Biophysics I

14. Nuclear radiations in the clinical practice

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10. 12. 2021.

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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

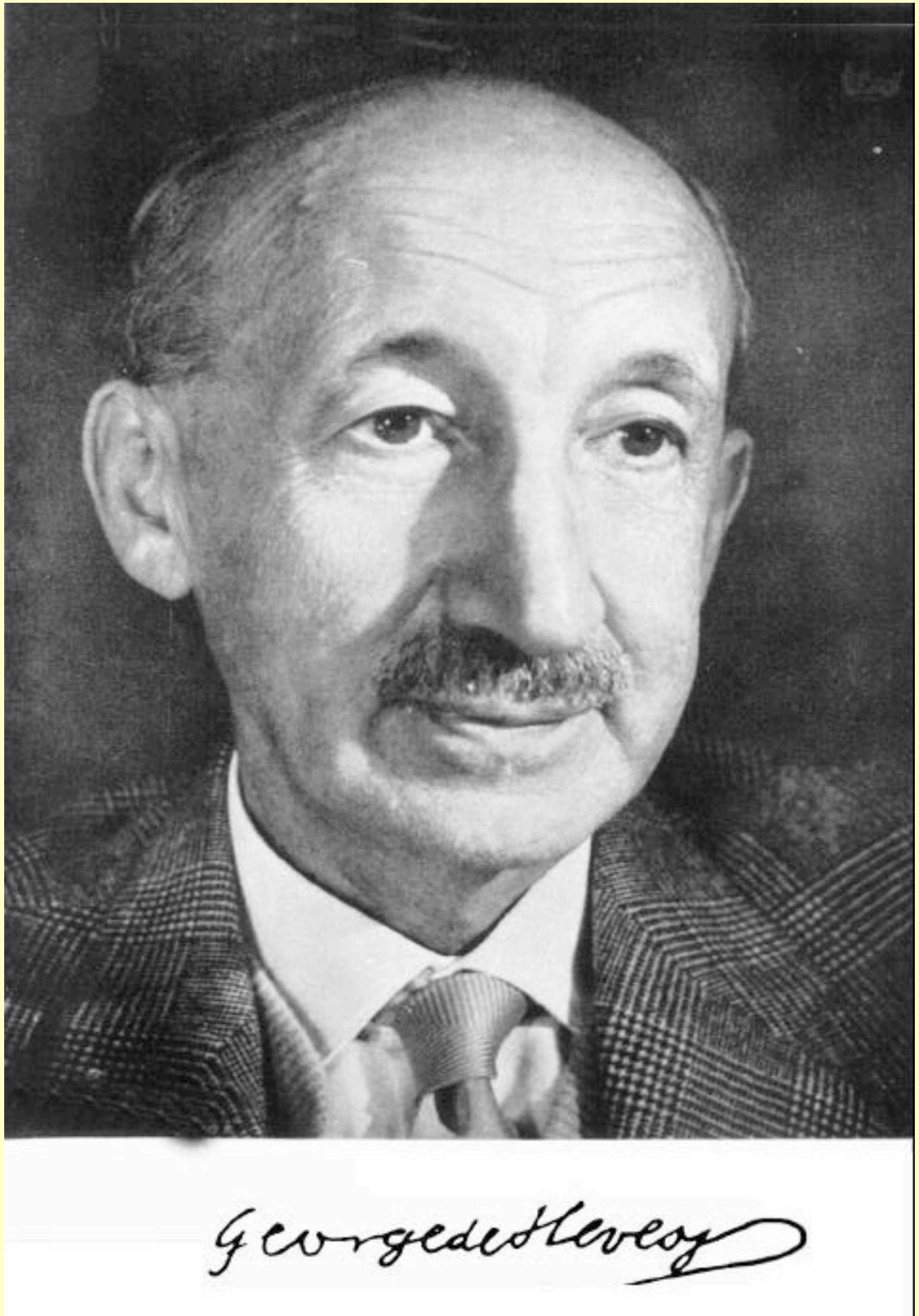
Structure	X-ray Ultrasound MRI	*differences according to the different physical parameters / properties of tissues*
Function	Isotope diagnostics MRI	*dynamic physiological / metabolic processes of different body organs can be followed*

X-ray

Shows the structure

Isotope diagnostics

Reports 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

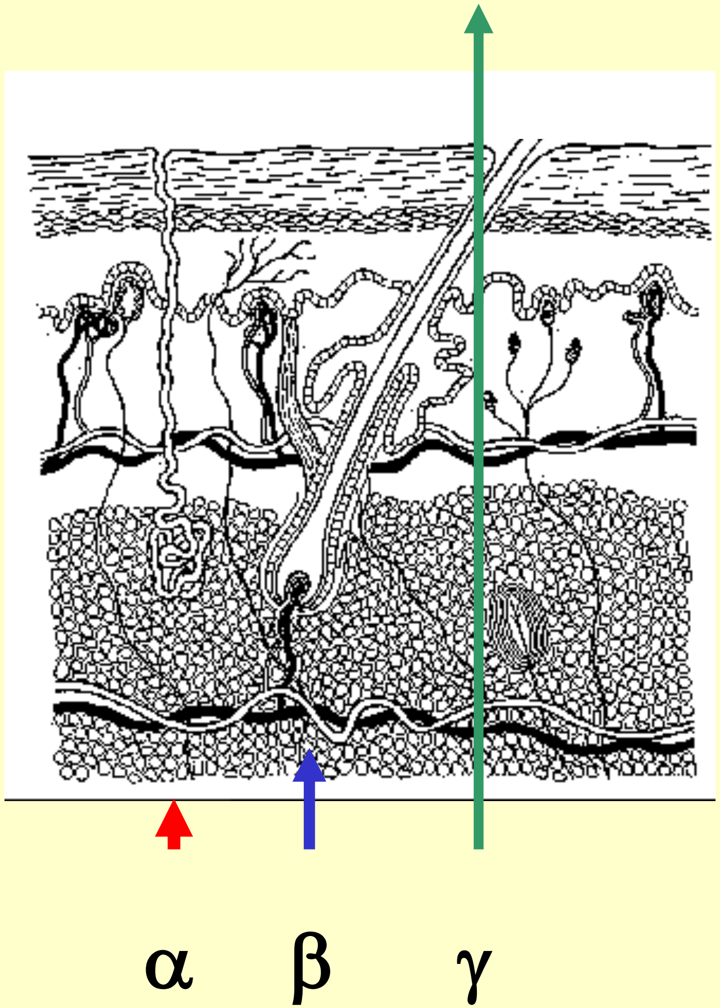
The choice of the appropriate radioisotope for nuclear imaging

Maximize the information – Minimize the risk

For that find the optimal

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

Type of radiation



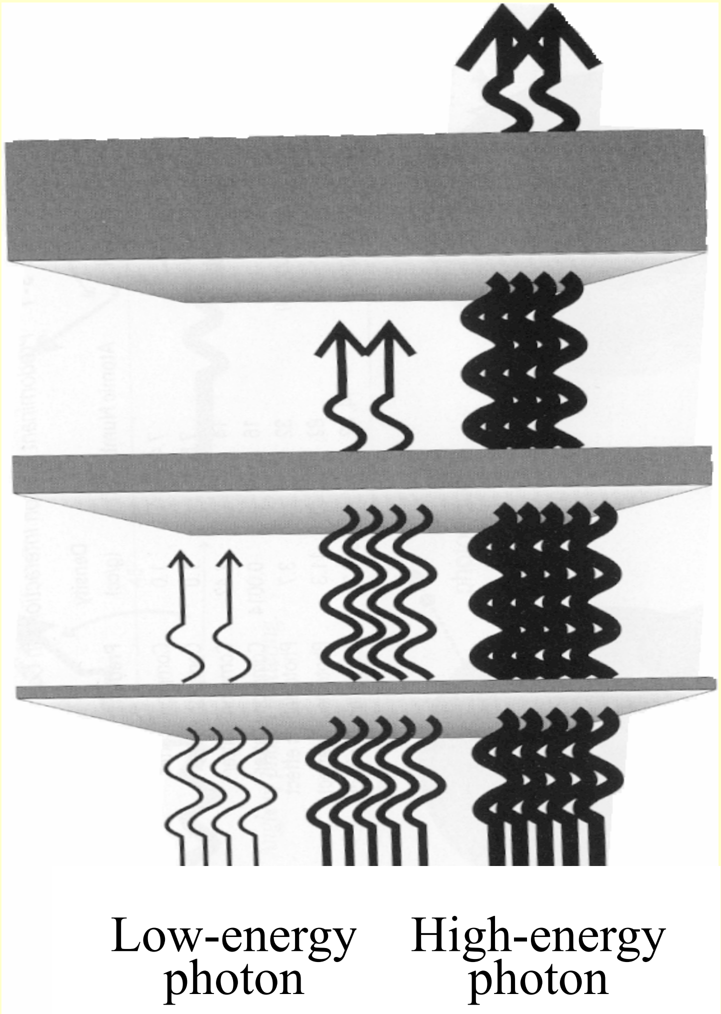
decay via photon emission to minimize absorption effects in body tissue

only **γ-radiation** has sufficient penetration depth

purely gamma-emitting isotope is 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

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

smaller is better
but
the value is limited by the sensitivity of the detector

smaller is better

dose considerations for patients

shorter is better

but

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

radiopharmaceutical – is a 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.

Factors 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

Gamma-emitting isotiopes

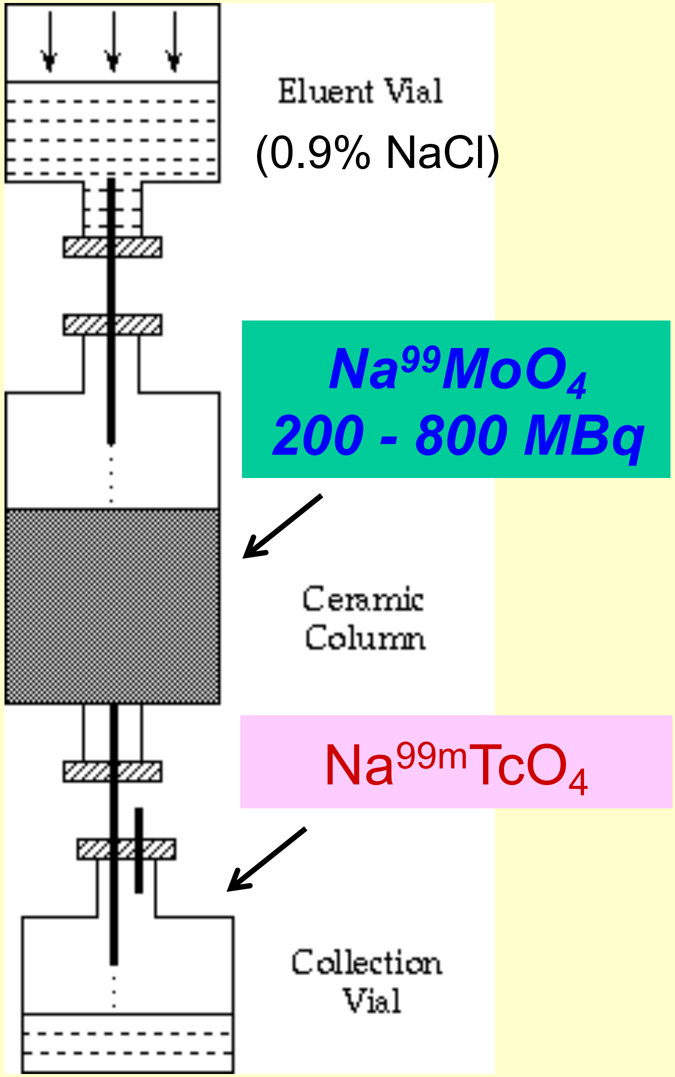
Isomeric transition: some excited states may have half-lifes ranging from hours up to more than 600 years

