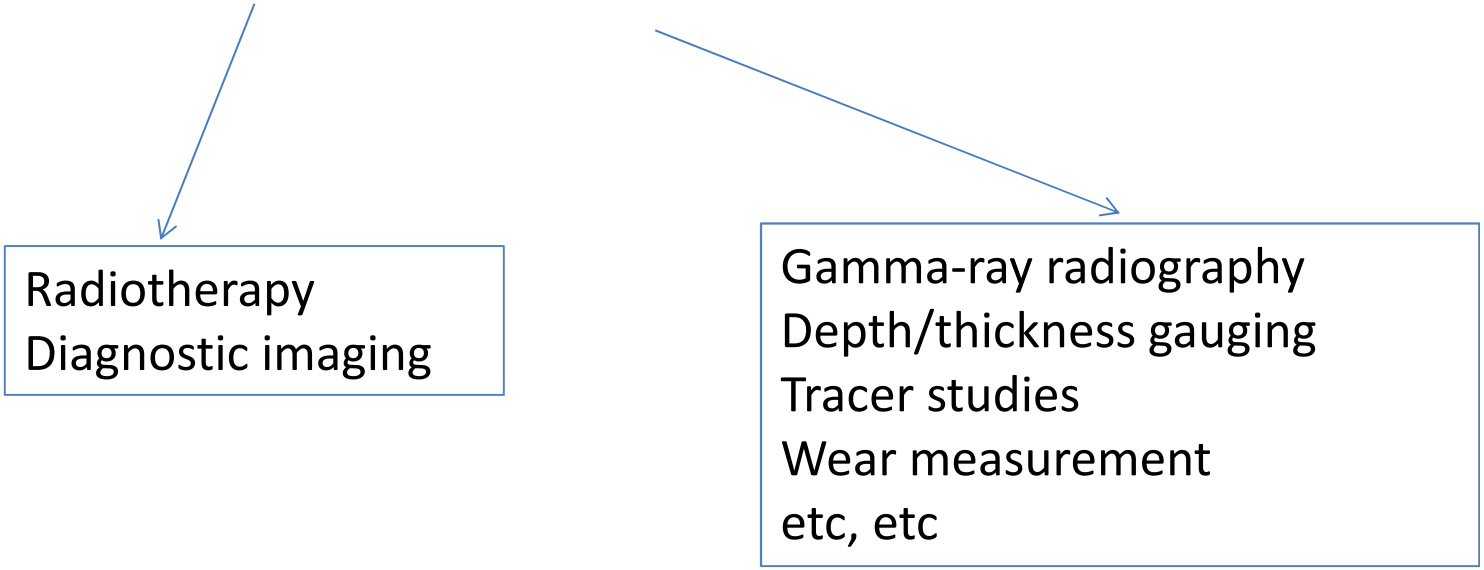
Applications of Nuclear Physics (especially radioisotopes) in medicine and industry



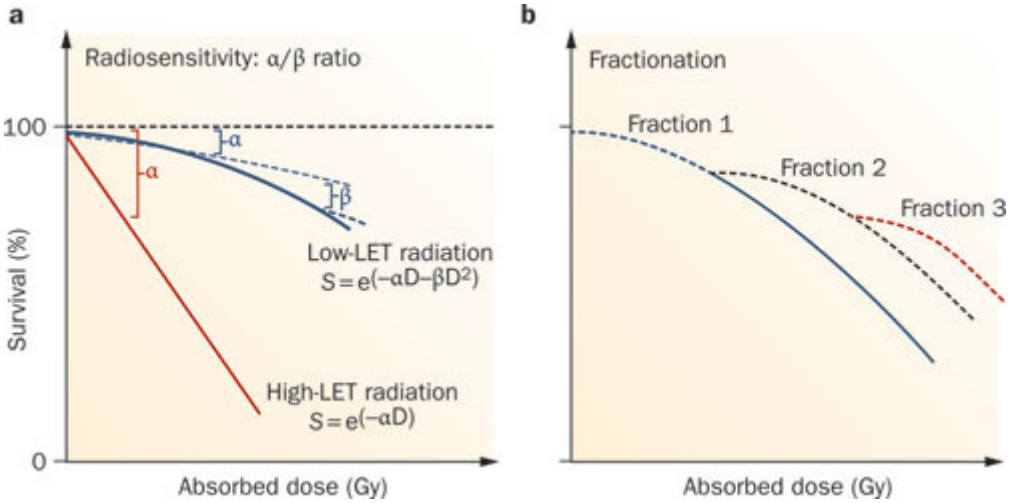
Lecture 1: Radiotherapy; isotope production
Lecture 2: Nuclear medicine imaging
Lecture 3: Industrial applications

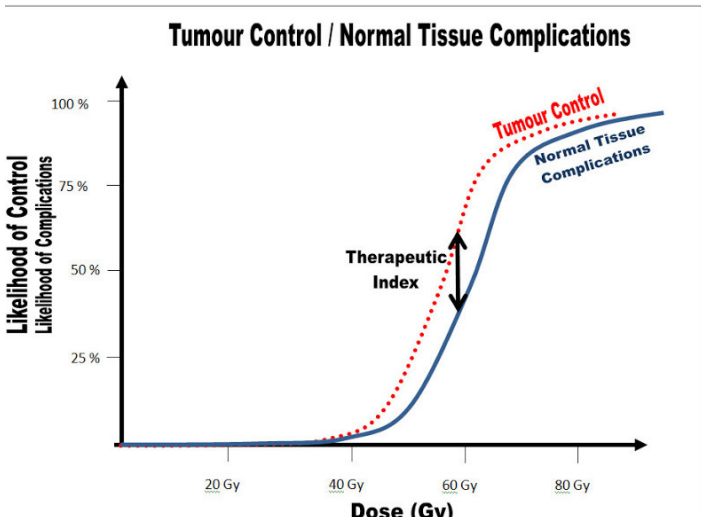
Radiotherapy – treatment of disease (usually cancer) using radiation

- complements surgery and chemotherapy
- used for 40% of cancer patients.

