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

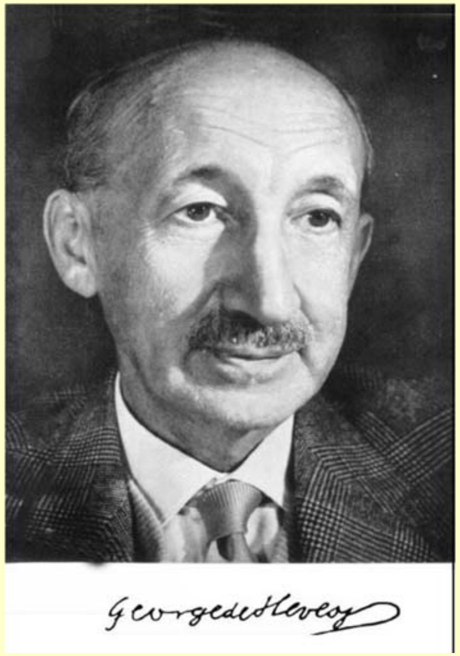
Structure	X-ray Ultrahang MRI	*differences according to the different physical parameters / properties of tissues*
Function	Isotope diagnostics MRI	*dynamic physiological / metabolic processes of different body organs can be followed*

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

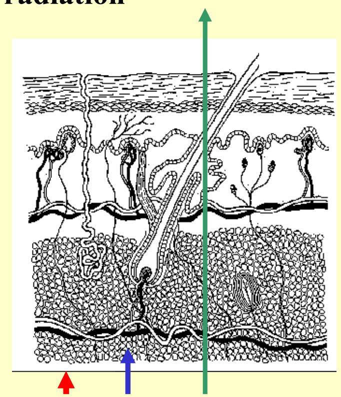
Maximize the information

Minimize the risk.

For that find the optimal

- type of radiation
- photon energy
- half-life
- radiopharmacon

Type of radiation



α β γ

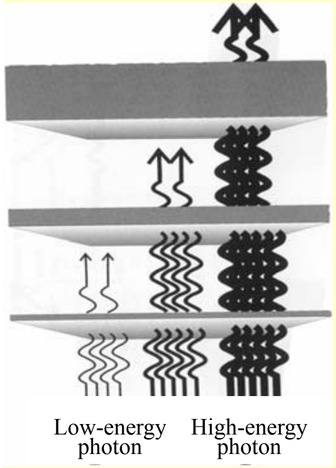
decay via photon emission to minimize absorption effects in body tissue

Only **γ-radiation** has sufficient penetration distance.

purely gamma-emitting isotope would be preferable

photon energy

$hf > 50$ 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

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

Λ: smaller is better

but

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

T: **shorter is better**

but

it has to be long enough for monitoring the physiological organ functions to be studied

N: smaller is better

dosimetric considerations for patients

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

Isomeric transition

Metastable excited nuclear state - half-life from few hours to 600 years

$$^{Am}_{Z}X \rightarrow {}^{A}_{Z}X + \gamma$$

$$^{99}_{42}Mo \rightarrow {}^{99m}_{43}Tc + \beta^- \rightarrow {}^{99}_{43}Tc + \gamma$$

