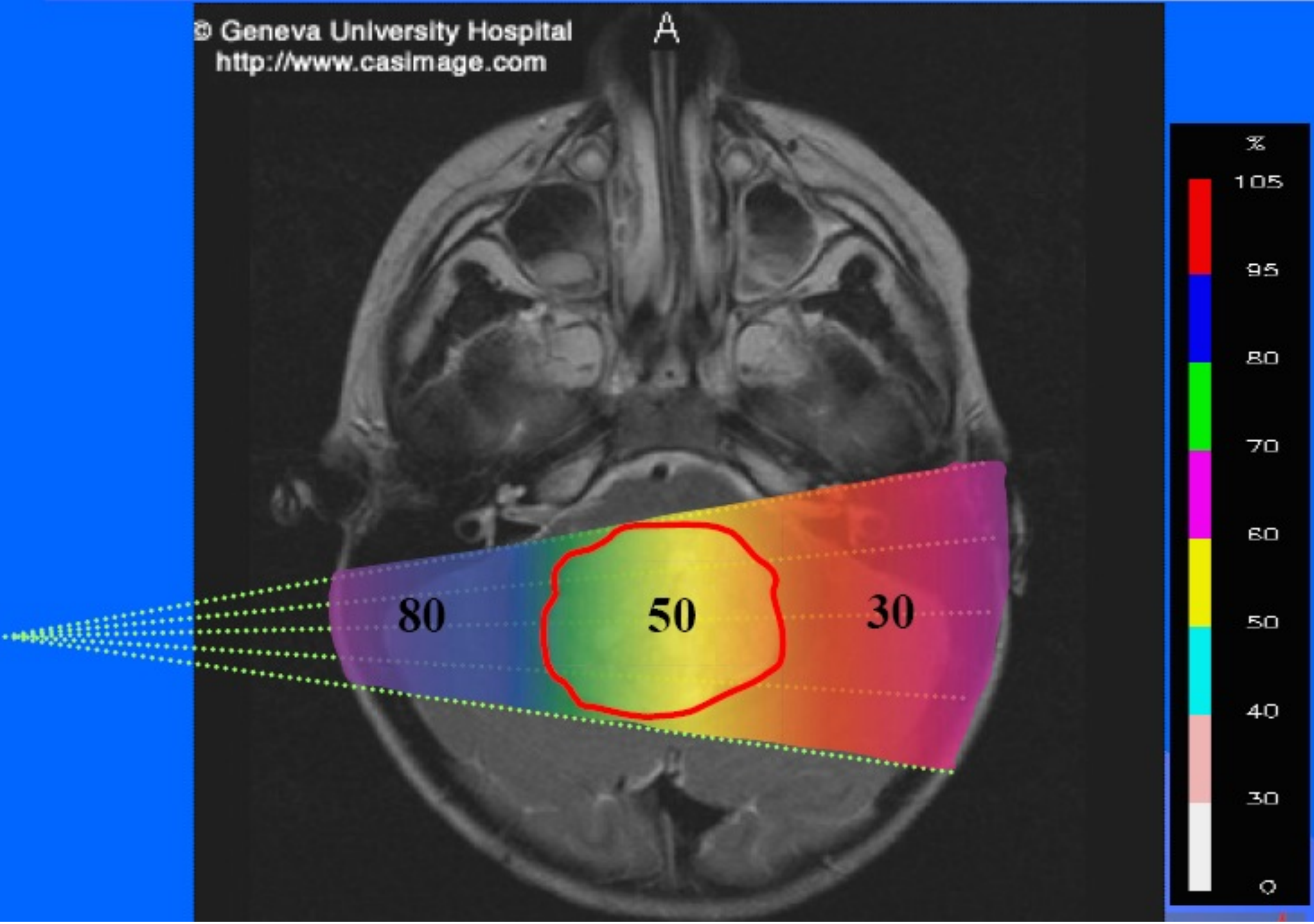
Deposition of Energy by a beam of photons as a function of penetration depth in tissue.



- **In the simplest form of radiation therapy a beam of radiation from a ^{60}Co source is collimated and directed on to the tumour. It is effective but inflexible.**
- **The photon beam deposits energy in normal tissue both in front of and behind the tumour.**
- **Photons also scatter sideways into normal tissue.**

In order to deliver the lethal dose to the tumour we inevitably irradiate healthy tissue in front of and behind the tumour.