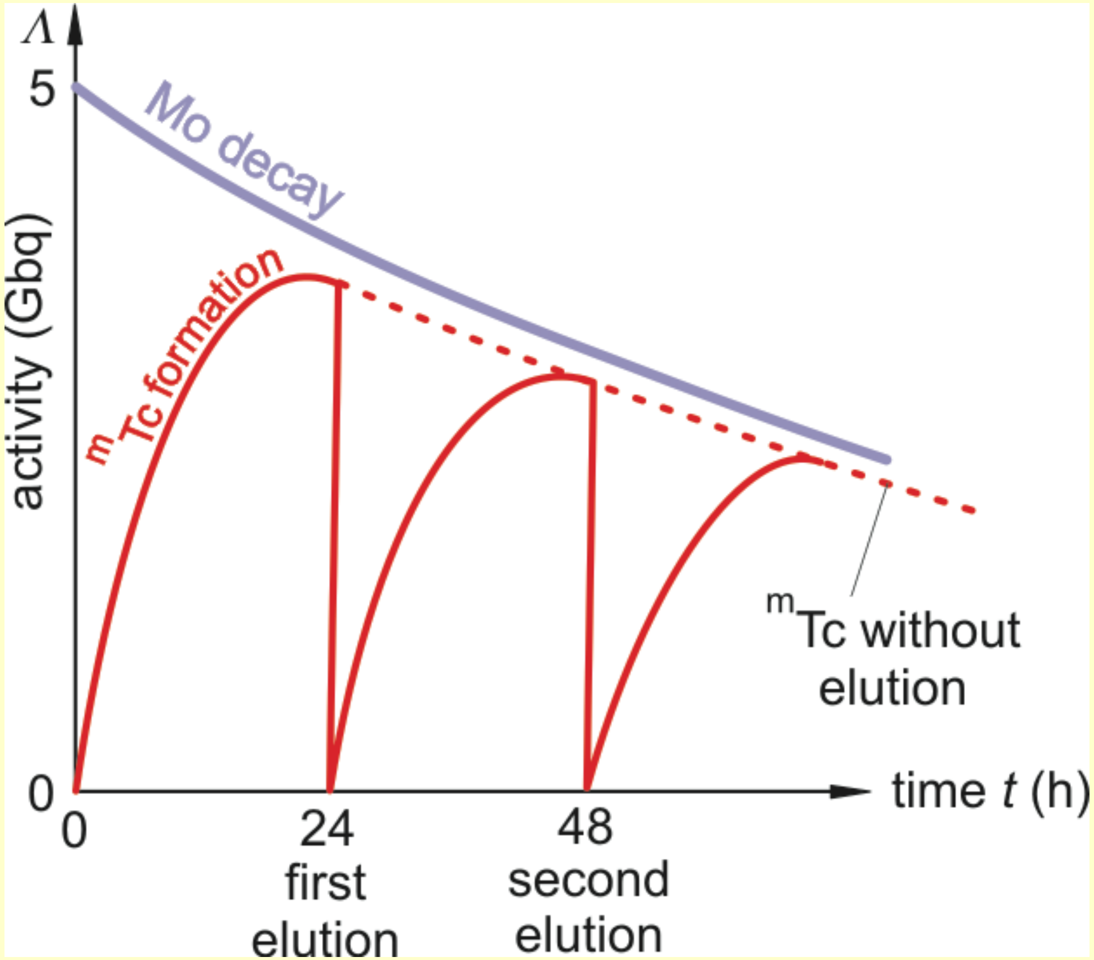
$$^{Am}_{Z}X \rightarrow {}^{A}_{Z}X + \gamma$$

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

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

Technetium-99m generator





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 image – spatial distribution of isotope / activity at a certain time

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

Static and dynamic image – series of static recordings

Emission CT

SPECT (Single Photon Emission Computed Tomography)

PET (Positron Emission Tomography)

Types of images

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

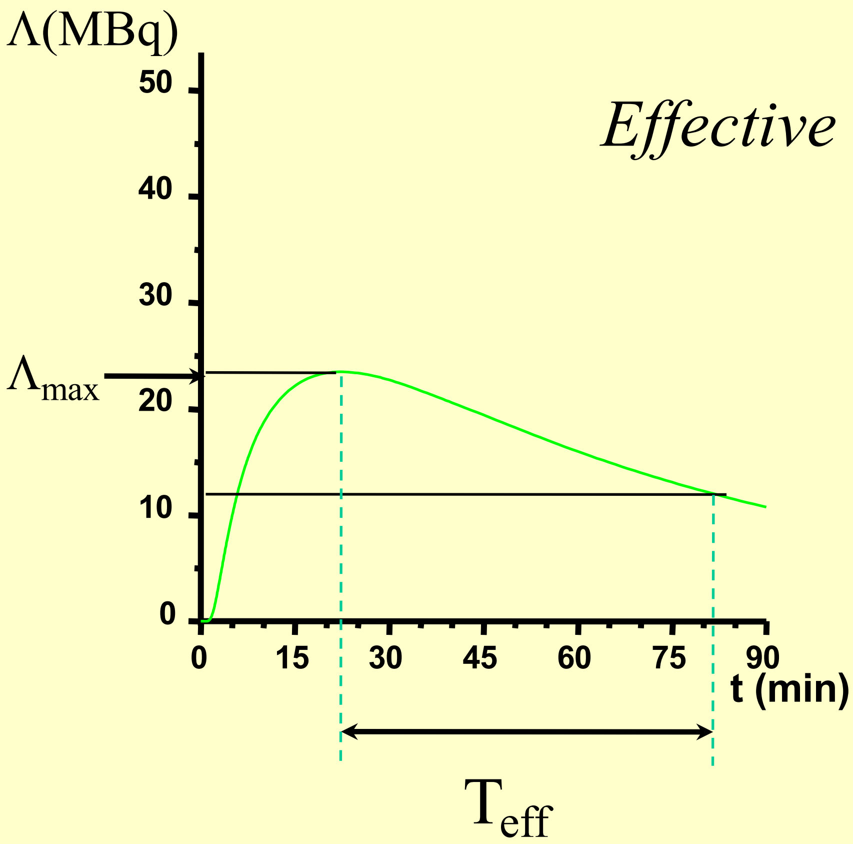
Isotope accumulation in

thyroid glands

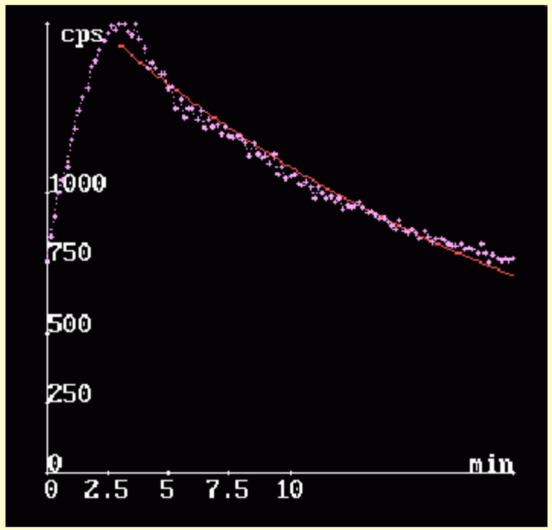
kidneys

Types of images

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

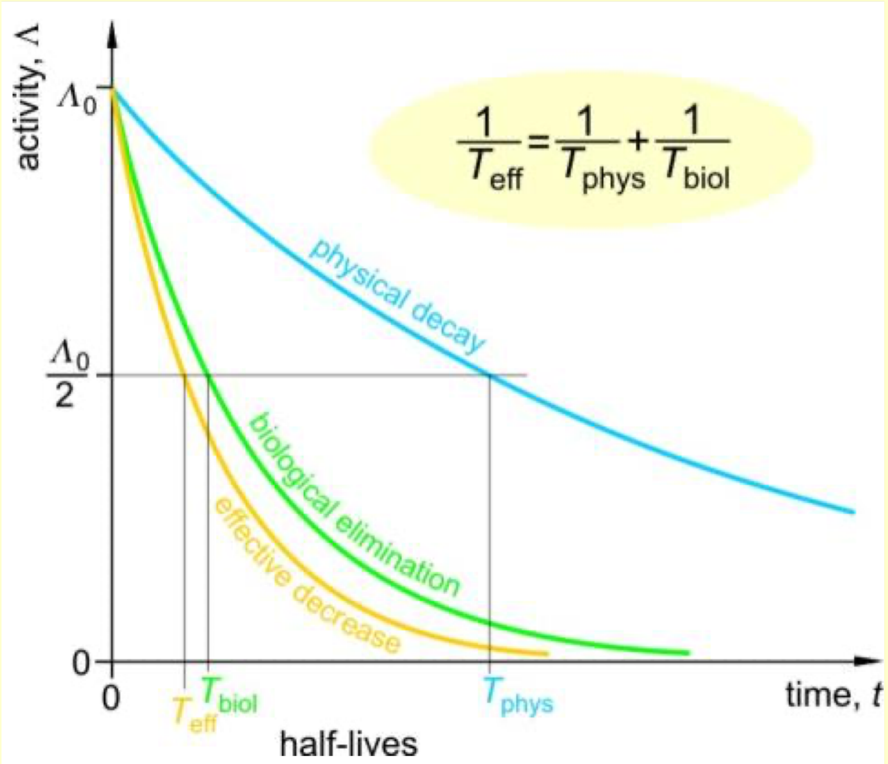


Effective half-life – activity decreases by half in the target organ



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

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

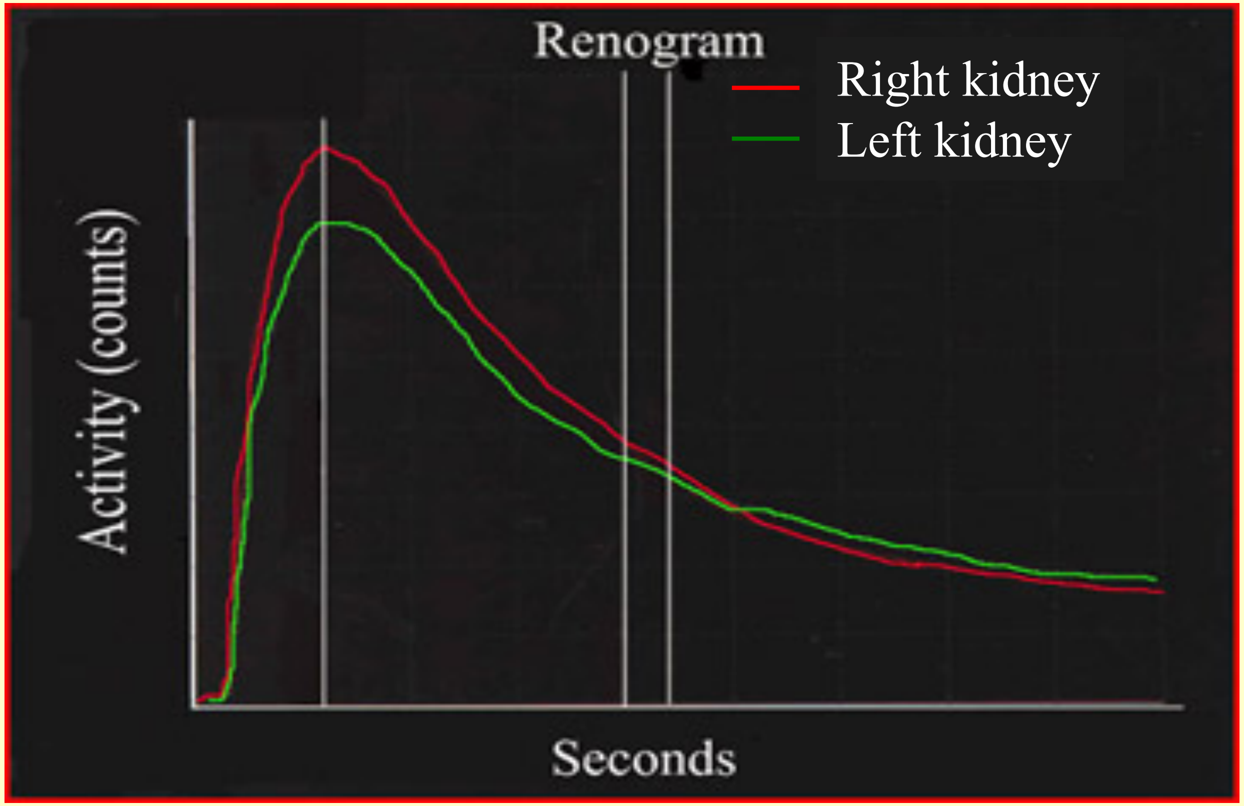


$$\lambda_{effective} = \lambda_{phys} + \lambda_{biol}$$

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

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.