$T_{1/2}$=67 hours $T_{1/2}$=6 hours

hf=140 keV

Isomeric transition

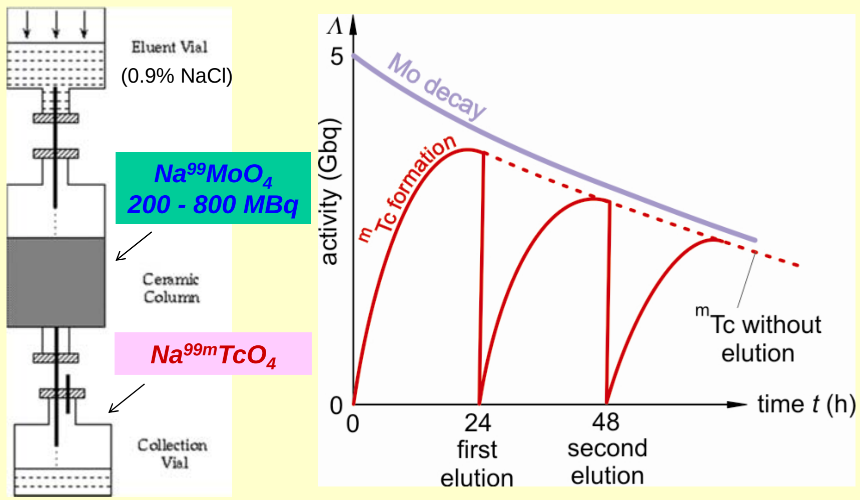
$$^{99}_{42}Mo \rightarrow {}^{99m}_{43}Tc + \beta^- \rightarrow {}^{99}_{43}Tc + \gamma$$

$T_{1/2}$=67 hours $T_{1/2}$=6 hours

hf=140 keV

One of the features that makes **Tc-99m** such an ideal radioisotope for diagnostic imaging is its ability to **readily bind to a wide variety of compounds** under physiological conditions.

Technetium-99m generator



Optimal activity for diagnostic procedure

Maximize the information

Minimize the risk

$\Lambda \sim 100$ 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

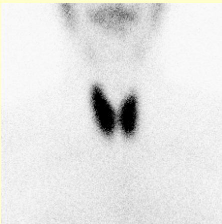
Emission CT

SPECT (Single Photon Emission Computed Tomography)

PET (Positron Emission Tomography)

Types of images

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

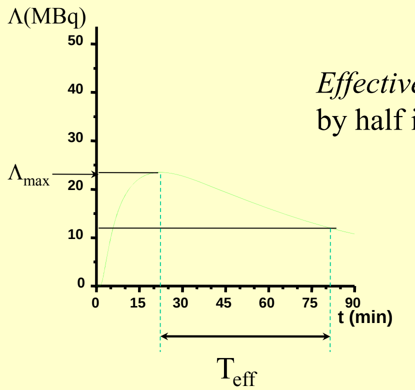


Isotope accumulation in

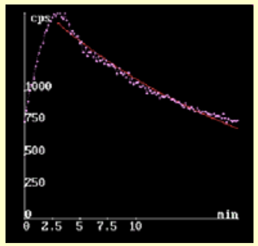
thyroid glands kidneys

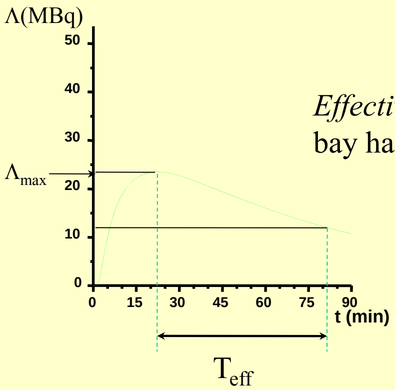
Types of images

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 bay half in the target organ

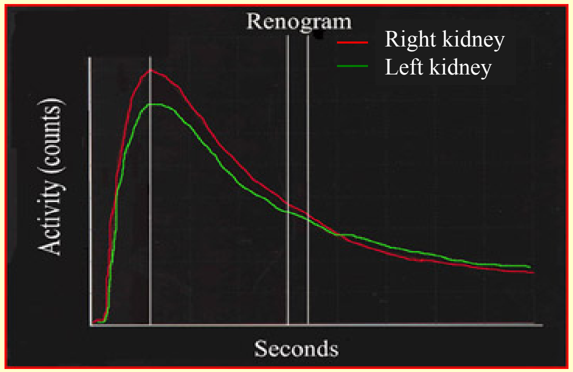
$$\Lambda = \Lambda_0 e^{-(\lambda_{phys} + \lambda_{biol})t}$$

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

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

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.

