Biophysics I

# 14. Nuclear radiations in the clinical practice

Dora Haluszka

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haluszkadora@gmail.com

Steps of diagnostic procedure

- Selection of **radioactive isotope**

- Selection of **radiopharmacon**

- Distribution and alteration of **activity** is detected

- Monitoring of **physiological pathways** and/or identification and localization of **pathological changes**

ISOTOPE DIAGNOSTICS

gamma radiation source

gamma-camera

gamma-camera
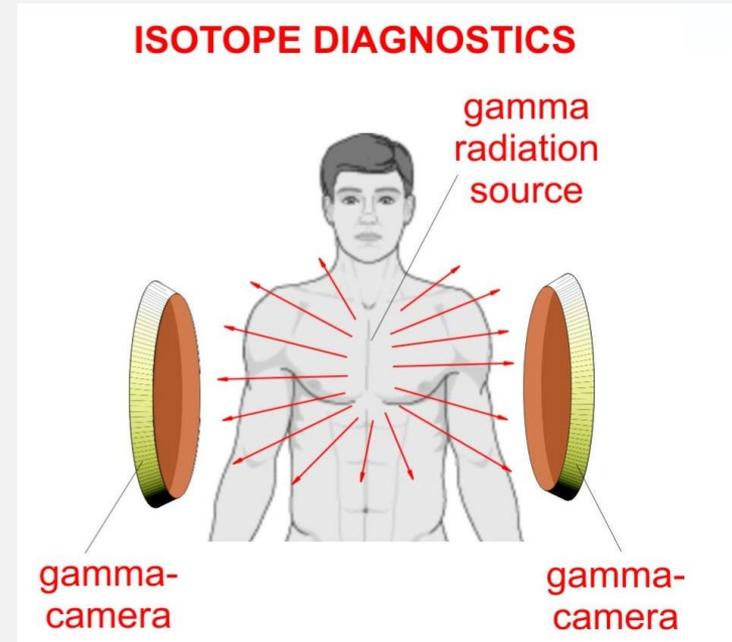
Informations provided by medical imaging

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
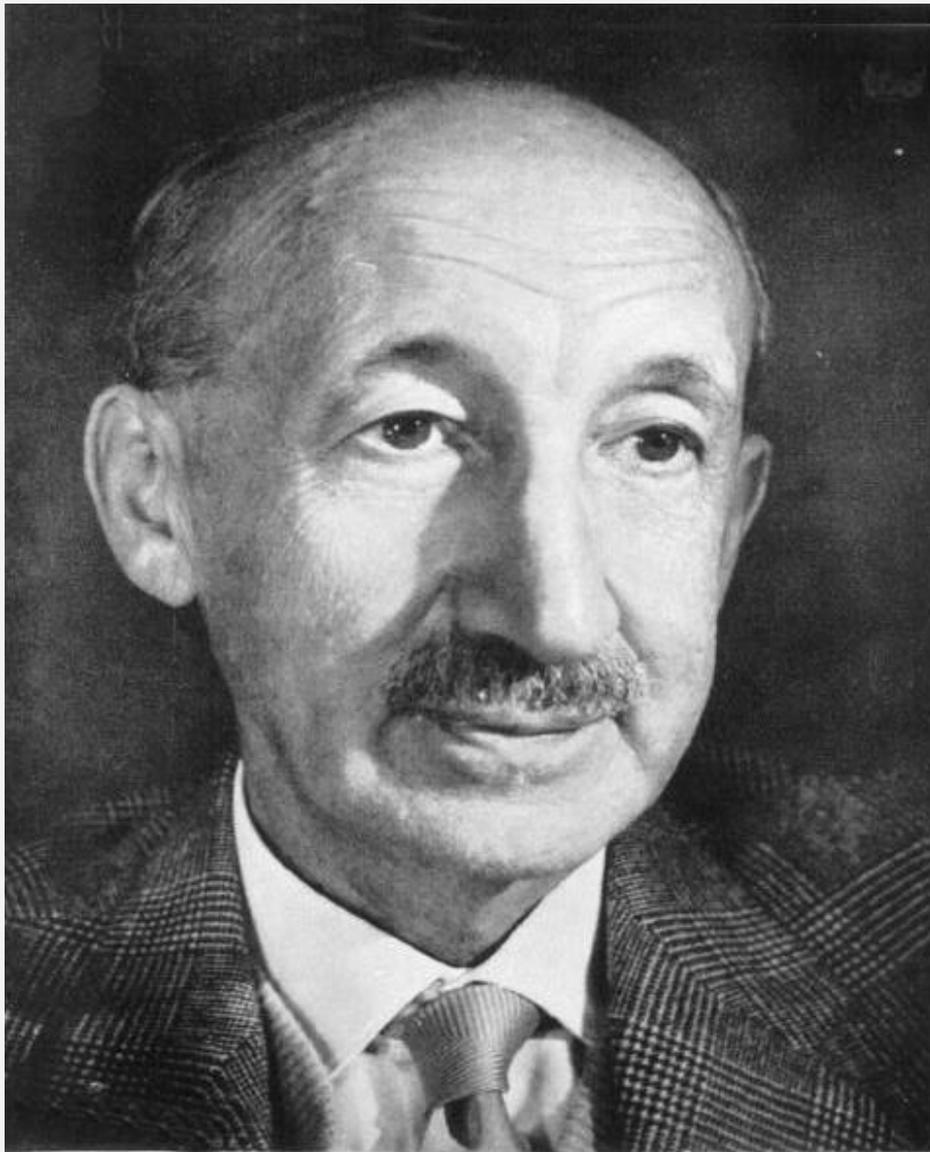
Father of Nuclear Medicine

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
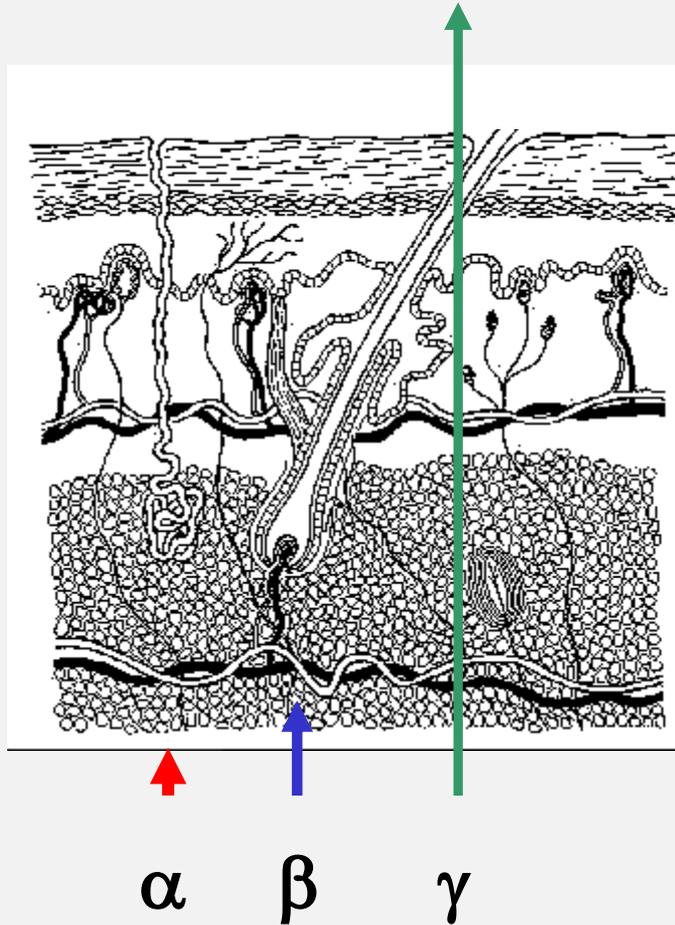
decay via photon emission to minimize absorption effects in body tissue

