

Radioisotopes in action



Diagnostic application of radioisotopes

Steps of diagnostic procedure

- Radioactive material introduced into the patient
- Distribution and alteration of activity is detected
- Monitoring of physiological pathways and/or identification and localization of pathological changes

Information from various medical imaging techniques

Structure	X-ray	<i>differences according to the different physical parameters / properties of tissues</i>
	Ultrasound	
	MRI	
Function	Isotope diagnostics	<i>dynamic physiological / metabolic processes of different body organs can be followed</i>
	MRI	



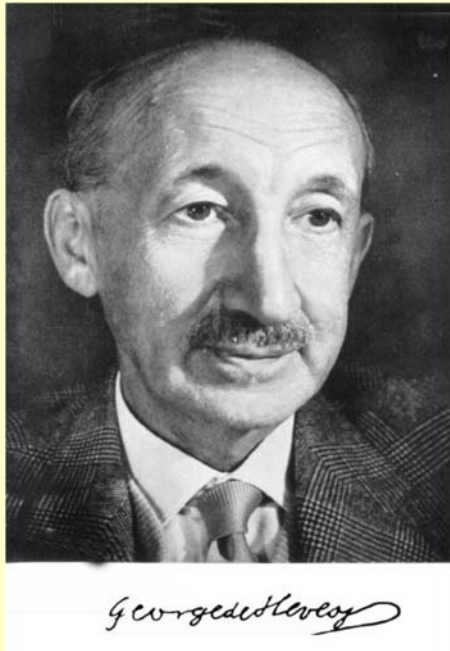
X-ray

Shows the structure



Isotope diagnostics

*Report the
metabolic activity*



Father of Nuclear Medicine

Georg Charles de Hevesy
(1885 - 1966)

Nobel Prize in Chemistry
1943

**for his work on the use of
isotopes as tracers in the
study of chemical
processes**

George Hevesy and his landlady



In any event, he became convinced that his landlady had a nasty habit of recycling food. Hevesy secretly spiked the leftovers on his plate with radioactive material. A few days later, the electroscope he smuggled into the dining room revealed the presence of the tracer

The choice of the appropriate radioisotope for nuclear imaging

Maximize the information

Minimize the risk.

For that find the optimal

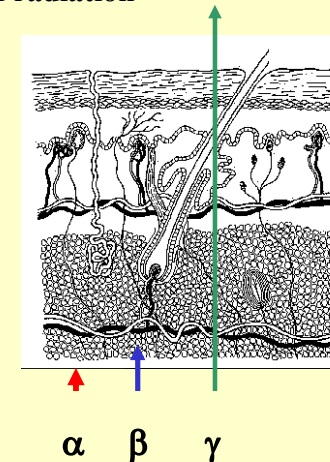
type of radiation

photon energy

half-life

radiopharmakon

Type of radiation

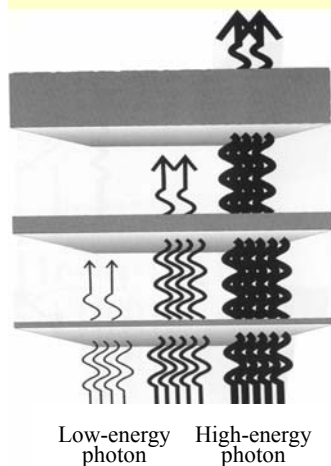


decay via photon emission
to minimize absorption
effects in body tissue
Only **γ-radiation** has
sufficient penetration
distance.

purely gamma-emitting isotope would be preferable

photon energy

$$hf > 50 \text{ keV}$$



Photon must have sufficient energy to penetrate body tissue with minimal attenuation

BUT!

Photon must have sufficiently low energy to be registered efficiently in detector and to allow the efficient use of lead collimator systems (must be absorbed in lead)

a suitable physical half-life

$$\Lambda = \lambda N = \frac{0,693}{T} N$$

smaller is better
but
the value is limited from below
e.g., by the sensitivity of the detector

smaller is better
dosimetric considerations for patients

shorter is better
but
it has to be long enough for monitoring the physiological organ functions to be studied

radiopharmaceutical – is substance that contain one or more radioactive atoms and are used for diagnosis or treatment of disease.

It is typically made of two components, the radionuclide and the chemical compound to which it is bound.

Basic requirements:

specific localizing properties;
high *target : non-target* ratio

have no pharmacological or toxicological effects which may interfere with the organ function under study.