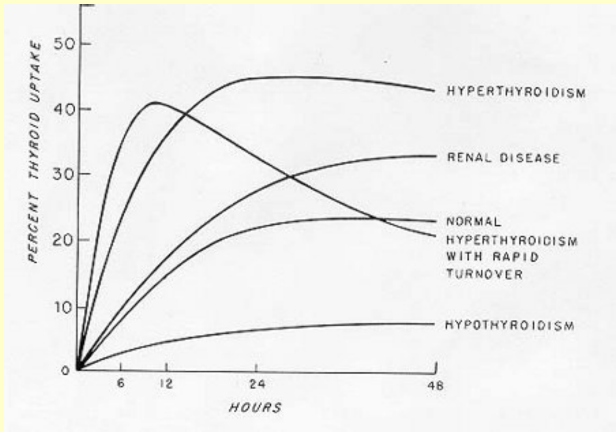
example



kidney

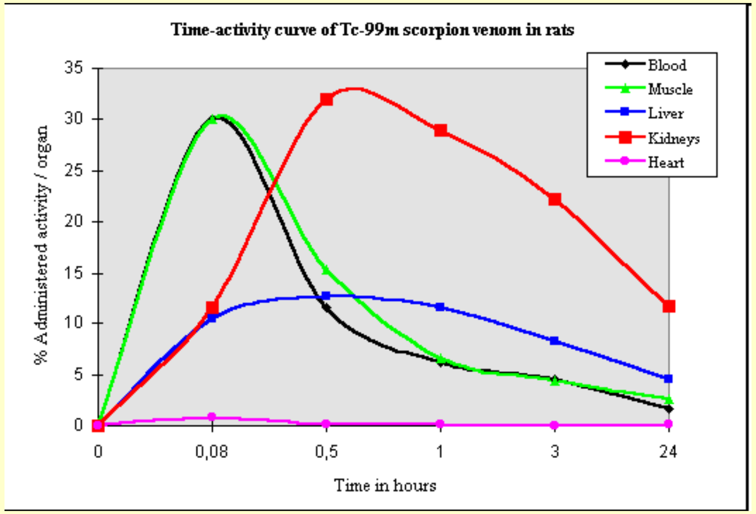
Isotope accumulation

example



Thyroid glands

Isotope accumulation



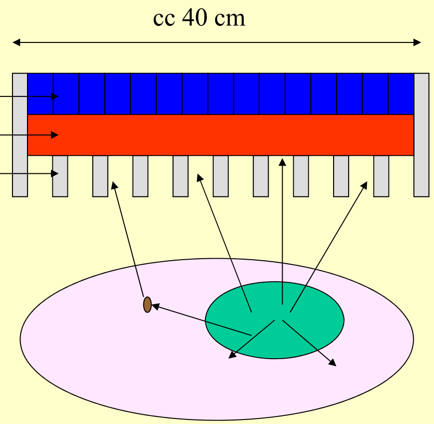
Hal Anger

1920-2005

Hal Anger and coworkers

1952

Gamma camera



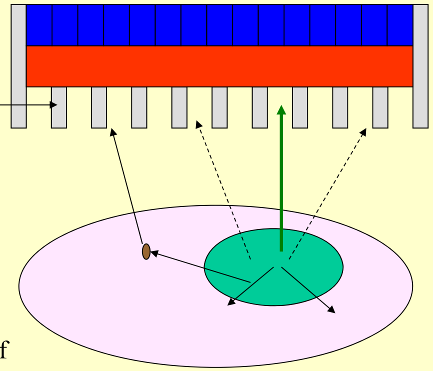
Photomultiplier tubes

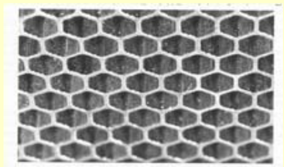
Scintillation crystal

Collimator

A radioactive source emits gamma ray photons in all directions.

collimator



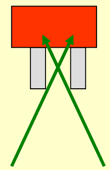


Collimators are composed of thousands of precisely aligned channels made of lead.