Because they are generally hypoxic (short of oxygen) tumours are usually LESS sensitive to radiation than healthy tissue
Need to concentrate radiation dose at tumour and minimise dose to surrounding tissues

Also tumour cells generally less good at repairing non-lethal damage, so can often improve situation by delivering dose in series of daily fractions
- typically 50 Gy in 2Gy fractions





Types of radiotherapy treatment

External beam RT

- X-ray – using bremsstrahlung spectrum from electron linac — ROUTINE
- Hadron therapy – using proton or carbon ion beams — JUST STARTING

Brachytherapy (“short distance”)

- insert sealed radioactive sources in body — OCCASIONALLY USED

Unsealed source internal therapy

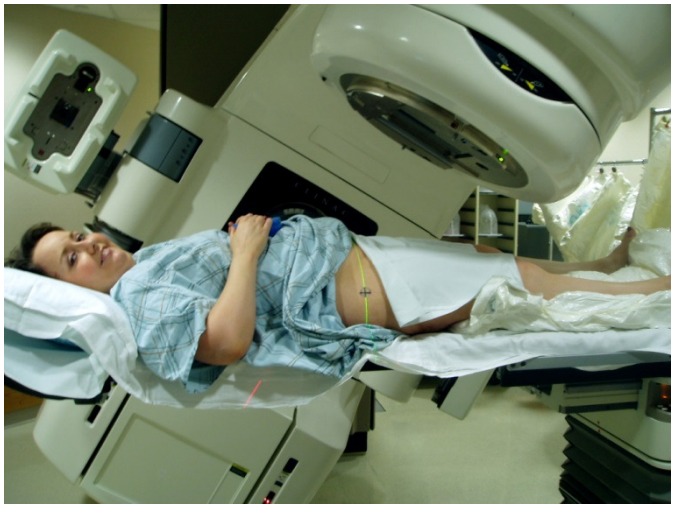
- Iodine for treating thyroid (malignant or benign) — FOR SPECIFIC CASES
- Targeted Alpha Therapy (TAT) — EXPERIMENTAL

Binary therapies – use carrier “drug” to sensitise tumour cells to radiation

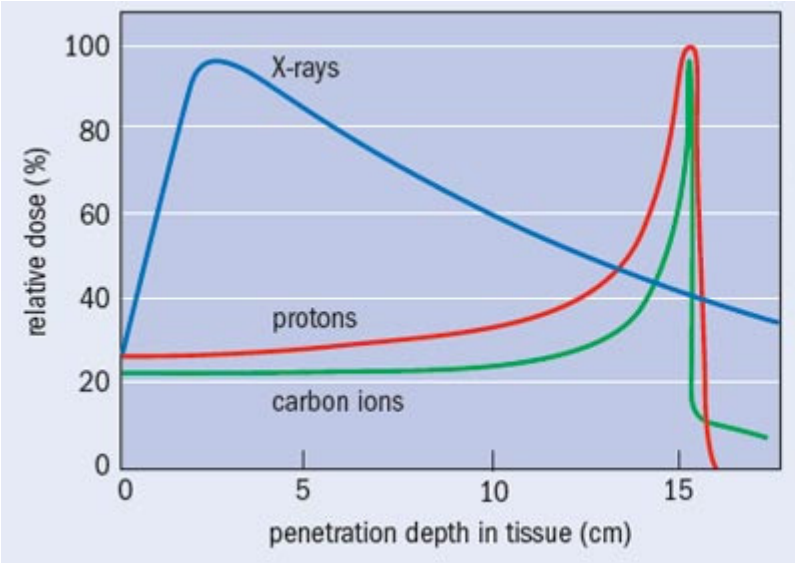
- Boron Neutron Capture Therapy (BNCT) — EXPERIMENTAL
- Photon Activation Therapy (PAT) — EXPERIMENTAL

X-ray therapy

Linac accelerates electrons to around 20 MeV.
Target produces continuous bremsstrahlung spectrum.



