

Biophysics I

14. Nuclear radiations in the clinical practice

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09. 12. 2022.

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Steps of diagnostic procedure

- Selection of radioactive isotope
- Selection of radiopharmakon
- Distribution and alteration of activity is detected
- Monitoring of physiological pathways and/or identification and localization of pathological changes

Informations provided by medical imaging

Structure

X-ray

Ultrasound

MRI



differences according to the different physical properties of tissues

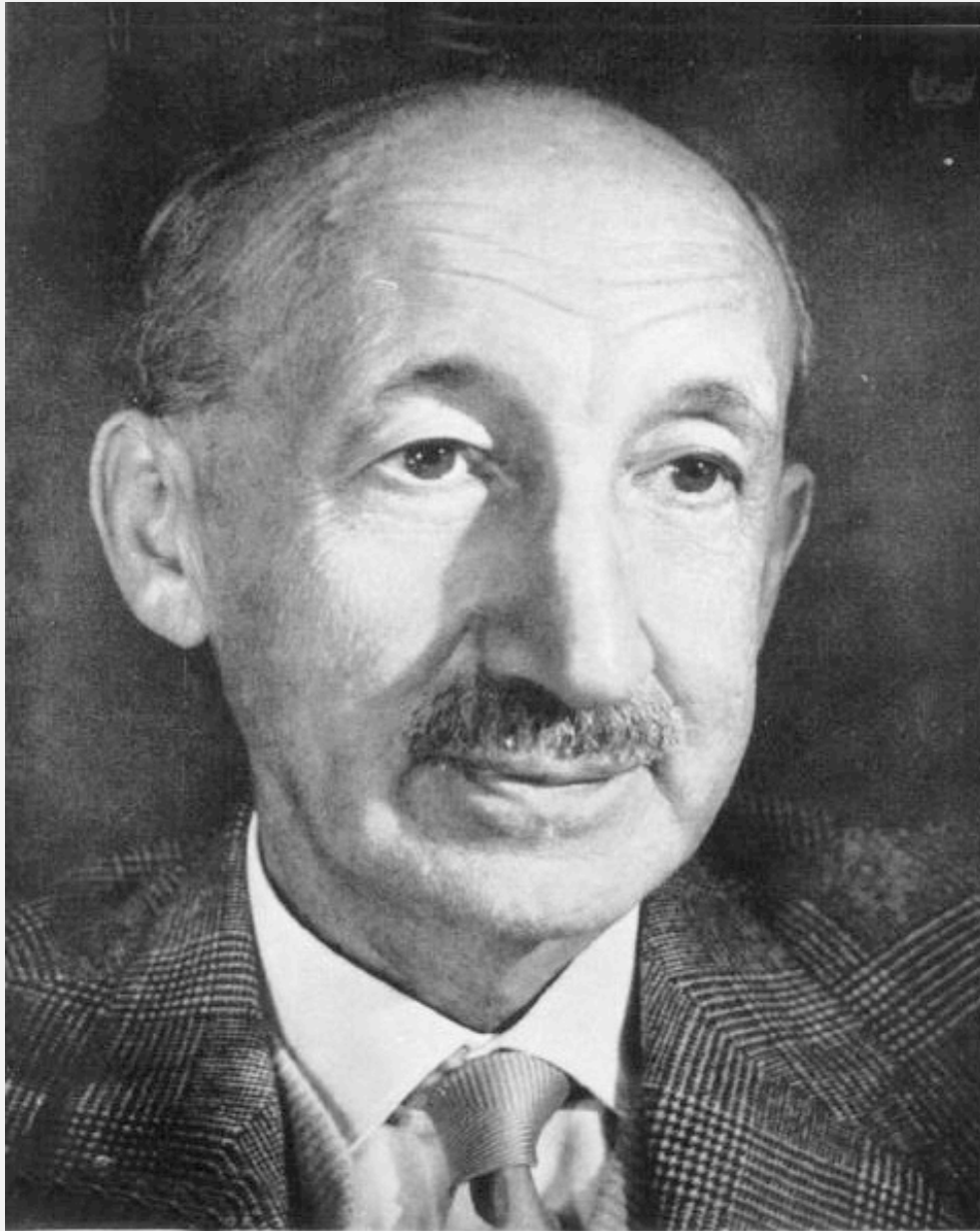
Function

Isotope diagnostics

MRI



dynamic physiological / metabolic processes can be followed



Georg de Hevesy

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**

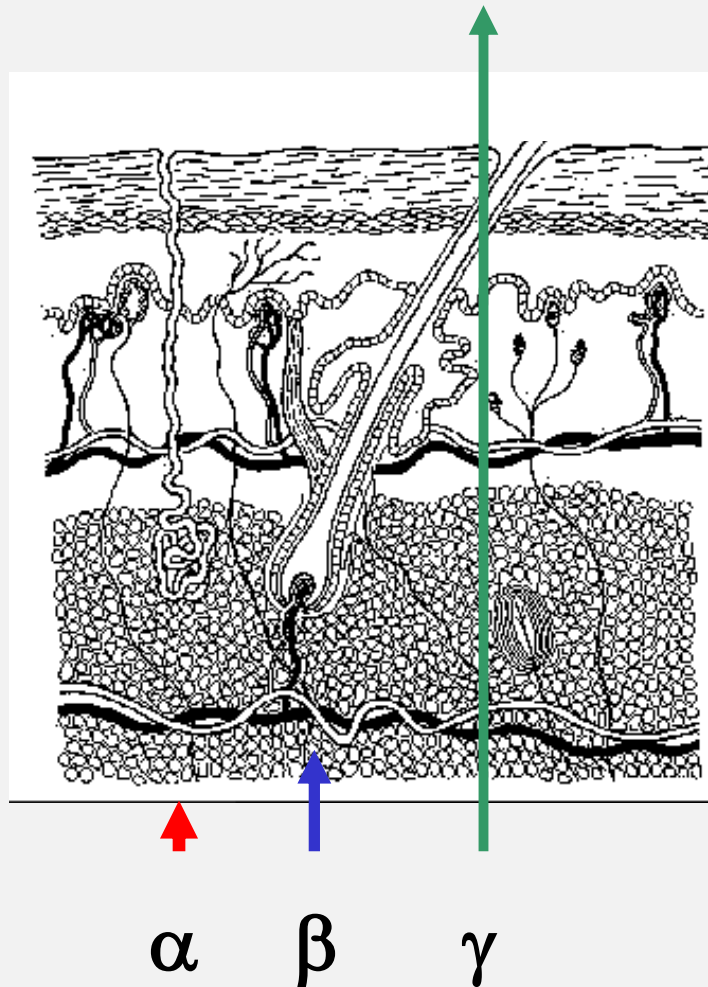
The choice of the appropriate radioisotope for nuclear imaging

Maximize the information — Minimize the risk

For that find the optimal

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

Type of radiation



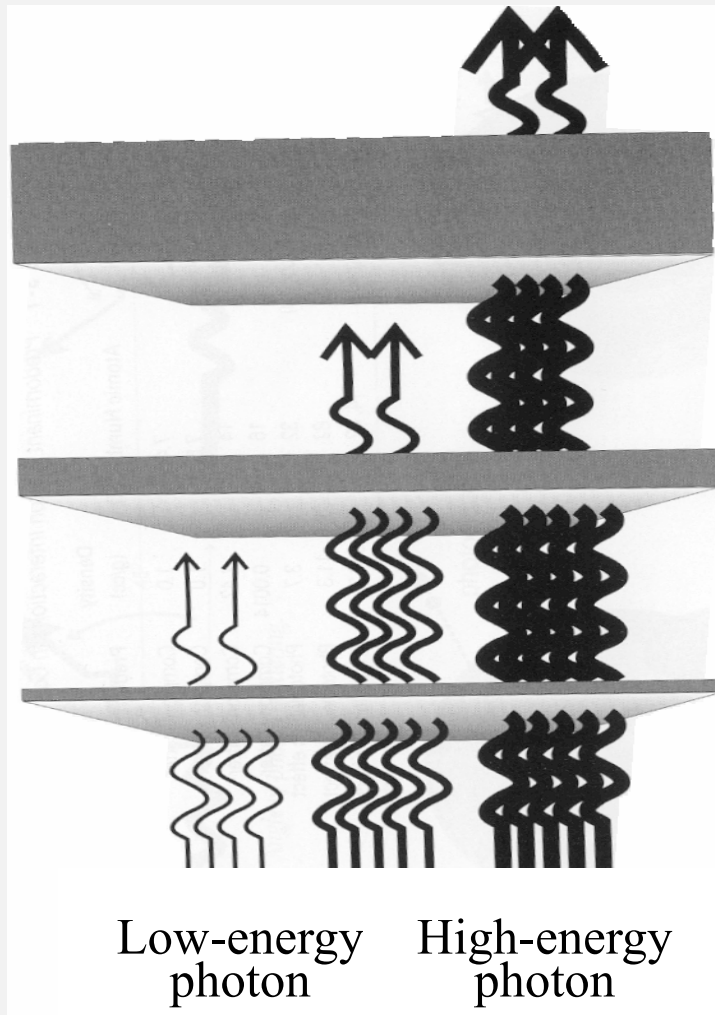
decay via photon emission
to minimize absorption
effects in body tissue

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

purely gamma-emitting isotope is preferable

photon energy

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



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 by the
sensitivity of the detector

smaller is better

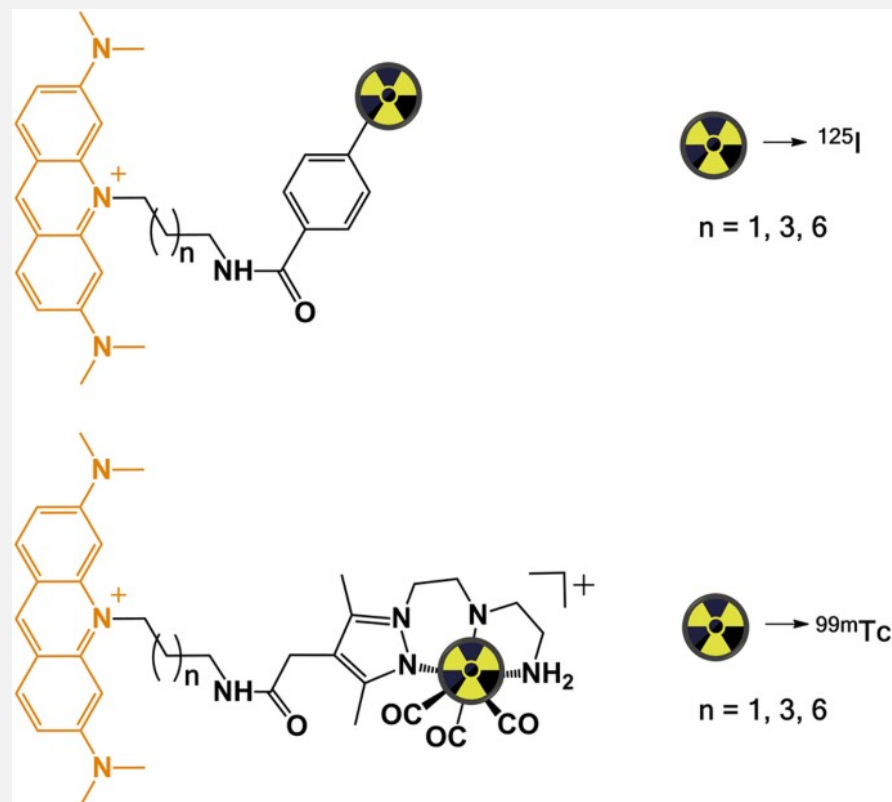
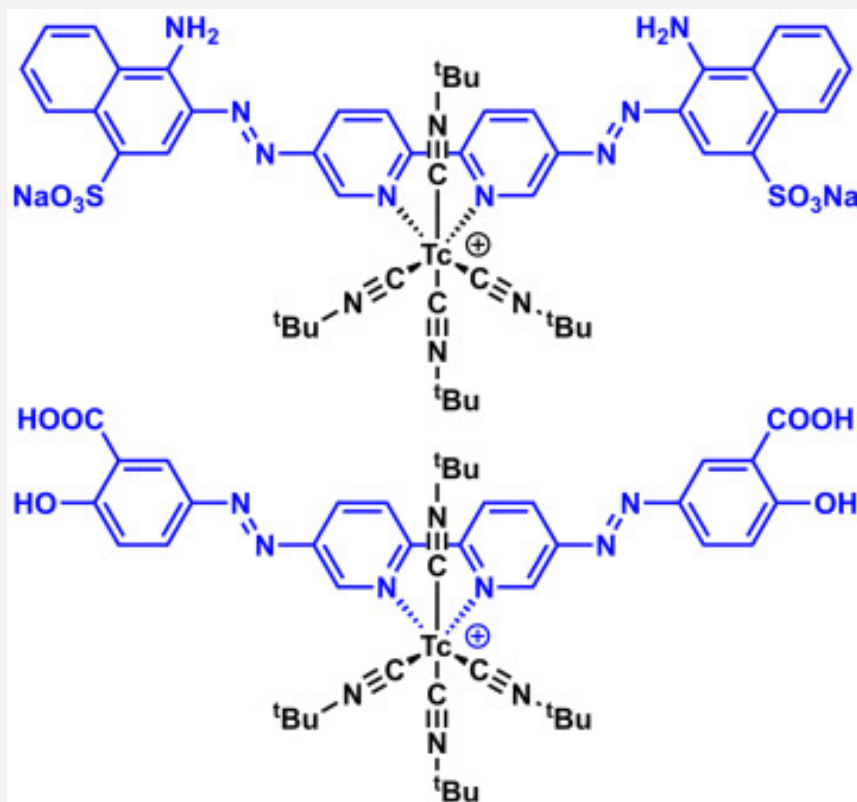
dose considerations for
patients