Two opposite photon beams



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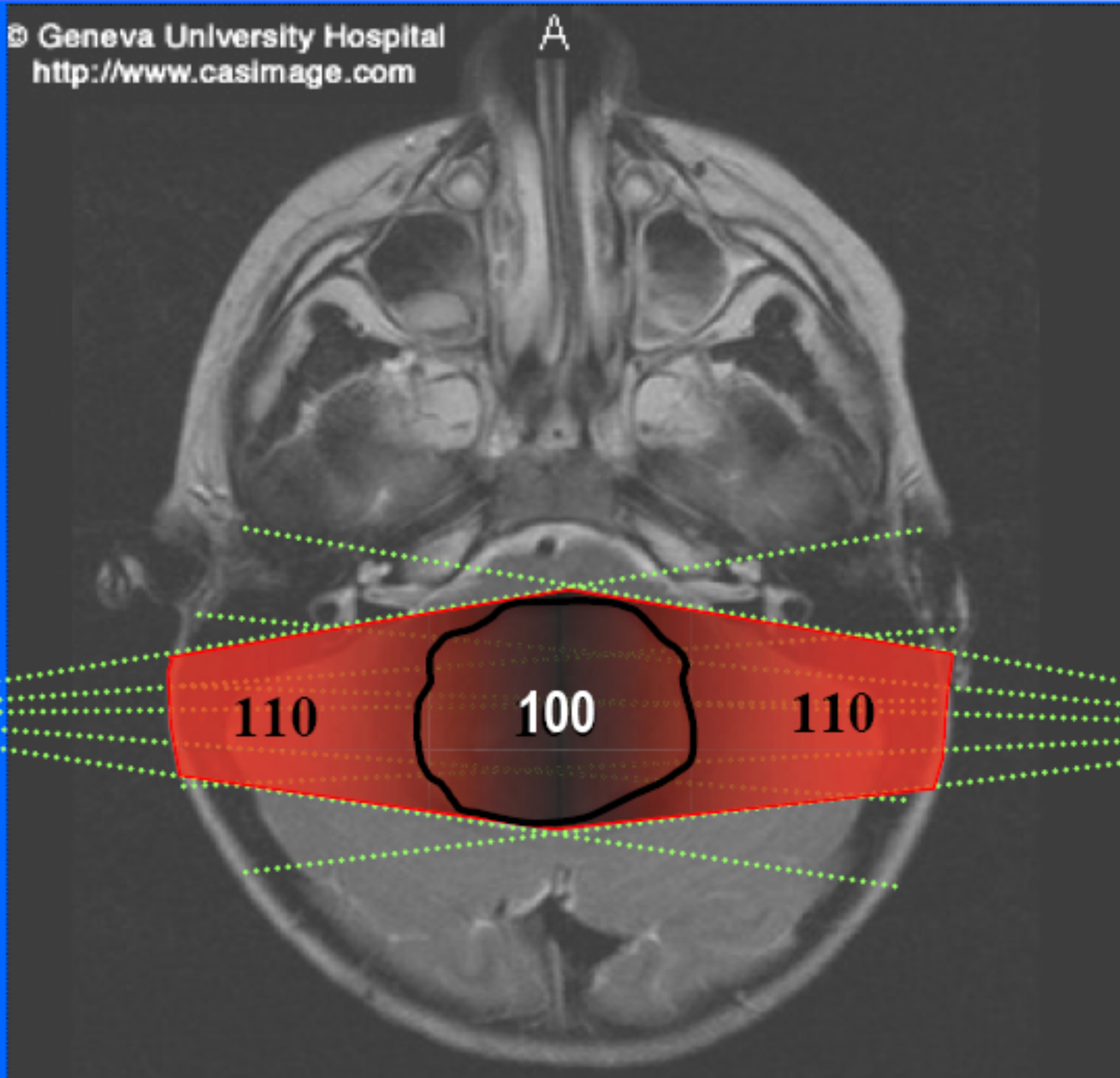


Intensity Modulated Radiation Therapy.

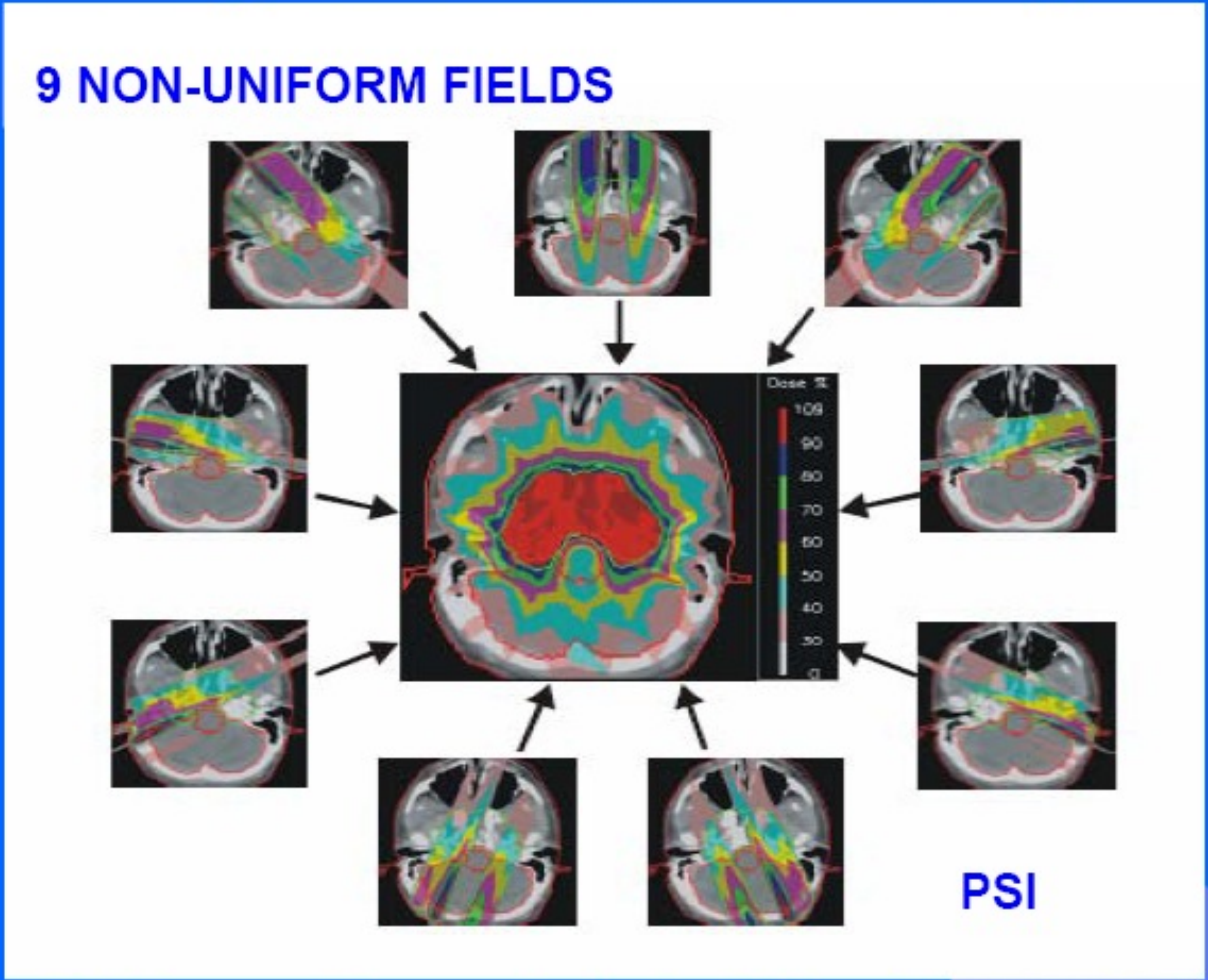
1. Using the two beams reduces the fraction of radiation in normal tissue