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

α   β   γ

purely gamma-emitting isotope is preferable

Photon energy

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

Low-energy photon   High-energy photon
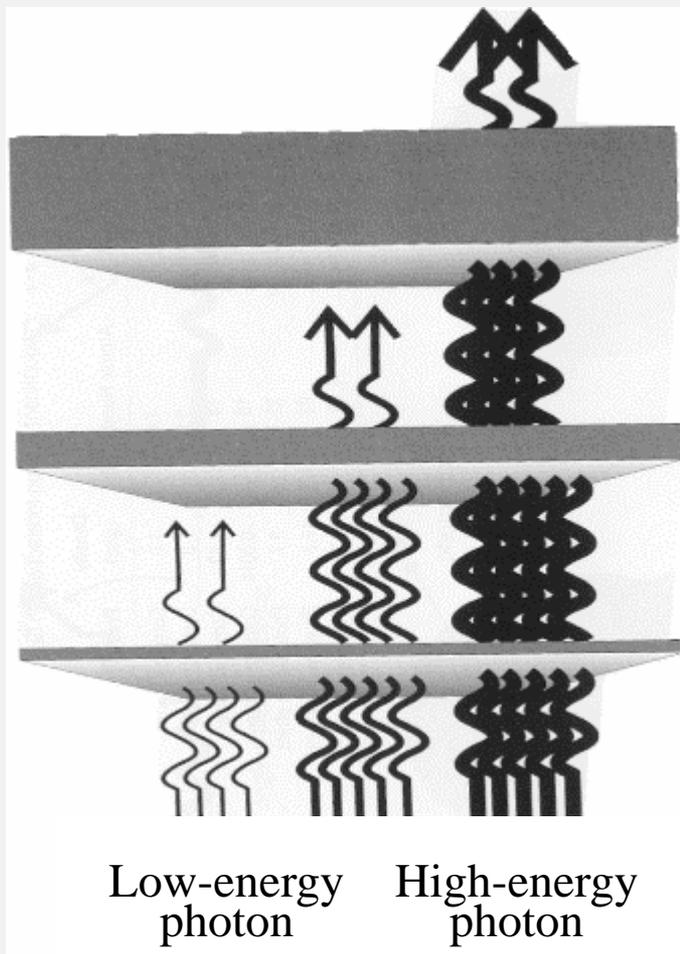
Photon must have sufficient energy to penetrate body tissue with minimal attenuation

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)

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

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

**shorter is better**

smaller is better

dose considerations for patients

but

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

Radiopharmacon

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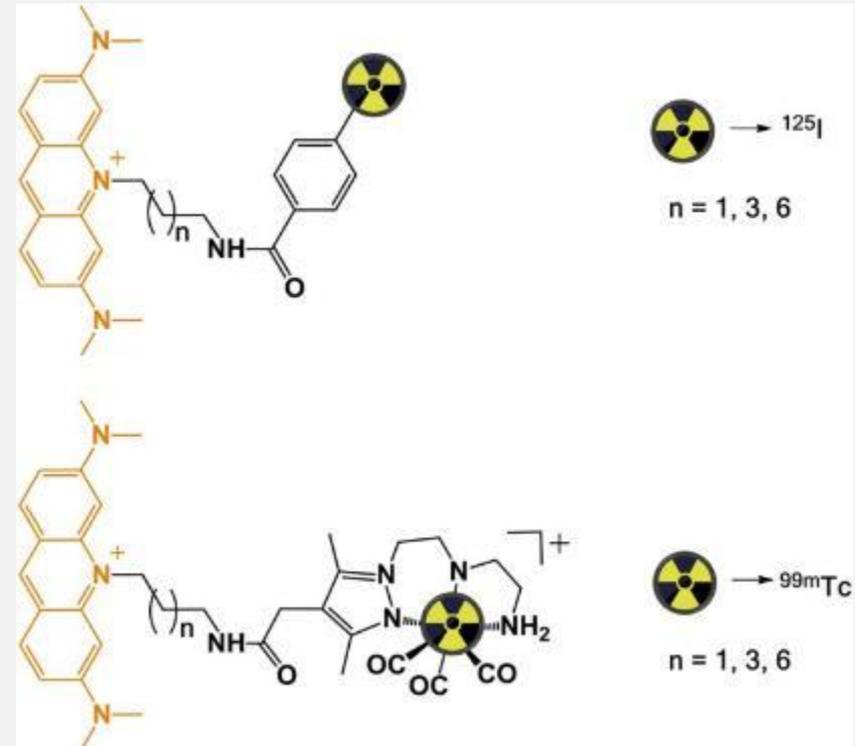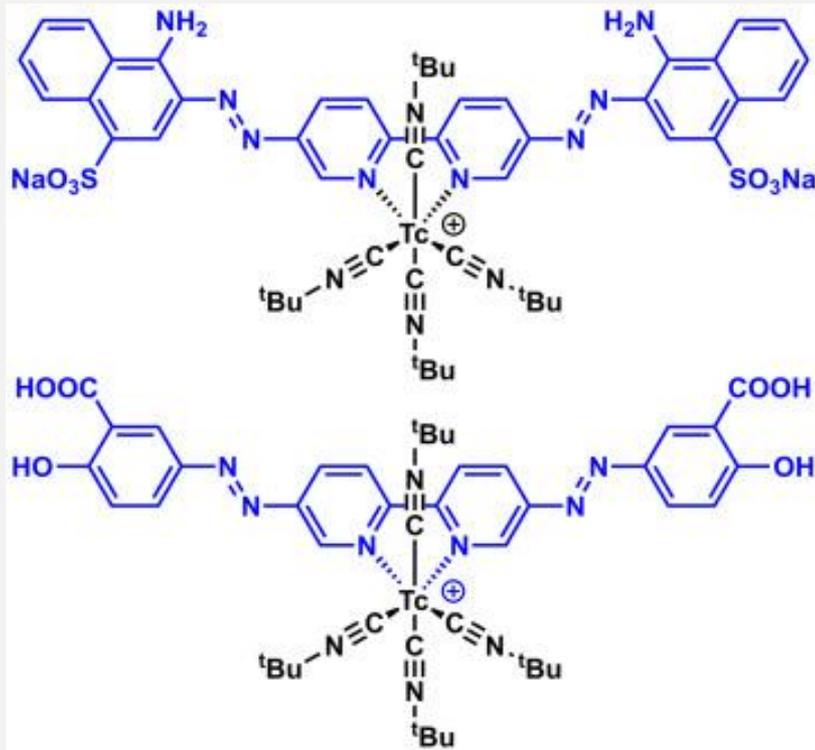

Basic requirements:
- high *target / non-target* ratio
- have no pharmacological or toxicological effects which may interfere with the organ function under study.