shorter is better

but

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

Radiopharmaceutical – is a substance that contains one or more radioactive atoms and are used for diagnosis or treatment of disease.

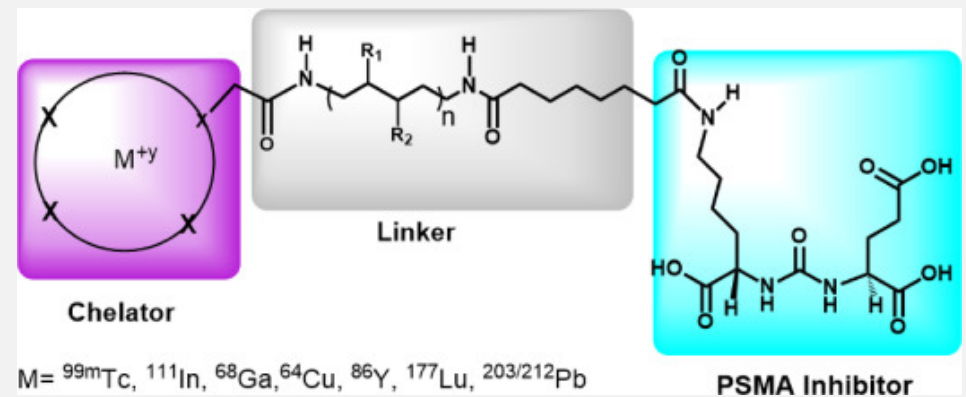


Basic requirements:

- high *target / non-target* ratio
- have no pharmacological or toxicological effects which may interfere with the organ function under study.

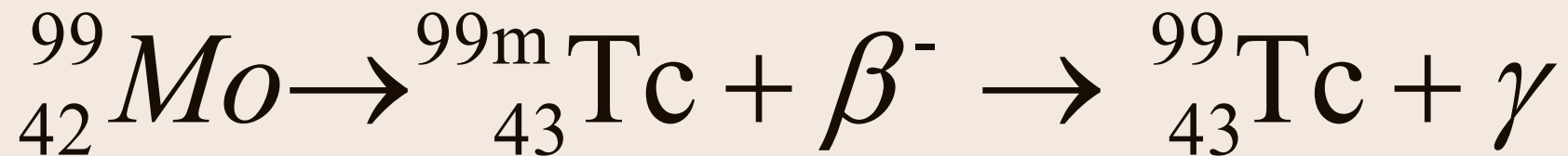
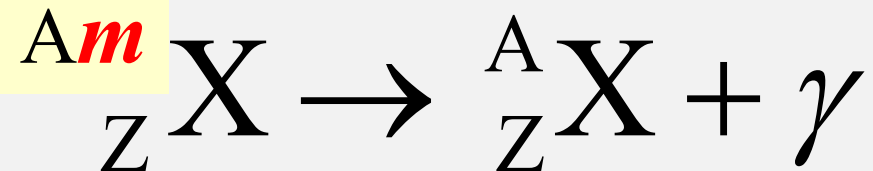
Factors responsible for ADME-TOX

- availability of compound to tissue, or the proportion of the tracer that is bound to proteins in the blood
- blood flow (percent cardiac input/output of a specific organ)
- basic shape, size, solubility, hydrophobicity, etc...



Gamma-emitting isotopes

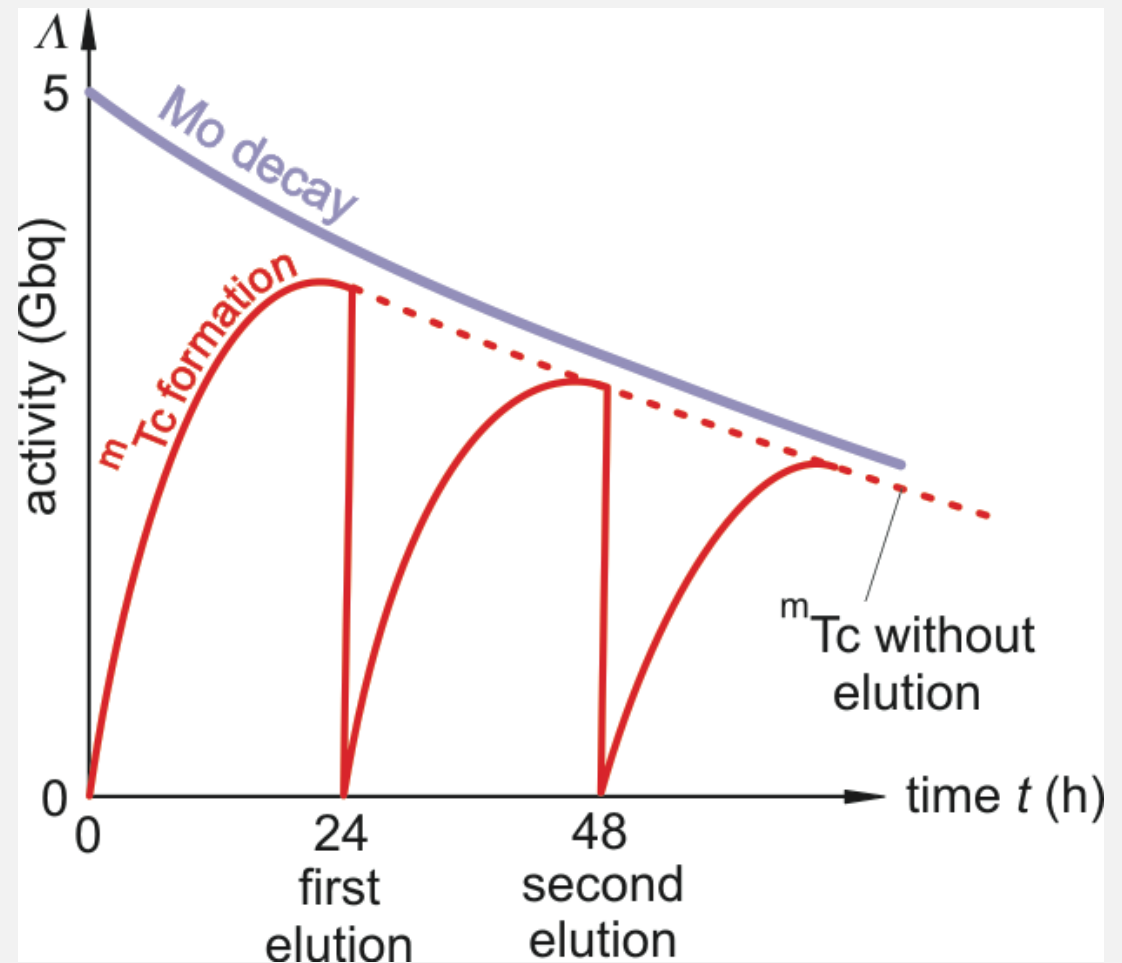
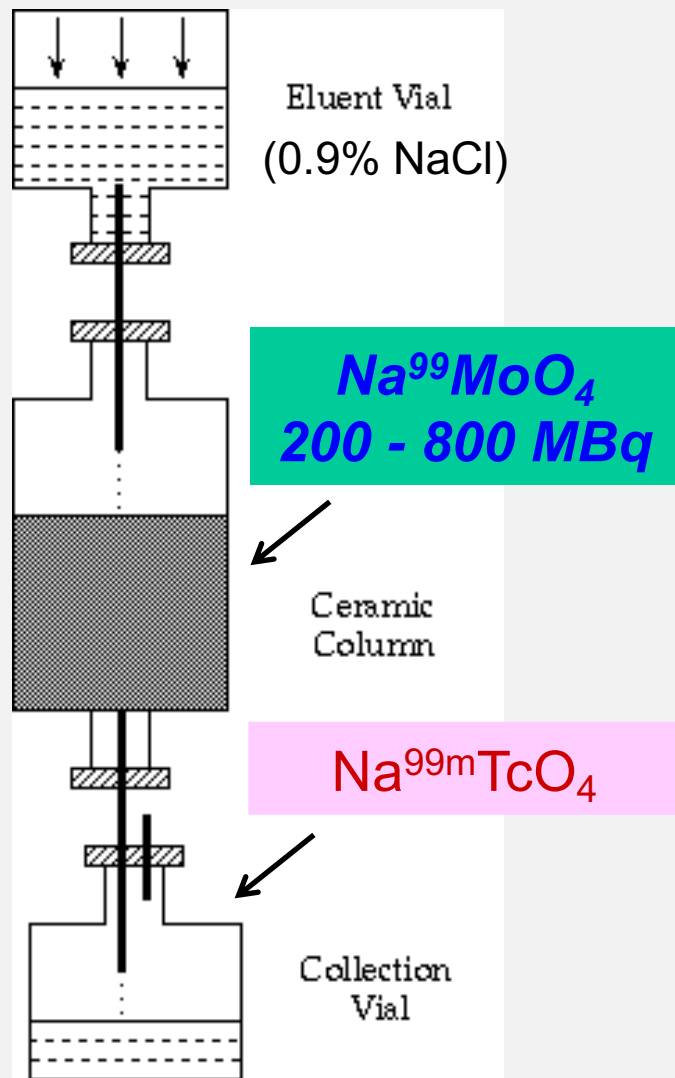
Isomeric transition: some excited states may have half-lives ranging from hours up to more than 600 years