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

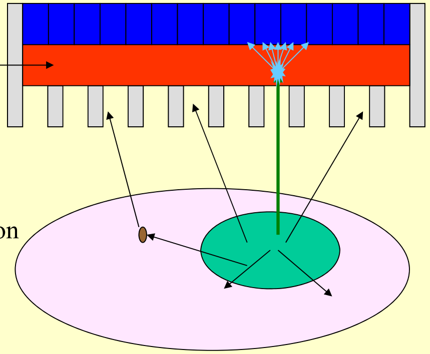
Photons emitted in other directions are absorbed by the septa between the holes.

Size and geometry of holes are essential for the resolution.



Scintillation crystal

NaI(Tl)



Sufficient detection efficiency

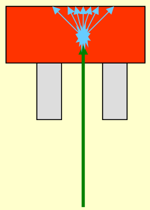
photons of 150 keV μ ~2.2 1/cm

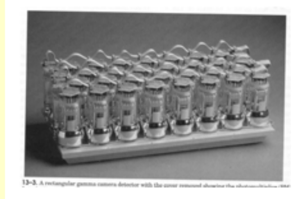
10 mm thickness ~ 90% attenuation

Proper wavelength – 415 nm – for PM photocathode

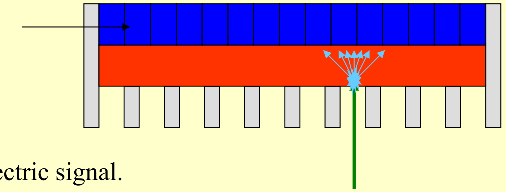
Problems:

- fragile
- temperature sensitive
- hygroscopic





Photomultiplier tubes

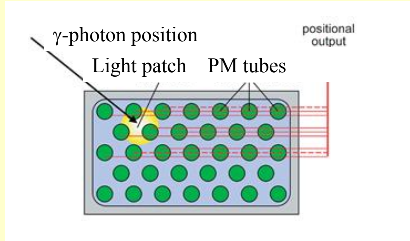


Transformation of light pulses to electric signal.

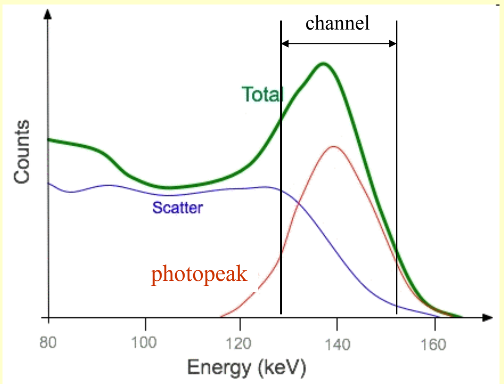
Typically 37-91 tubes, 5.1-7.6 cm diameter each

Amplitude of electric pulses varies in a wide range, because

- absorption of one γ-photon induces electric signals in more then 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.



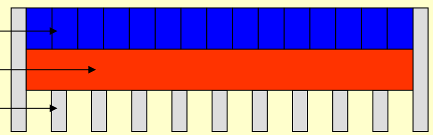
These electric pulses can be distinguished by discrimination (DD).