Factors responsible for ADME-TOX
(absorption, distribution, metabolism, excretion, toxicology)

– 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...

M= ^{99m}Tc, ^{111}In, ^{68}Ga, ^{64}Cu, ^{86}Y, ^{177}Lu, $^{203/212}$Pb

Chelator

Linker

PSMA Inhibitor
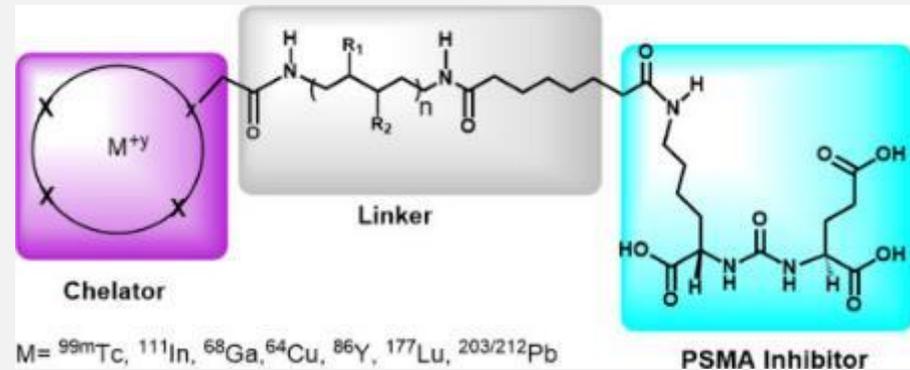
Gamma-emitting isotopes

Isomeric transition: some excited states may have half-lives ranging from hours up to more than 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 $\qquad\qquad T_{1/2}=6$ hours
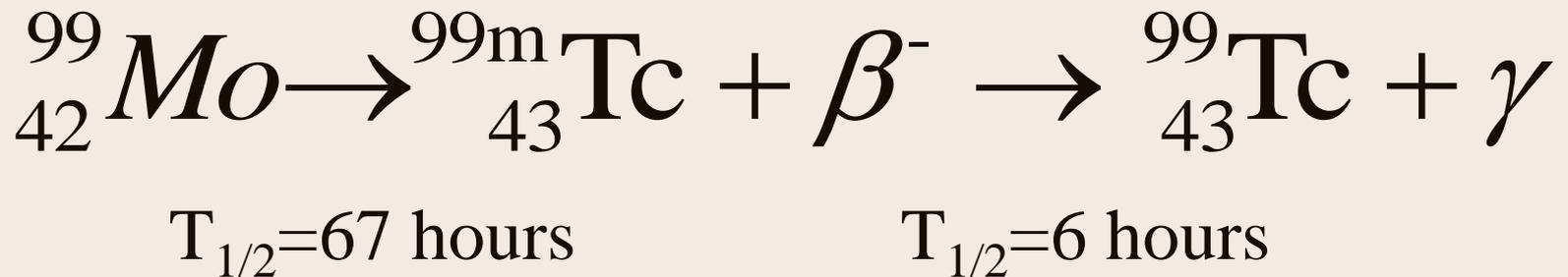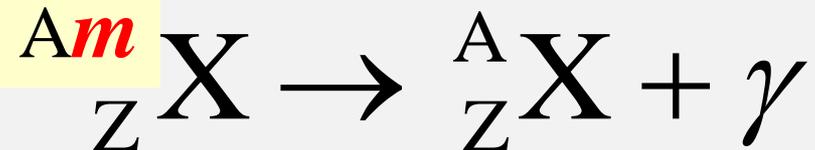
Technetium-99ᵐ generator
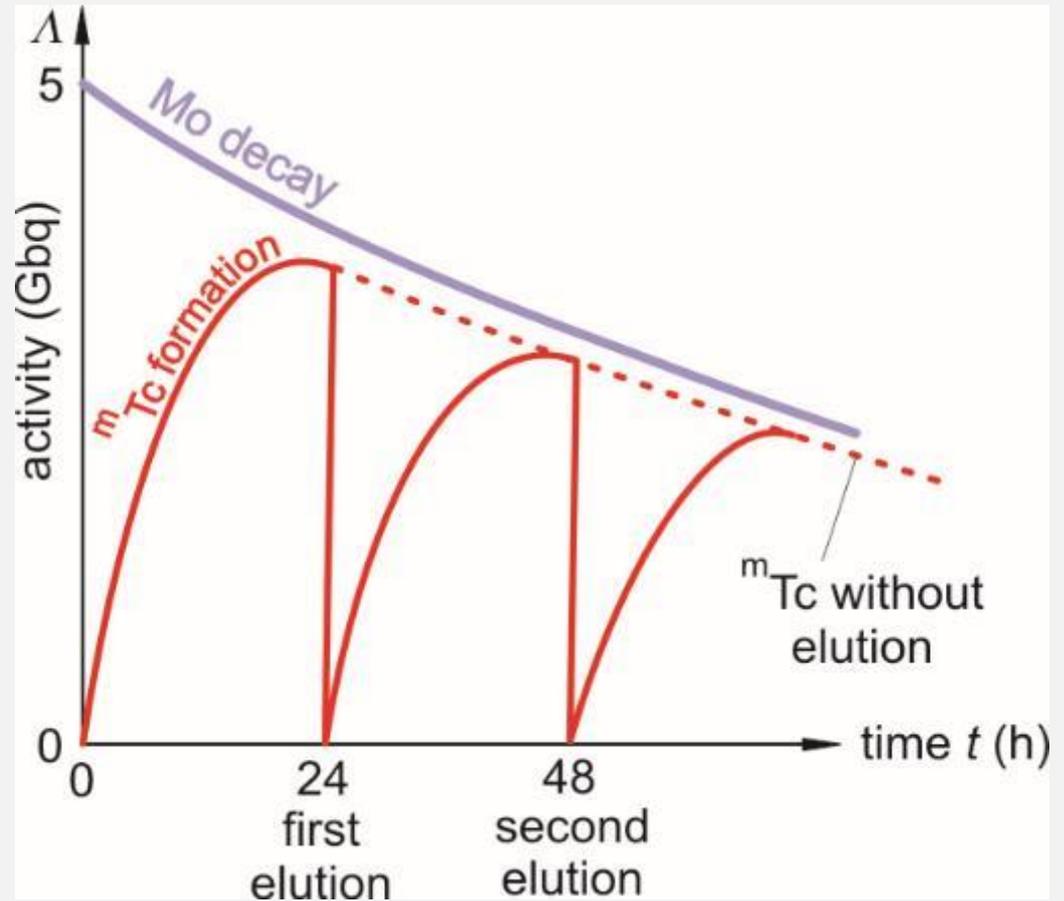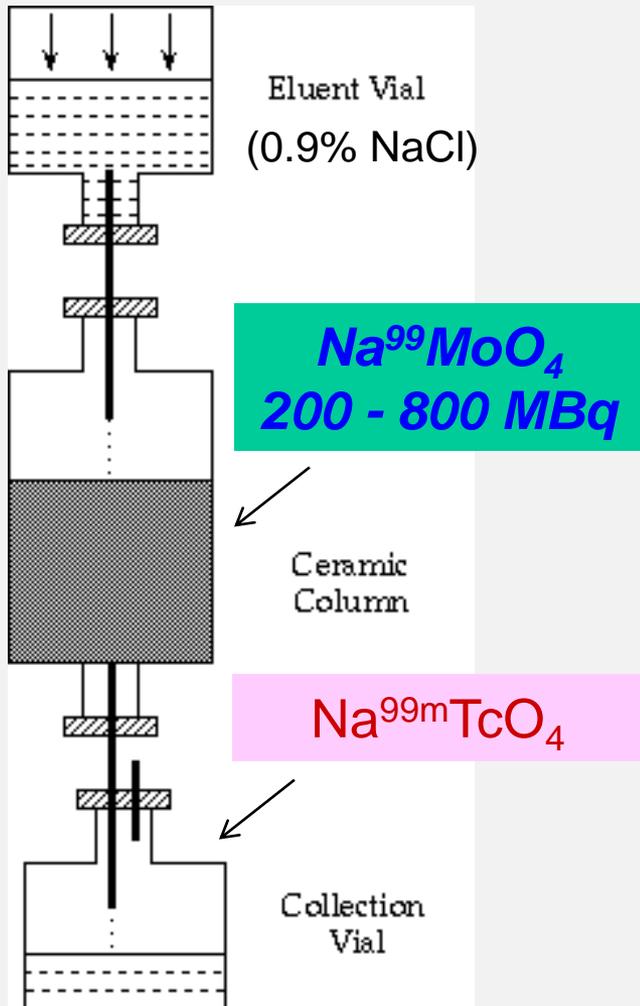
pharmaceutical	radioisotope	activity (MBq)	target organ
Pertechnetate	^{99m}Tc	550 - 1200	brain
Pirophosphate	^{99m}Tc	400 - 600	heart
Diethylene Triamine Penta Acetic Acid (DTPA)	^{99m}Tc	20 - 40	lung
Mercaptoacetyltriglycine (MAG3)	^{99m}Tc	50 - 400	kidney
Methylene Diphosphonate (MDP)	^{99m}Tc	350 - 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)