A number of factors is responsible for the ultimate distribution of the radioisotope:

- blood flow (percent cardiac input/output of a specific organ)
- availability of compound to tissue, or the proportion of the tracer that is bound to proteins in the blood
- basic shape, size, and solubility of molecule which controls its diffusion capabilities through body membranes

examples

pharmaceutical	radioisotope	activity (MBq)	target organ
Pertechnetate	^{99m}Tc	550 - 1200	brain
Pirophosphate	^{99m}Tc	400 - 600	heart
Diethylene Triamine Penta Acetic Acid (DTPA)	^{99m}Tc	20 - 40	lung
Mercaptoacetyltriglycine (MAG3)	^{99m}Tc	50 - 400	kidney
Methylene Diphosphonate (MDP)	^{99m}Tc	350 - 750	bones

Optimal activity for diagnostic procedure

Maximize the information

Minimize the risk

$$\Lambda \sim 100 \text{ MBq}$$

Types of images

Static picture – spatial distribution of isotope / activity
at a certain time

Dynamic picture – variation of the amount of isotope /
activity in time

Static and dynamic picture – series of static recordings

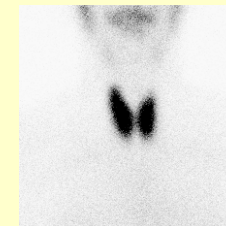
Emission CT

SPECT (Single Photon Emission Computed Tomography)

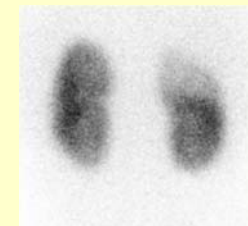
PET (Positron Emission Tomography)

Types of images

Static picture – spatial distribution of isotope / activity
at a certain time



thyroid glands

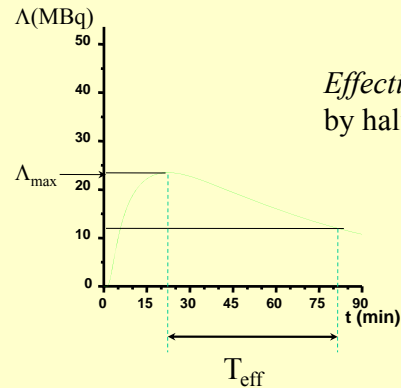


kidneys

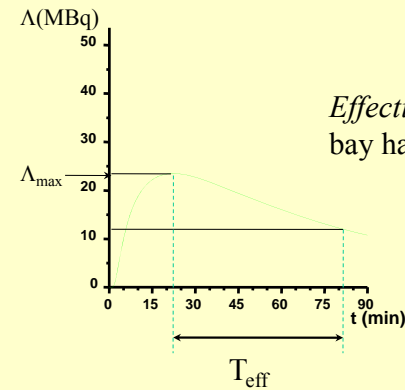
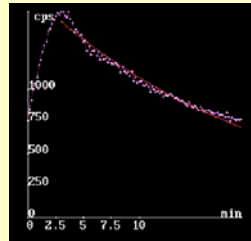
Isotope accumulation in

Types of images

Dynamic picture – variation of the amount of isotope / activity in time



Effective half-life – activity decreases by half in the target organ



Effective half-life – activity decreases by half in the target organ

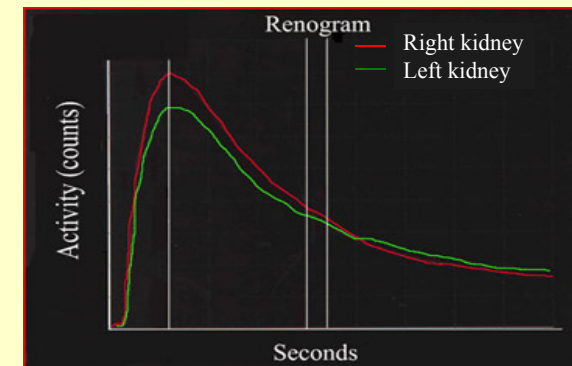
$$\Lambda = \Lambda_0 e^{-(\lambda_{\text{phys}} + \lambda_{\text{biol}})t}$$

$$\lambda_{\text{effective}} = \lambda_{\text{phys}} + \lambda_{\text{biol}}$$

$$\frac{1}{T_{\text{eff}}} = \frac{1}{T_{\text{phys}}} + \frac{1}{T_{\text{biol}}}$$

The final fate of the radiotracer depends on how the addressed organ deals with the molecule, whether it is absorbed, broken down by intracellular chemical processes or whether it exits from the cells and is removed by kidney or liver processes. These processes determine the **biological half-life** T_{biol} of the radiopharmaceutical.