Gamma camera

Photomultiplier tubes

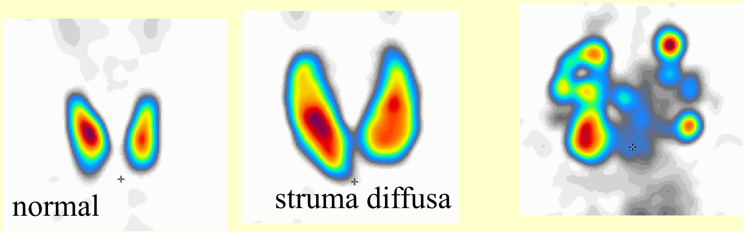
Scintillation crystal

Collimátor



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

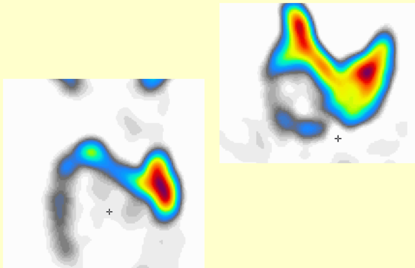
Pertechnetate (intravenous 80 MBq) distribution in thyroid glands



normal

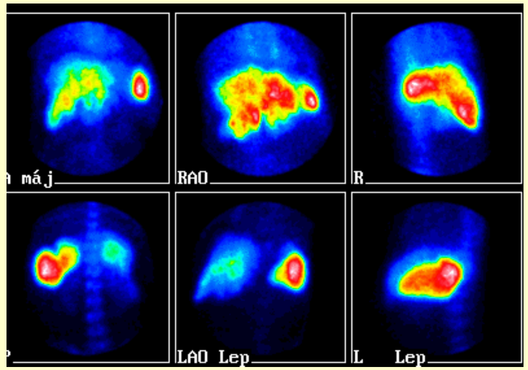
struma diffusa

struma multinodularis



Cold nodules

Liver lesion nodules

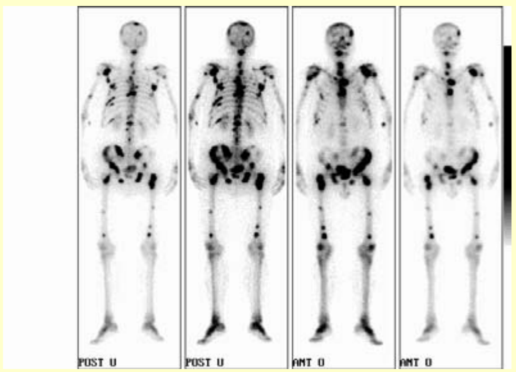


^{99m}Tc- fyton

Bone scintigraphy

^{99m}Tc-MDP: 600 MBq

normal



imaging in bone metastases

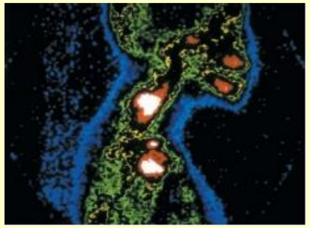
Gamma camera – space and time distribution can be recorded

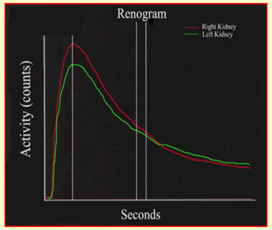
static and dynamic pictures can be reconstructed

Camera parameters:

- spatial resolution
- energy resolution
- efficiency of detection

Gamma camera image:
summation image

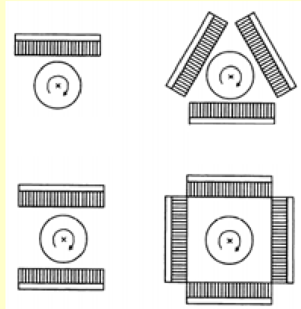




For depth resolution: tomographic device is necessary

SPECT

Single Photon Emission Computed Tomography



Variouos camera arrangements

SPECT

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

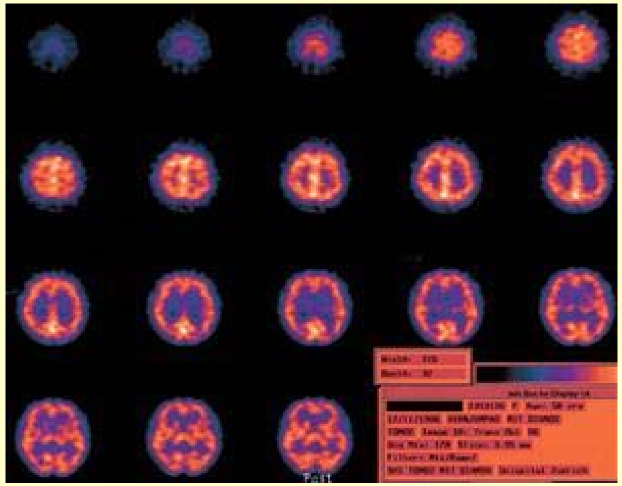
Cross-sectional image can be reconstructed.

Measurement from a series of projections.