2. We can readily extend this idea to the use of multiple beams from different directions. This is now the method of choice since it reduces the risk of secondary malignancies.

3. Typically irradiation from 9 directions is used.

4. How does it work?
   - First a CT scan is used to define the position and extent of the tumour and the positions of any nearby structures.
   - Computer simulation is then used to plan the beam direction, shape etc so that the full extent of the tumour is irradiated.
   - Number of beams is decided.

IMRT = Intensity Modulated Radiation Therapy with photons



60-70 grays given typically in 30 fractions to allow healthy tissues to repair

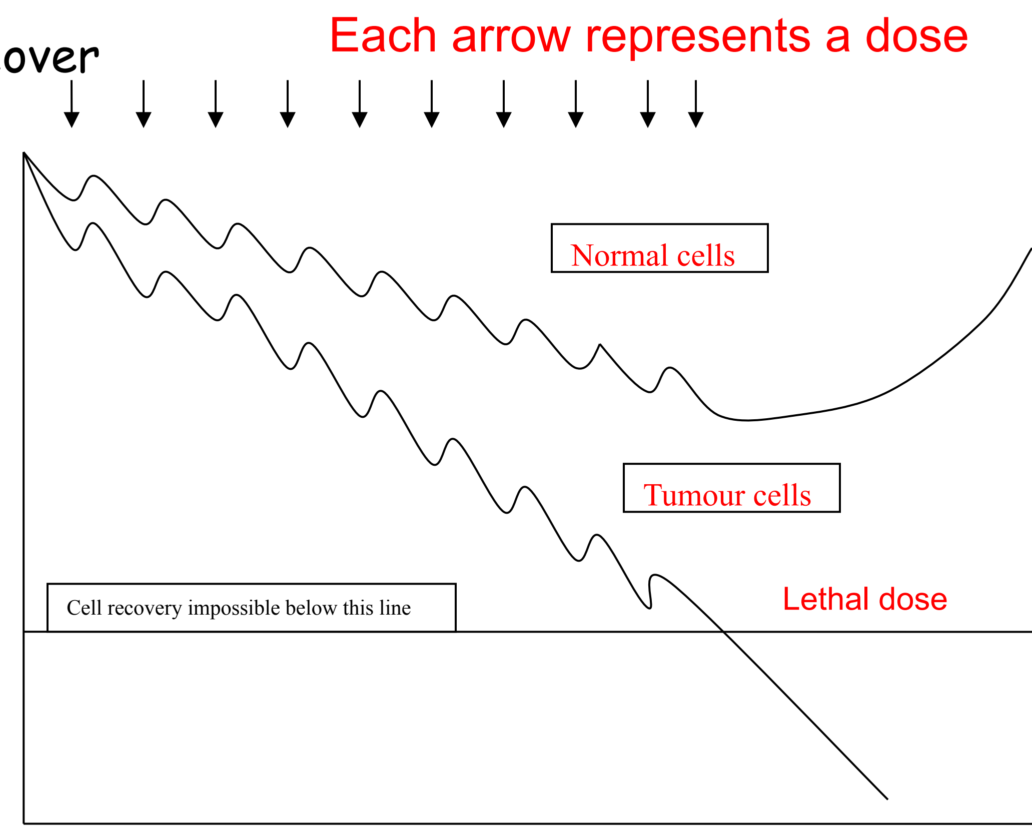
Fractionation in Radiation Therapy.

1. As indicated on the previous slide the radiation is not all delivered at once.

   Typically in the U.K. and elsewhere it is delivered in a series of "fractions"

   - a dose of about 60-70Gy is delivered 1.8-2 Gy at a time.