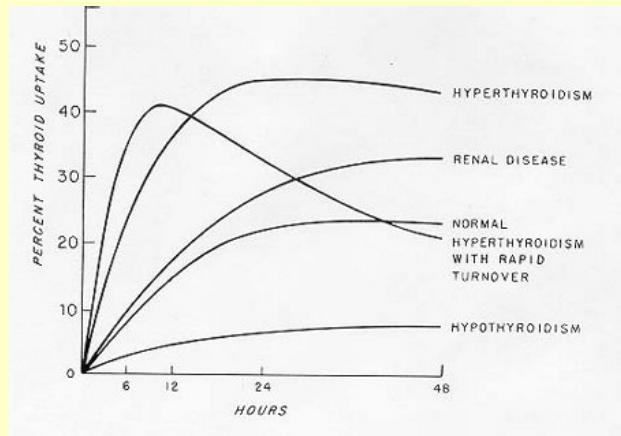
example



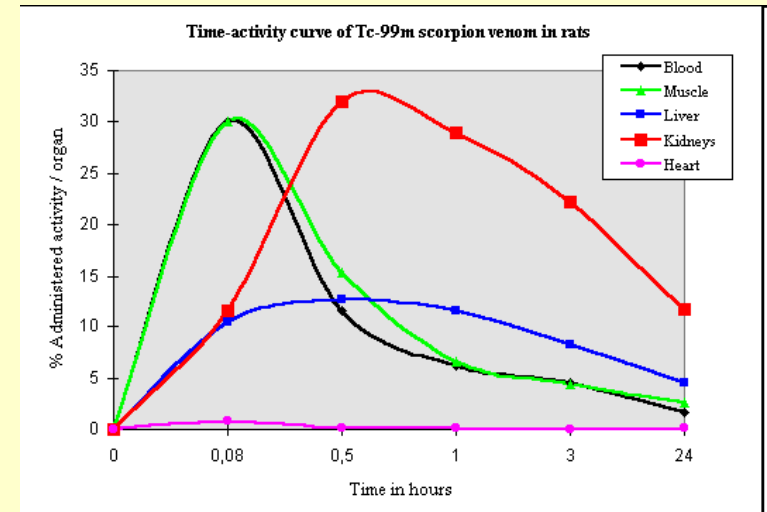
kidney

Isotope accumulation

example



Thyroid glands
Isotope accumulation



Hal Anger
1920-2005

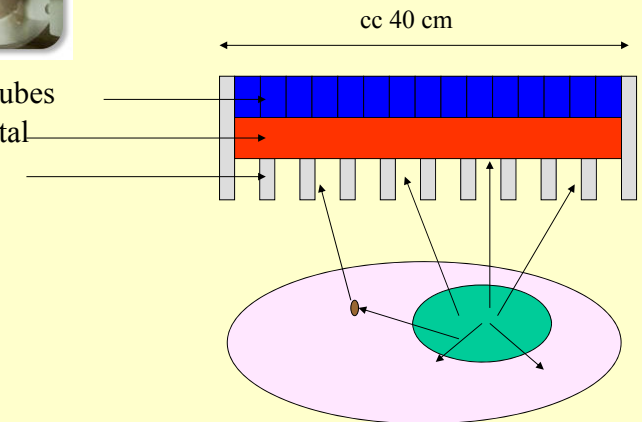


Hal Anger and coworkers
1952



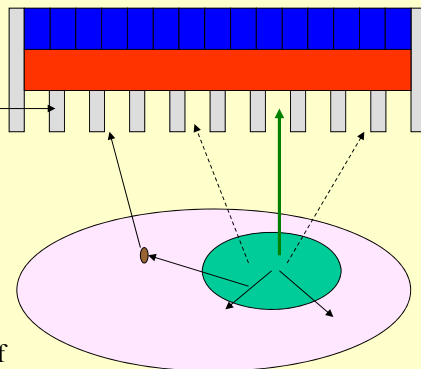
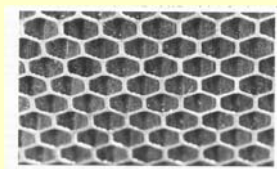
Gamma camera

Photomultiplier tubes
Scintillation crystal
Collimator



A radioactive source emits gamma ray photons in all directions.

collimator

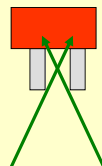


Collimators are composed of thousands of precisely aligned channels made of lead.