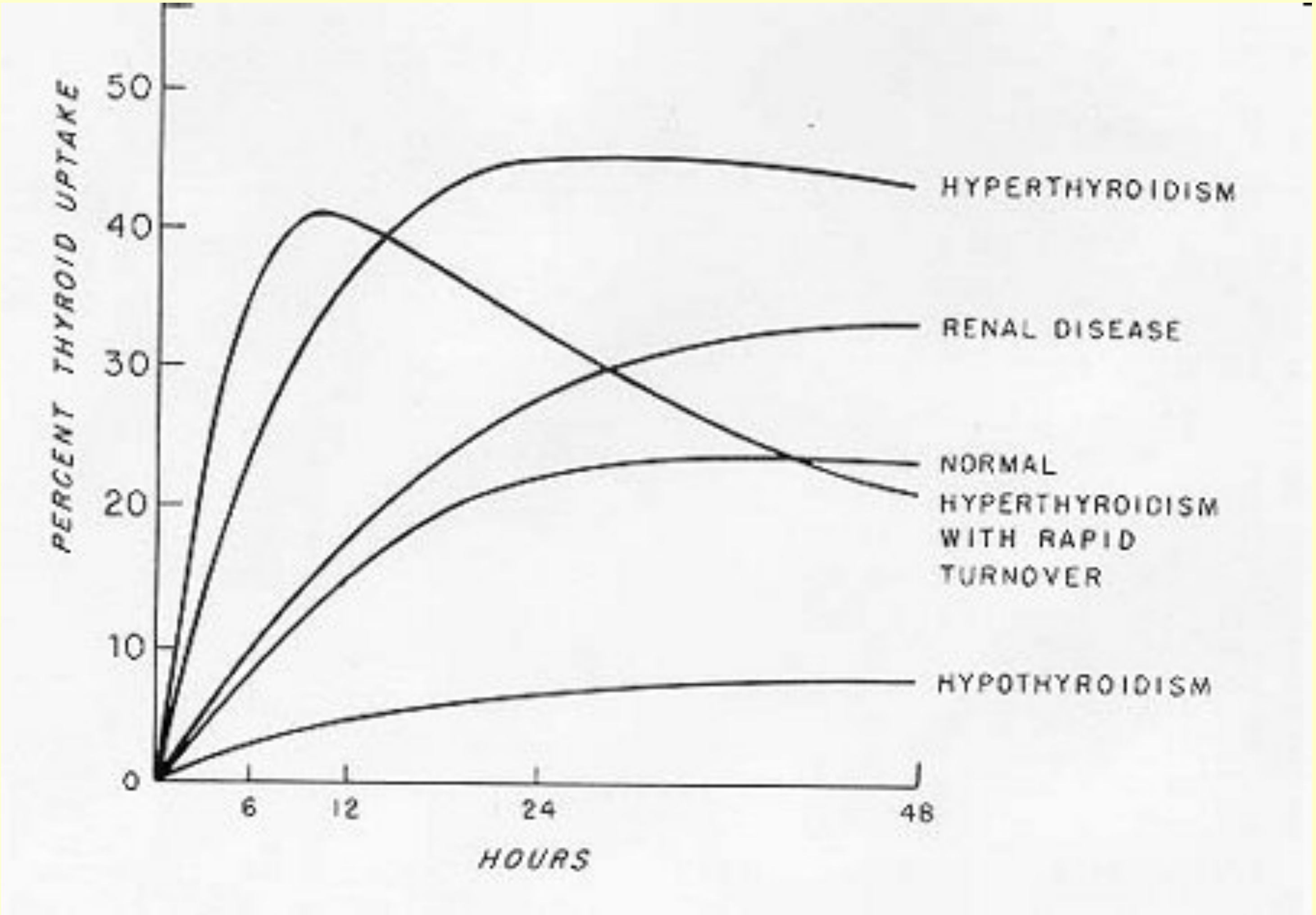
example



kidney

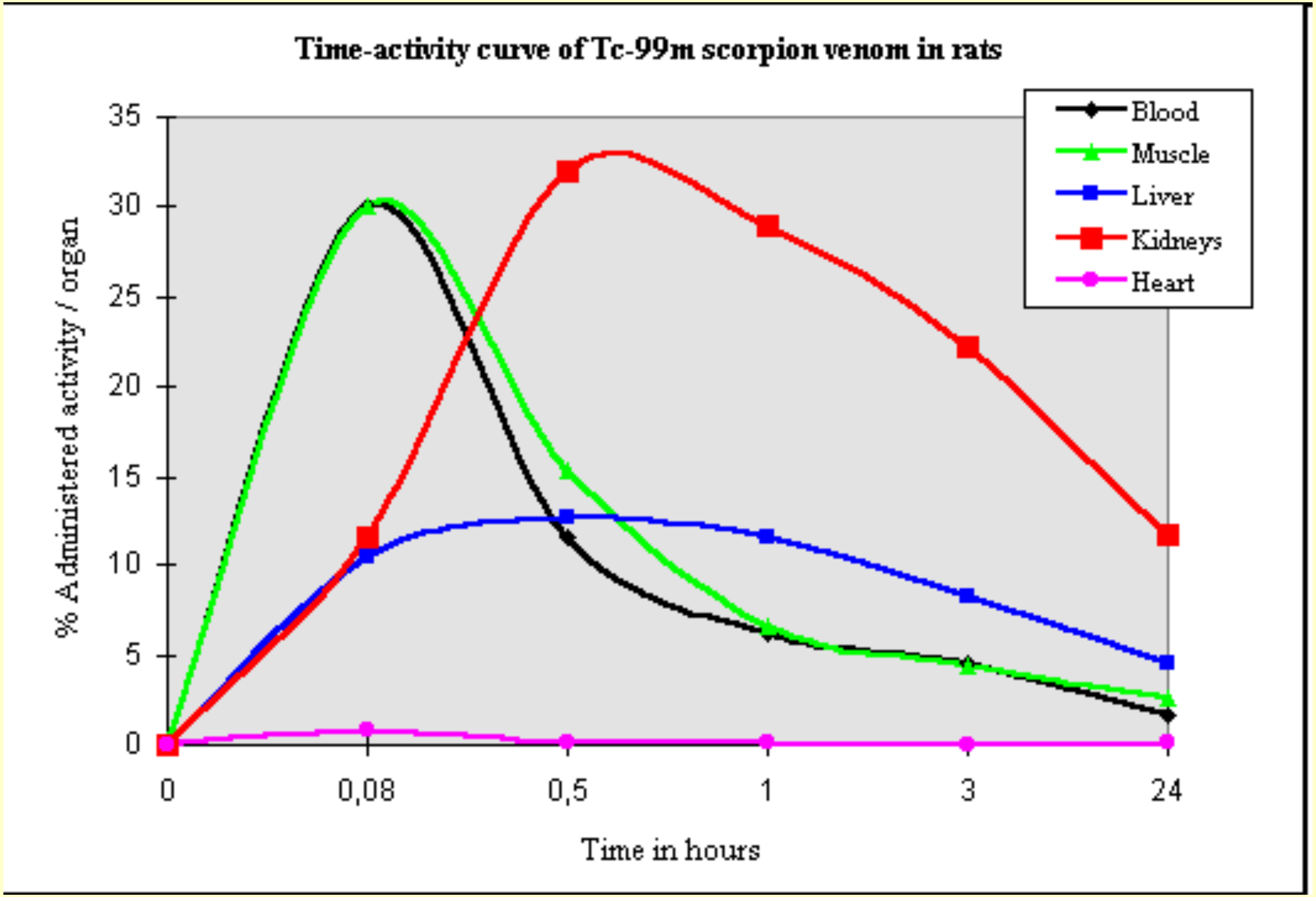
Isotope accumulation traces

example



Thyroid glands

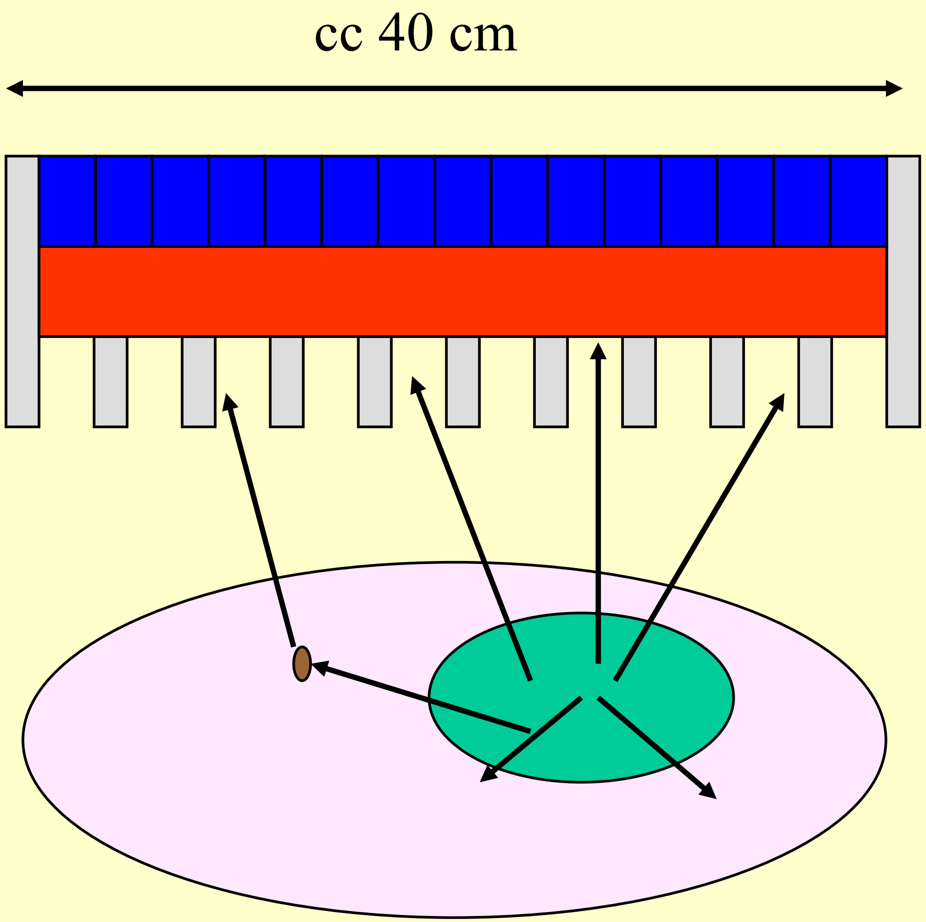
Isotope accumulation traces


Time-activity curve of Tc-99m scorpion venom in rats
35
30
25
20
15
10
5
0
% Administered activity / organ
0
0,08
0,5
1
3
24
Time in hours
Blood
Muscle
Liver
Kidneys
Heart