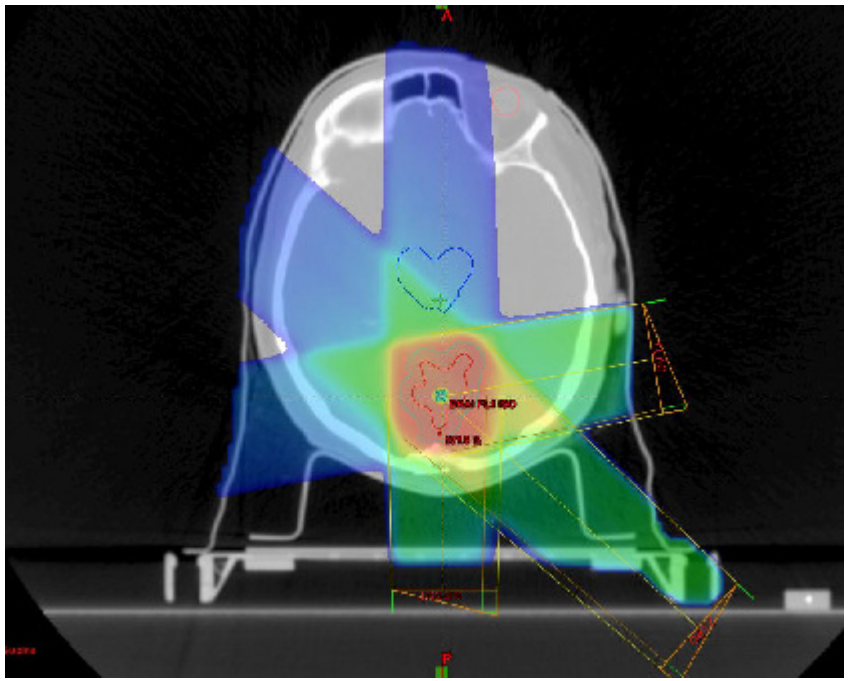
Depth/dose curve peaks at a few cm (electron range gives initial build-up – “skin sparing”) and then falls off exponentially



To concentrate dose in tumour, must superimpose irradiations from several angles – linac head rotates about patient

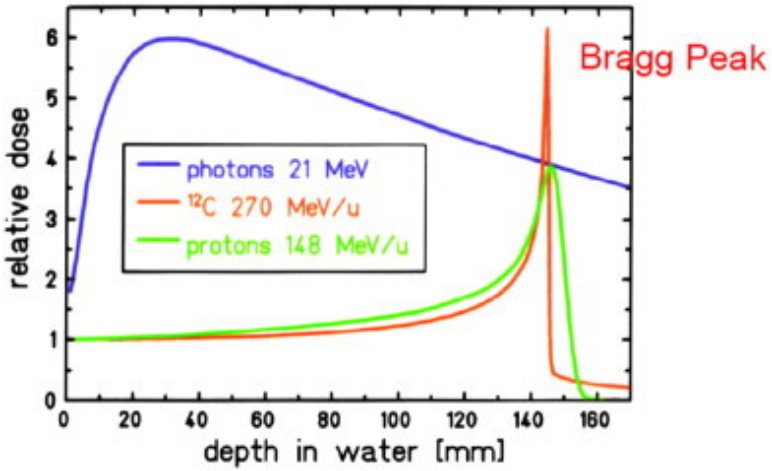
Multileaf collimators are used to shape beam
Latest development is Intensity Modulated RT (IMRT) where collimators move continuously during irradiation

Physicists perform treatment planning

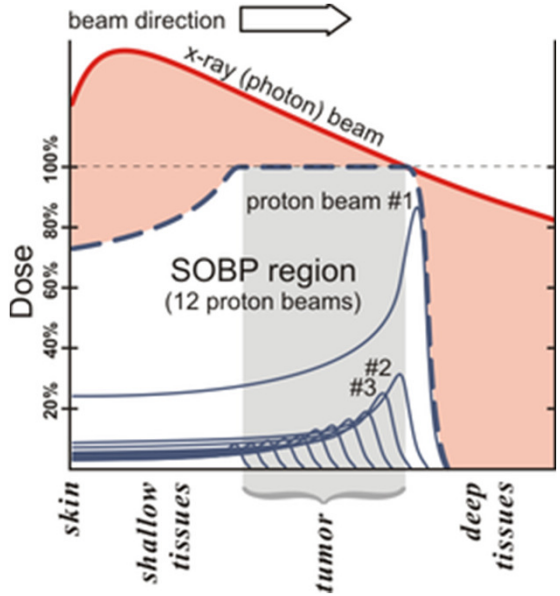


Hadron therapy

A beam of protons deposits most of its energy near the end of range (“Bragg peak”) so dose can be concentrated effectively in tumour – in particular there is NO dose to organs beyond the end of range – good for treating tumours close to very sensitive organs (also for children).