$T_{1/2}=67$ 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



thyroid glands

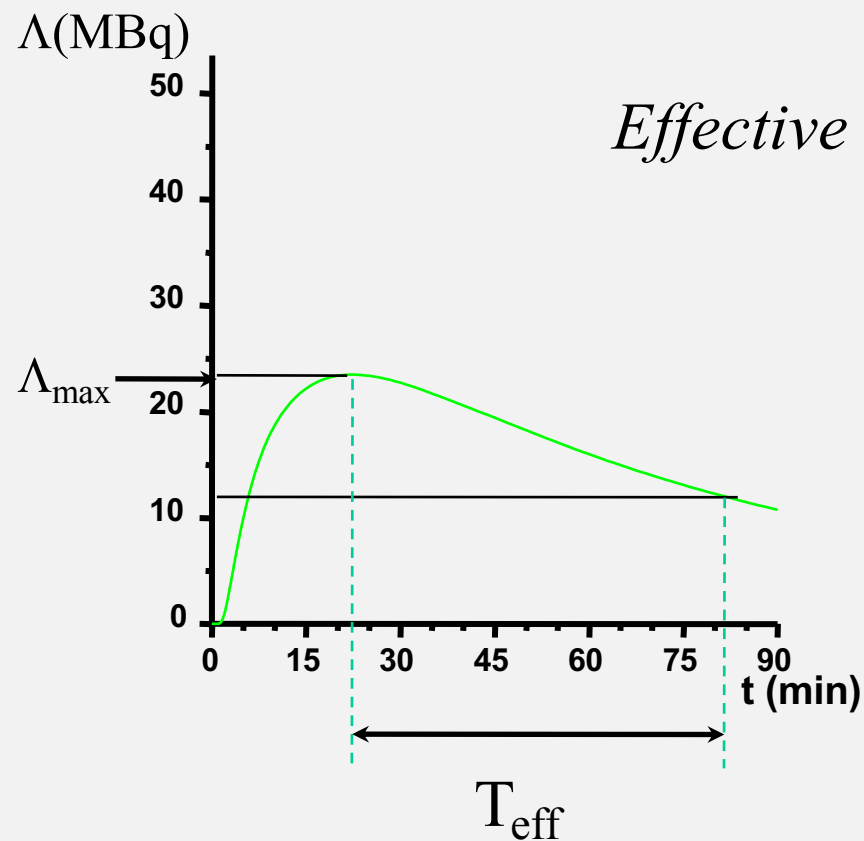


kidneys

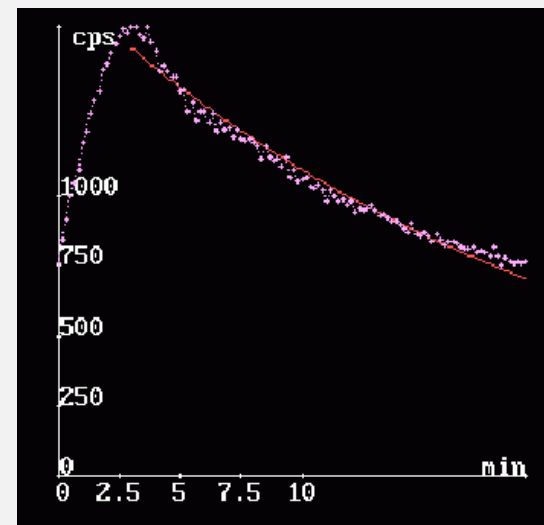
Isotope accumulation in

Types of images

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

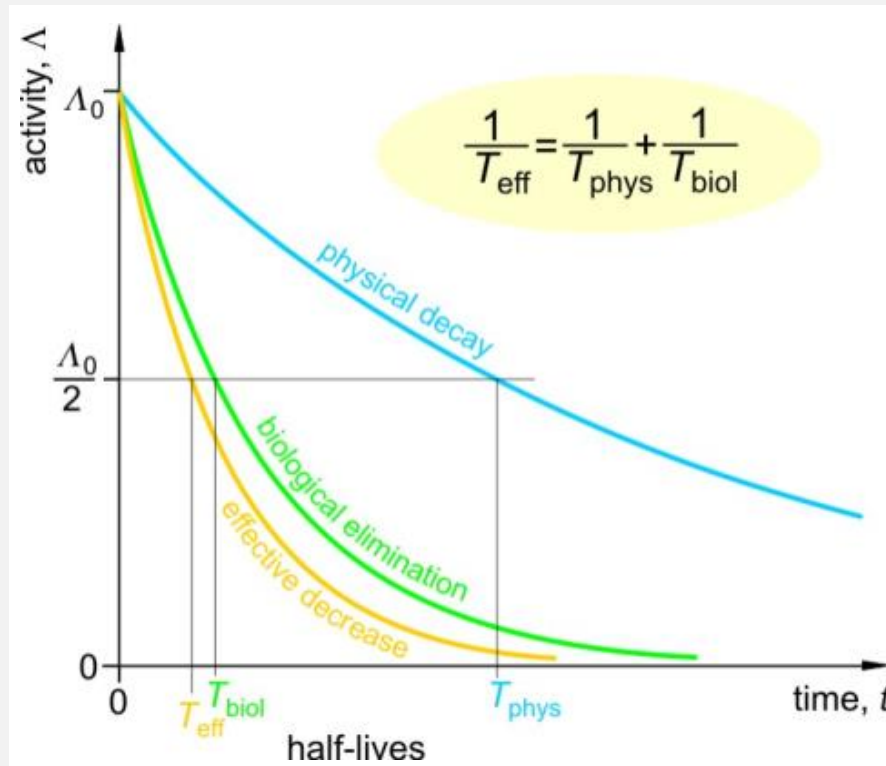


Effective half-life – activity decreases by half in the target organ



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

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

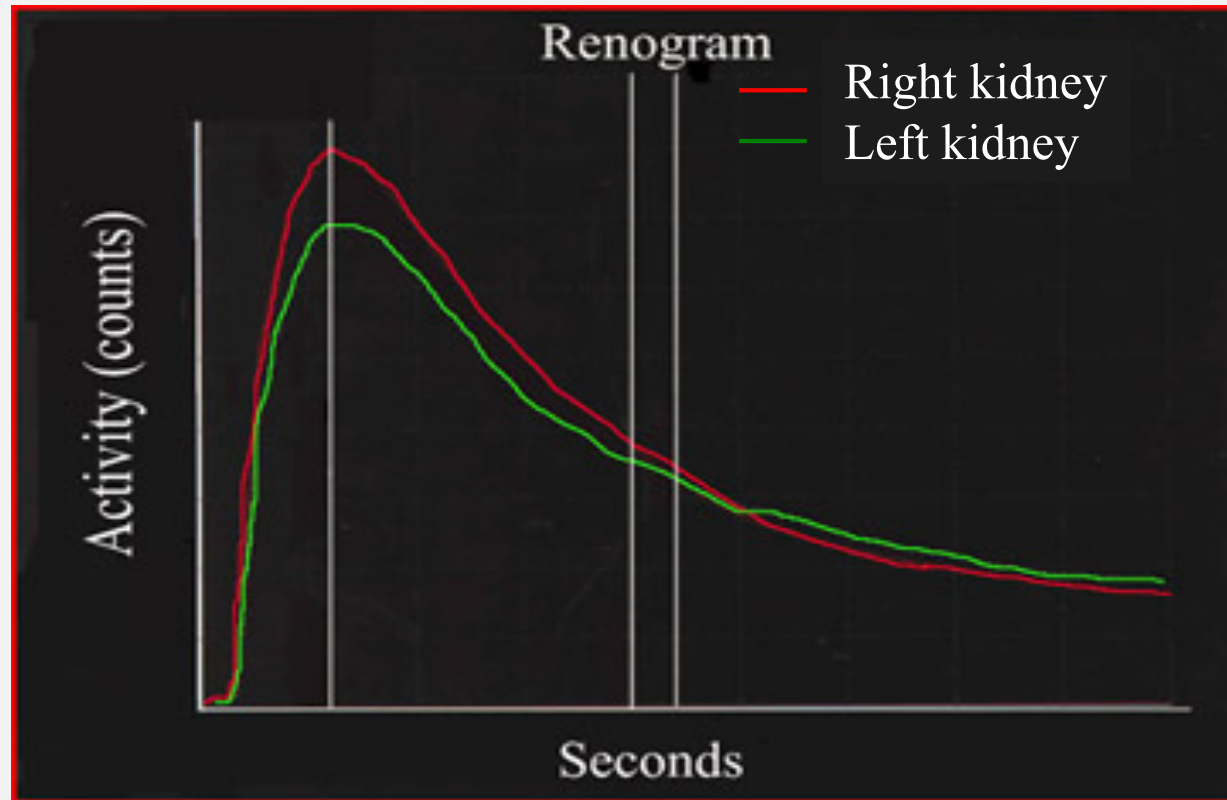


$$\lambda_{\text{effective}} = \lambda_{\text{phys}} + \lambda_{\text{biol}}$$

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

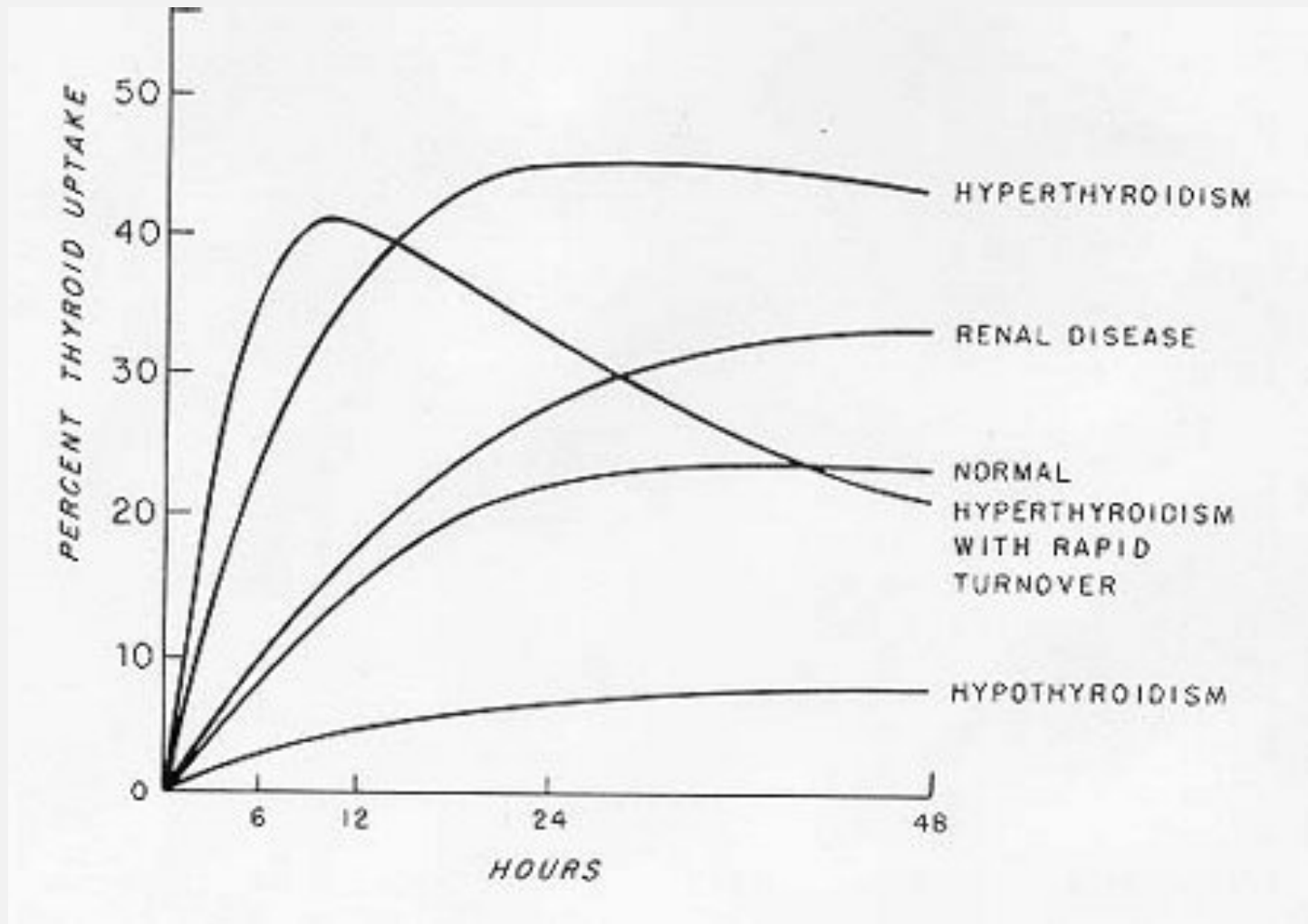
The final fate of the radiotracer depends on how the addressed organ deals with the molecule, whether it is absorbed, broken down by intracellular chemical processes or whether it exits from the cells and is removed by kidney or liver processes. These processes determine the **biological half-life**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