Gamma camera

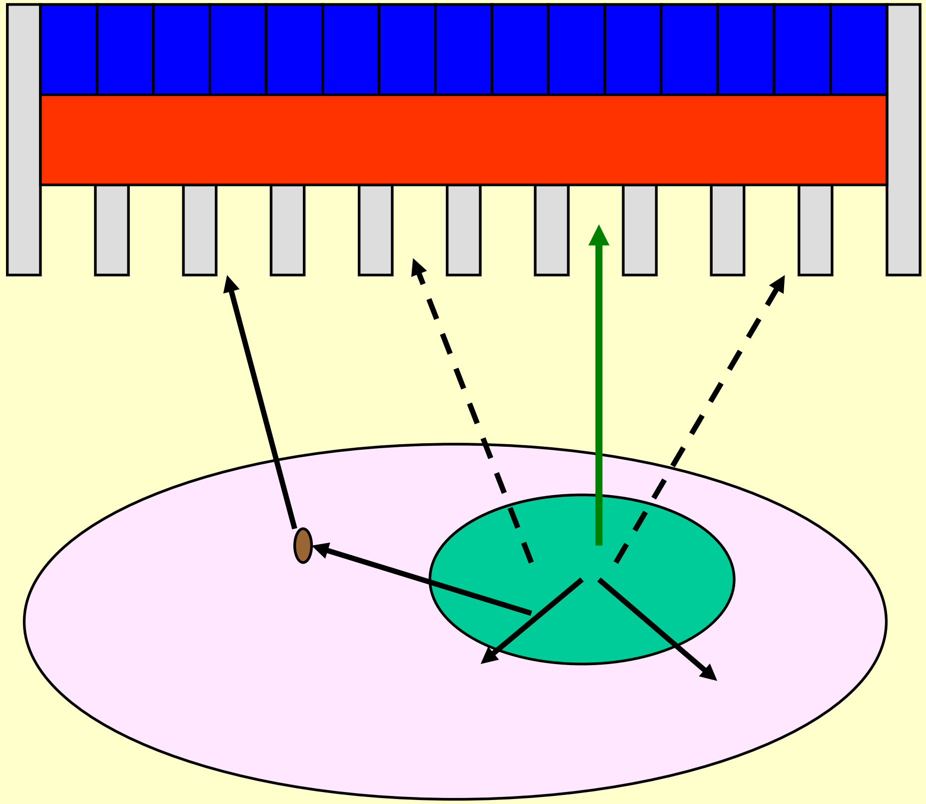
Hal Anger
1920-2005

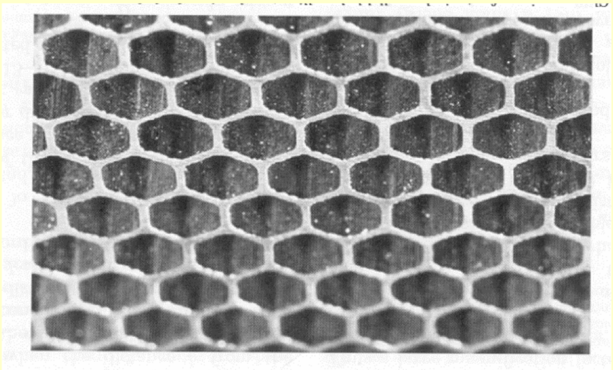
Photomultiplier tubes
Scintillation crystal
Collimator



A radioactive source emits gamma photons in all directions.

collimator →

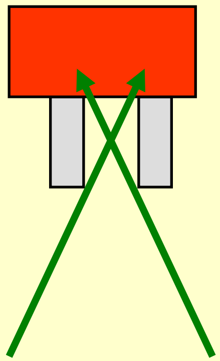




Collimators are composed of thousands of precisely aligned channels made of lead.

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

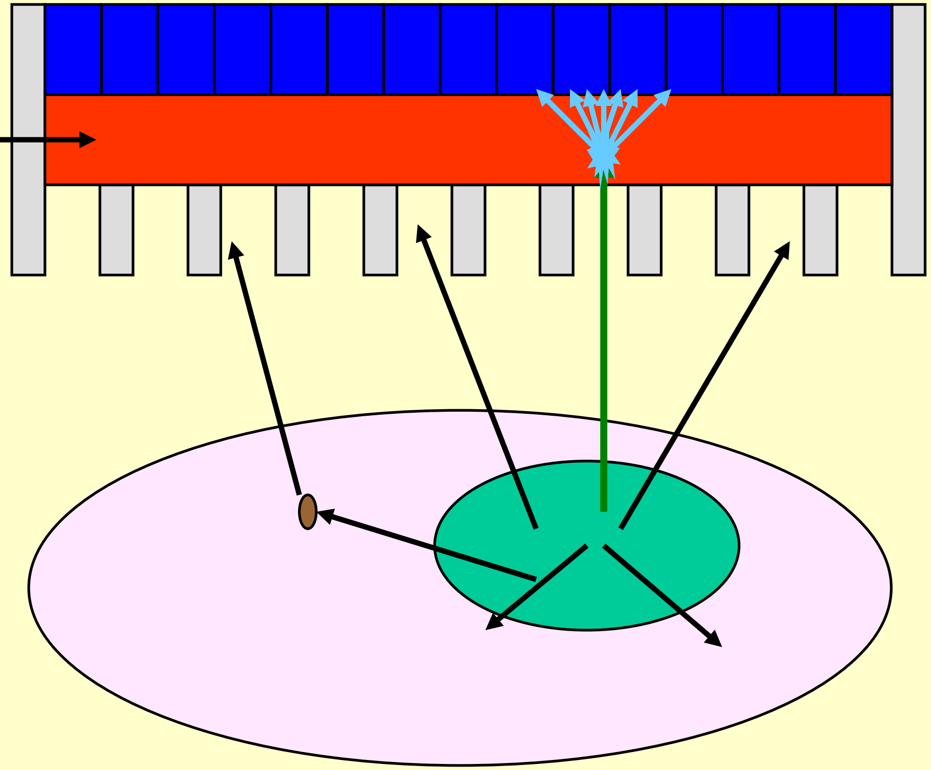
Photons emitted in other directions are absorbed by the septa between the holes.



Size and geometry of holes determine resolution.

Scintillation crystal

NaI(Tl)

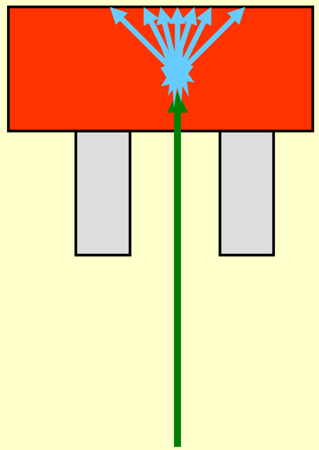


Sufficient detection efficiency

photons of 150 keV, μ ~2.2 1/cm

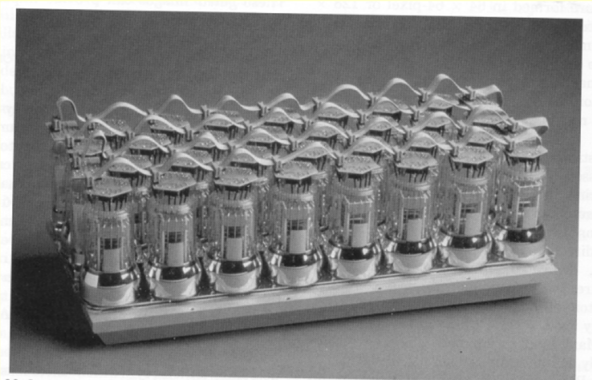
10 mm thickness ~ 90% attenuation

Proper wavelength – 415 nm – for PM photocathode

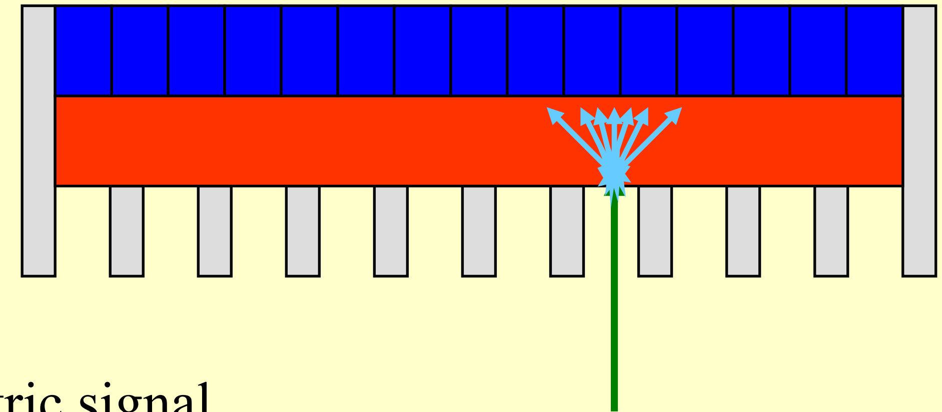


Problems with NaI:

- fragile
- temperature sensitive
- hygroscopic


13-3. A rectangular gamma camera detector with the cover removed showing the

Photomultiplier tubes

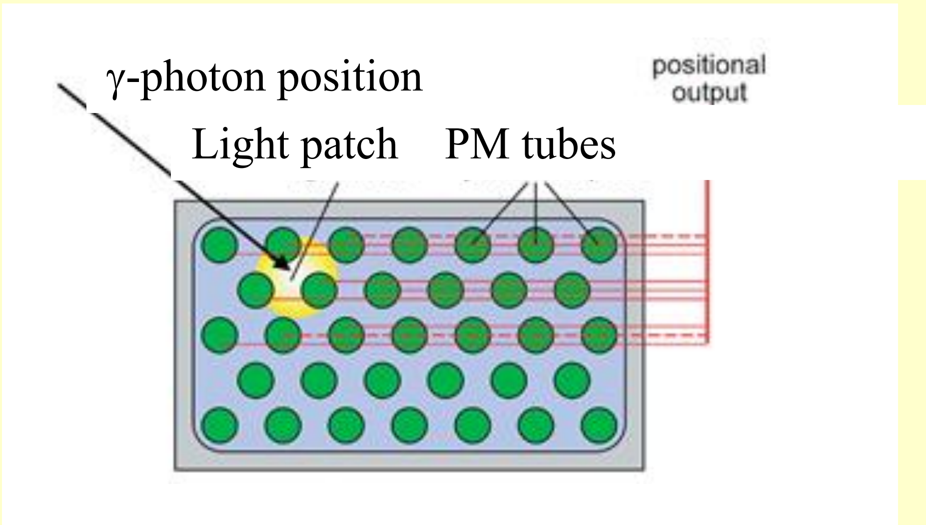


Transformation of light pulses to electric signal.