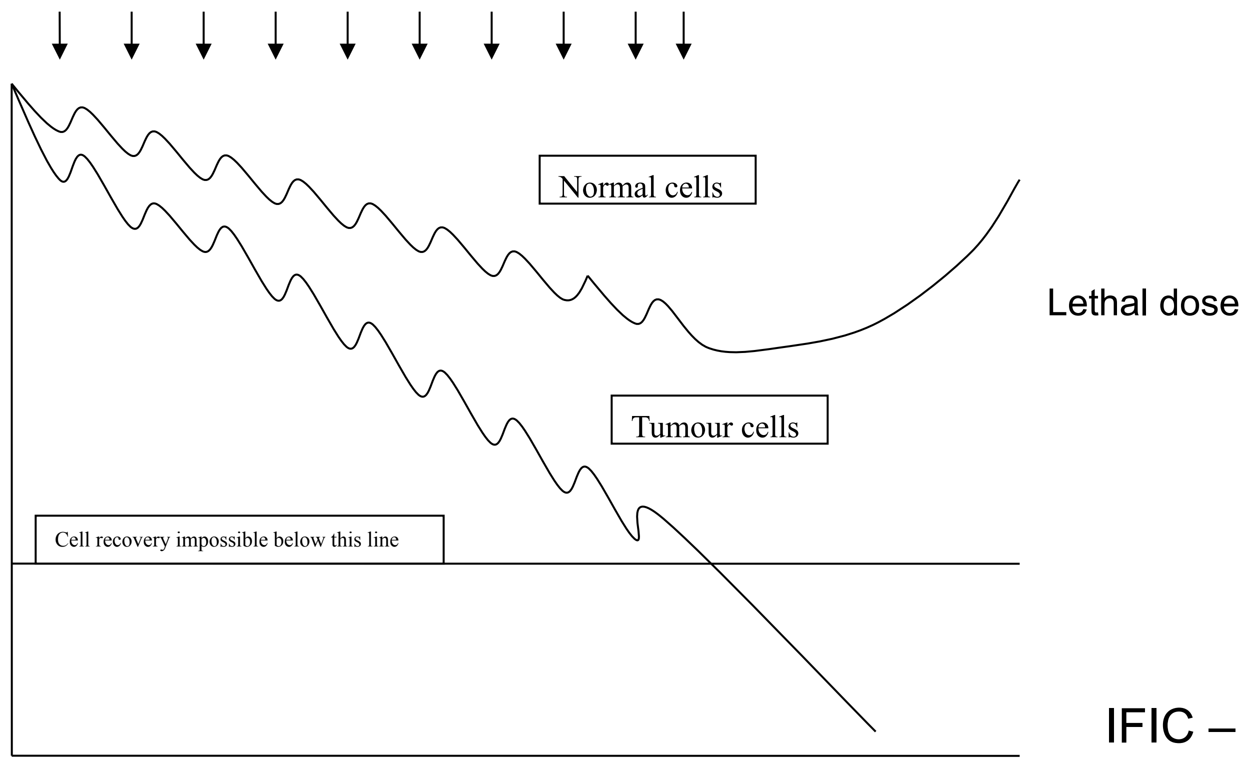
2. Why fractionation?
   - a) It allows normal cells time to recover
     Tumour cells are generally less efficient in repair between fractions.
   - b) tumour cells in relatively radio-resistant phase may cycle into sensitive phase
   - c) Tumour cells chronically or acutely hypoxic may re-oxygenate between fractions.