example



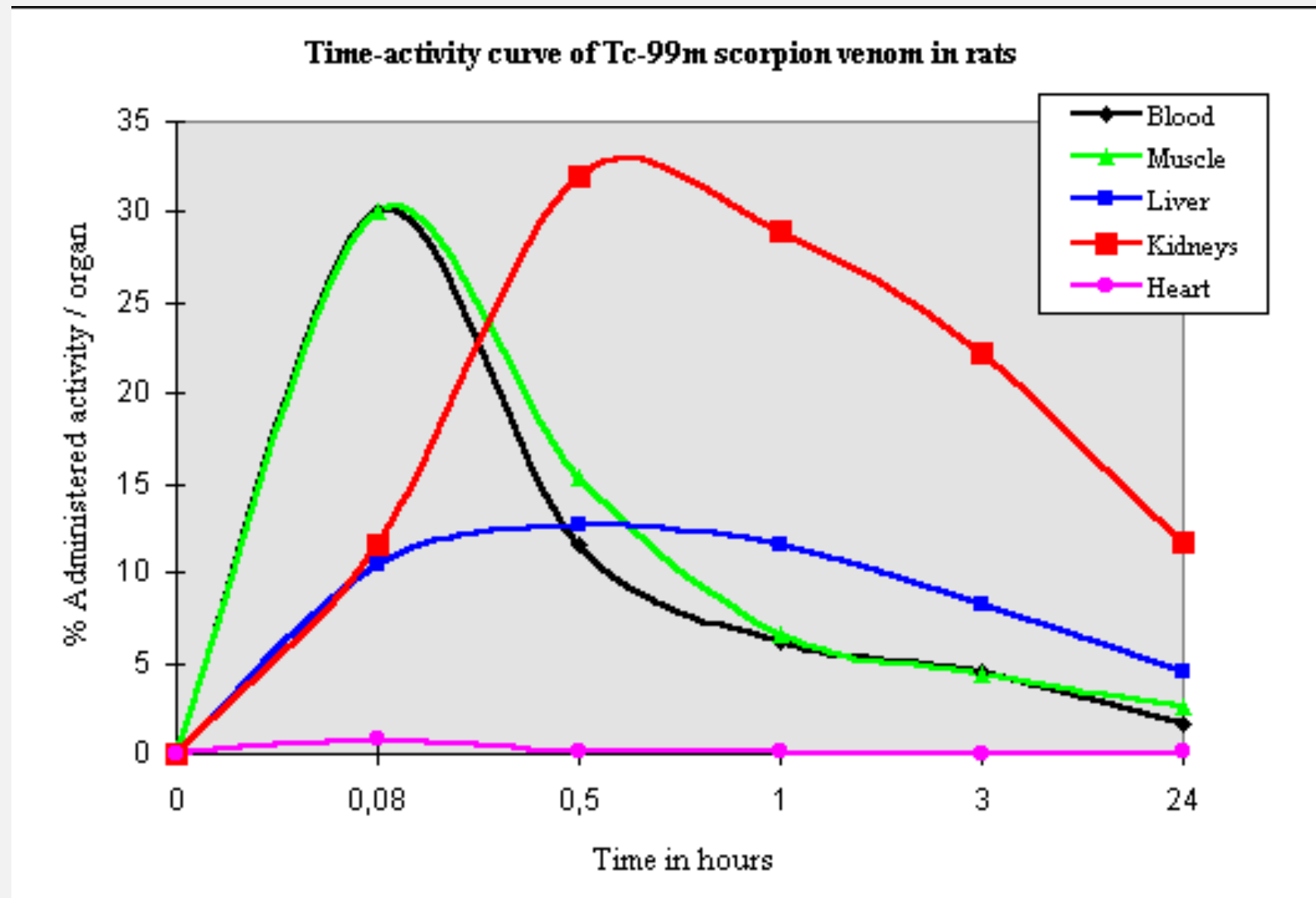
Isotope accumulation traces of kidney.

example



Thyroid glands' isotope accumulation traces

Pulse-chase experiments

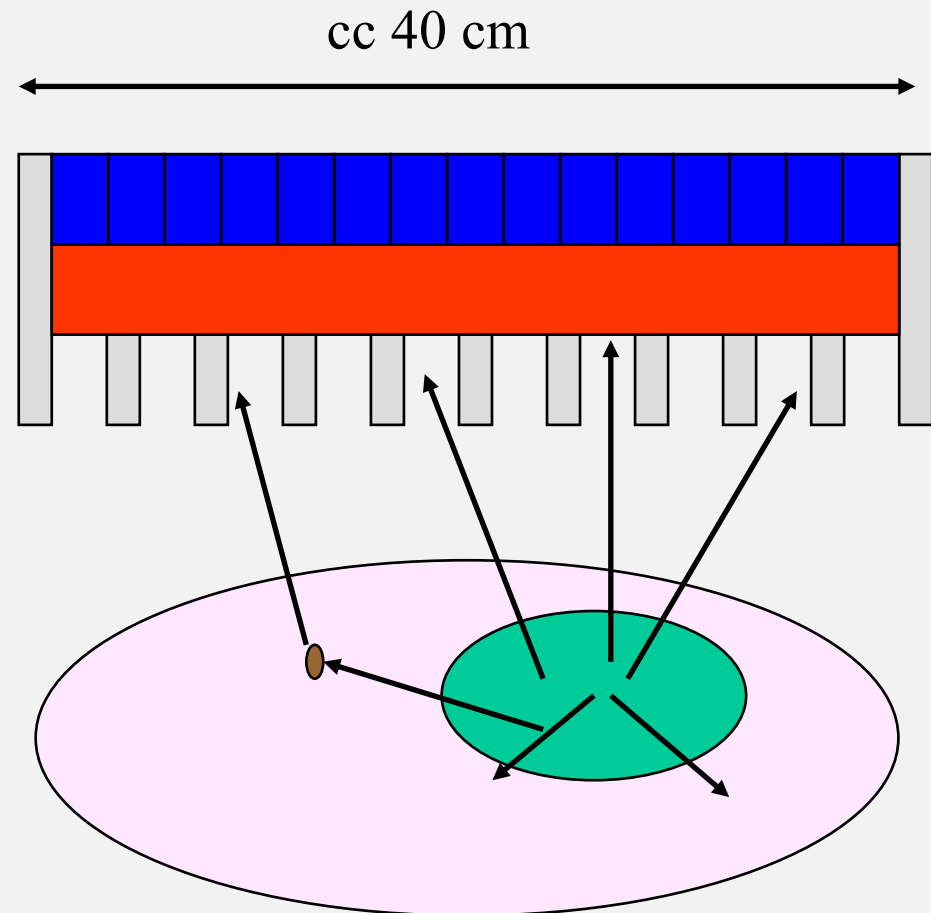




Hal Anger
1920-2005

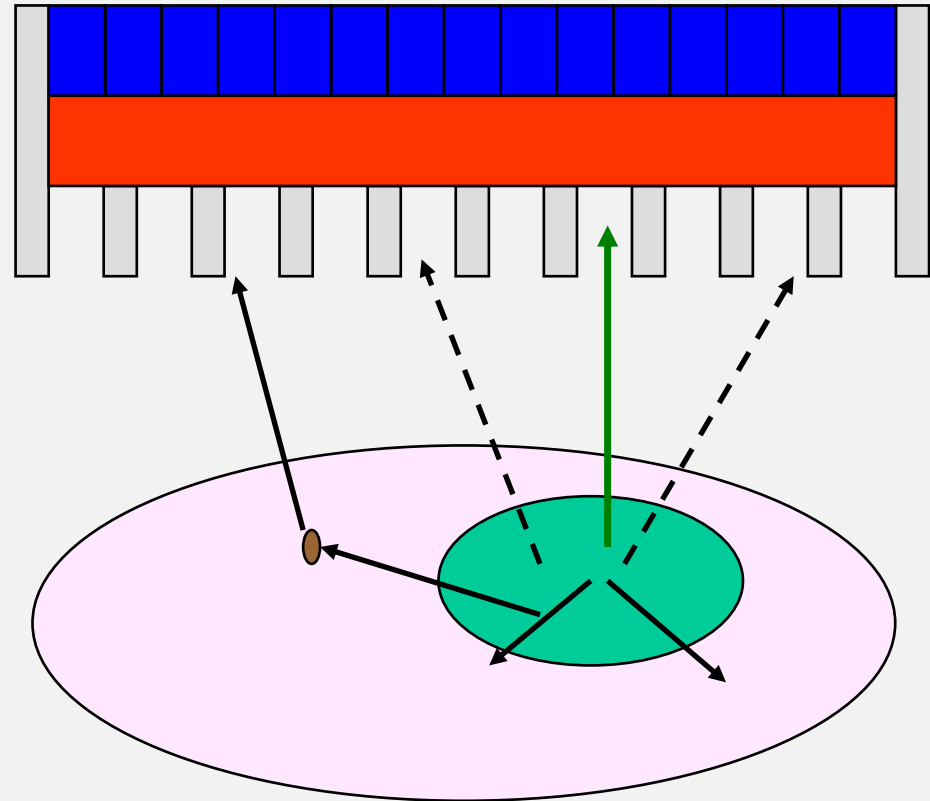
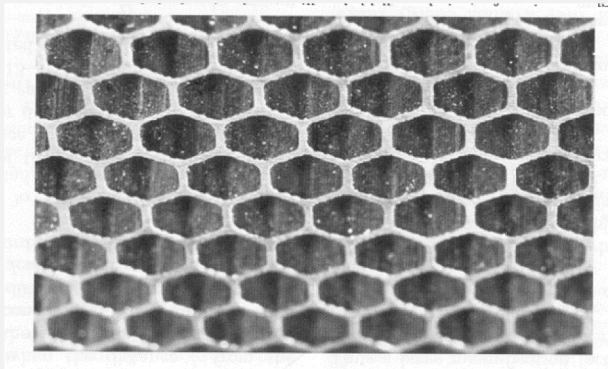
Gamma camera

Photomultiplier tubes →
Scintillation crystal →
Collimator →



A radioactive source emits gamma photons in all directions.

collimator

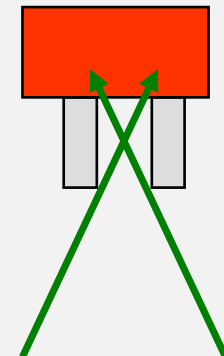


Collimators are composed of thousands of precisely aligned channels made of lead.