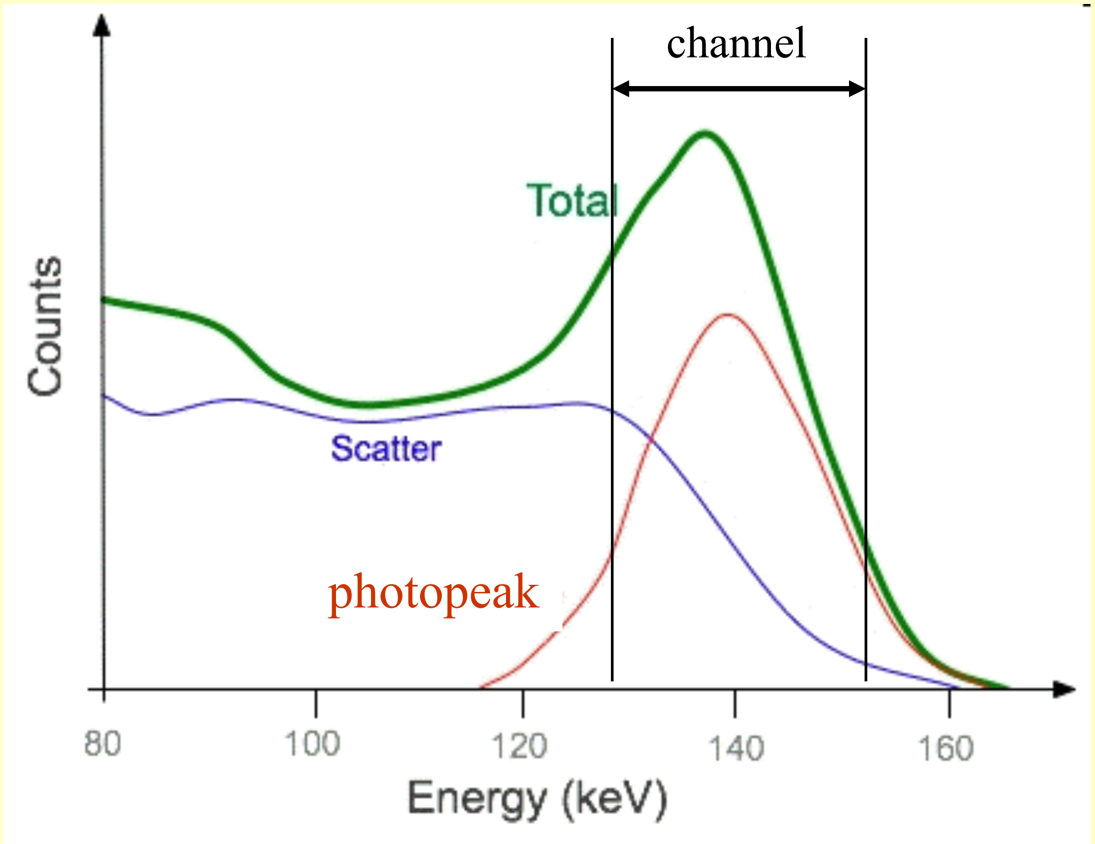
Typically 37-91 tubes, 5.1-7.6 cm diameter each

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-scattering.

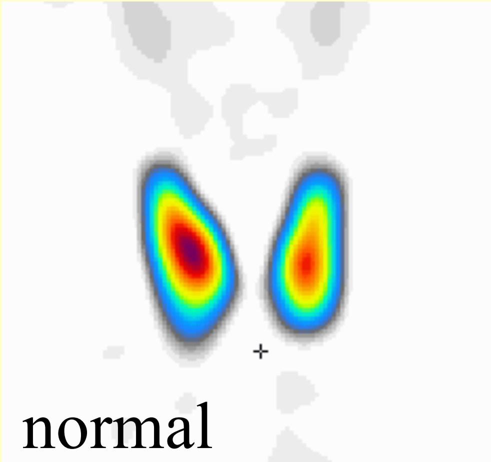


Pulse amplitude spectrum – Amplitude of an electric pulse generated by a γ-photon absorption in photoeffect is proportion to the photon energy.

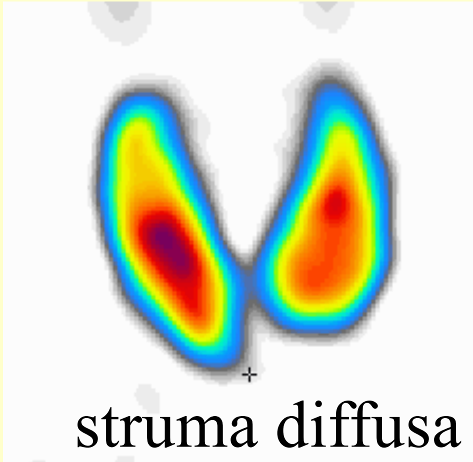


These electric pulses can be distinguished by discrimination (DD).