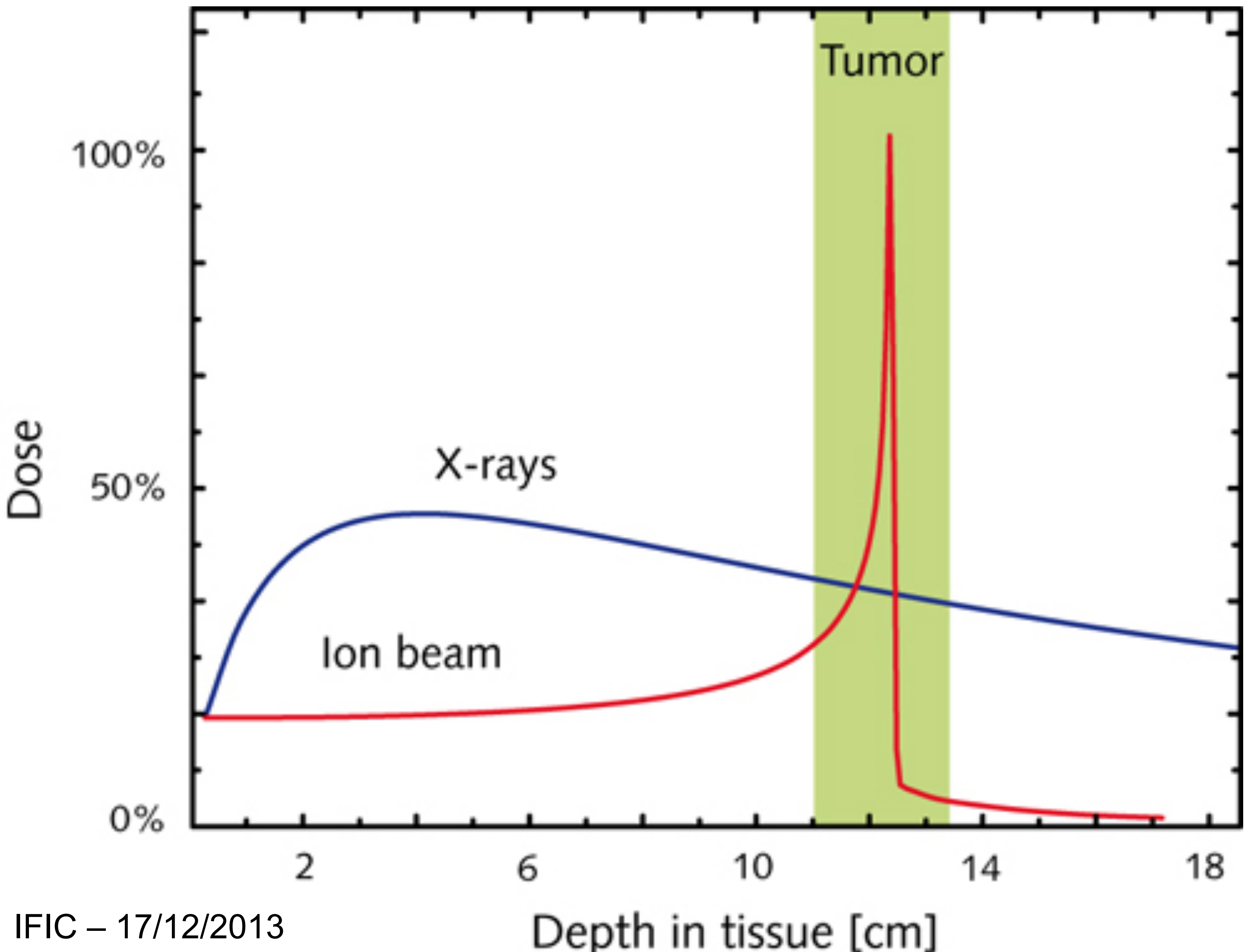


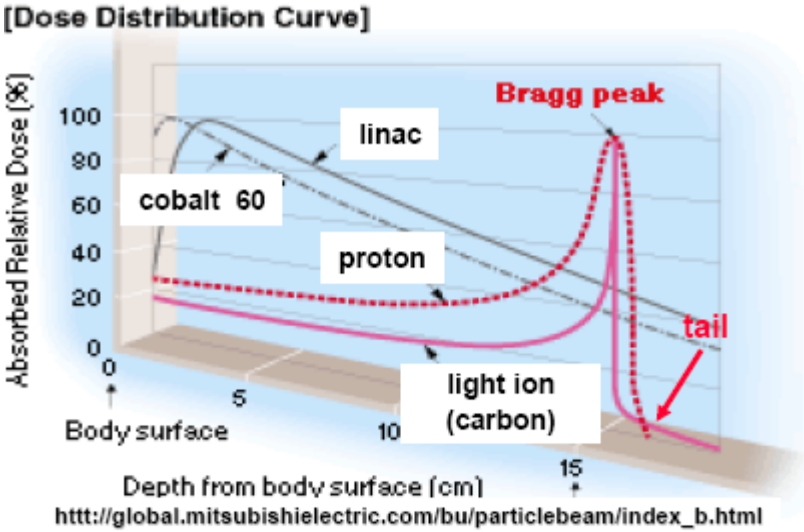
Repopulation

- Sometimes the fractionation has to be speeded up because if it takes too long the tumour may have time to repopulate.
- For children fractions are often smaller to reduce the incidence of late onset side effects.
- Sometimes two fractions/day are used towards the end because tumours regenerate more quickly when smaller.