Isotope accumulation in

thyroid glands   kidneys

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

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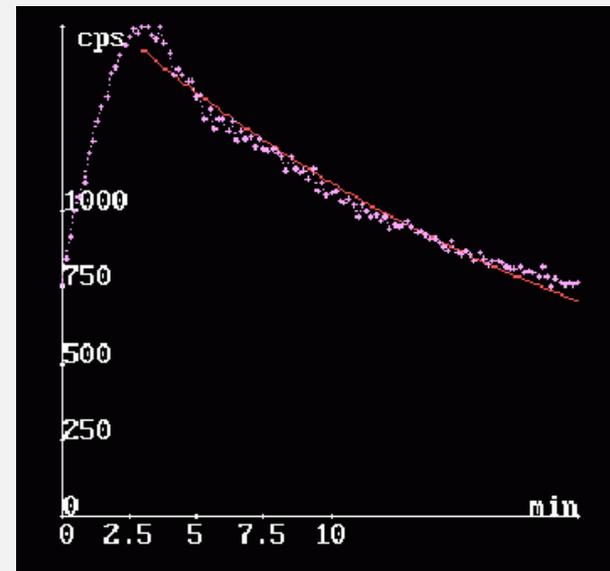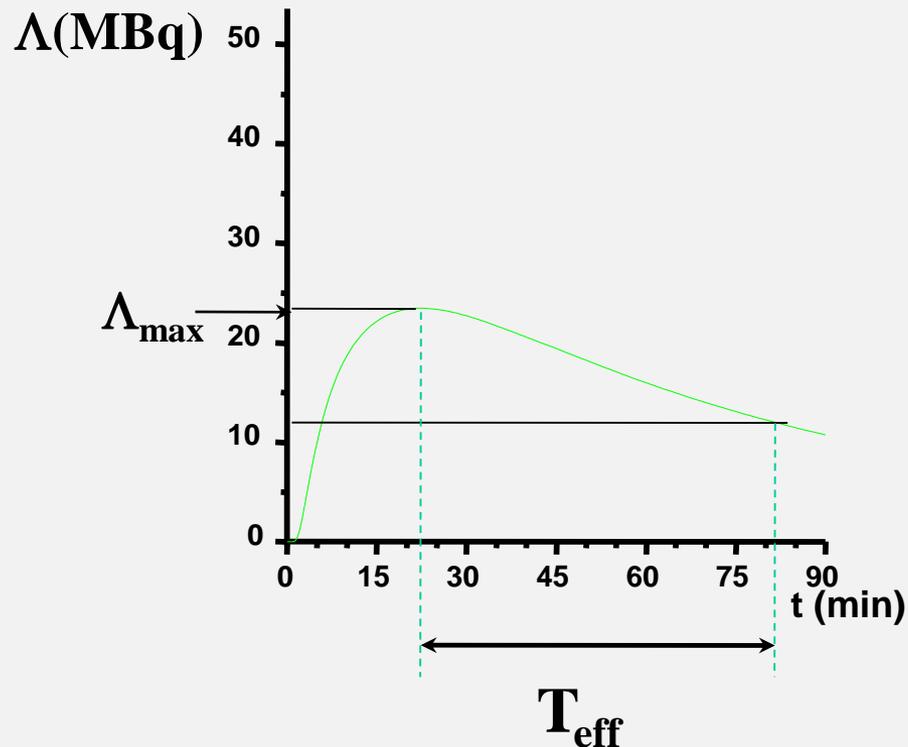
Effective half-life – activity decreases by half in the target organ

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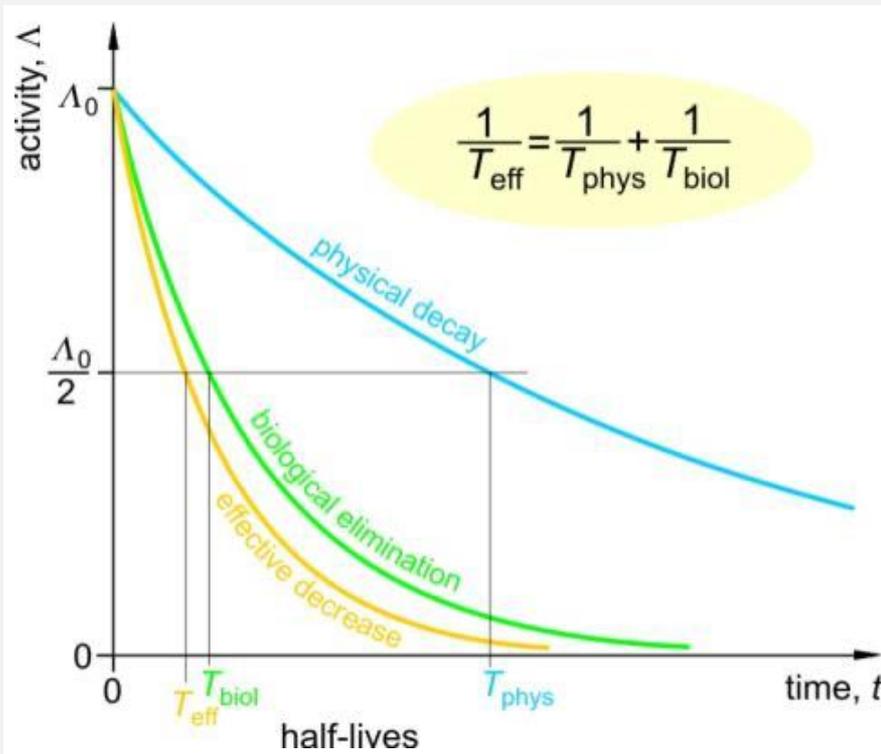
$$\lambda_{effective} = \lambda_{phys} + \lambda_{biol}$$