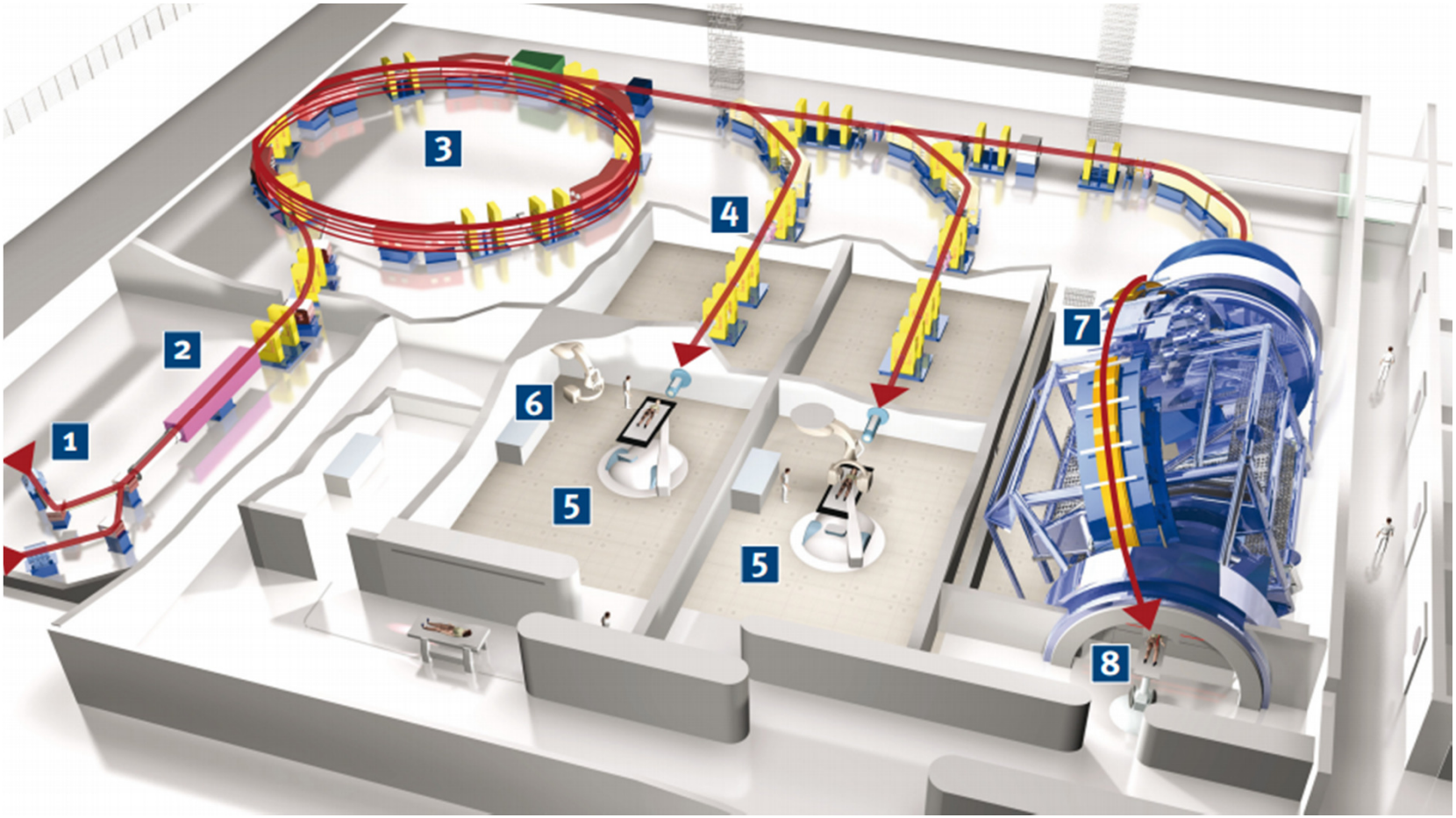
Using carbon ions the Bragg peak is even sharper, but has a deeper tail due to alpha fragmentation



In practice the depth distribution is usually spread out to cover the extent of the tumour by varying the beam energy

Heidelberg: synchrotron accelerates protons or carbon ions to up to 400 MeV/u

600 tonne gantry moving with sub-mm precision directs beam onto patient from any angle

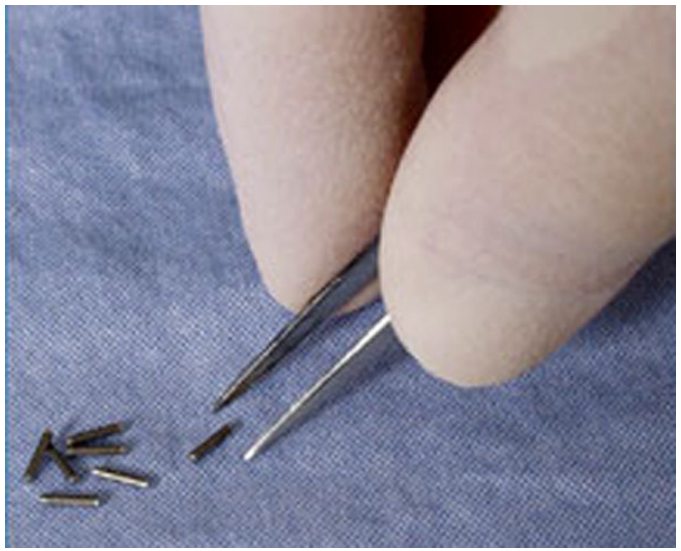


Brachytherapy

For localised tumours close to sensitive organs a better way of delivering required dose distribution may be using short-range radioactive sources inserted into body - e.g treatment of prostate cancer.

Usually ^{192}Ir pellets inside wires inserted into body for ~ 1 hour
(patient anaesthetised)

^{192}Ir (half-life 74 days) decays by β^- decay (plus some EC) emitting gammas of mean energy 380 keV



Unsealed source internal therapy

^{131}I (half-life 8 days) is used for treating overactive thyroid/thyroid cancer
- Decays by β- decay – betas destroy local tissue

Targeted alpha therapy
- idea is to attach alpha-emitter to a drug that concentrates in tumour (e.g. antibody)

- Usually ^{211}At : half-life 7 hours, decays partly by alpha decay (6 MeV alpha) and partly by EC to very short-lived ^{211}Po which alpha decays (7.5 MeV alpha)

- Controversial !