Each arrow represents a dose of radiation

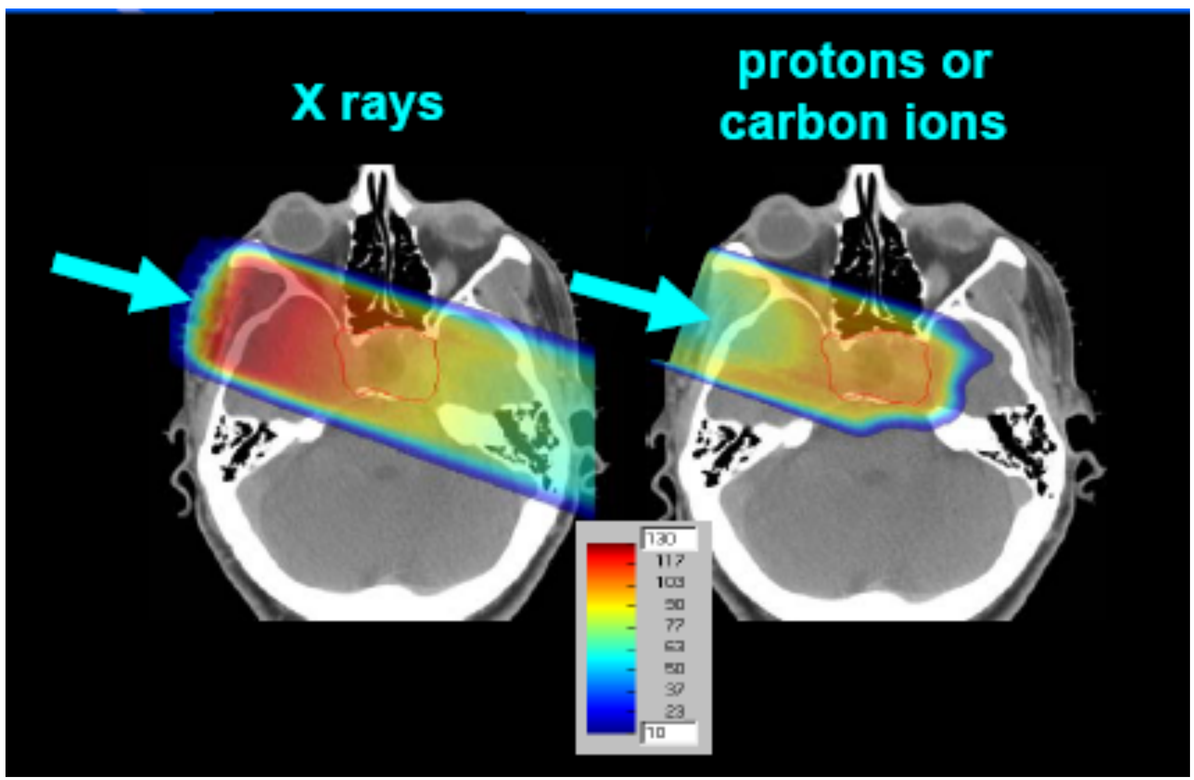



Tumor
100%
50%
0%
Dose
X-rays
Ion beam
2
6
10
14
18
Depth in tissue [cm]

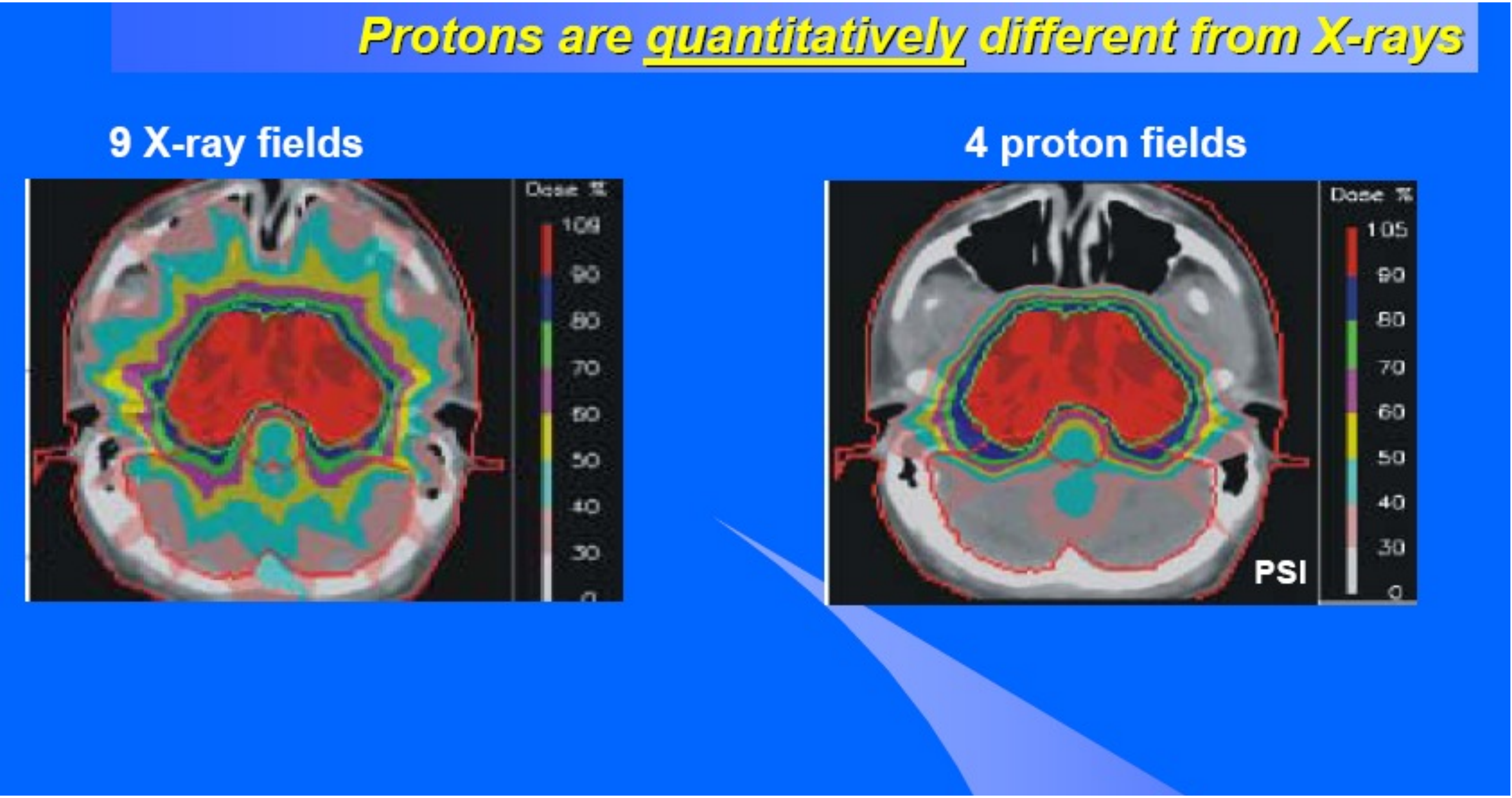


Dose Distributions for Photons (X-rays) and hadrons (protons and carbon ions)