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

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
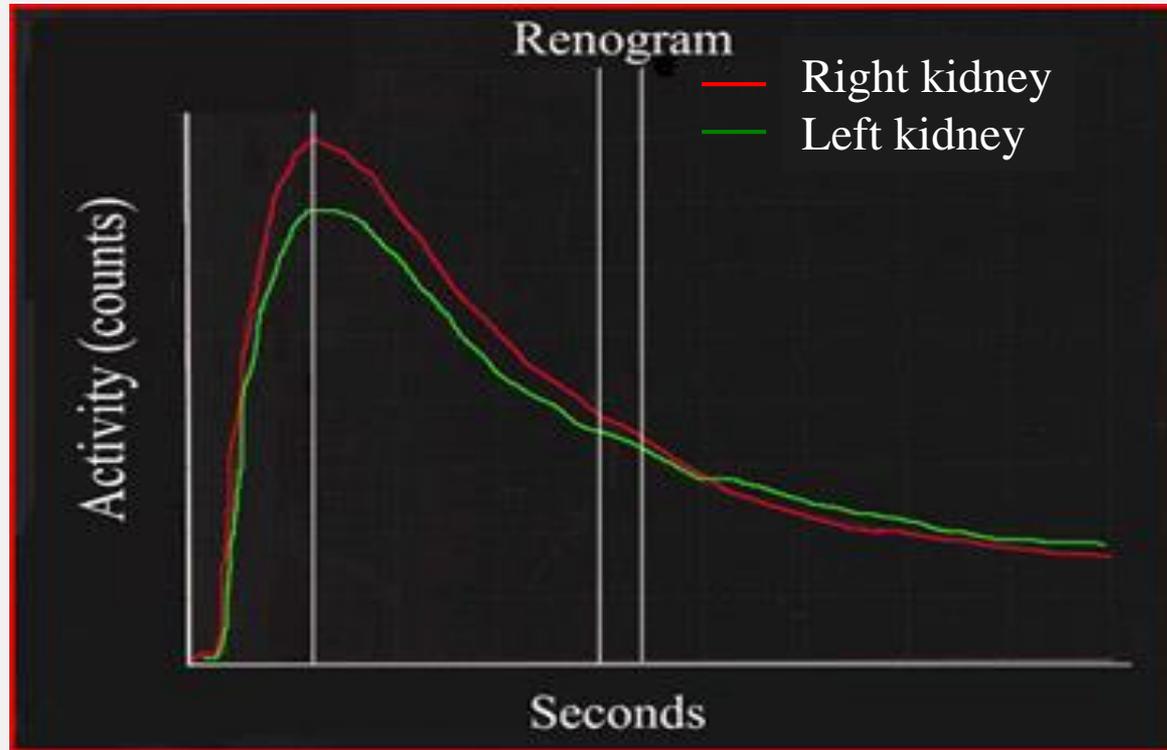
Isotope accumulation traces of kidney

example
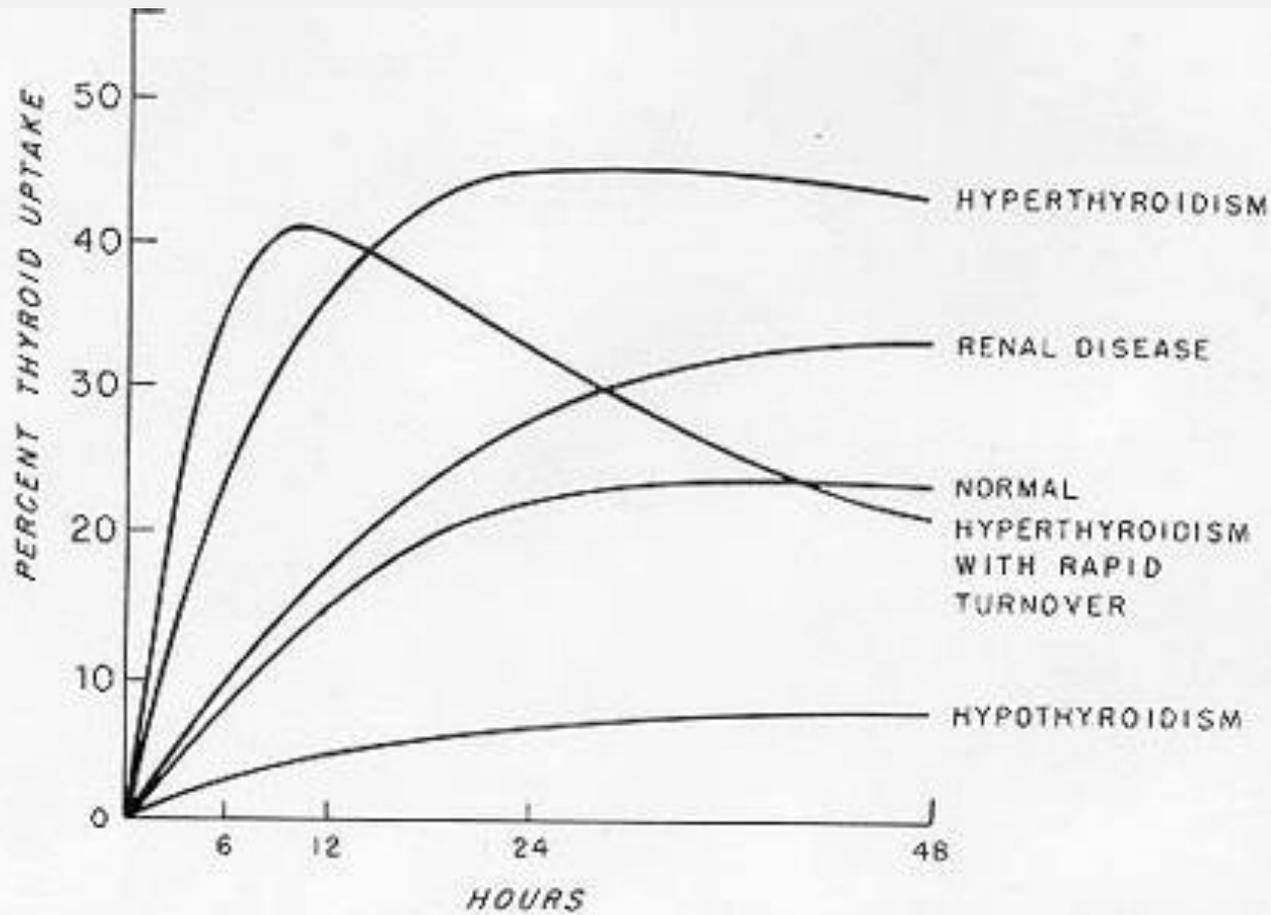
Thyroid glands' isotope accumulation traces