Pertechnetate (intravenous 80 MBq) distribution in thyroid glands

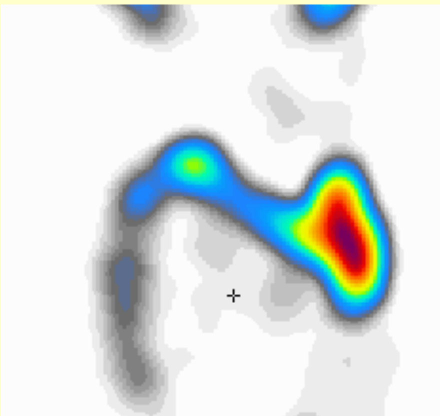


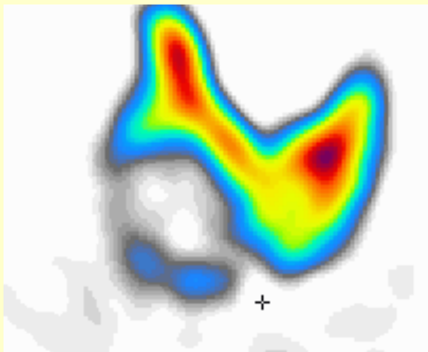
normal



struma diffusa

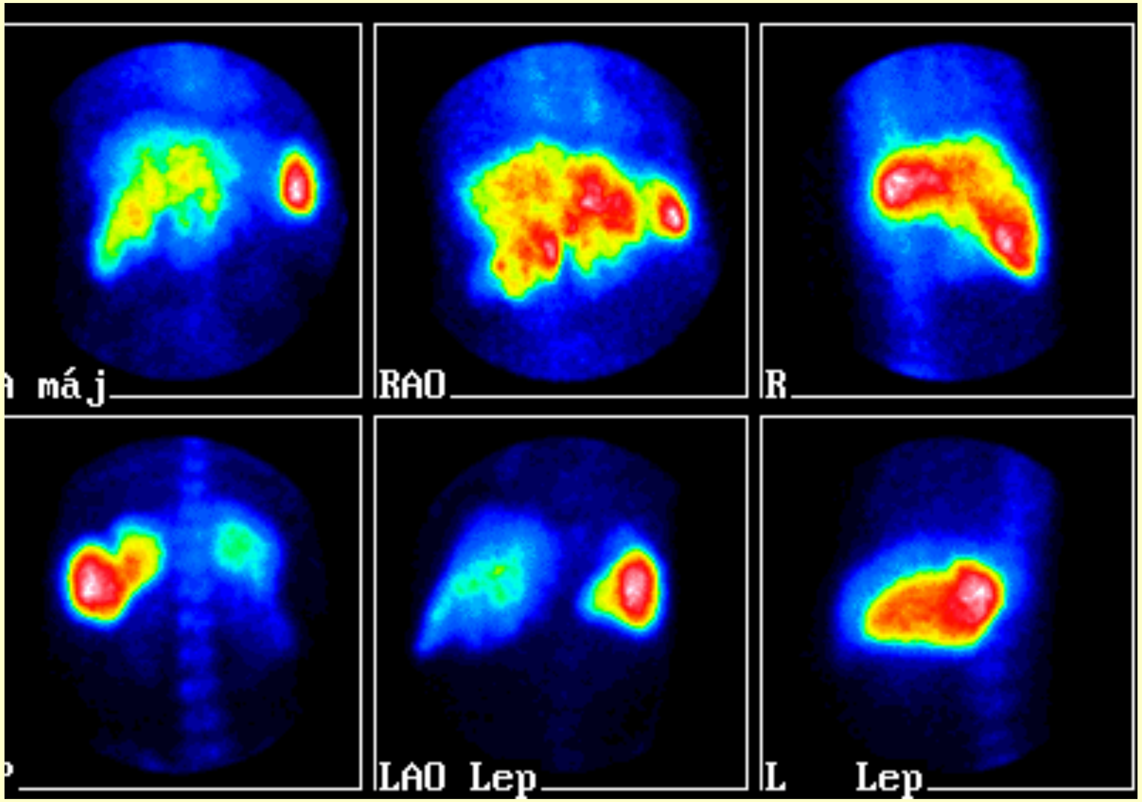
struma multinodularis





Cold nodules

Liver lesion nodules

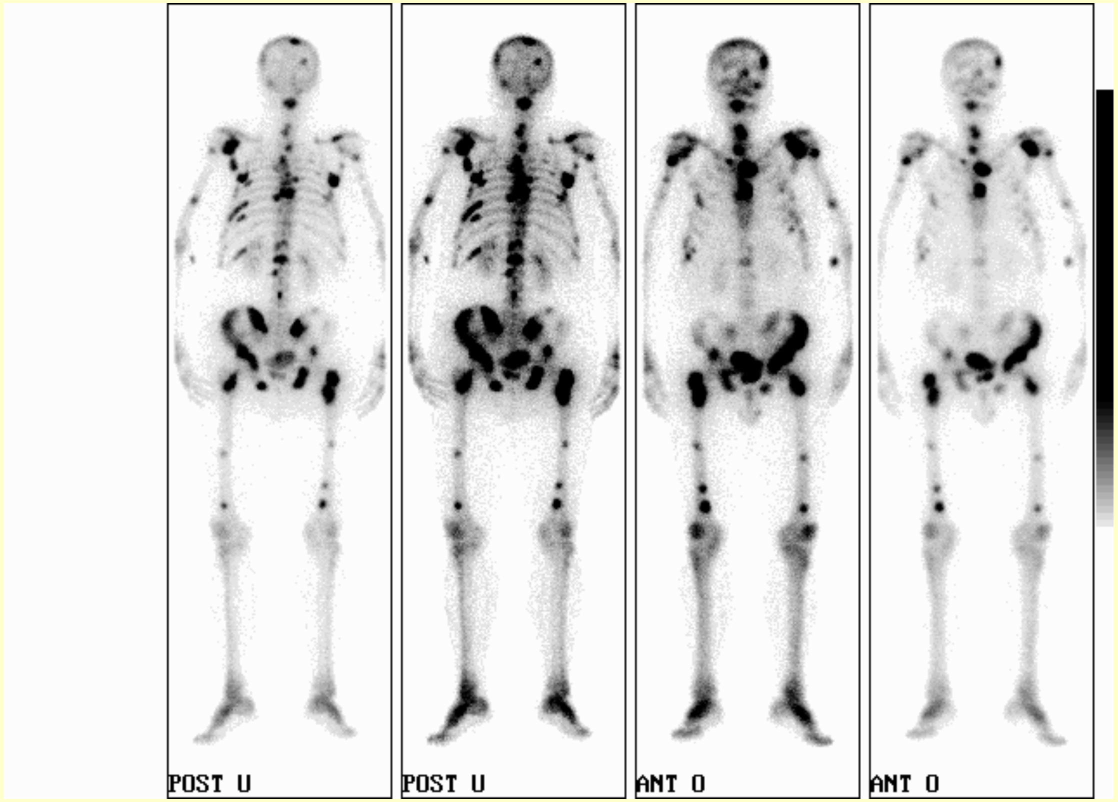


^{99m}Tc- fyton

Bone scintigraphy

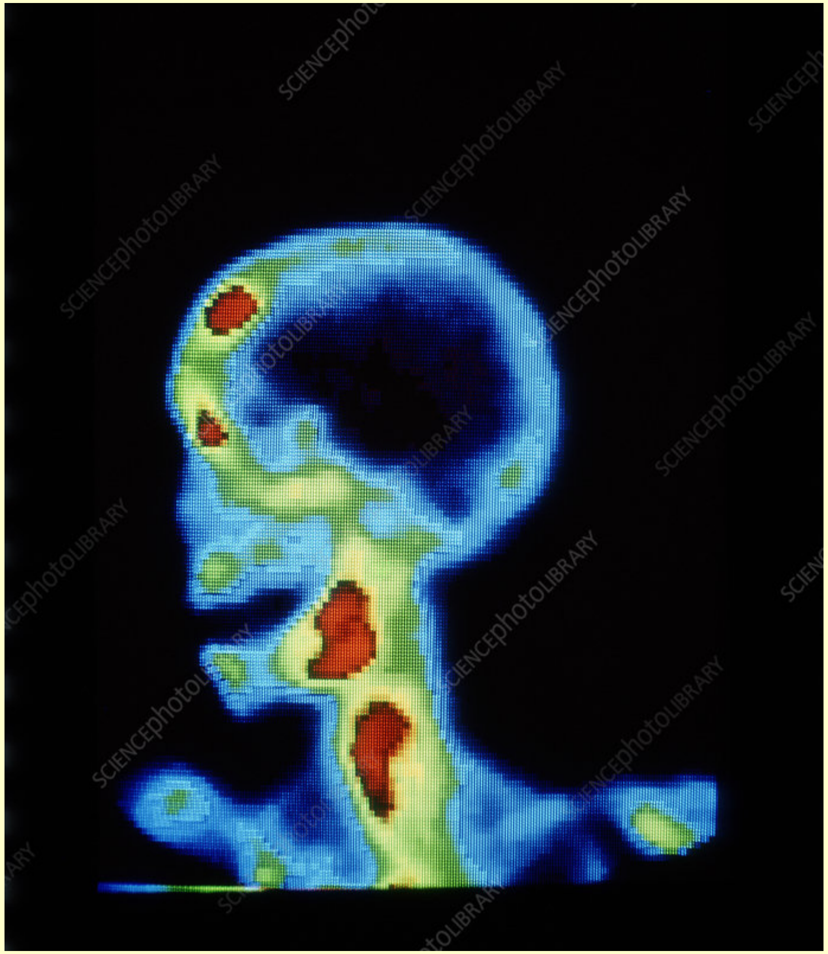
^{99m}Tc-MDP: 600 MBq

normal



imaging bone metastases

Gamma camera image: summation image



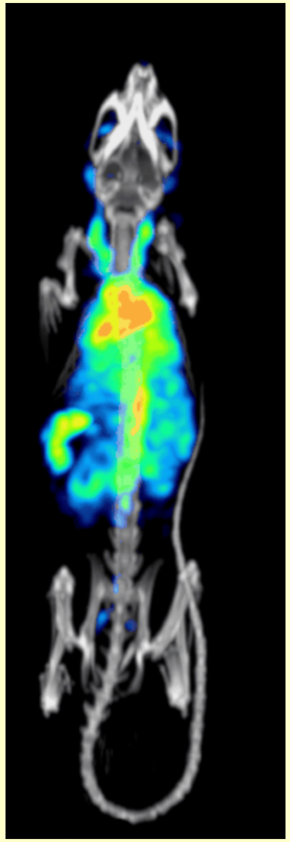
For depth / 3D resolution: tomographic device is necessary

SPECT – Single Photon Emission Computed Tomography

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

Measurement of a series of projections.

3D image can be reconstructed from projections.