Single field of Photons or hadrons



We can also irradiate from different directions with hadrons. In other words Intensity Modulated Hadron Therapy

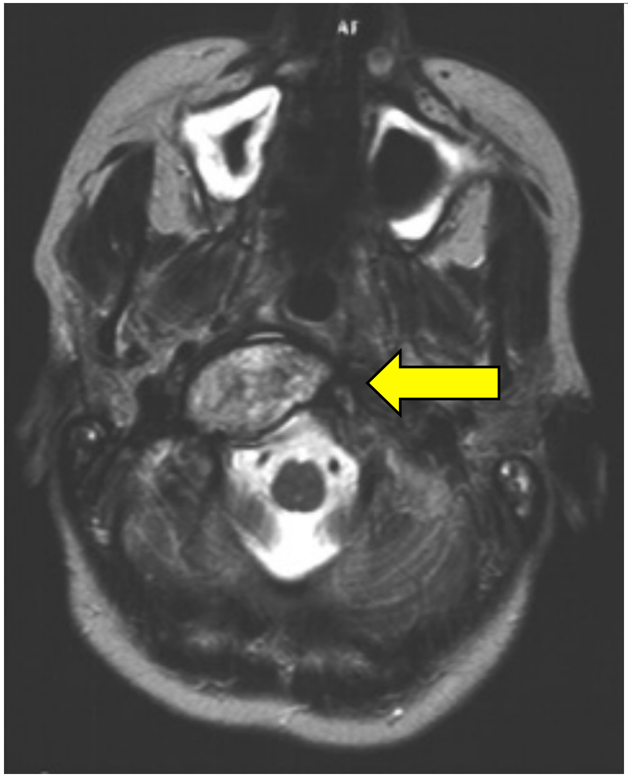


Dose map for Photons (X-rays) and Protons

Tumor regression

Prior to therapy

Tumor regression (Chordoma)



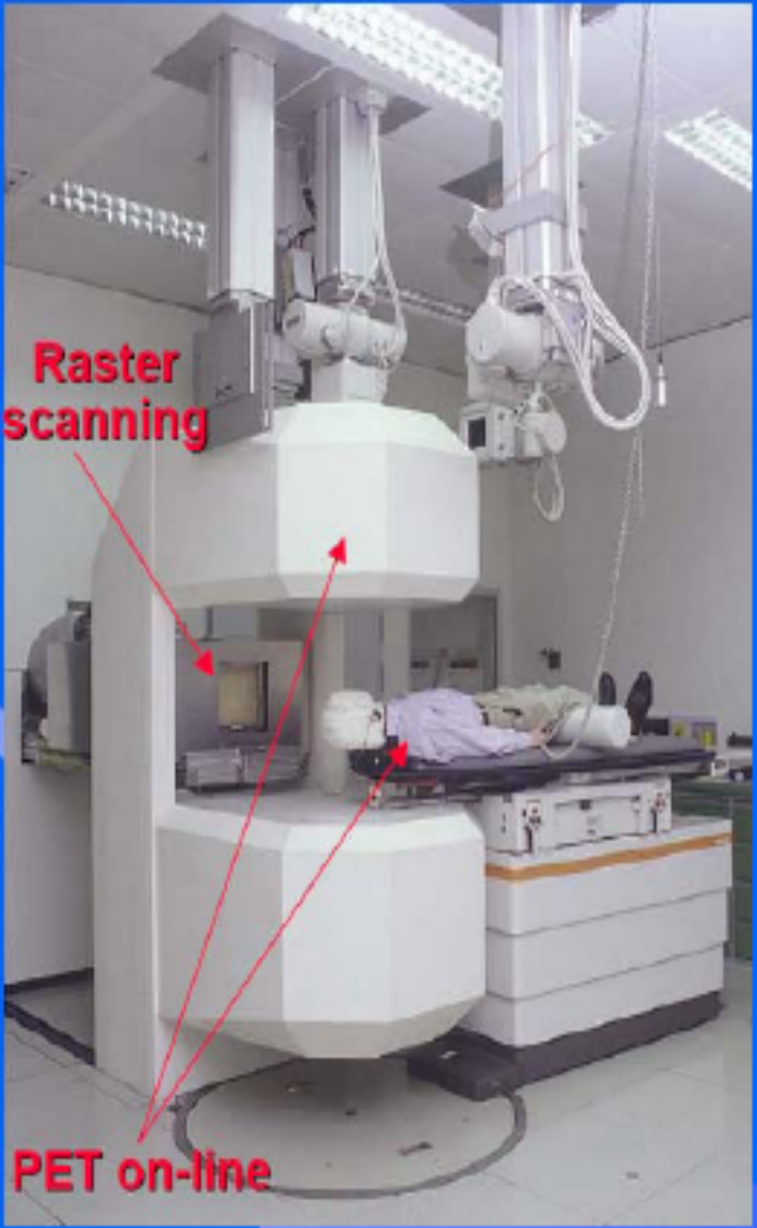
Prior to therapy
(Axial NMRI Scan)