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

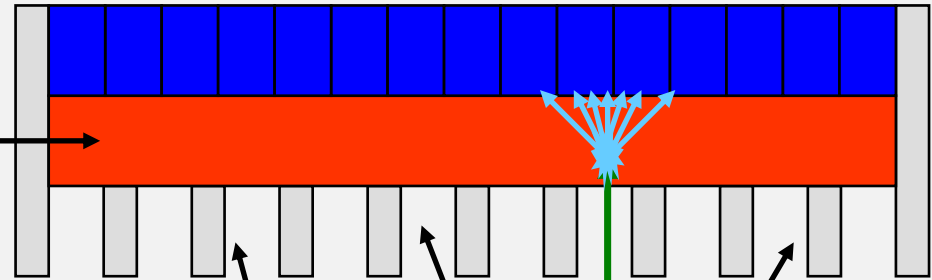
Photons emitted in other directions are absorbed by the septa between the holes.

Size and geometry of holes determine resolution.



Scintillation crystal

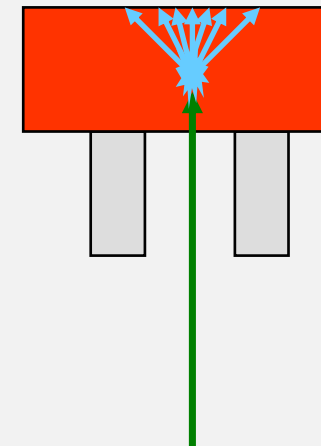
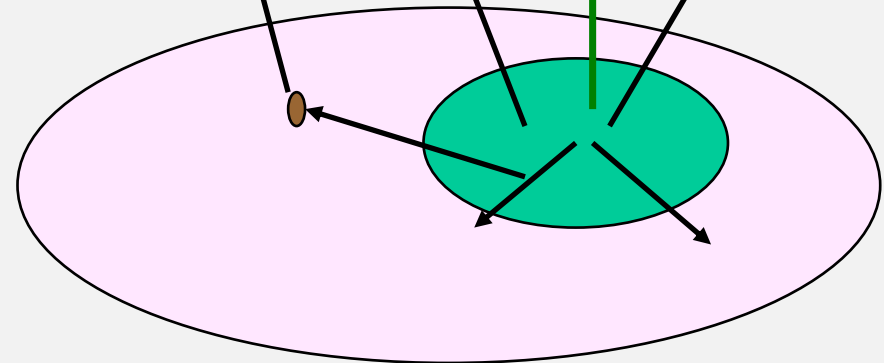
NaI(Tl)



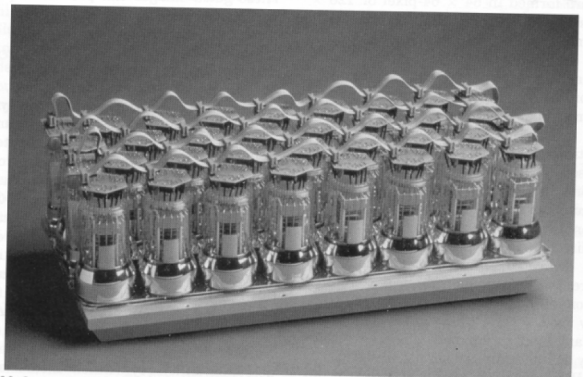
Sufficient detection efficiency
photons of 150 keV: $\mu \sim 2.2 \text{ 1/cm}$

Proper wavelength – 415 nm – for
PM photocathode

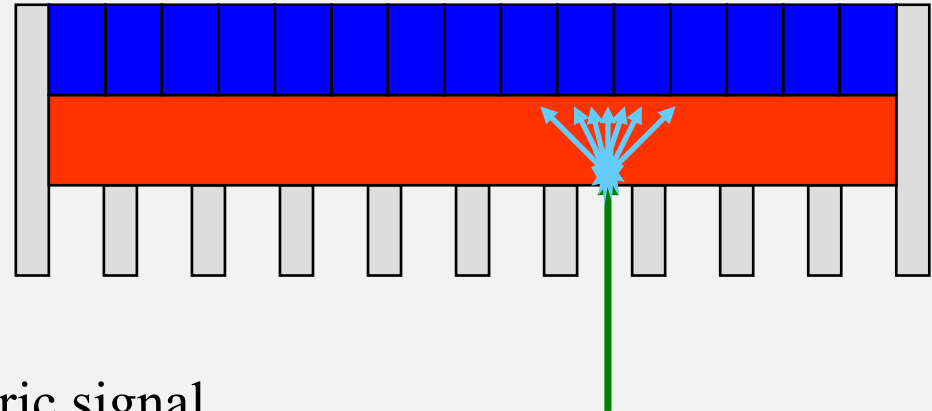
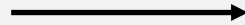
Problems with NaI:
fragile
temperature sensitive
hygroscopic



Photomultiplier tubes



13-3. A rectangular gamma camera detector with the cover removed showing the photomultiplier tubes (PMTs).

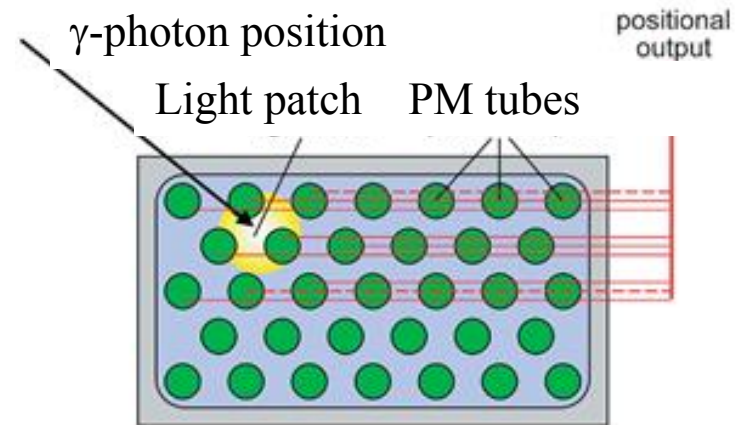


Transformation of light pulses to electric signal.

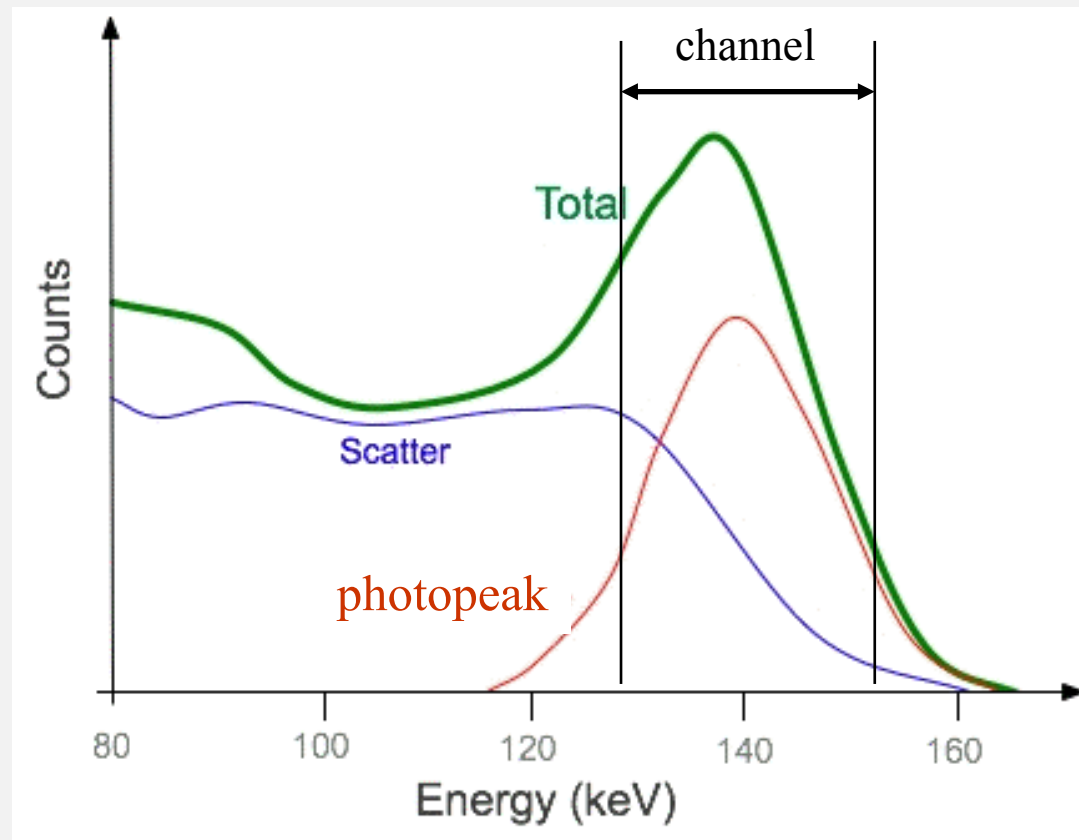
Typically 37-91 tubes, 5.1-7.6 cm diameter each

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-scattering.

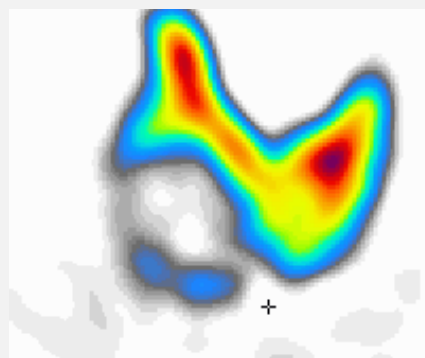
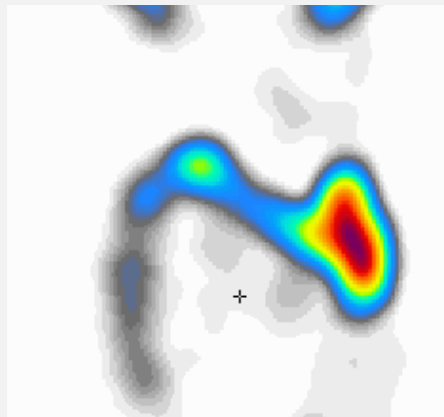
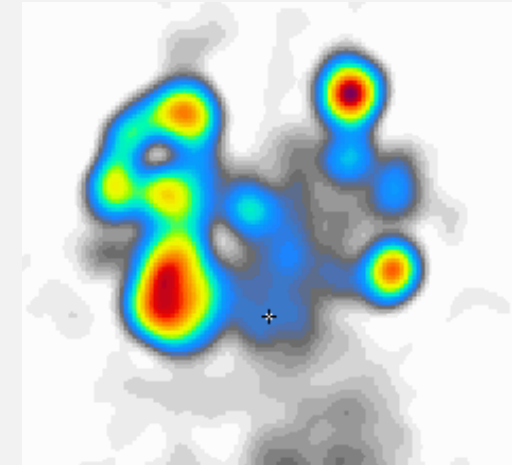
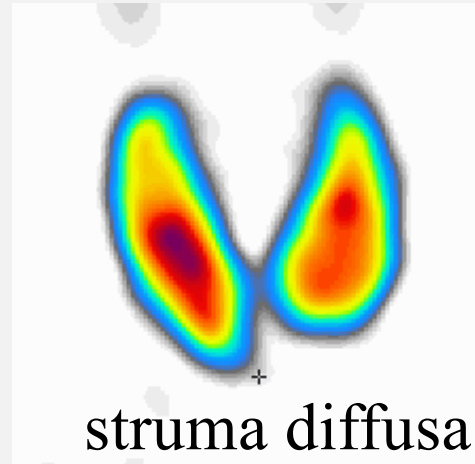
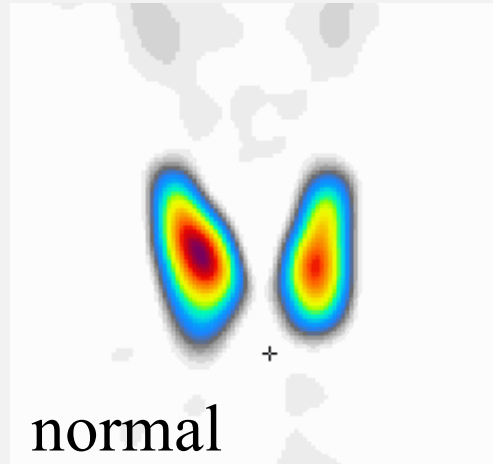


Pulse amplitude spectrum – Amplitude of an electric pulse generated by a γ -photon absorption in photoeffect is proportion to the photon energy.