Pulse-chase experiments

Time-activity curve of Tc-99m scorpion venom in rats

Legend:
- Blood
- Muscle
- Liver
- Kidneys
- Heart

Y-axis: % Administered activity / organ
X-axis: Time in hours
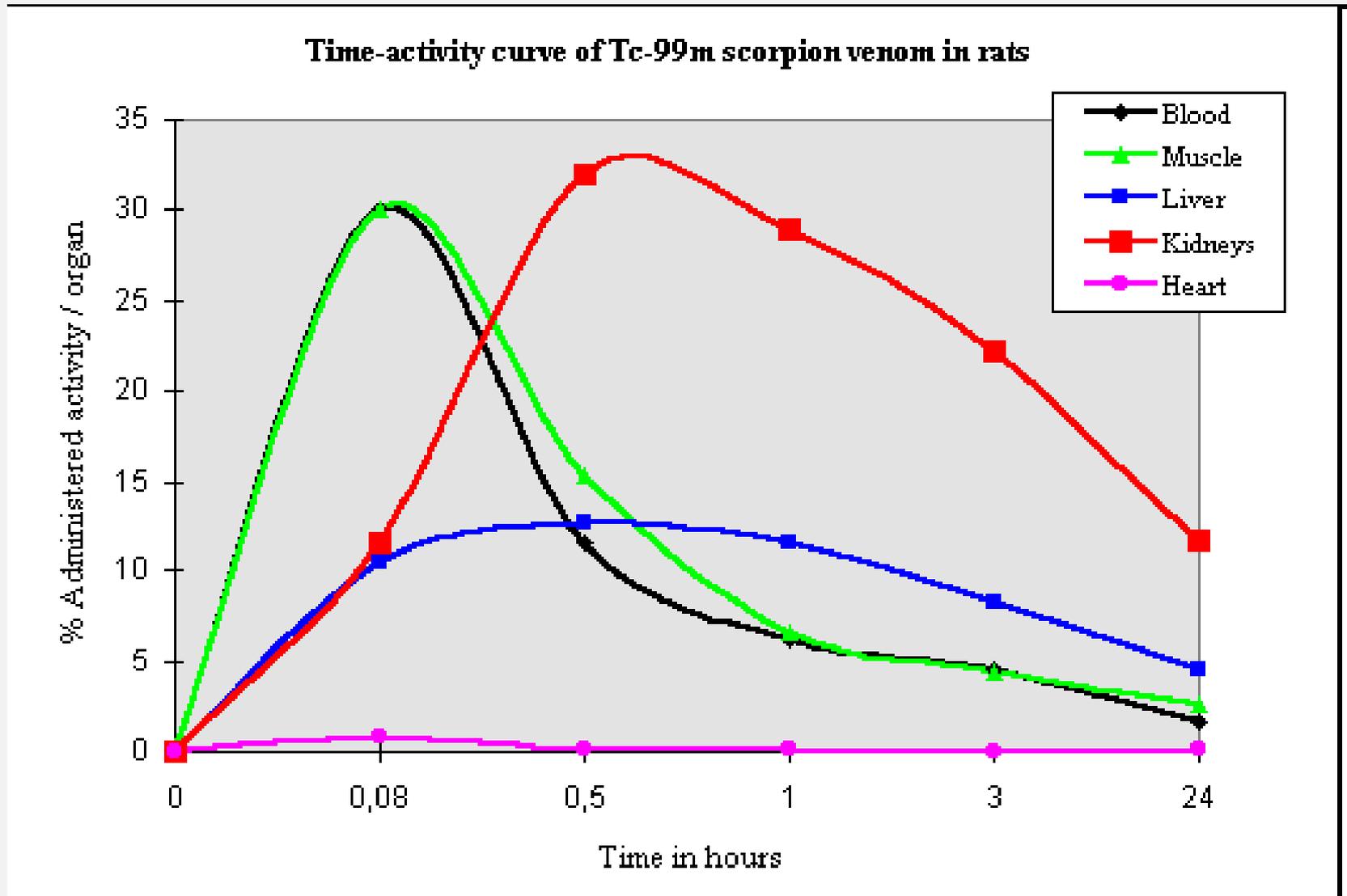
Hal Anger
1920-2005