Boron Neutron Cancer Therapy (BNCT)

For treatment of glioblastoma (invasive cancer of the brain, which cannot be effectively removed by surgery)

Idea is to deliver stable ^{10}B to tumour cells, then irradiate with thermal neutrons.

$^{10}B(n, \alpha)^{7}Li$ reaction (Q=2.3 MeV) gives alpha and lithium ion which deposit all their energy within the tumour cell

Only as good as boron carrier drugs

Also complicated by other dose components (neutron, gamma…)

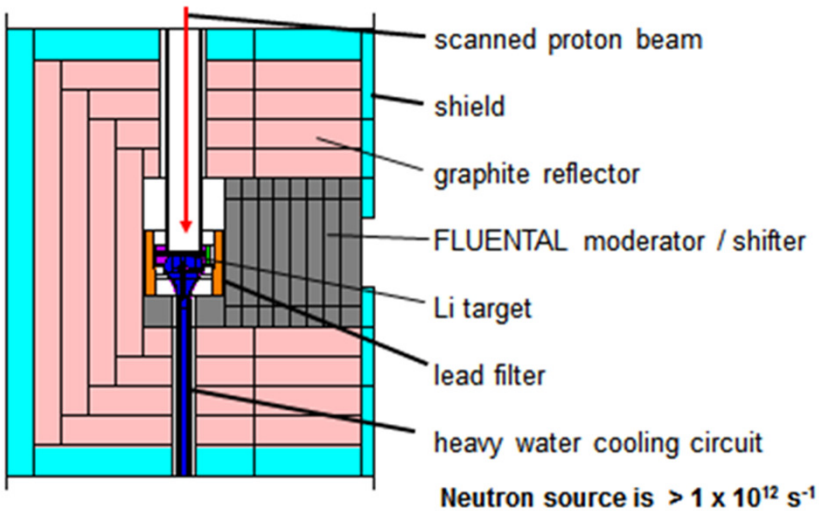
Originally investigated using neutrons from reactors

Now accelerator sources being developed.

Seems promising when used in conjunction with other therapies.

At Birmingham, the 3 MV Dynamitron
is used to generate neutrons using a lithium target

Boron neutron capture therapy: $^{7}Li(p,n)^{7}Be$
Neutron generation and moderation



Neutron source is > 1 x 10^{12} s^{-1}

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Production of radionuclides

Using reactor – as fission products (e.g. ^{99}Mo) or by neutron activation (e.g. ^{192}Ir)

- products generally neutron-rich

Using accelerator (cyclotron)

- products generally proton-rich (e.g. ^{18}F, ^{81}Rb, ^{211}At)

Fission products

Fission is random but generally asymmetric

Figure shows yields of different masses produced in thermal neutron induced fission of ^{235}U

The ^{236}U nucleus is most likely to fission into one fragment of mass ~ 93 and one of mass ~ 140, plus ~ 3 neutrons

Symmetric fission into two fragments of mass ~ 117 is possible but ~ 1000x less likely

Each fission fragment has a neutron/proton ratio similar to that of the original ^{236}U, viz 144/92=1.56

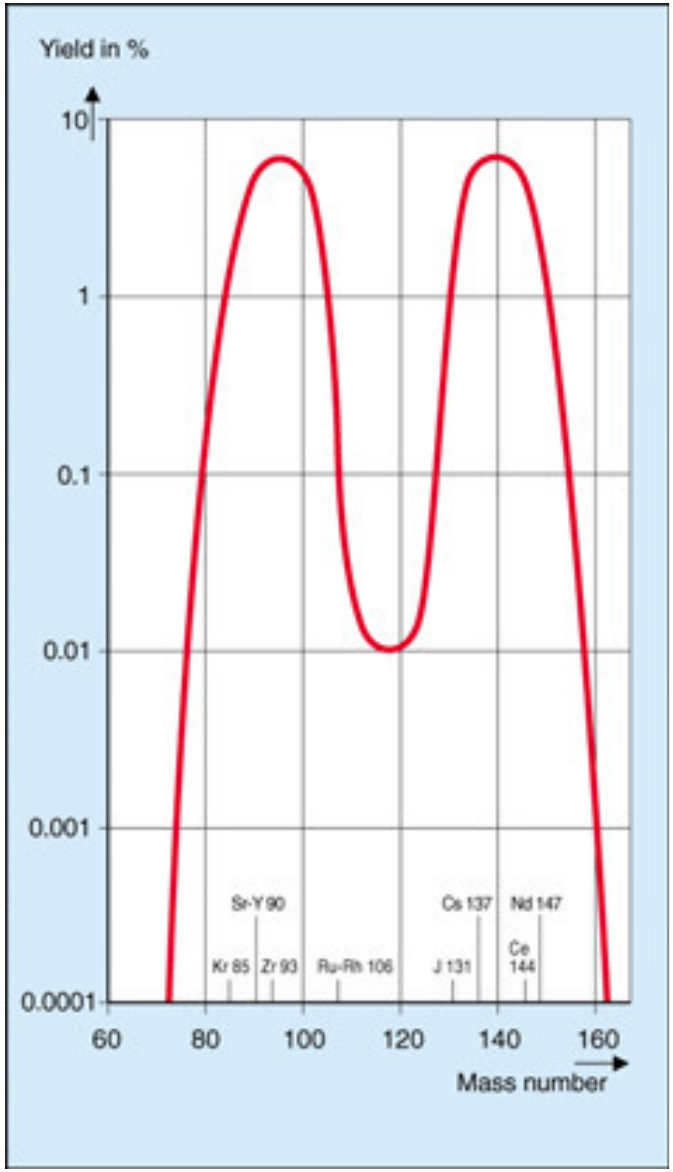
Because of the bend in the valley of stability, fission fragments are neutron rich, and decay by beta- emission (generally several times).