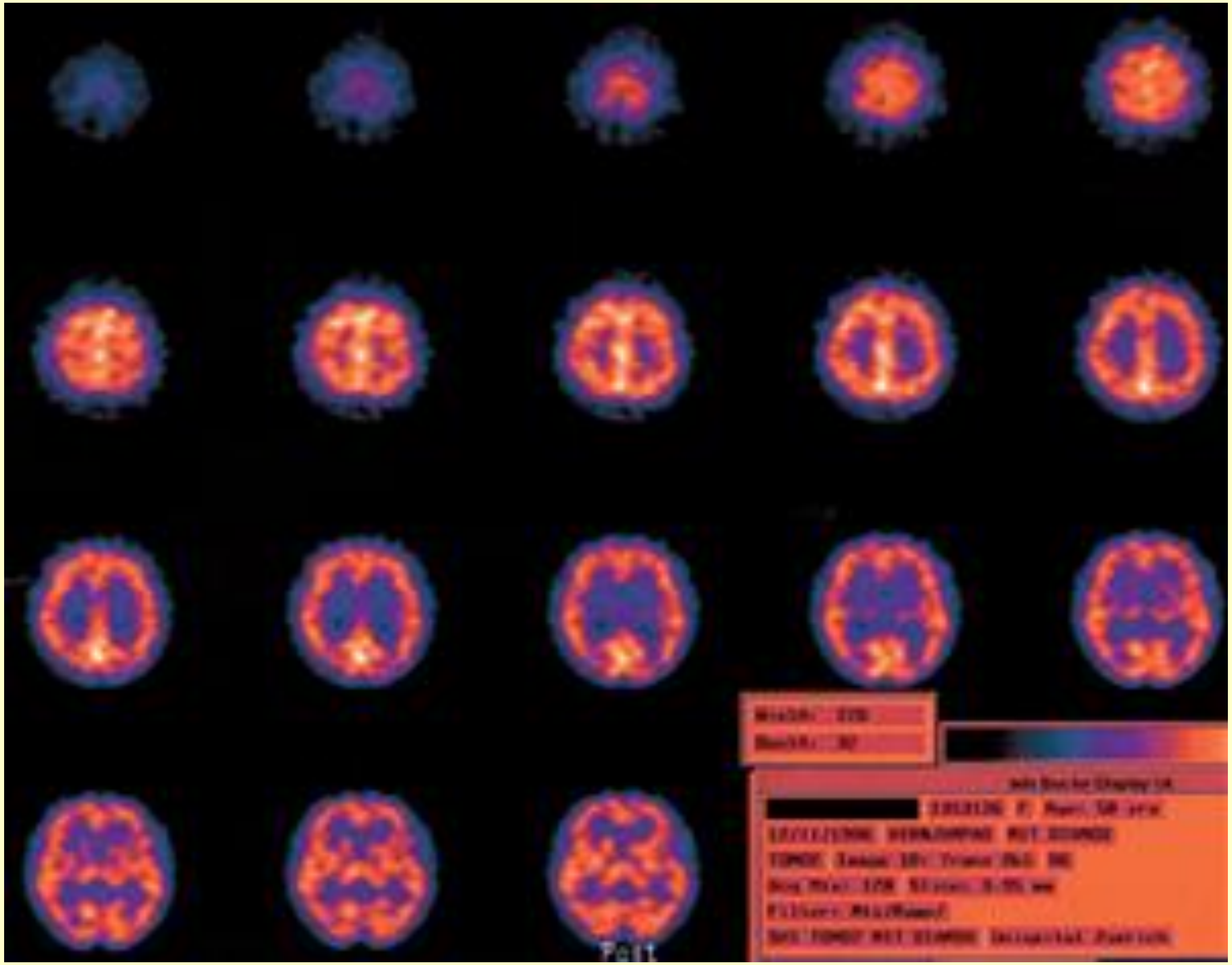


Various camera arrangements

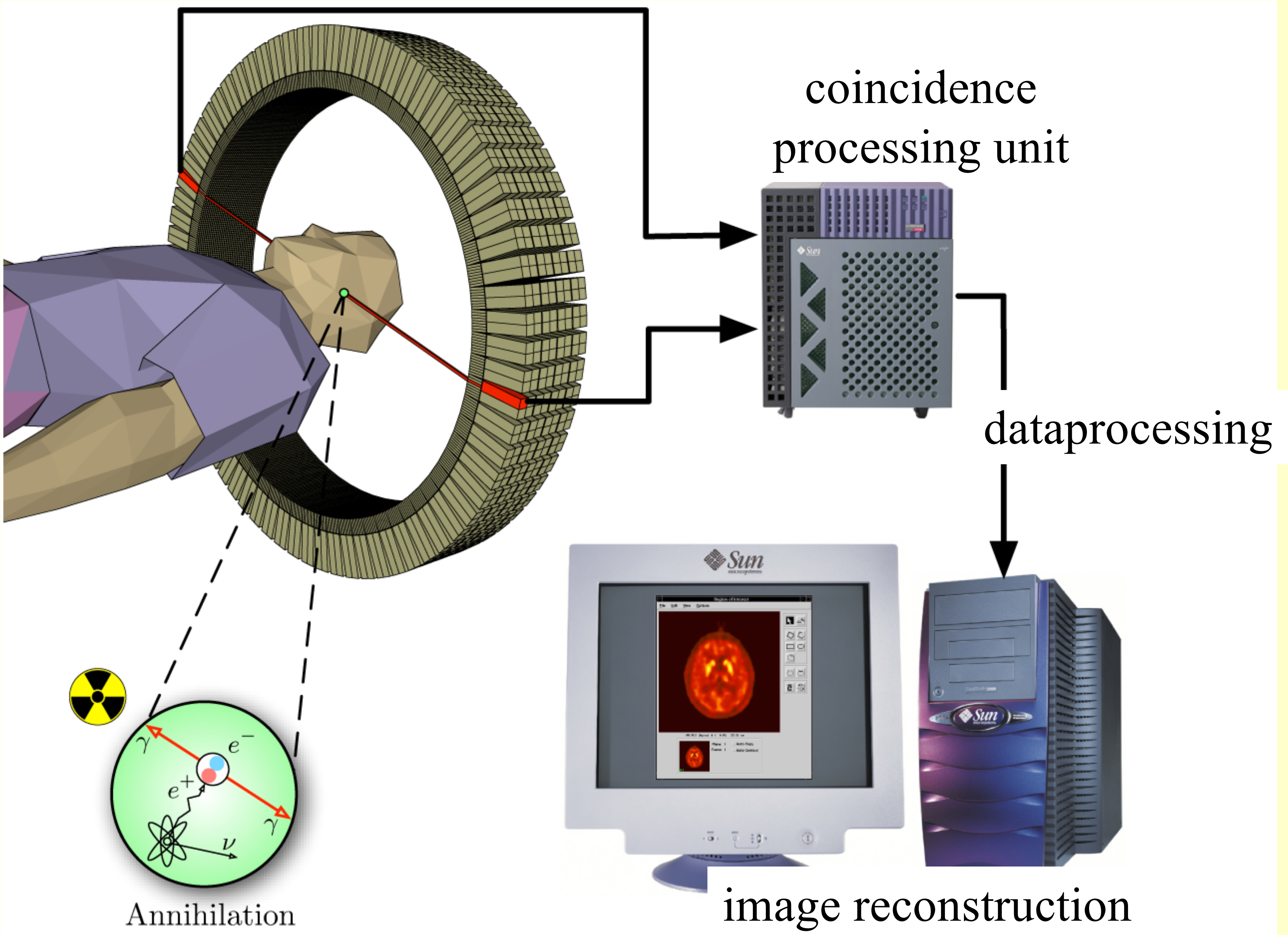
SPECT

SPECT – images of scalp

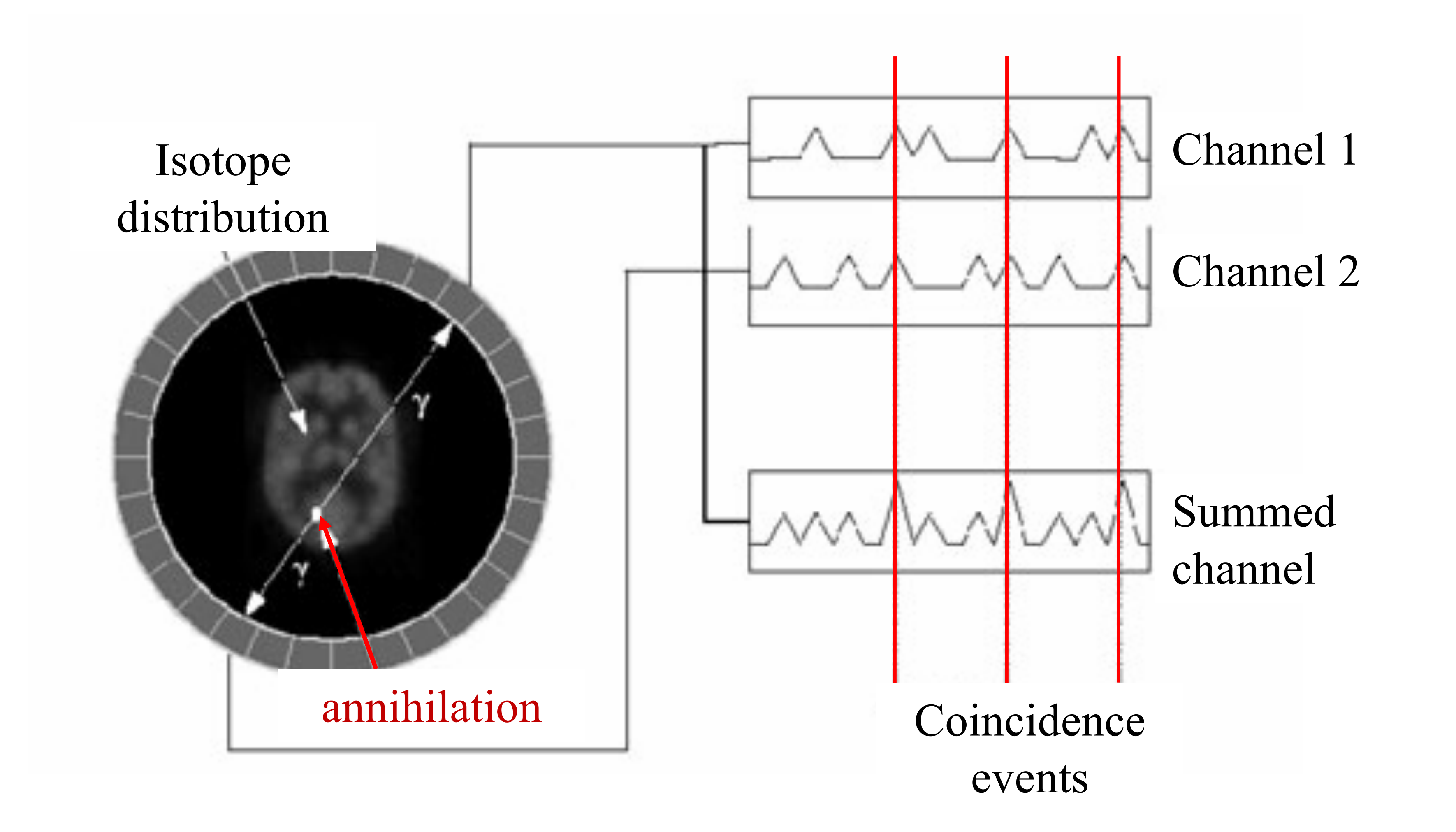
^{99m}Tc- HMPAO



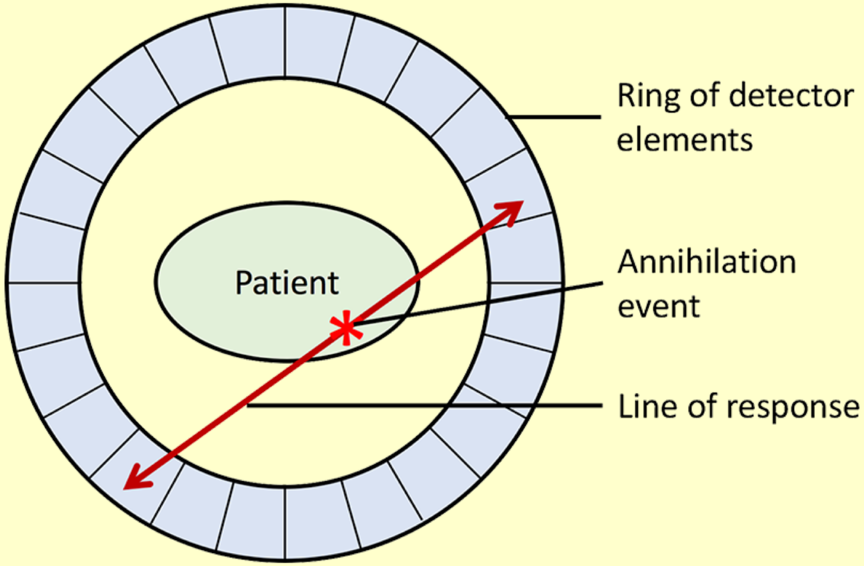
Positron Emission Tomography PET

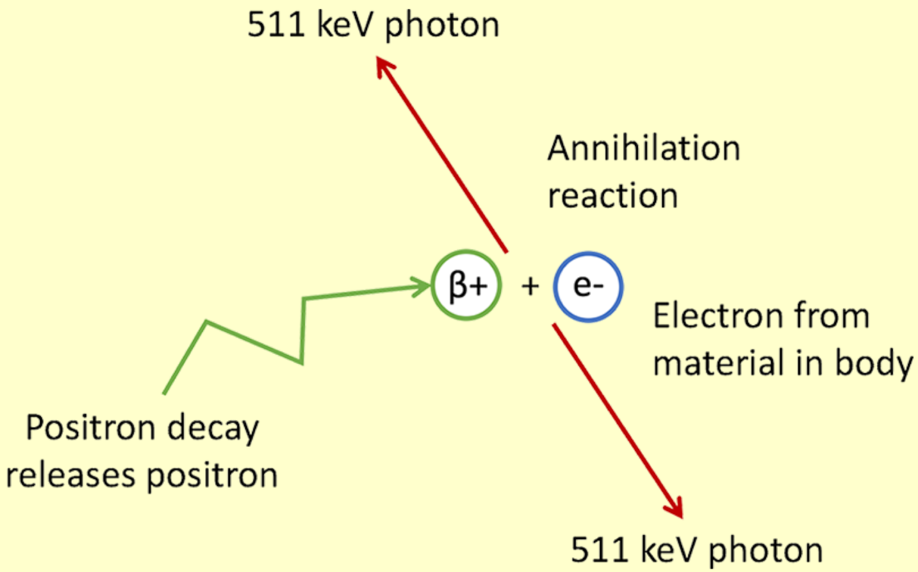


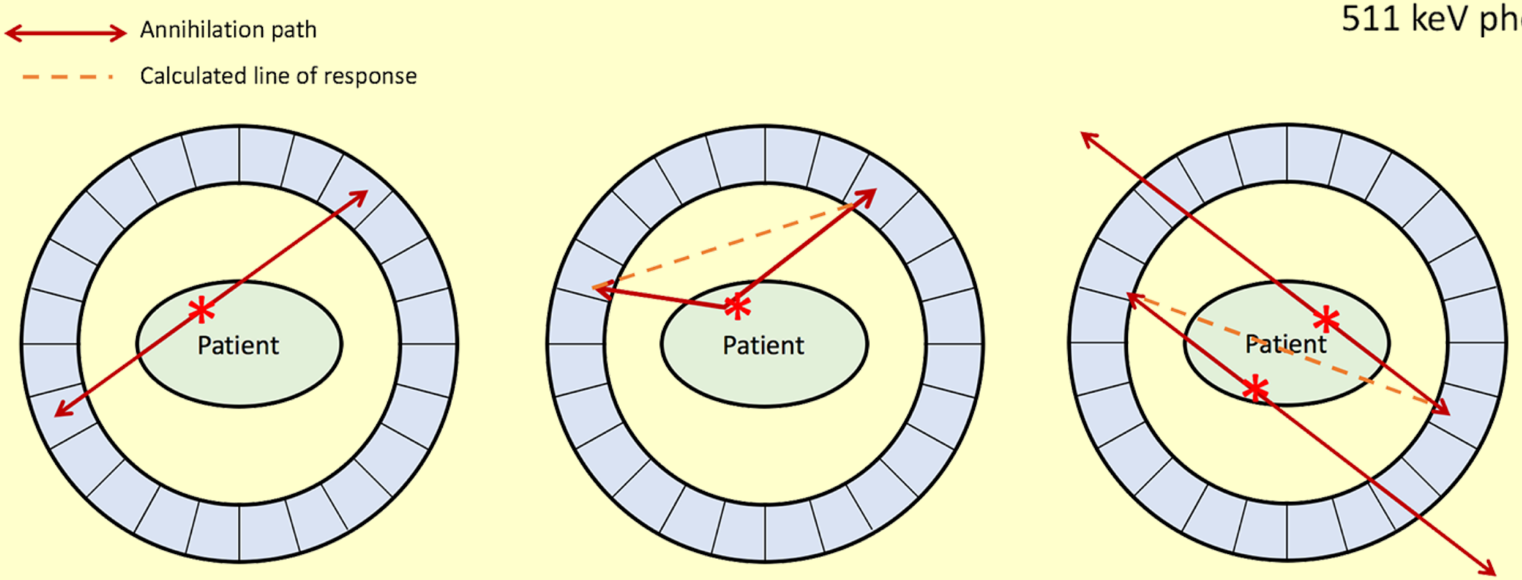
Coincidence detection



Coincidence detection







True coincidence

- One annihilation
- Straight path photons in opposite directions

Scatter coincidence

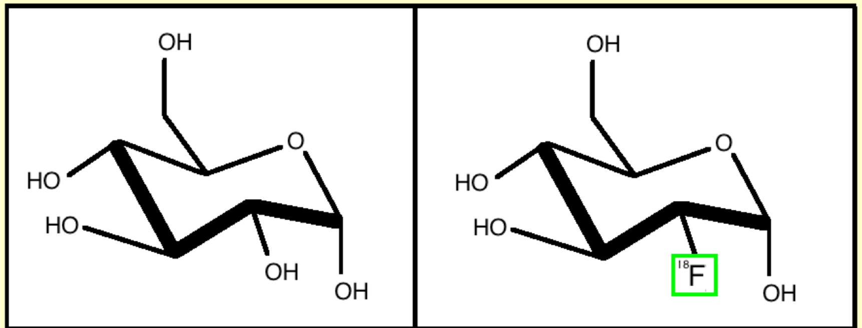
- One annihilation
- Photons scatter
- Measured line of response places annihilation reaction along artefactual projection

Random coincidence

- More than one annihilation
- Photons from different annihilations are detected simultaneously
- Artefactual line of response calculated