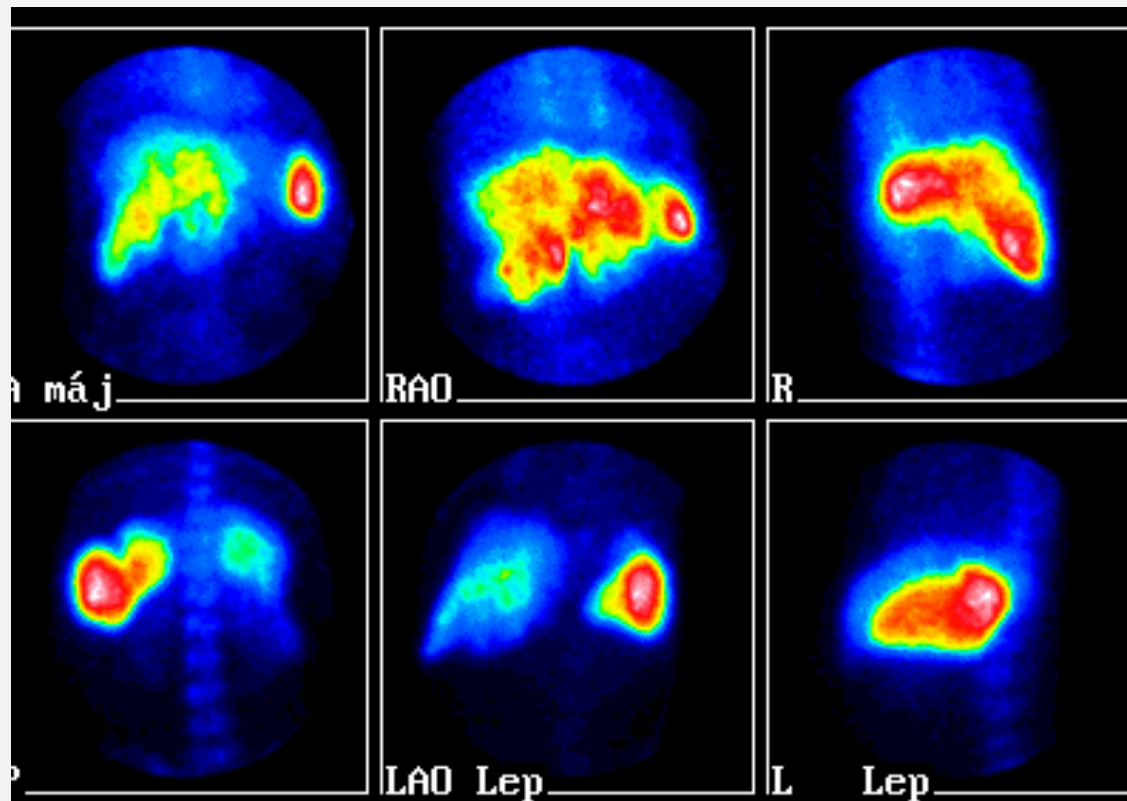
These electric pulses can be distinguished by discrimination (DD).

Pertechnetate (intravenous 80 MBq) distribution in thyroid glands



Cold nodules

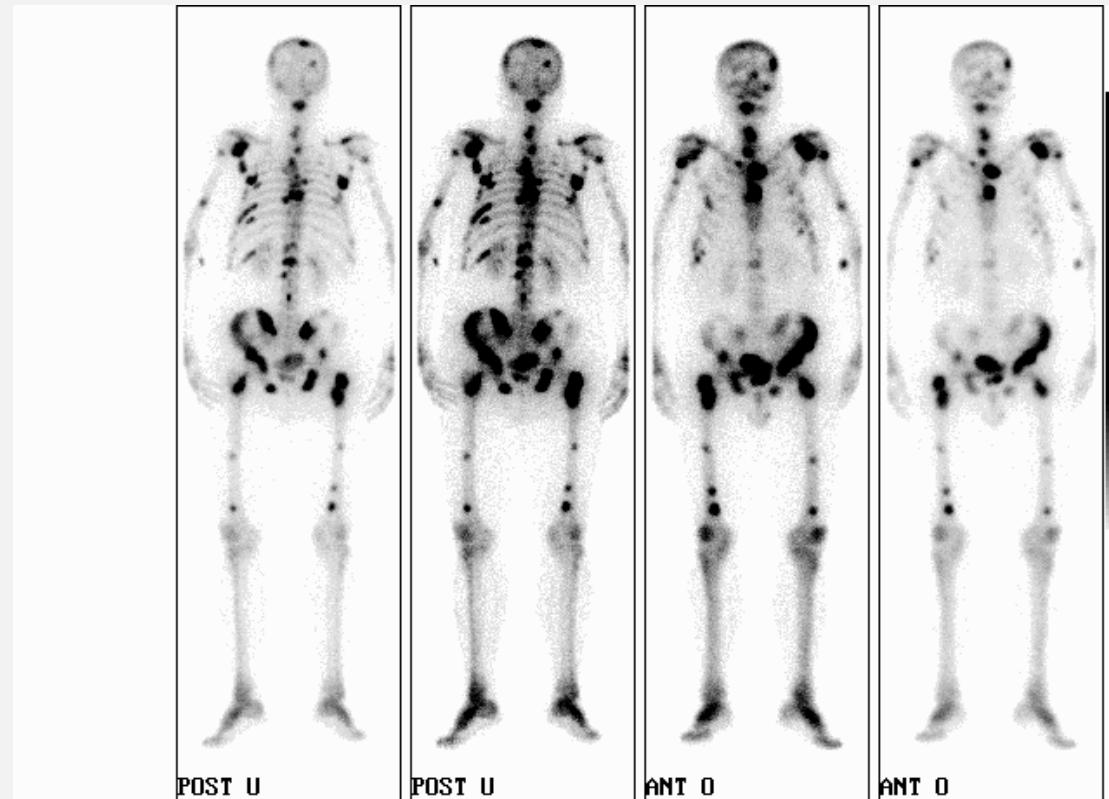
Liver lesion nodules



^{99m}Tc - fyton

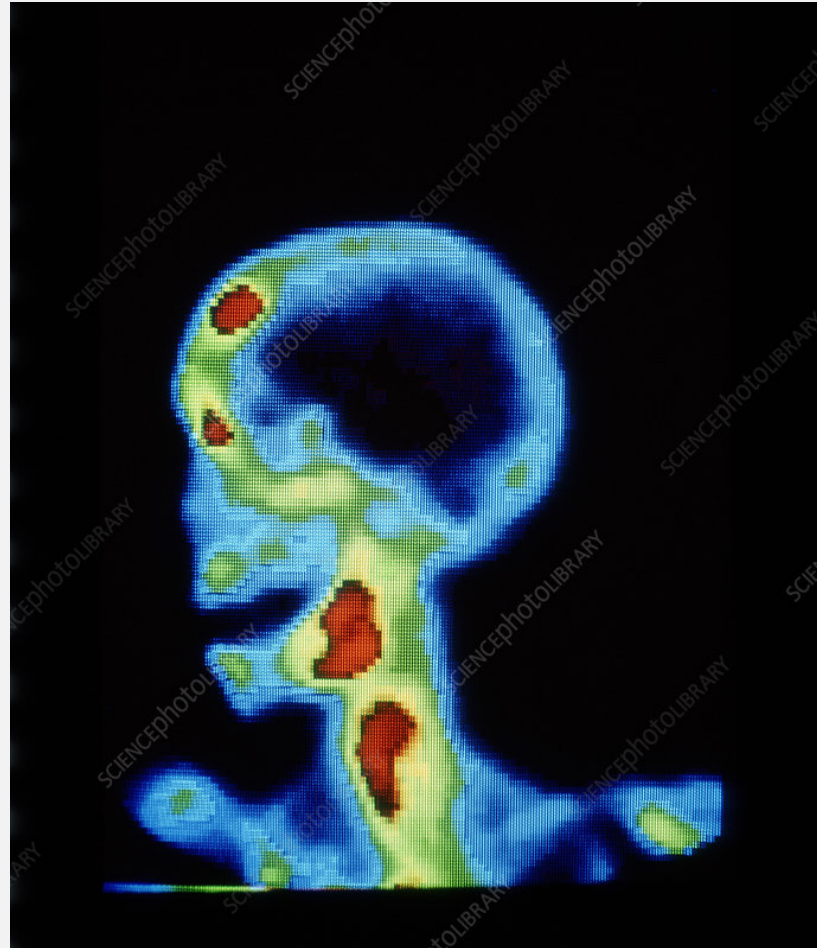
Bone scintigraphy

^{99m}Tc -MDP: 600 MBq



imaging bone metastases

Gamma camera image: summation image



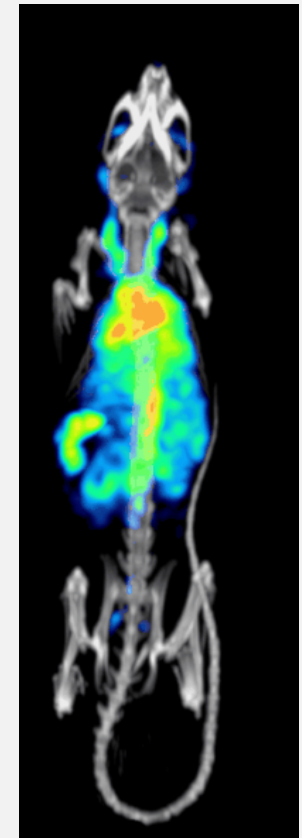
For depth / 3D resolution: tomographic device is necessary

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.