^{99}Mo is obtained as a fission product, e.g. following

$$^{236}_{92}U \rightarrow ^{134}_{52}Te + ^{99}_{40}Zr + 3n$$

In example given,

$^{99}Zr \rightarrow ^{99}Nb \rightarrow ^{99}Mo$ [$\rightarrow ^{99}Tc \rightarrow ^{99}Ru$ (stable)]



Activation products

Thermal neutrons are captured by nuclei, creating heavier isotopes

These may be stable [eg: in control rods $^{10}B+n \rightarrow {}^{11}B+\gamma$] but in general this process produces neutron-rich radionuclides

Samples may be deliberately introduced into neutron flux to produce RNs

(usually in dedicated research reactors):

Eg: Natural iridium is 37% ^{191}Ir

If a sample of iridium is placed in neutron flux from a reactor, ^{192}Ir is produced:

$^{191}Ir+n \rightarrow {}^{192}Ir+\gamma$

Probability of reaction (for a given target atom) per unit time = $\varphi\sigma$

where φ is neutron flux (number crossing unit area per unit time)

and σ is "cross section" for this particular reaction

Example:

"typical" research reactor gives flux ~ 10^{13} neutrons cm^{-2} s^{-1}

Cross section for thermal neutron capture by ^{191}Ir ~ 950 barns = 950×10^{-24} cm^2

So probability of conversion to ^{192}Ir is ~ 10^{-8} per second

In 1 month (2.6×10^6 s), around 2.6% of ^{191}Ir atoms will be converted

[But note that "high flux" reactors can give a flux of up to 10^{15} neutrons cm^{-2} s^{-1}]

As RN is produced (at constant production rate *R*) it also decays, so number of atoms obeys $\frac{dN}{dt} = R - \lambda N$

Solution (if N=0 initially) activity =λN=R(1-exp(-λt))

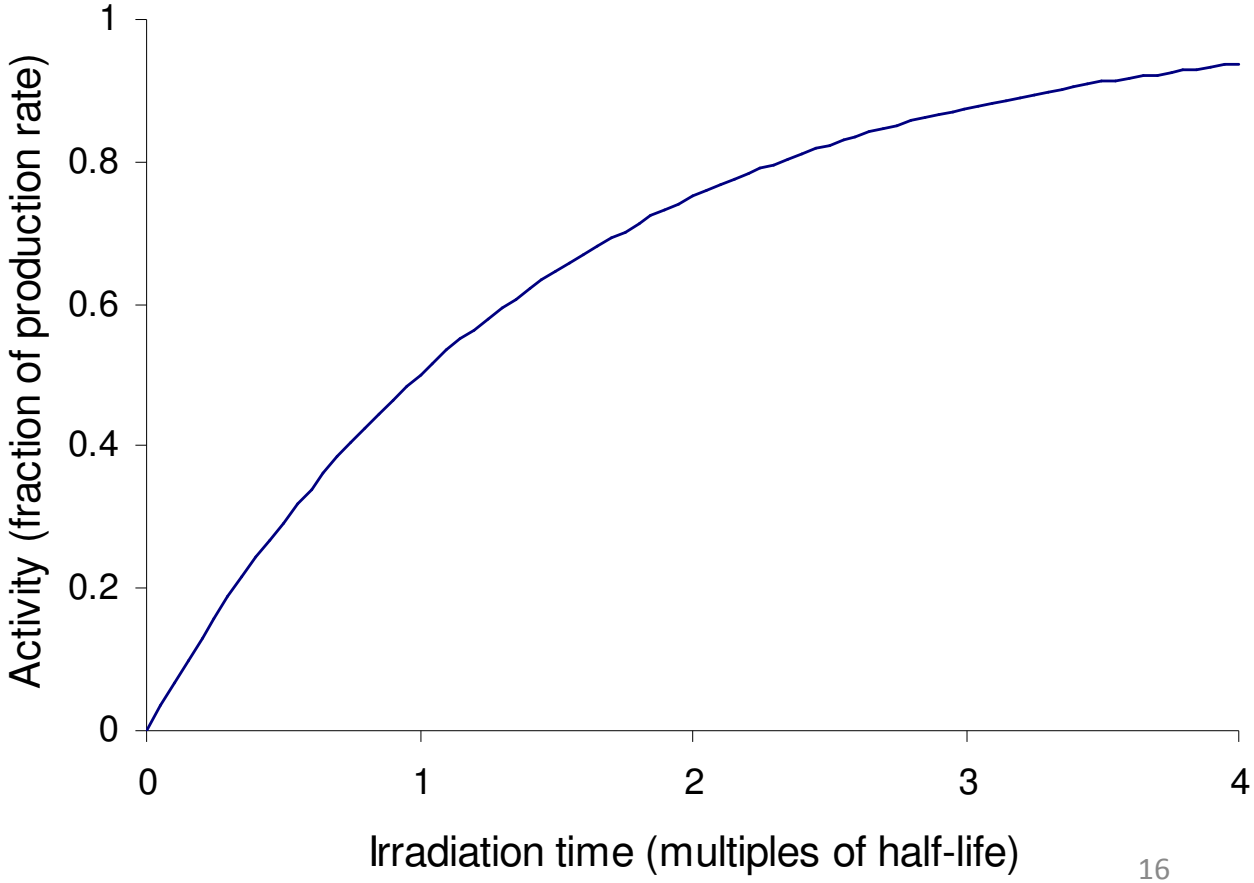
If we irradiate the sample for a long time, eventually RN would reach "saturated" activity R, when it is decaying as fast as it is produced