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

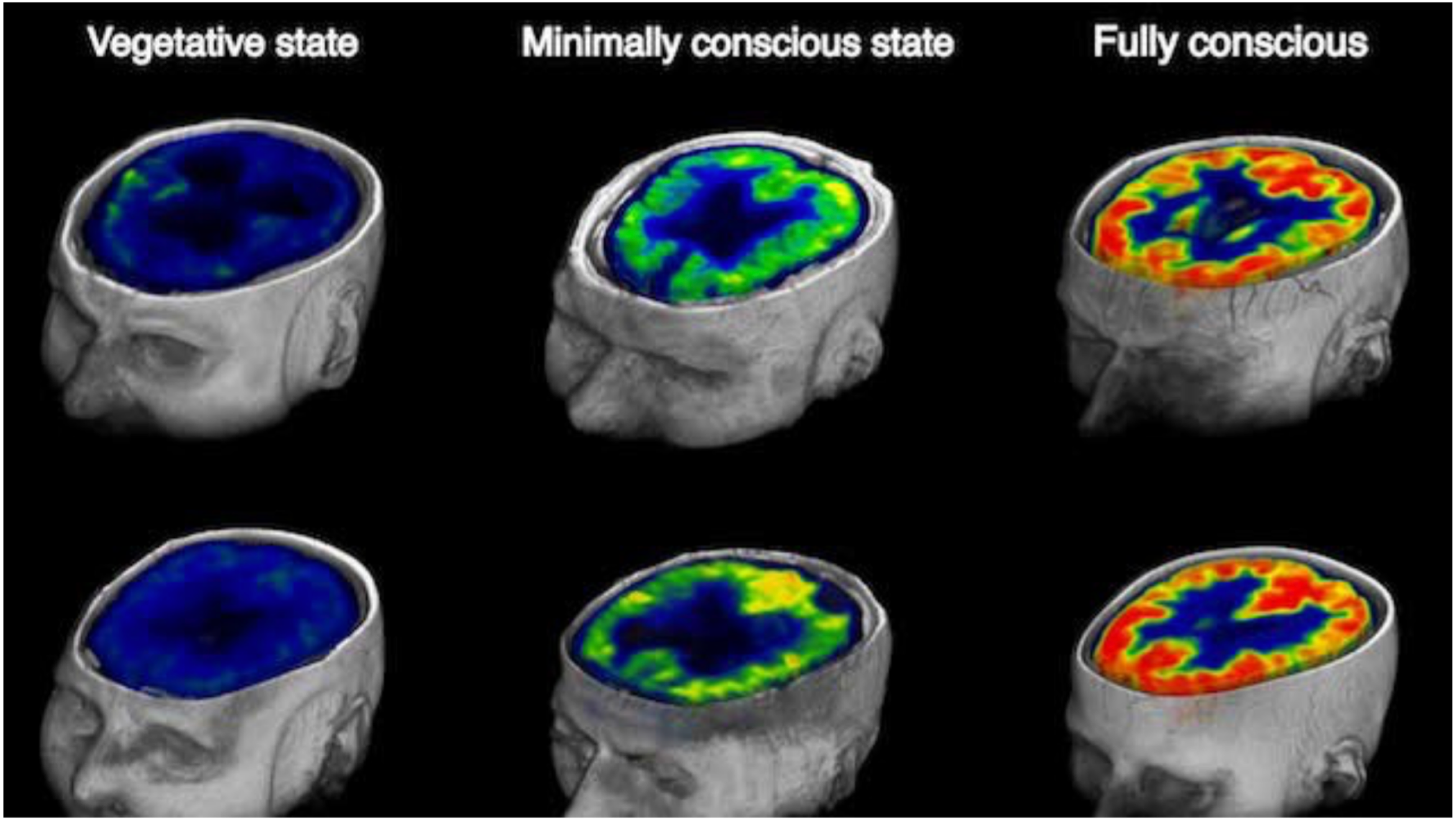
Isotope	β^+ energy (MeV)	β^+ range (mm)	1/2-life	Applications
^{11}C	0.96	1.1	20.3 min	receptor studies
^{15}O	1.70	1.5	2.03 min	stroke/activation
^{18}F	0.64	1.0	109.8 min	oncology/neurology
^{124}I	2.1350/1.5323	1.7/1.4	4.5 days	oncology



Glucose	2-deoxy-2-[^{18}F]-D-glucose

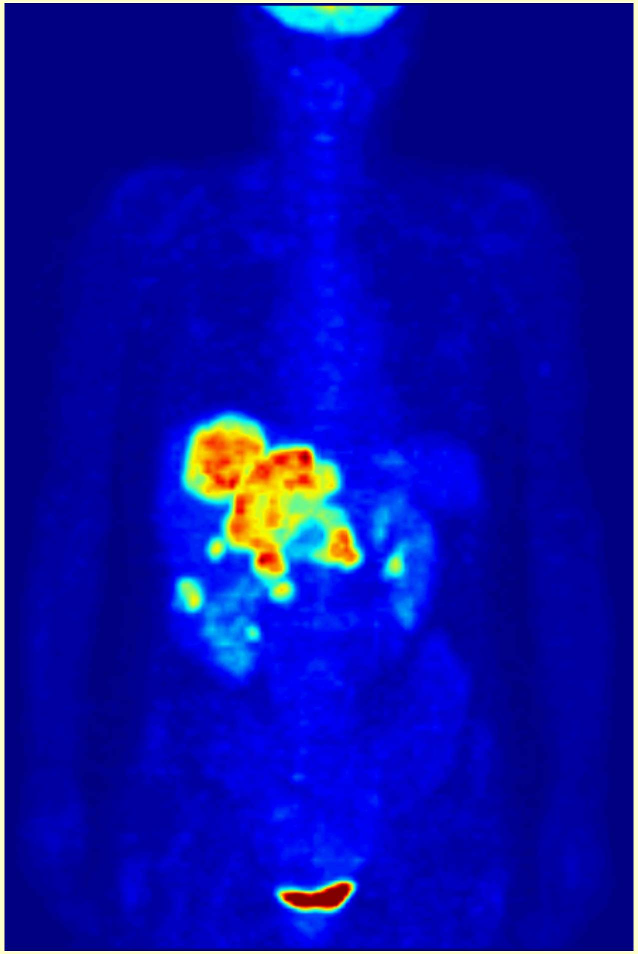
Isotope manufacturing must be nearby the site of application (see half-lives).

[^{18}F]-fluorodeoxyglucose (FDG) – showing glucose metabolism



Global cerebral metabolic rate of glucose as an indicator of consciousness. 42% of normal cortical activity represents the minimal energetic requirement for the presence of conscious awareness (middle).

$[^{18}F]$-fluorodeoxyglucose (FDG) – showing glucose metabolism

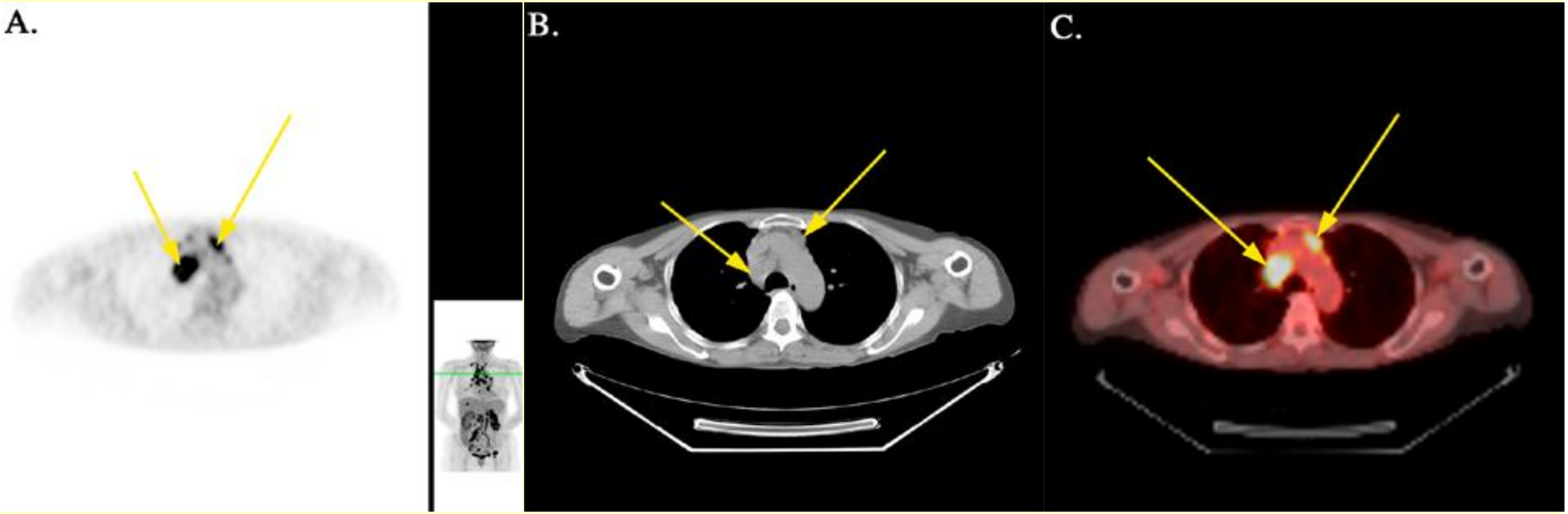


3D reconstruction of tissue metabolic activity from a $[^{18}F]$-FDG PET scan. Notably, we see increased activity along the chest walls, indicating carcinoma, as well as the supraclavicular fossa.

Information like this cannot be obtained from a regular CT scan, and is thus invaluable to many specialties, particularly oncology and neurology

PET/CT

Combination of structural and functional imaging



Radiotherapy

Which radiation is the best?

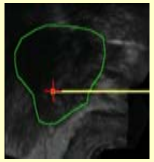
What is the optimal dose of radiation?

What is the best technique for generating radiation?

Irradiation selectivity – protection of healthy structures?

Radiotherapy

α



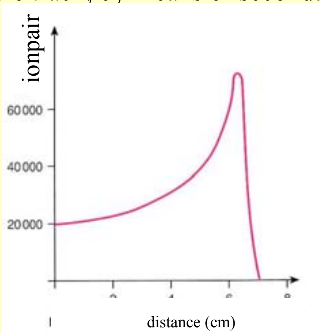
Internally deposited radioactivity

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. $(nE_{ionpair}/l)$

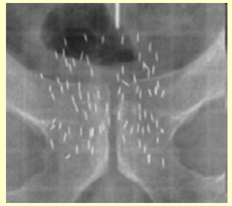
In the air: $E_{ionpair}=34\ eV$



α

β⁻:

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



Internally seeded radioactivity

e⁻: accelerated electron - 10-20 MeV

γ,
Rtg,
p
n

production: linear accelerator

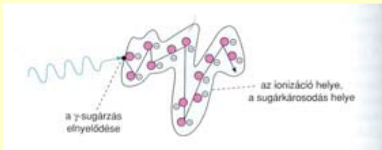
Efficient distance! ≈1cm/3MeV

In the practice 6-21 Mev => 2-7 cm
treatment of superficial tumours

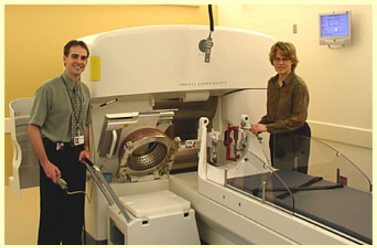
γ : external radiation source

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

Penetration distance
is energy dependent



γ-knife: focused dose of radiation

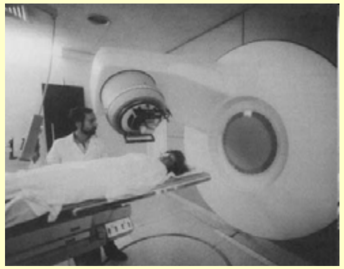


about 200 portals in a specifically designed helmet

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.

Radiotherapy

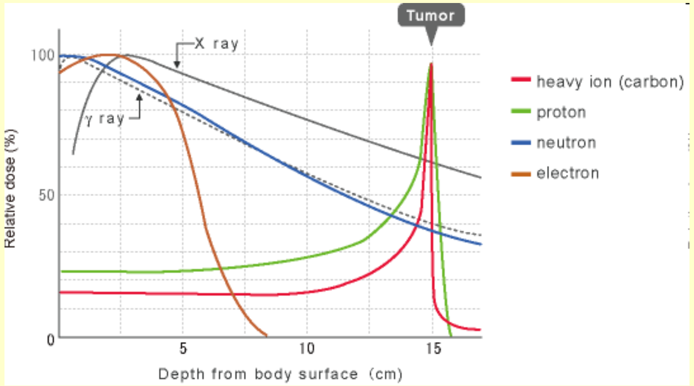
Would be ideal, but very expensive!

γ,

Rtg,

p :

n



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

Cheklist

Selection rules of radioactive markers

- physical parameters
- biological and pharmacological characteristics

Information provided by isotope diagnostics

Types of isotope diagnostic images

- static pictures
- dynamic pictures

Gamma-camera, SPECT

Physical concept of PET

PET scanners – coincidence detectors

Radiotherapy, gamma-knife, LET

Damjanovich, Fidy, Szöllősi: Medical biophysics

II. 3.2.3
3.2.4
3.2.5

VIII. 3.2
VIII. 4.4

IX.3