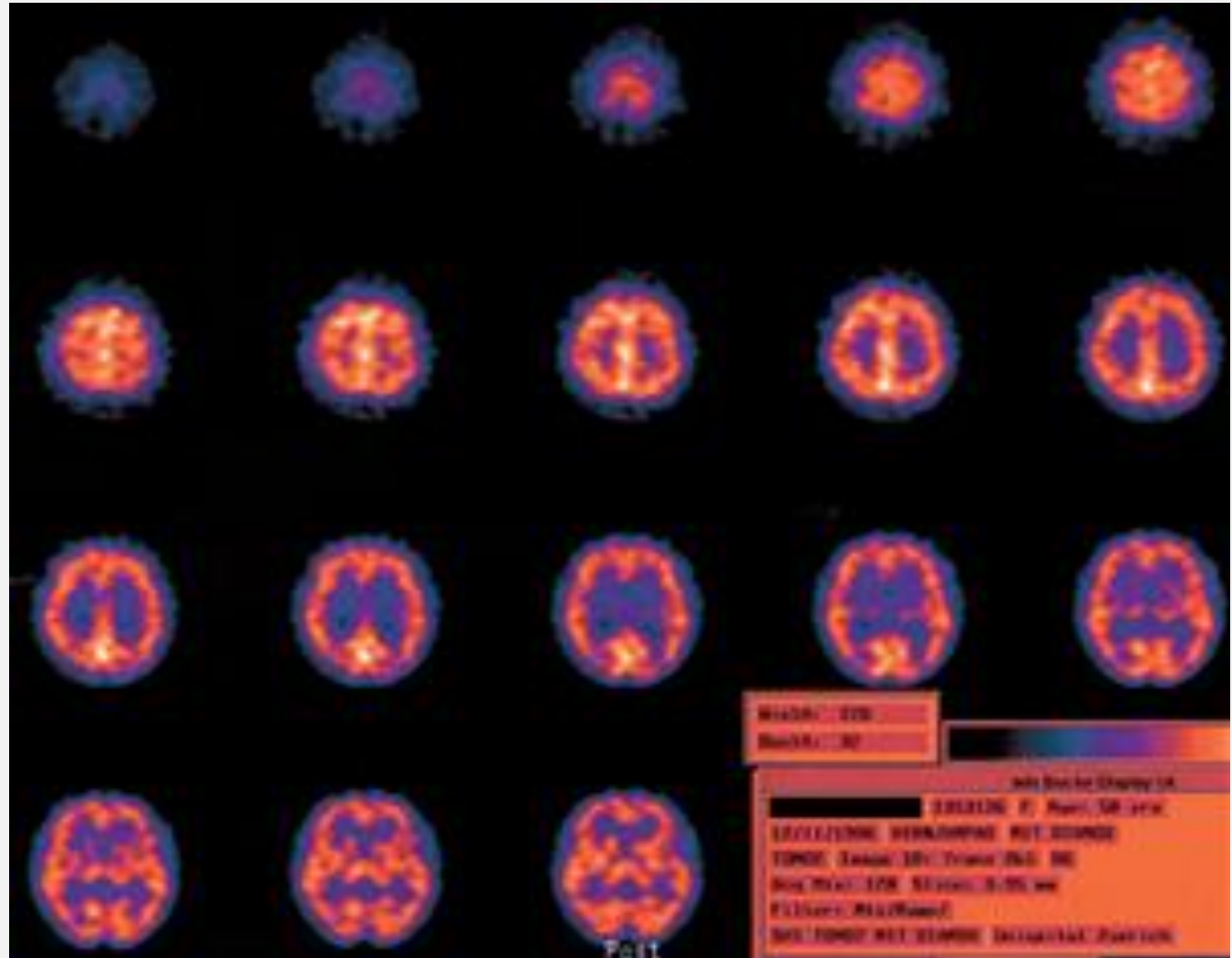


Various camera arrangements

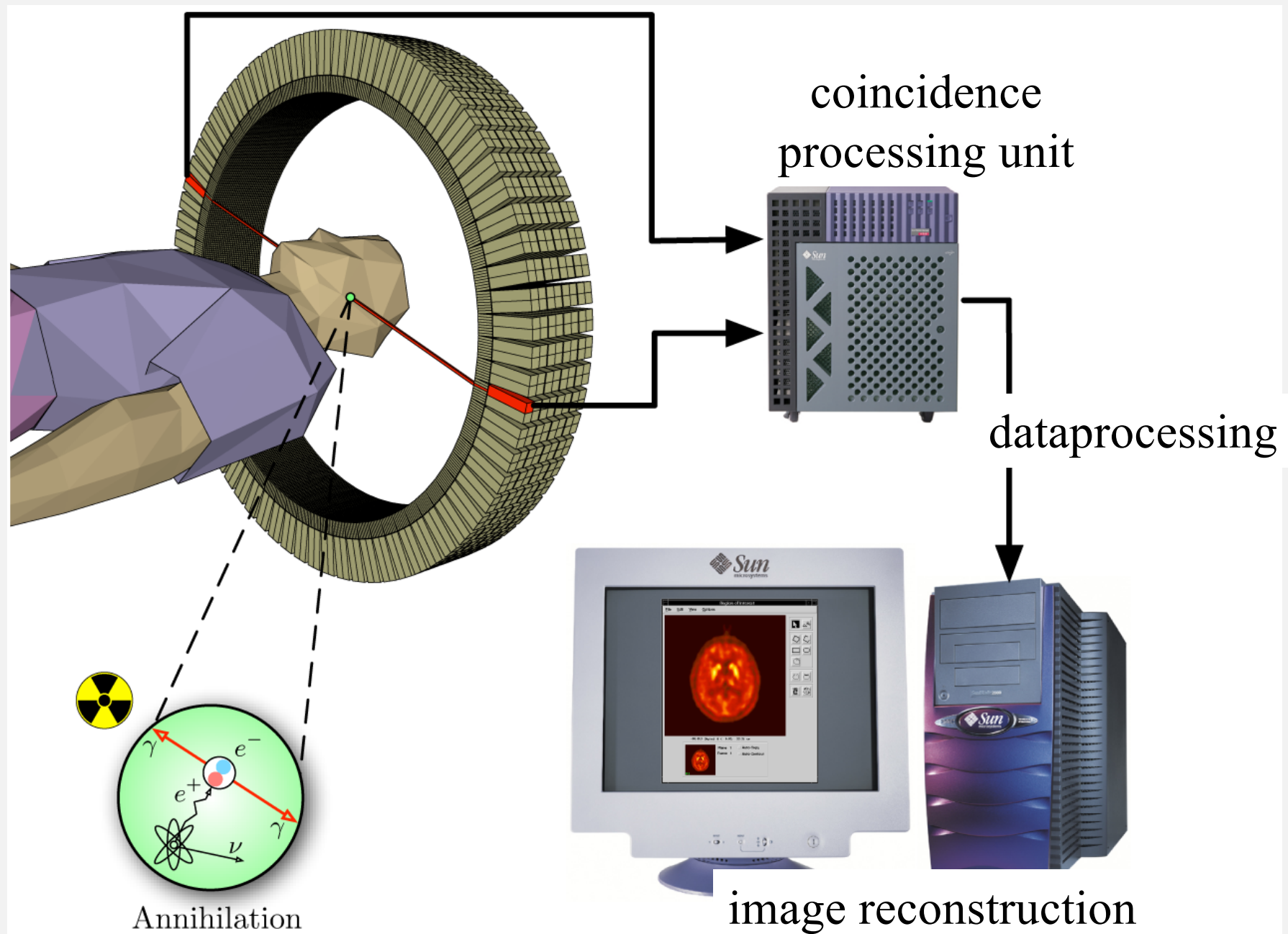
SPECT



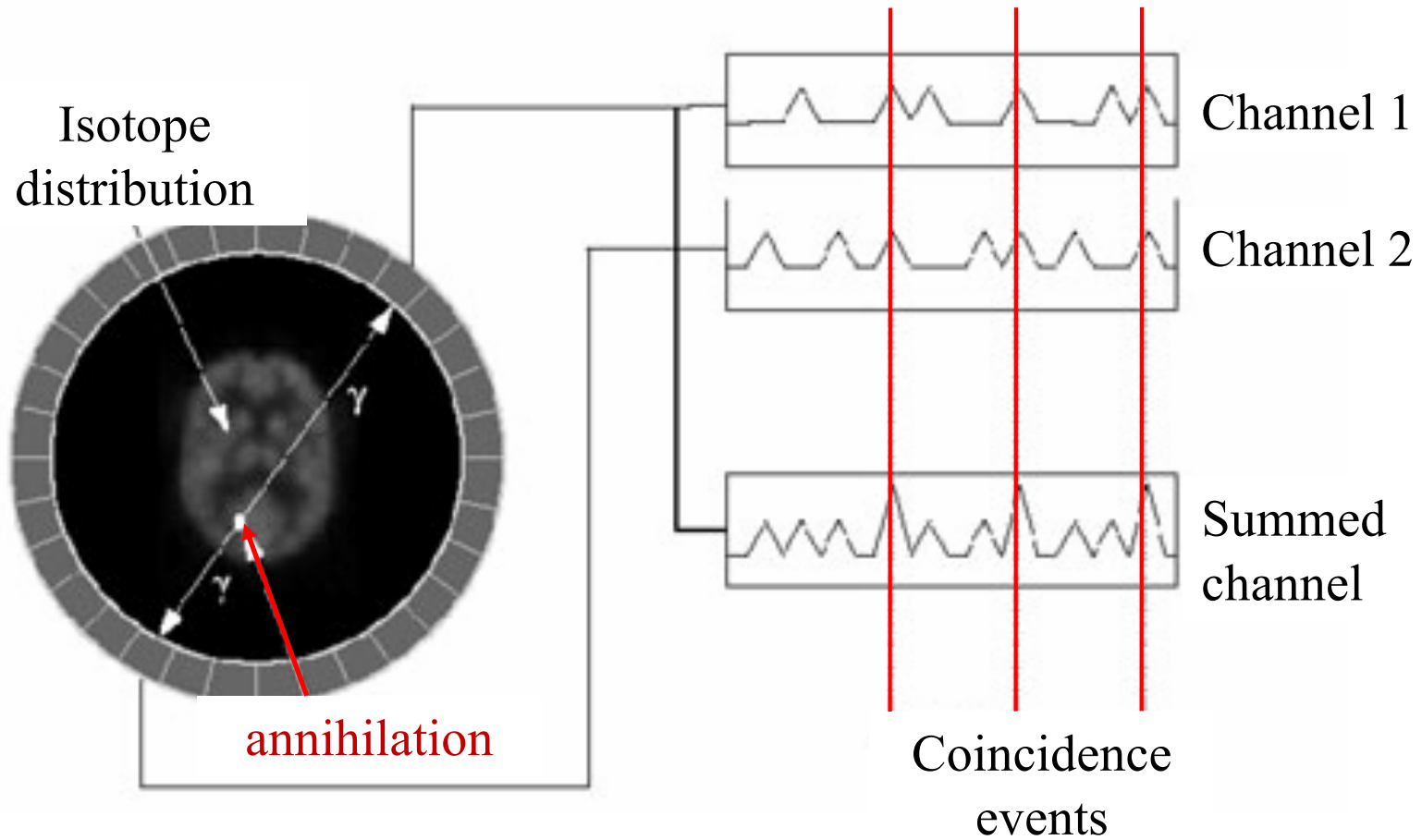
SPECT – images of scalp

 $^{99\text{m}}\text{Tc-HMPAO}$ 

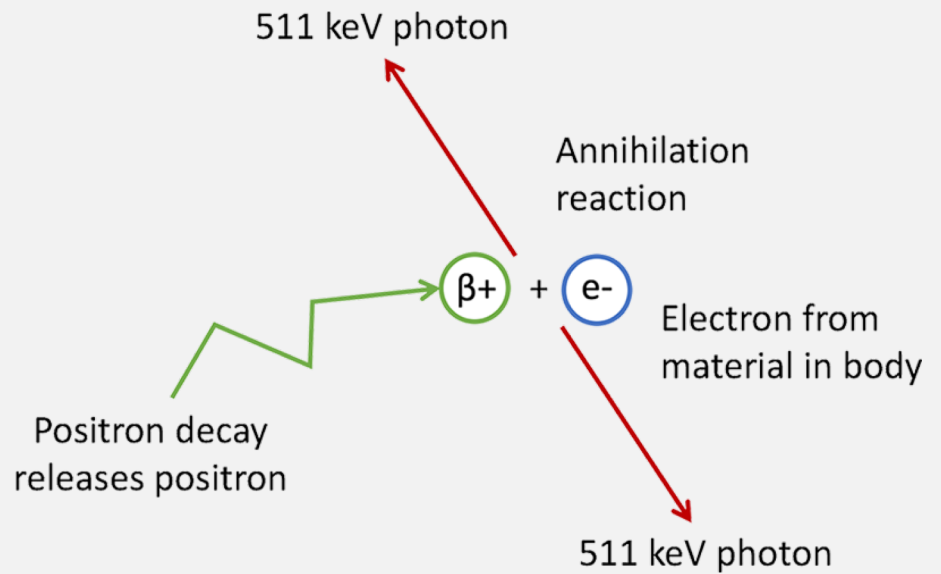
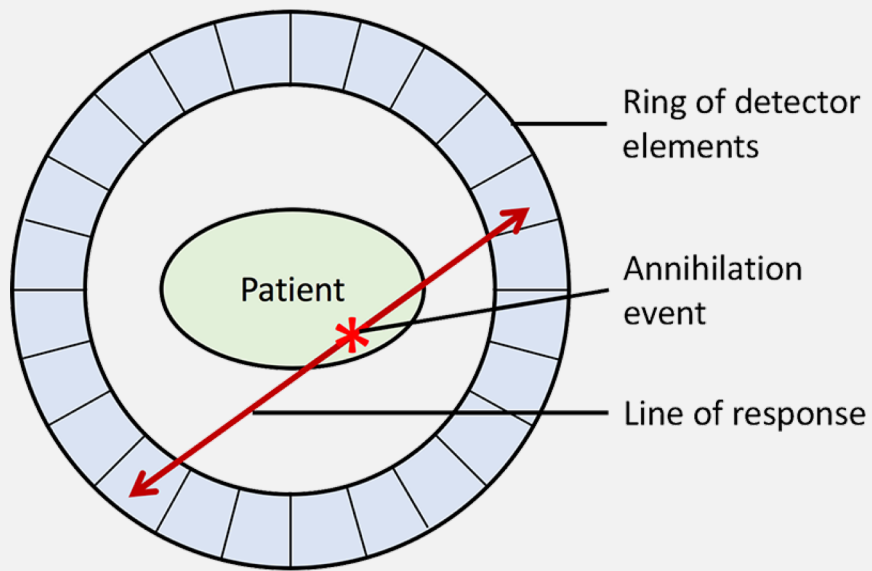
Positron Emission Tomography PET