The collimator conveys only those photons traveling directly along the long axis of each hole.

Photons emitted in other directions are absorbed by the septa between the holes.

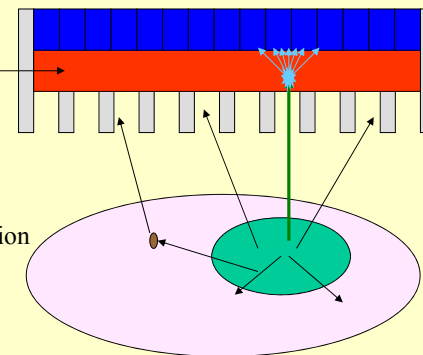
Size and geometry of holes are essential for the resolution.



Scintillation crystal

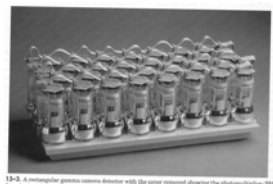
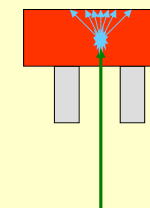
NaI(Tl)

Sufficient detection efficiency
photons of 150 keV $\mu \sim 2.2 \text{ 1/cm}$
10 mm thickness $\sim 90\%$ attenuation
Proper wavelength – 415 nm – for PM photocathode

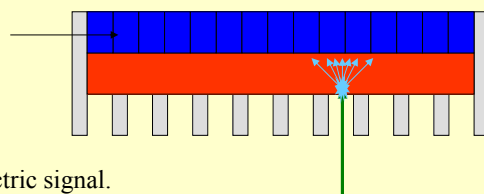


Problems:

fragile
temperature sensitive
hygroscopic



Photomultiplier tubes

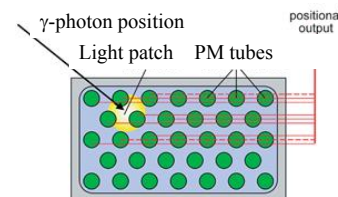


Transformation of light pulses to electric signal.

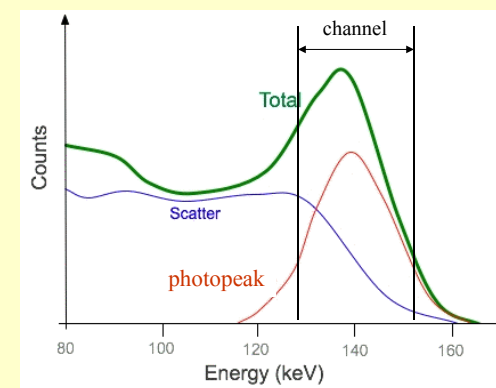
Typically 37-91 tubes, 5.1-7.6 cm diameter each

Amplitude of electric pulses varies in a wide range, because

- absorption of one γ -photon induces electric signals in more than one tubes.
- attenuation mechanism can be photoeffect and Compton-scatter.

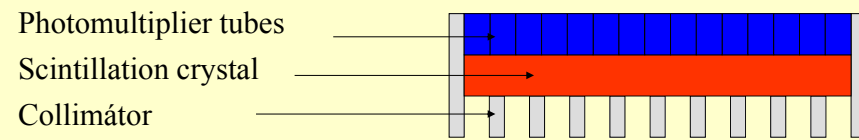


Pulse amplitude spectrum – Amplitude of an electric pulse generated by a γ -photon absorption in photoeffect is proportion to the photon energy.