Approaches saturated level exponentially:

Reaches 50% after one half-life

75% after two half-lives

Generally no point in irradiating for much longer than this



Saturated activity = production rate

$= N \varphi\sigma$ where N is no of atoms in sample

For previous example, saturated activity in 1 g of iridium (~10^{21} ^{191}Ir atoms) is

$10^{21} \times 10^{-8}\ s^{-1} = 10^{13}$ Bq (10 TBq)

Since half-life of ^{192}Ir is 74 days, a 37 day irradiation produces half this activity

Proton-rich RNs are generally produced in charged particle induced reactions, using **particle accelerators** (eg cyclotrons)

Accelerate ions (proton, deuteron, alpha particle) to sufficient energy to overcome the Coulomb barrier

$$E_{Coulomb} = \frac{e^2}{4\pi\varepsilon_o}\frac{Z_1 Z_2}{(R_1 + R_2)} \approx \frac{Z_1 Z_2}{\left(A_1^{1/3} + A_2^{1/3}\right)} MeV$$

~ few MeV

Examples: $^{18}O(p,n)^{18}F$ - 10 MeV p

$^{82}Kr(p,2n)\ ^{81}Rb$ - 30 MeV p

$^{209}Bi(\alpha, 2n)\ ^{211}At$ - 30 MeV alphas

The MC40 cyclotron

is the third cyclotron to be operated at the University of Birmingham

In 2002-2004 transferred from Minneapolis

to Birmingham

In a “thin target”, reaction rate given by $J\sigma nt$

where J is the incident beam current (protons/s)

n is the number of atoms per unit volume in the target

t is the target thickness

(so the product nt is the no of atoms per unit area seen by the beam)

Typical cyclotron current is ~50 μA ($50\times10^{-6}/1.6\times10^{-19} = 3\times10^{14}$ protons/s)

If this is spread over an area of ~1 cm^2, proton flux is similar to neutron flux in a high flux reactor

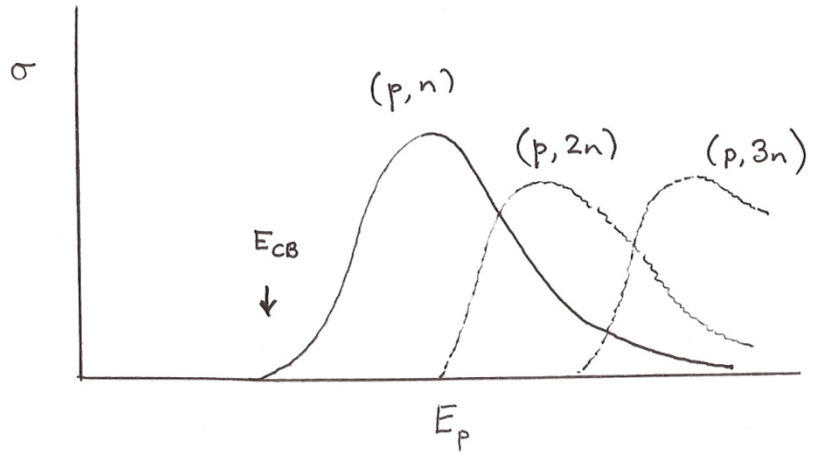
But cross sections for charged particle reactions rarely exceed 0.5 barns

Only a very small fraction of target atoms undergo nuclear reactions

Also the target thickness is limited

As energy of incident proton increases, other reactions become energetically possible, and cross-section for (p,n) decreases

There is an optimum energy range inducing the desired reaction.



In a thick target, the protons lose energy with depth in a well defined way (stopping power dE/dx), so that the cross section depends on depth

Production rate = *JY*, where *Y* is the "thick target yield"

$$Y = n\int_0^{E_0} \sigma(E)\frac{1}{\frac{dE}{dx}(E)}dE$$

As before, this rate also defines the saturated activity after long irradiation time

Y is often quoted in activity per μA

Eg: The thick target yield of ^{18}F from 18 MeV protons on $H_2{}^{18}O$ water is ~ 8 Gbq/μA

Since the half life of ^{18}F is 110 mins, a 2 hour irradiation produces ~ half this yield

Generator systems

Helpful if the desired radionuclide is the daughter of a longer-lived parent, and can be readily separated – hospital is supplied with parent "generator".