In Germany the GSI pilot project (1997-2008)

G. Kraft

350 patients treated with carbon ions

J. Debus (Heidelberg Univ.)



Numbers of potential patients

X-ray therapy (≥ 40 linacs)

every 10 million inhabitants: 20'000 pts/year

Protontherapy

12% of X-ray patients 2'400 pts/year

Therapy with Carbon ions for radio-resistant tumour

3% of X-ray patients 600 pts/year

TOTAL every 10 M **about 3'000 pts/year (*)**

(*) In Italy : 17'000 patients
5 proton centres and 1 carbon centre (AIRO-2004)

Some other Considerations

- All of that seems very straightforward – It is not so easy in practice

- There are some other things to consider

  - Effect of nuclear reactions – charged particles
    - neutrons

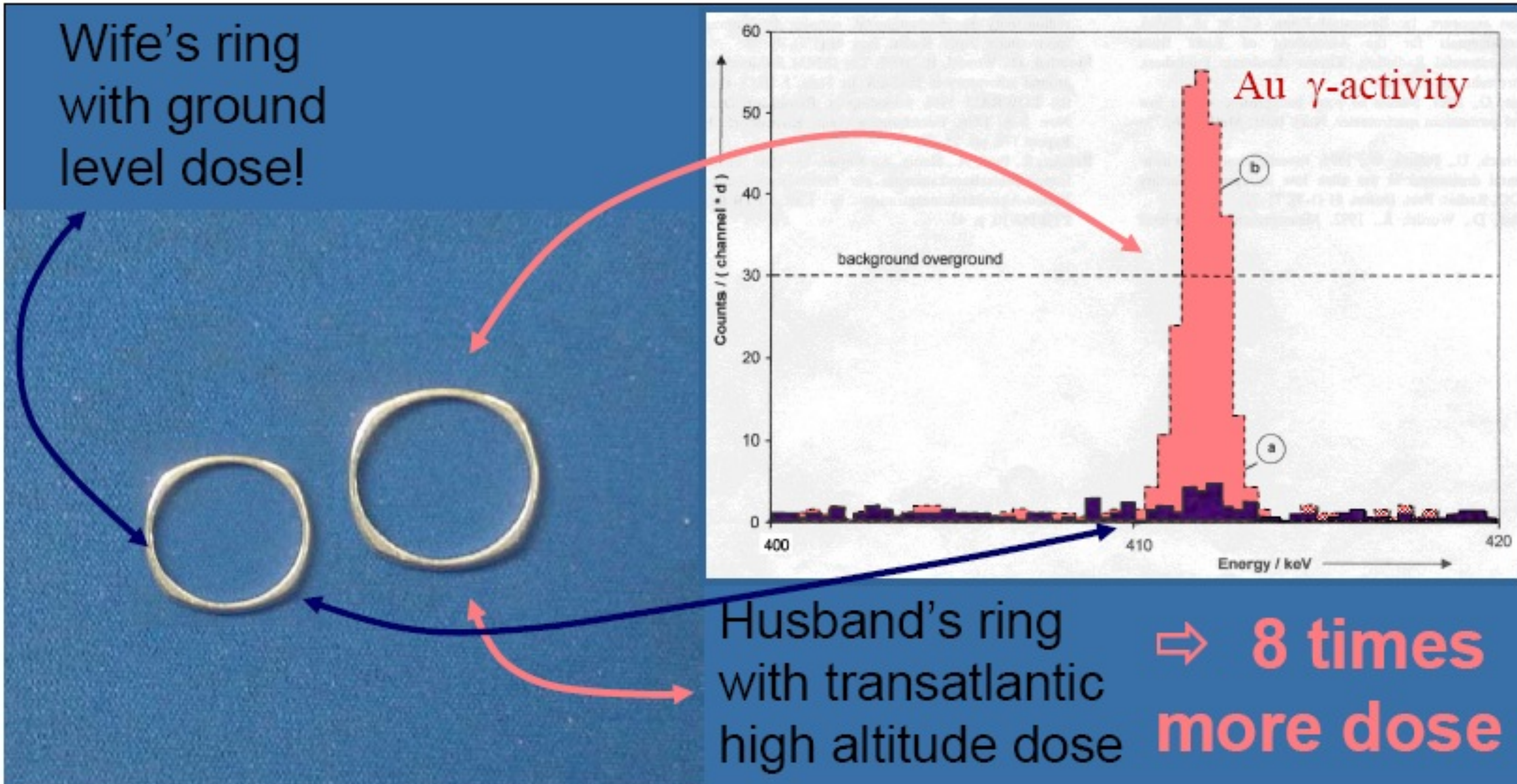
  - choice of accelerators

  - beam transport

  - moving organs

  - Treatment planning and dose verification

Observable Effects!



Husband = Michael Wiescher

There are 2 main types of radiation damage in biological systems:

Somatic Damage (also known as 'radiation sickness'): This refers to damage to cells which are not associated with reproduction. The degree of somatic damage depends on the organ exposed and the age of the individual (younger = more susceptible to somatic damage). Effects of somatic damage include:

- reddening of the skin,
- hair loss,
- ulceration,
- reduction of white blood cells,
- cataracts in the eyes,
- fibrosis of the lungs.

Genetic Damage: This refers to damage to cells associated with reproduction which can lead to genetic mutations in the offspring.