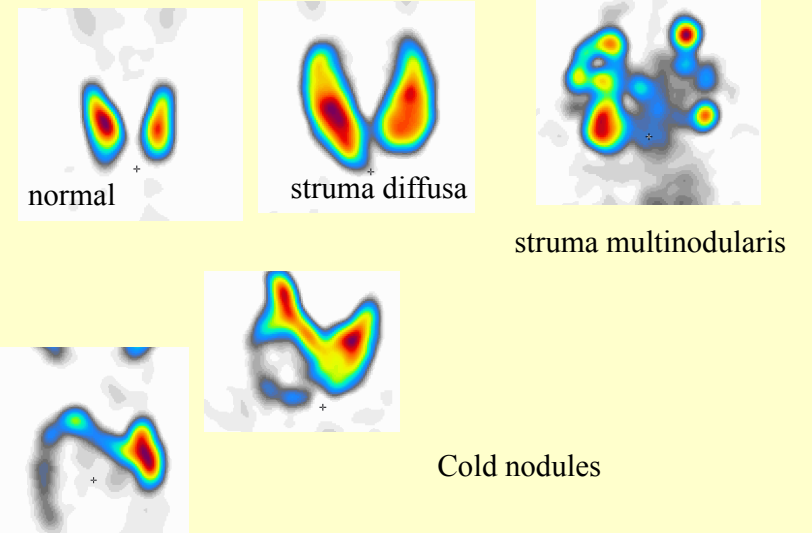
These electric pulses can be distinguished by discrimination (DD).

Gamma camera

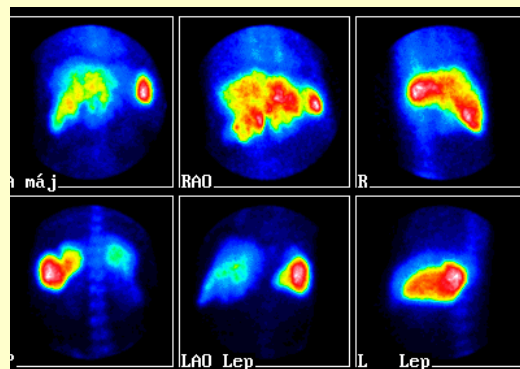


Identification of source position is facilitated by
the collimator
the PM tubes
the discrimination.

Pertechnetate (intravenous 80 MBq) distribution in thyroid glands



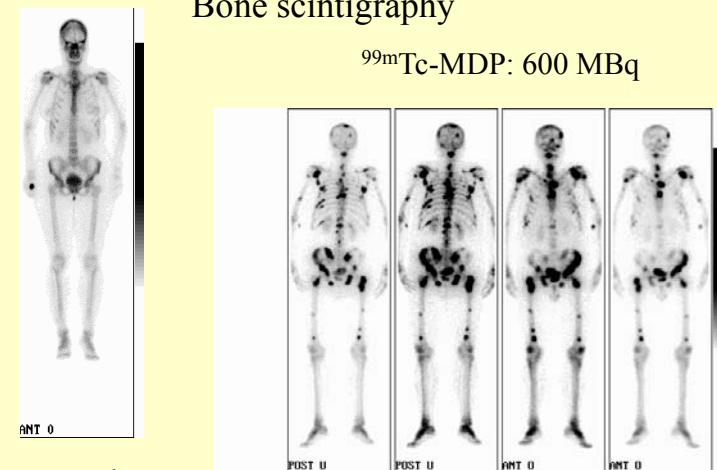
Liver lesion nodules



^{99m}Tc - fytion

Bone scintigraphy

^{99m}Tc -MDP: 600 MBq



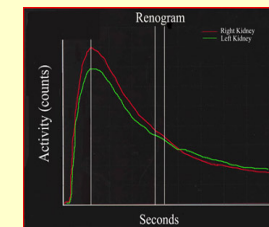
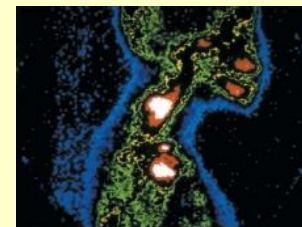
normal

imaging in bone metastases

Gamma camera – space and time distribution can be recorded
static and dynamic pictures can be reconstructed