Examples:

- ^{99m}Tc (6 hours) from ^{99}Mo (66 hours) – insoluble parent, soluble daughter
- ^{81m}Kr (13s) from ^{81}Rb (4.6 hours) – daughter is gas
- ^{62}Cu (10 min) from ^{62}Zn (9 hours)

Numbers of atoms of parent and daughter N_p , N_d obey $\frac{dN_p}{dt} = -\lambda_p N_p$ $\frac{dN_d}{dt} = \lambda_p N_p - \lambda_d N_d$

Parent follows usual decay $N_p = N_o e^{-\lambda_p t}$

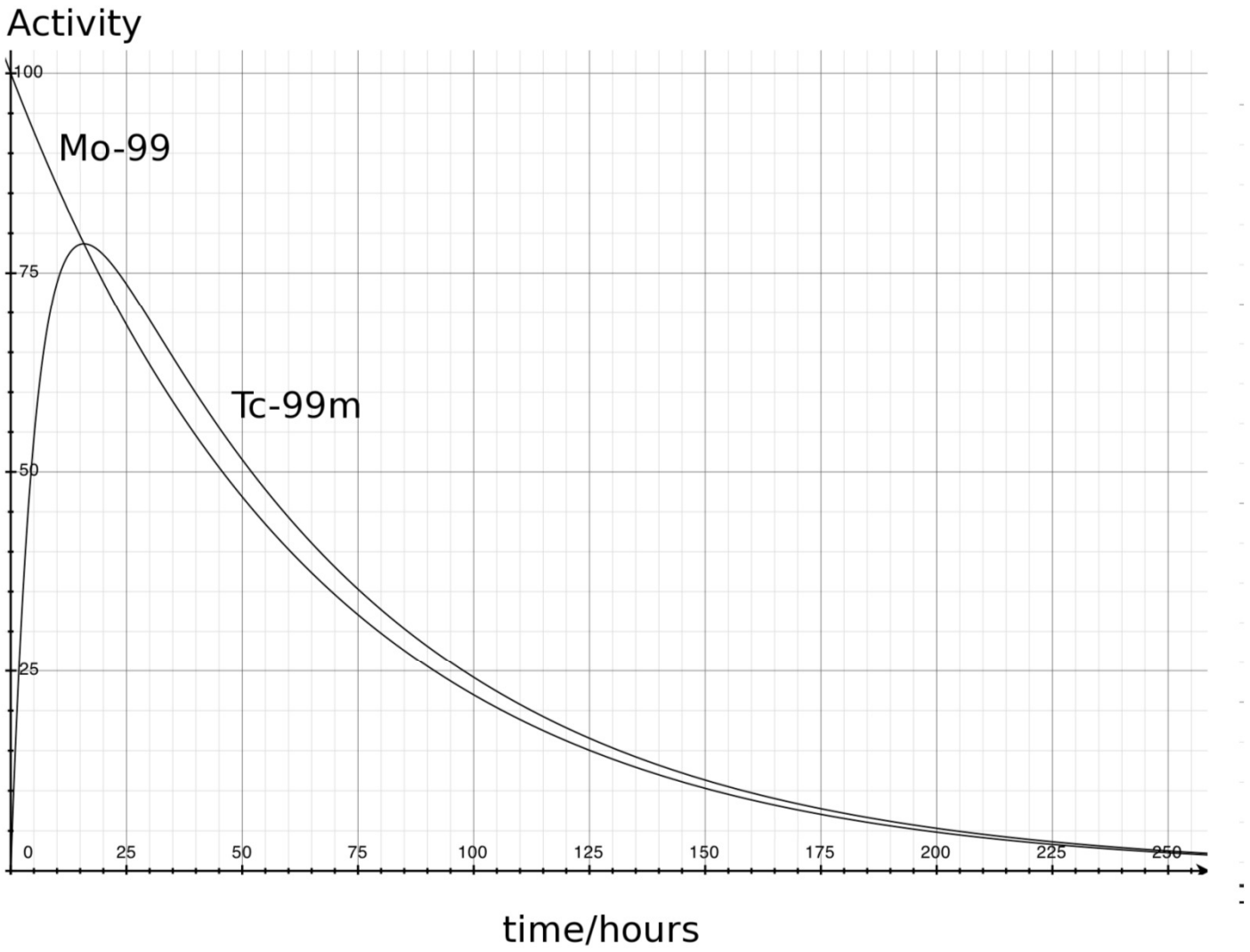
Substituting this in second equation, daughter follows $N_d = \frac{\lambda_p N_o}{\lambda_d - \lambda_p}\left[e^{-\lambda_p t} - e^{-\lambda_d t}\right]$

activity given by $A_d = \frac{\lambda_d A_o}{\lambda_d - \lambda_p}\left[e^{-\lambda_p t} - e^{-\lambda_d t}\right]$

At large t, second term becomes negligible, so $A_d = \frac{\lambda_d}{\lambda_d - \lambda_p} A_o e^{-\lambda_p t} = \frac{\lambda_d}{\lambda_d - \lambda_p} A_p$ (transient equilibrium)

Daughter activity follows parent activity but is higher by factor $\frac{\lambda_d}{\lambda_d - \lambda_p}$

For $^{99}Mo \rightarrow ^{99m}Tc$, delay factor is 1.1



But actually only 87% of ^{99}Mo decays to the metastable state!!!