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

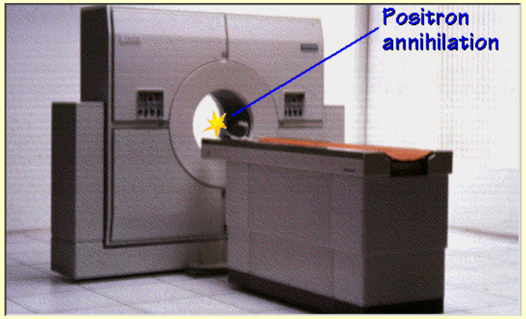
SPECT – images of scalp

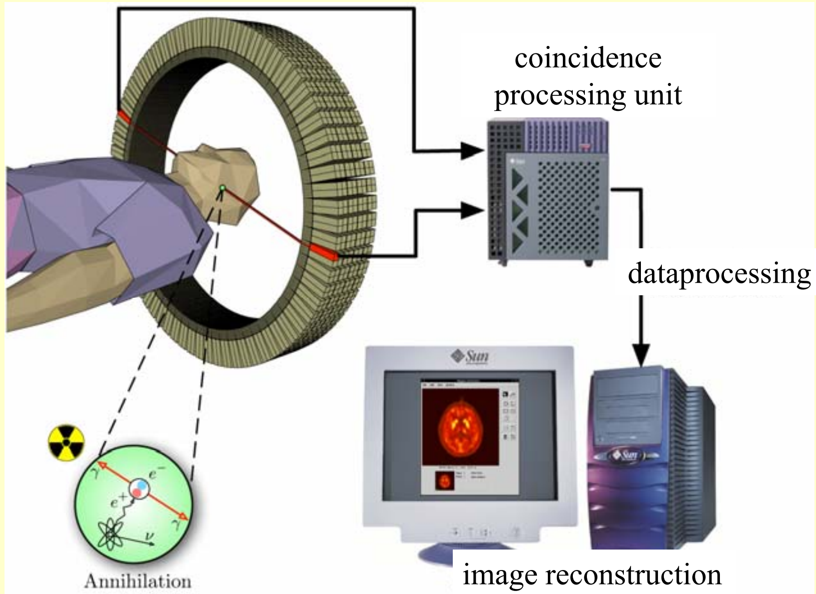
^{99m}Tc- HMPAO



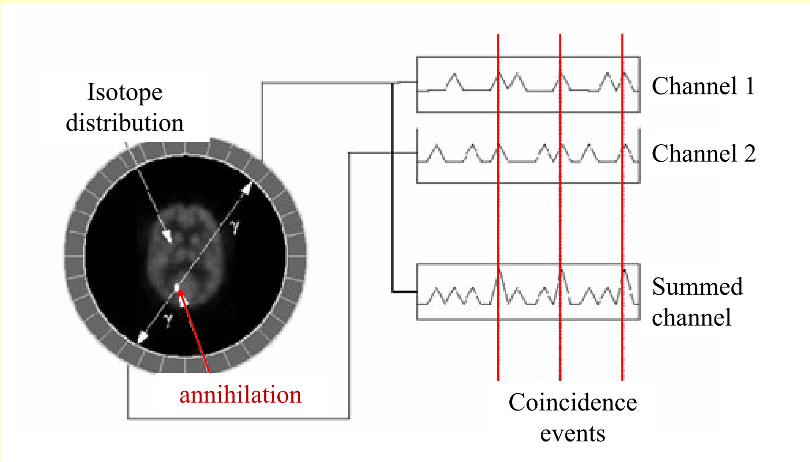
PET

Positron Emission Tomography





coincidence processing



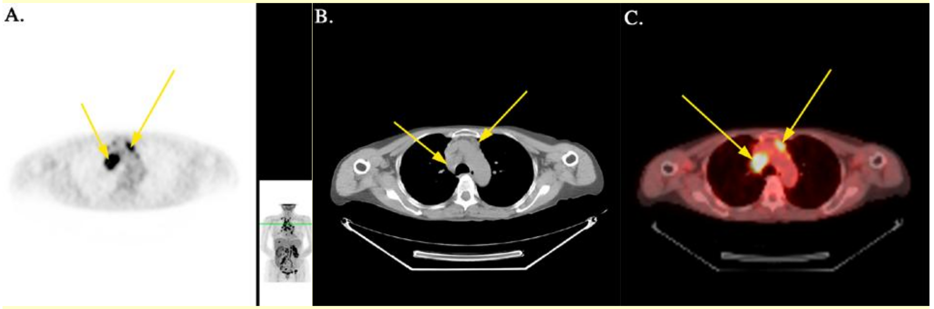
The most frequently used radionuclides in PET are radioisotopes of structural elements of natural organic molecules.

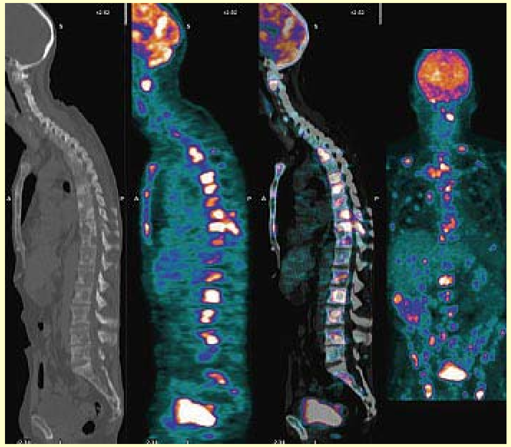
Isotope	β^+ energy (MeV)	β^+ range (mm)	1/2-life	Applications
^{11}C	0.96	1.1	20.3 min	receptor studies
^{15}O	1.70	1.5	2.03 min	stroke/activation
^{18}F	0.64	1.0	109.8 min	oncology/neurology
^{124}I	2.1350/1.5323	1.7/1.4	4.5 days	oncology

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

PET/CT

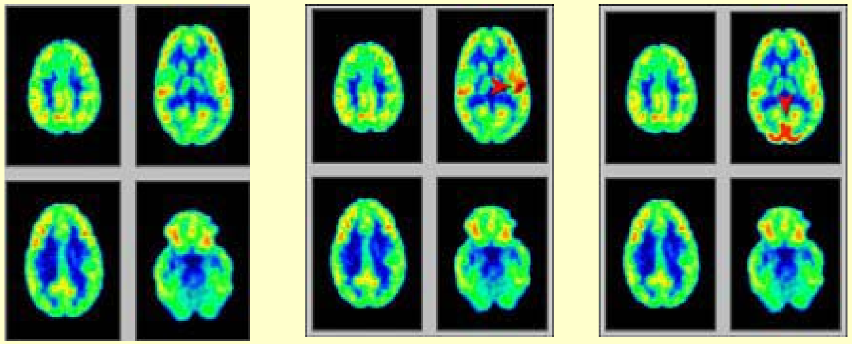
Combination of structural and functional imaging