Camera parameters:
spatial resolution
energy resolution
efficiency of detection

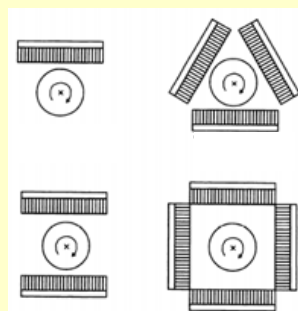
Gamma camera image:
summation image



For depth resolution: tomographic device is necessary

SPECT

Single Photon Emission Computed
Tomography



Various camera arrangements

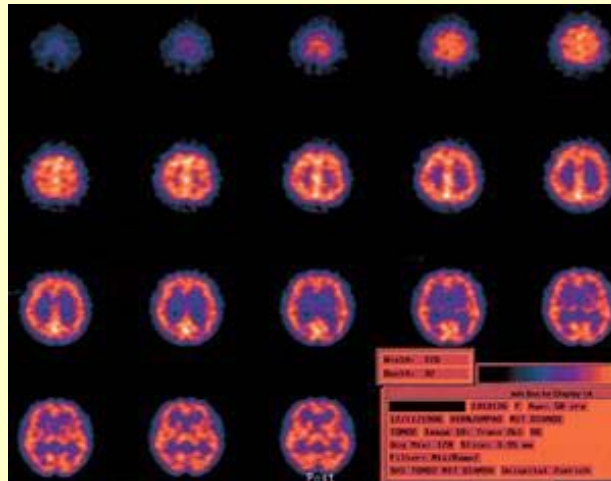
SPECT

Tomographic application of γ -cameras – data collection in 360° .

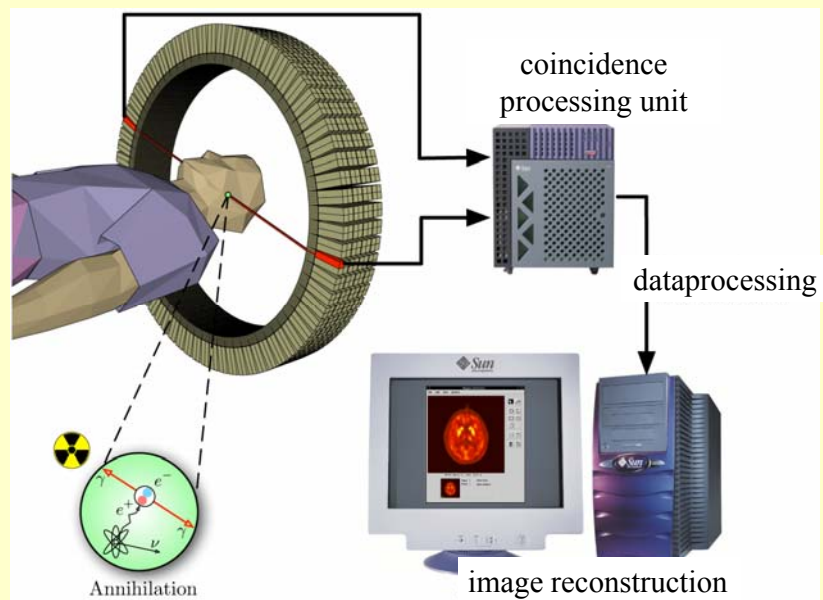
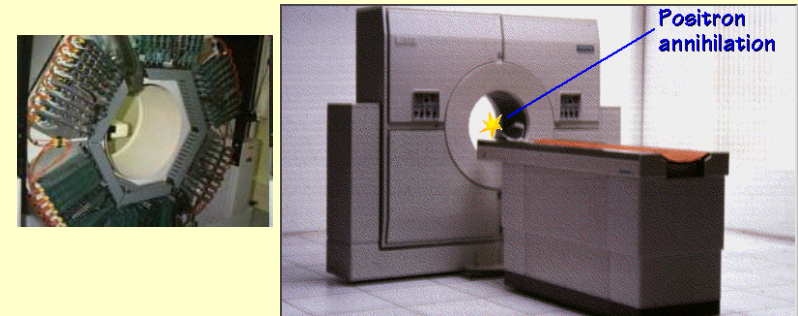
Cross-sectional image can be reconstructed.

Measurement from a series of projections.

Computer directs the movement of the detector, stores the data,
reconstruct the cross-sectional image

^{99m}Tc - HMPAO

Positron Emission Tomography



The diagram illustrates the PET scanner setup. On the left, a circular cross-section of the scanner is shown, labeled "Isotope distribution" and "annihilation". Inside the circle, a central region is labeled "Isotope distribution". Two arrows labeled γ point outwards from the center, representing the annihilation of a positron and an electron. A red line labeled "annihilation" points to the center. On the right, three signal waveforms are shown, labeled "Channel 1", "Channel 2", and "Summed channel". Three vertical red lines labeled "Coincidence events" indicate the detection of coincident gamma rays. The "Summed channel" waveform shows the combined signal of the two channels.

The most frequently used radionuclides in PET are radioisotopes of structural elements of natural organic molecules.