Gamma camera

cc 40 cm
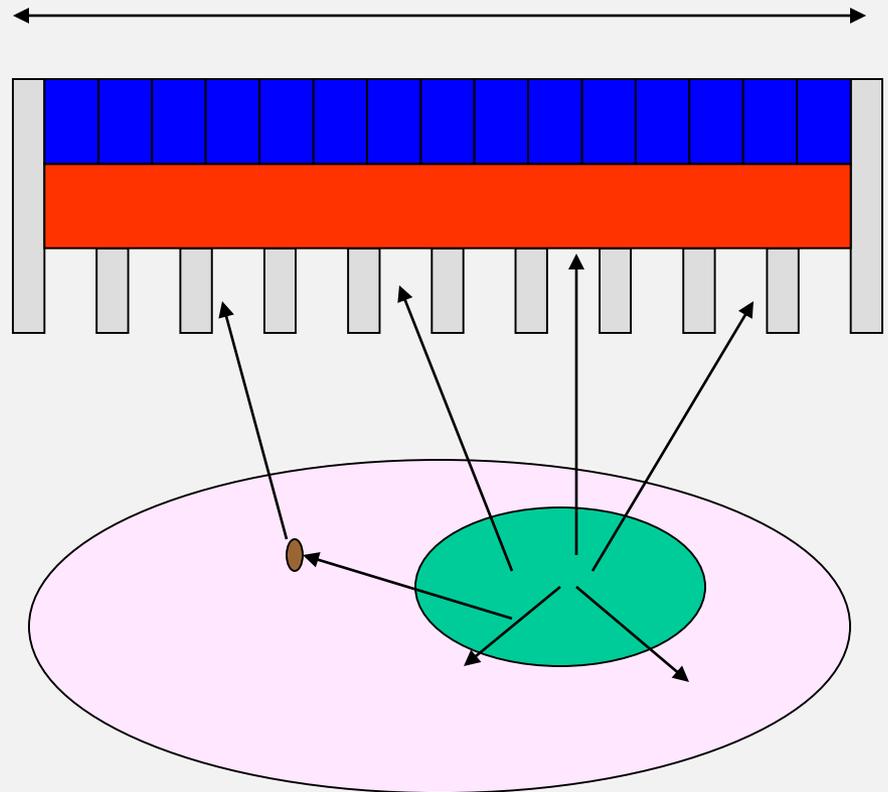
3. Photomultiplier tubes

2. Scintillation crystal

1. Collimator

A radioactive source emits gamma
photons in all directions

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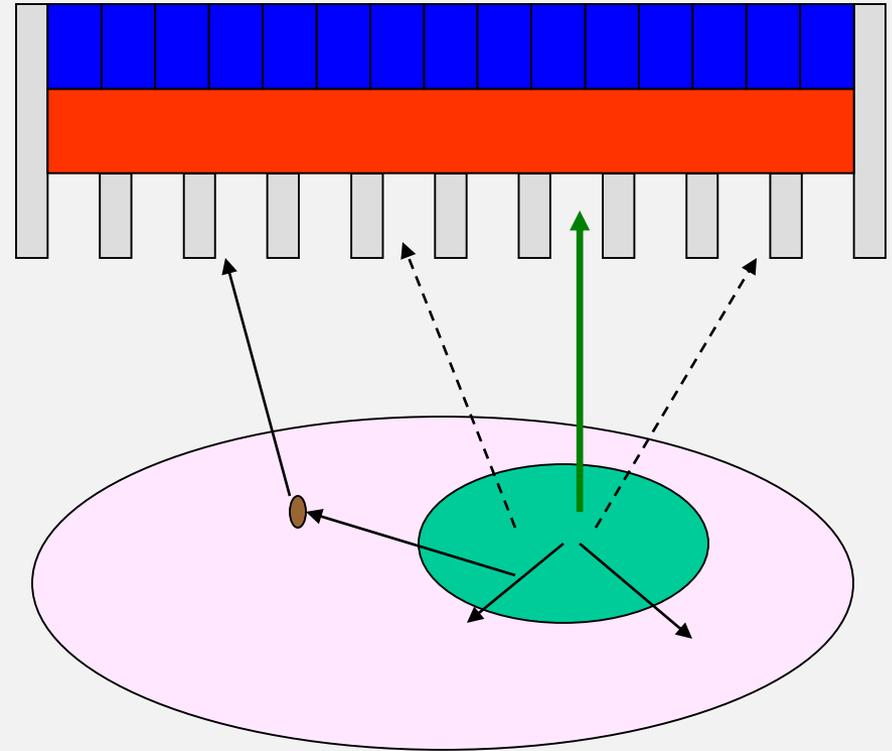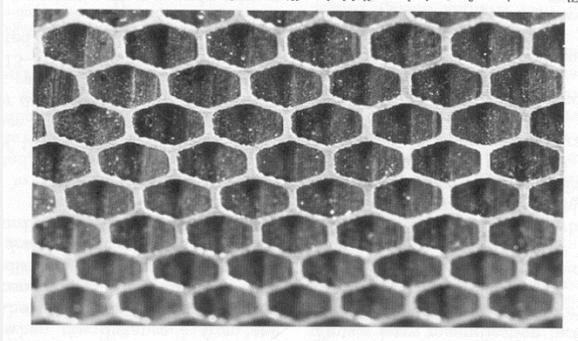
Collimators are composed of thousands
of precisely aligned channels made of lead.

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.
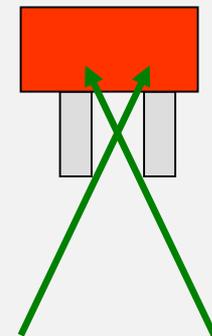
2. Scintillation crystal

NaI(Tl)
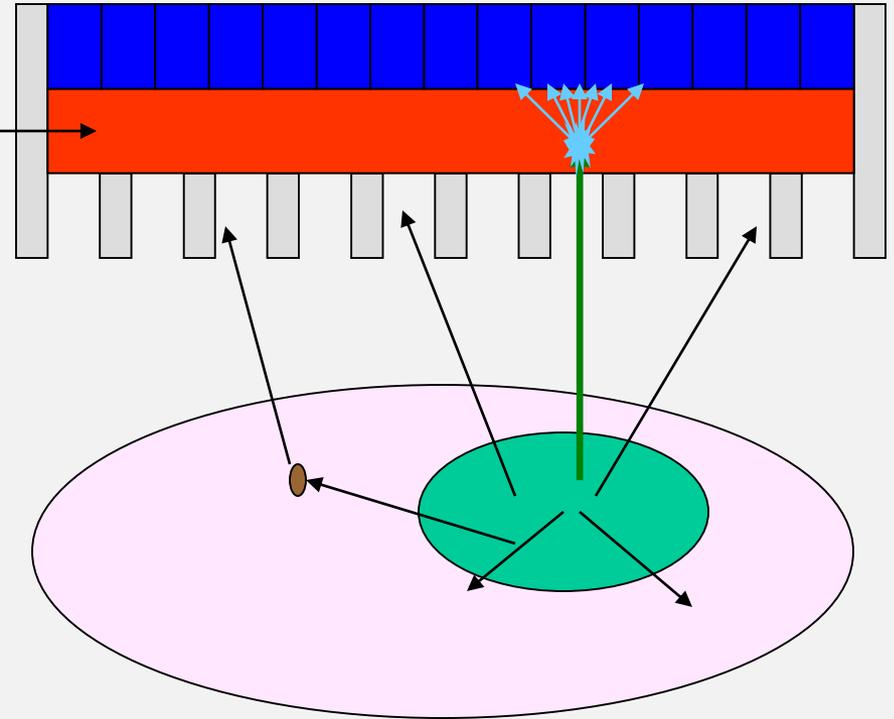
Sufficient detection efficiency
photons of 150 keV: μ ~2.2 1/cm

Proper wavelength – 415 nm ─ for PM photocathode

Problems with NaI:
      fragile
   temperature sensitive
      hygroscopic
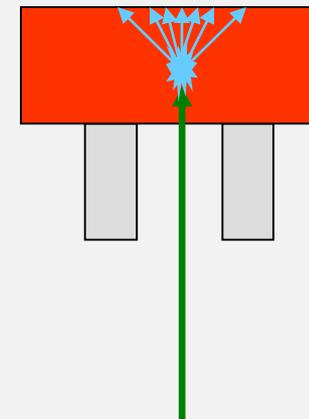
3. Photomultiplier tubes
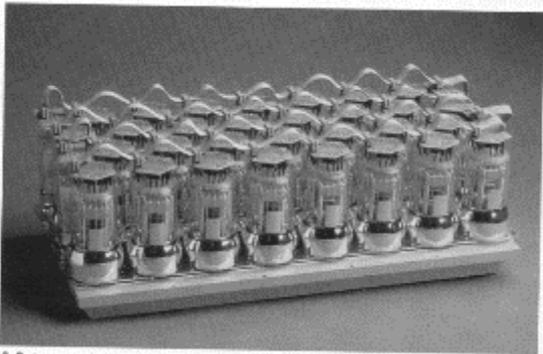
13-3. A rectangular gamma camera detector with the cover removed showing the photomultiplier tubes.
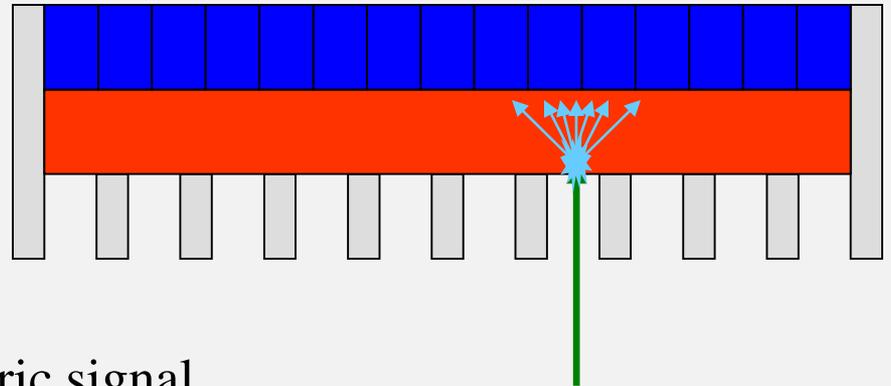

Transformation of light pulses to electric signal.