CT PET PET/CT PET

Activity of brain areas



In rest hearing vision

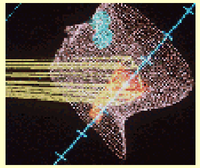
Radiation therapy

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

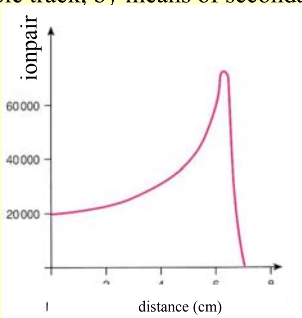
Internally deposited radioactivity

β-,
e-,
γ,
Rtg,
p
n

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

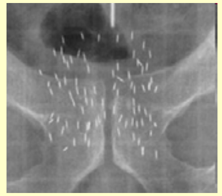
LET (Linear Energy Transfer : the energy transferred to the material surrounding the particle track, by means of secondary electrons. *($nE_{ionpair}/l$)*

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



α

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



Internally seeded radioactivity

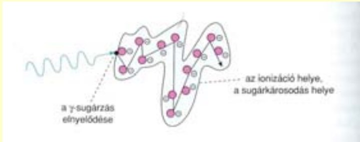
e⁻: accelerated electron - 10-20 MeV
production: linear accelerator
Efficient distance! ≈1cm/3MeV
In the practice 6-21 Mev => 2-7 cm
treatment of superficial tumours

γ,
Rtg,
p
n

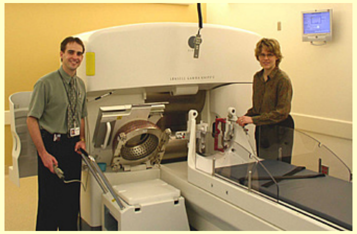
γ : external radiation source

Site of absorption≠ sites of ionization = site of radiation damages

Penetration distance
is energy dependent



γ-knife: focused dose of radiation

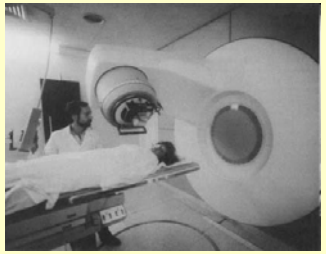


about 200 portals in a specifically designed helmet

e.g., ^{60}Co Eγ≈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.

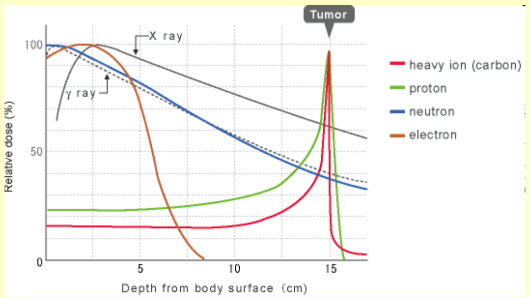
Would be ideal, but very expensive!

γ,

Rtg,

p :

n

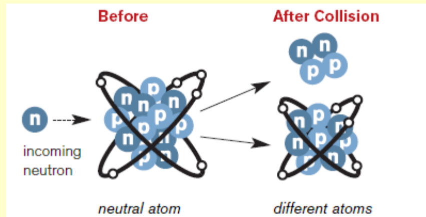


Neutron radiation:collision of high energy protons (66 MeV) into berillium target (p(66) +Be)

α

β-

Neutrons induce nuclear reactions.



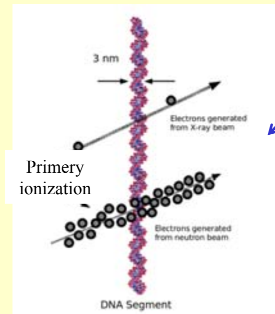
γ,

Rtg,

P,

n :

High LET



Typical LET values

LET	Radiation	Energy(MeV):	LET(keV/µm):
high	α – particles	5.0	90
	fast neutron s	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