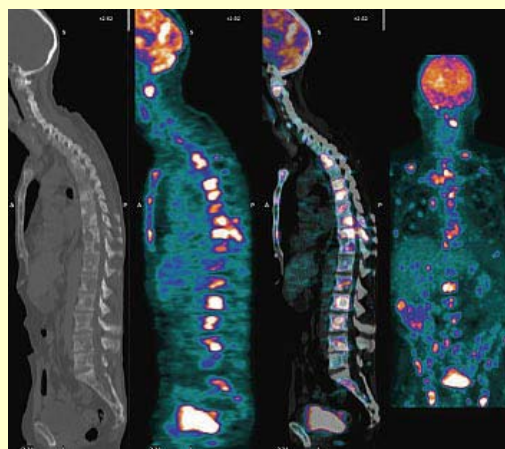
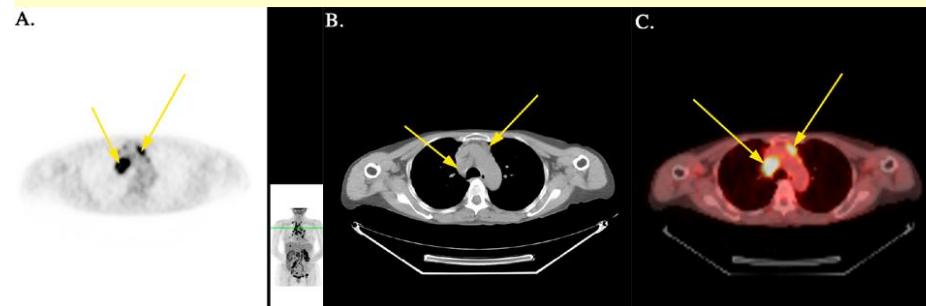
Isotope	β^+ energy (MeV)	β^+ range (mm)	1/2-life	Applications
^{11}C	0.96	1.1	20.3 min	receptor studies
^{15}O	1.70	1.5	2.03 min	stroke/activation
^{18}F	0.64	1.0	109.8 min	oncology/neurology
^{124}I	2.1350/1.5323	1.7/1.4	4.5 days	oncology

Isotope manufacturing nearby the site of application (see half-lives).



PET/CT

Combination of structural and functional imaging



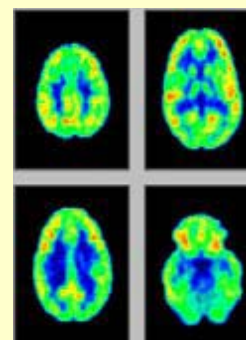
CT

PET

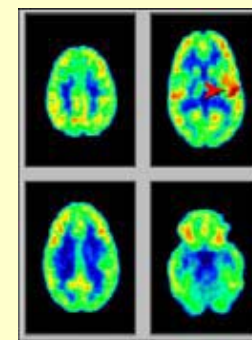
PET/CT

PET

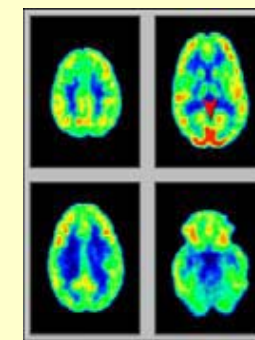
Activity of brain areas



In rest

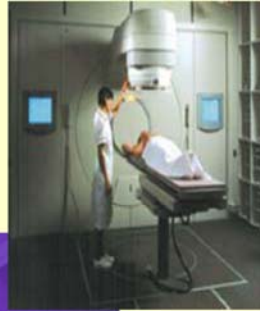


hearing



vision

Radiation therapy

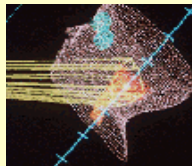


Radiotherapy : ionizing radiation induces damages at molecular and cellular level. This can be beneficial against tumour tissues

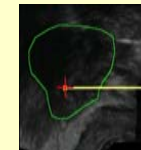
1. Which radiation is the best?
2. What is the optimal dose of radiation?
3. What is the best technique for generation radiation?
4. Irradiation selectivity – protection of healthy structures?