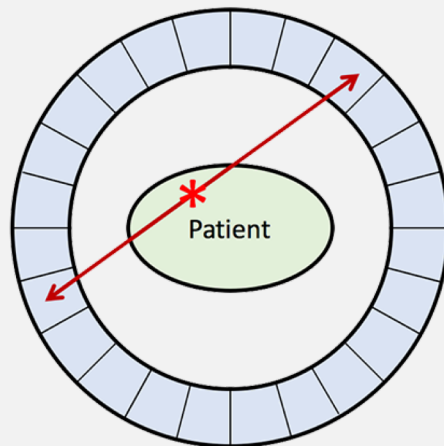
Coincidence detection



Coincidence detection

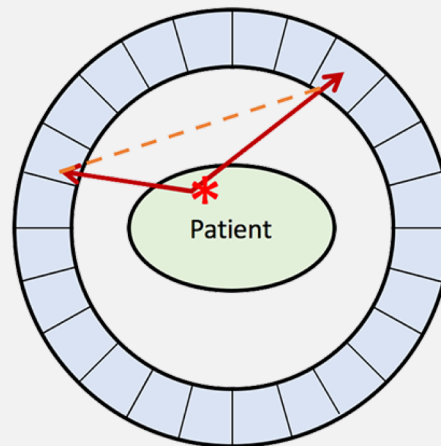


↔ Annihilation path
 - - - - - Calculated line of response



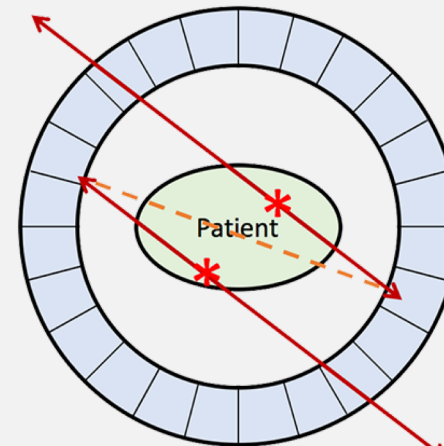
True coincidence

- One annihilation
- Straight path photons in opposite directions



Scatter coincidence

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

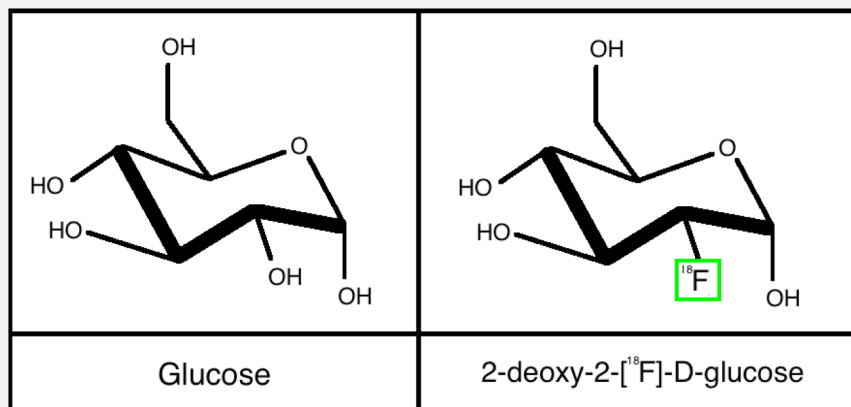


Random coincidence

- 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.

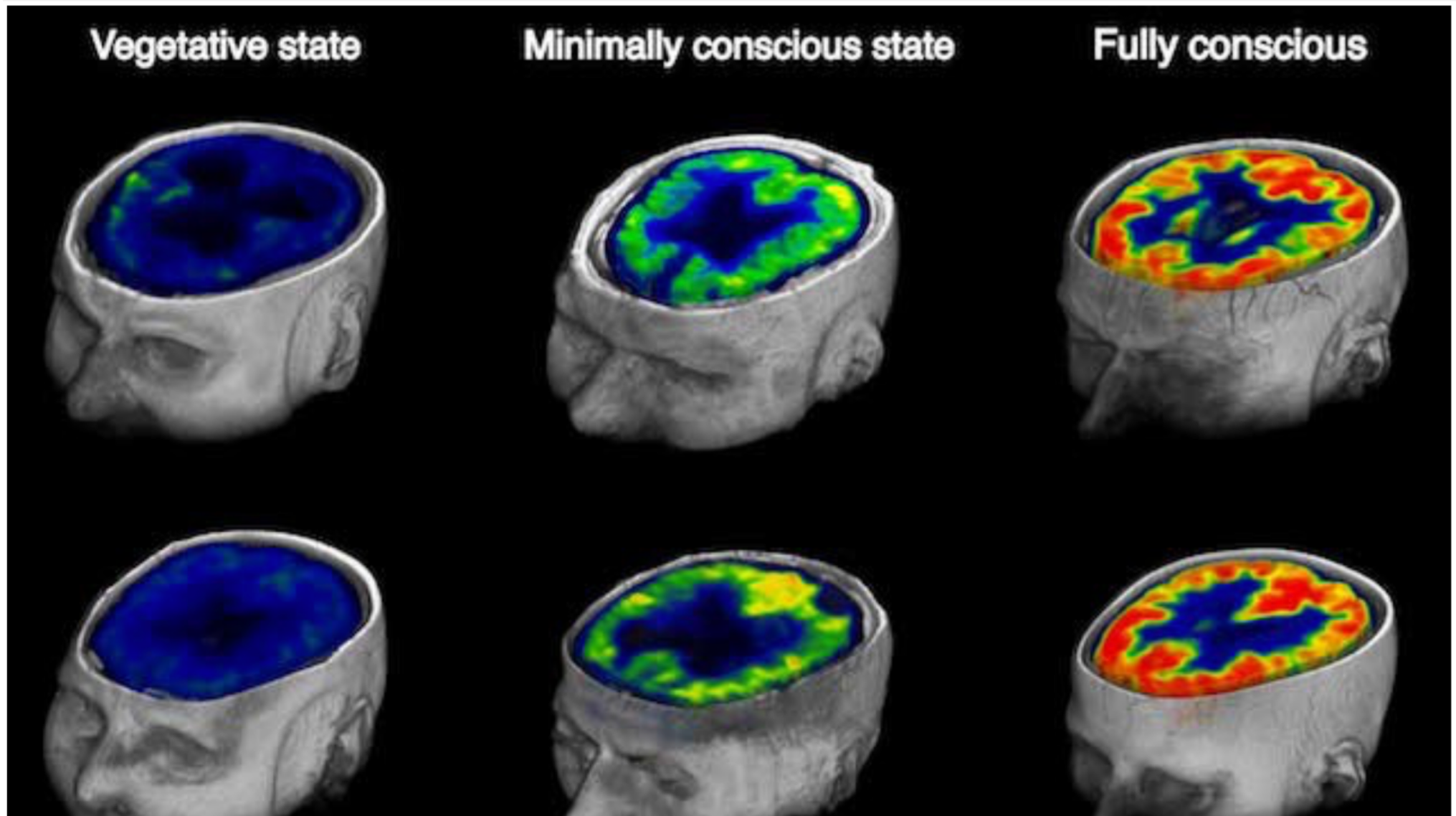
| Isotope | β^+ energy (MeV) | β^+ range (mm) | 1/2-life | Applications |
|------------------|------------------------|----------------------|-----------|--------------------|
| ^{11}C | 0.96 | 1.1 | 20.3 min | receptor studies |
| ^{15}O | 1.70 | 1.5 | 2.03 min | stroke/activation |
| ^{18}F | 0.64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



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

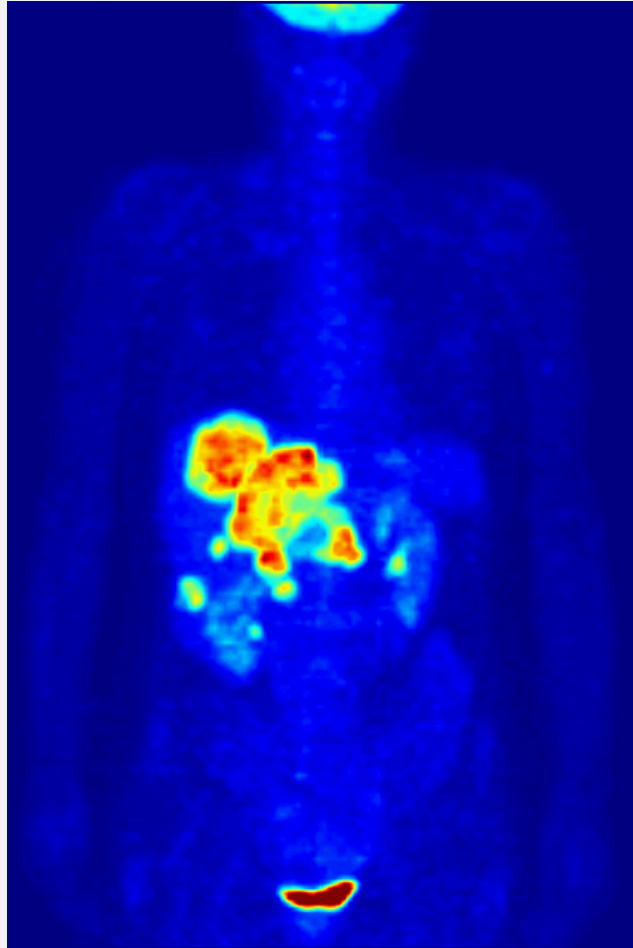


$[^{18}\text{F}]$ -fluorodeoxyglucose (FDG) – showing glucose metabolism



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



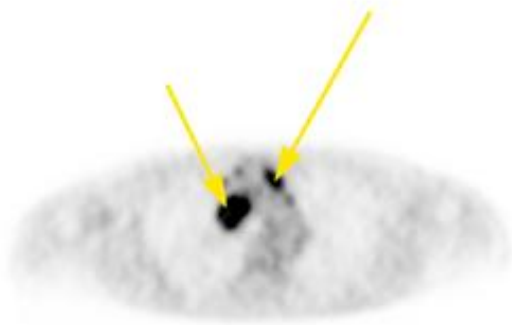
3D reconstruction of tissue metabolic activity from a [^{18}F]-FDG PET scan. Notably, we see increased activity along the chest walls, indicating carcinoma, as well as the supraclavicular fossa.

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

A.



B.



C.



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?



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