Approaches

- **Palliative radiotherapy** to reduce pain and address acute symptoms – e.g. bone metastasis, spinal cord compression etc.,
- **Radical radiotherapy** as primary modality for cure – e.g. head and neck
- **Adjuvant treatment** in conjunction with surgery – e.g. breast cancer



α



Internally deposited radioactivity

β^-

e^-

γ

R_{tg}

p

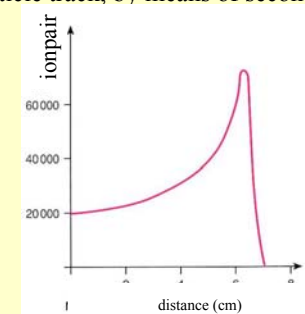
n

Linear ion density:

the amount of ion pairs in a line generated in a unit distance (n/l)

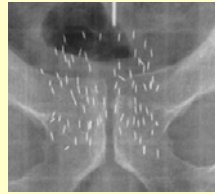
LET (Linear Energy Transfer) : the energy transferred to the material surrounding the particle track, by means of secondary electrons. ($nE_{ionpair}/l$)

In the air: $E_{ionpair} = 34 \text{ eV}$



α

Particle energy is not optimal
continuous energy spectrum
typical energy: few MeV



β^- :

Internally seeded radioactivity

e^- :

accelerated electron - 10-20 MeV

γ ,

production: linear accelerator

Rtg,

Efficient distance! $\approx 1\text{cm}/3\text{MeV}$

p

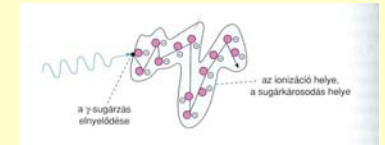
In the practice 6-21 MeV \Rightarrow 2-7 cm
treatment of superficial tumours

n

γ : external radiation source

Site of absorption \neq sites of ionization = site of radiation damages

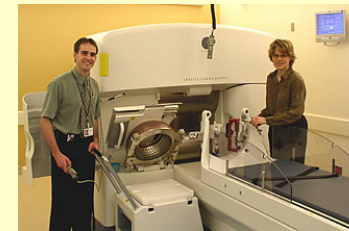
Penetration distance
is energy dependent



γ -knife: focused dose of radiation

about 200 portals in a specifically
designed helmet

e.g., ^{60}Co $E_\gamma \approx \text{MeV}$,
about TBq activity



Treat tumours and lesions in the brain

X/ray:



The X-rays are generated by a linear accelerator .

Few MeV photon energy.



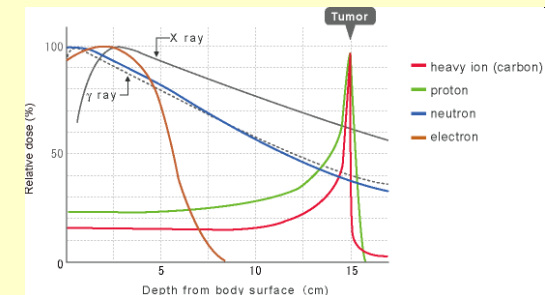
Would be ideal, but very
expensive!

γ ,

Rtg,

p :

n



Neutron radiation: collision of high energy protons (66 MeV) into berillium target ($p(66) + Be$)

α

R-

Neutrons induce nuclear reactions.

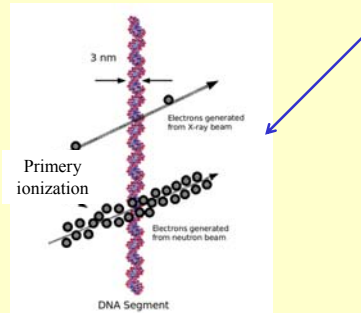
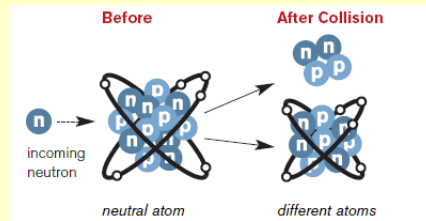
γ ,

Rtg,

P,

n :

High LET



Typical LET values

LET	Radiation	Energy(MeV):	LET(keV/ μ m):
high	α – particles	5.0	90
	fast neutrons	6.2	21
	protons	2.0	17
low	X-rays	0.2	2.5
	^{60}Co γ –radiation	1.25	0.3
	β – particles	2.0	0.3
	accelerated electrons	10.0	

Damjanovich, Fidy, Szöllősi: Medical biophysics

II. 3.2.3

3.2.4

3.2.5

VIII. 3.2

VIII. 4.4

IX.3