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.

γ-photon position

Light patch   PM tubes

positional output
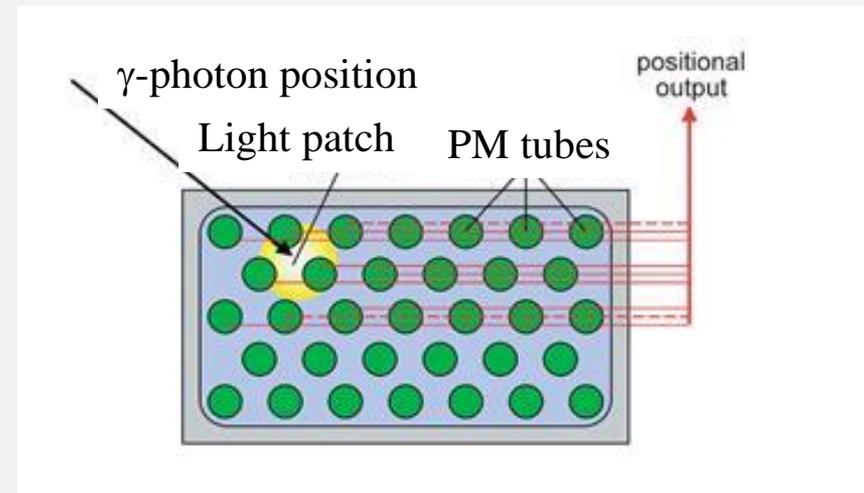
Pulse amplitude spectrum

Amplitude of an electric pulse generated by a γ-photon absorption in photoeffect is proportional to the photon energy.
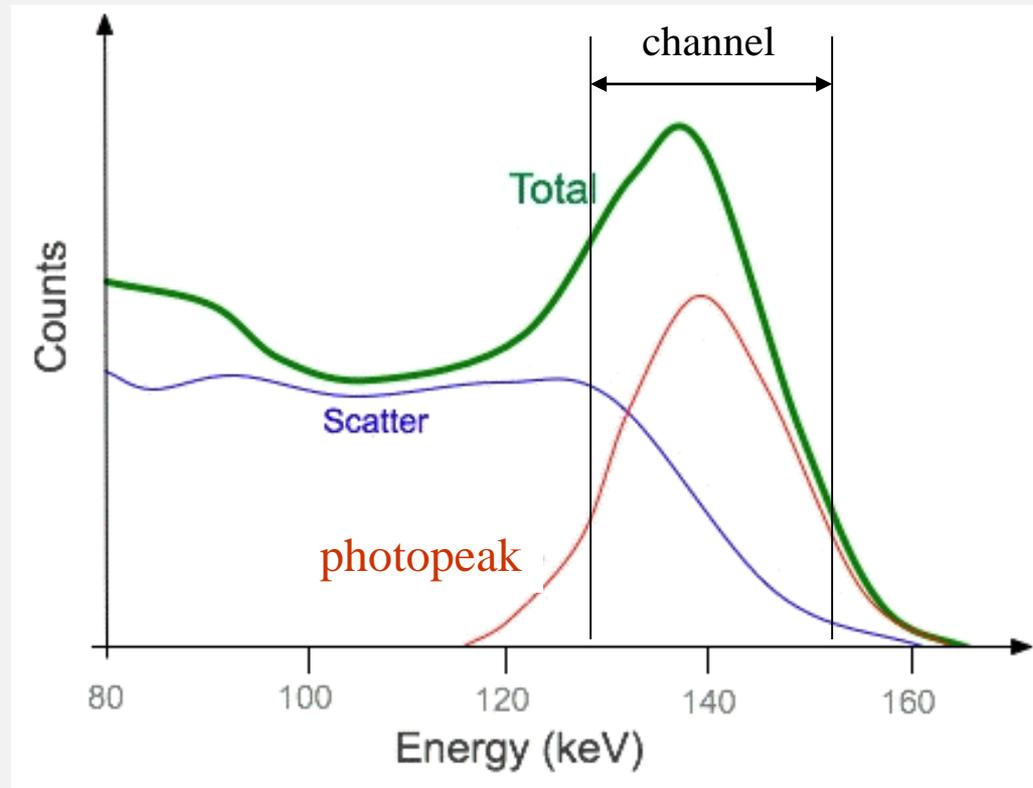

These electric pulses can be distinguished by discrimination (DD).

Pertechnetate (intravenous 80 MBq) distribution in thyroid glands

normal

struma diffusa

struma multinodularis
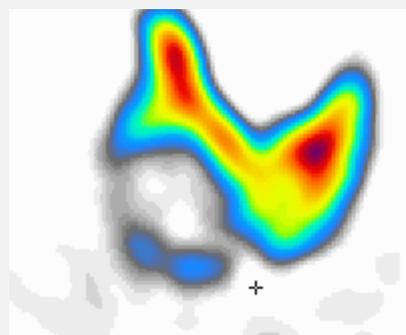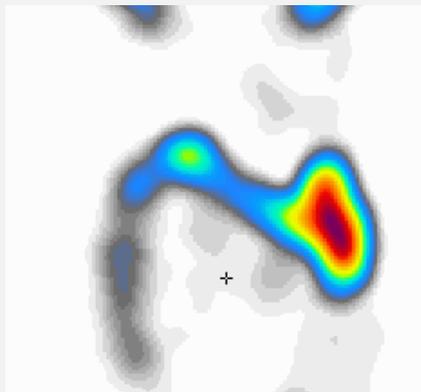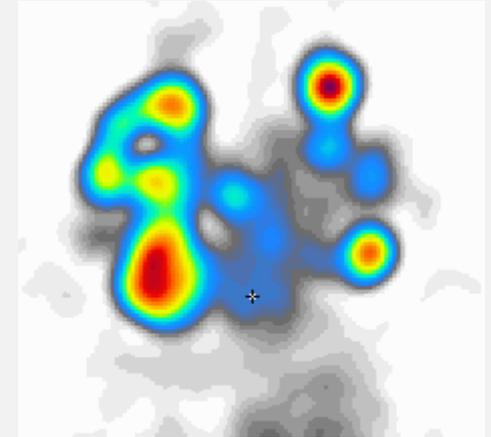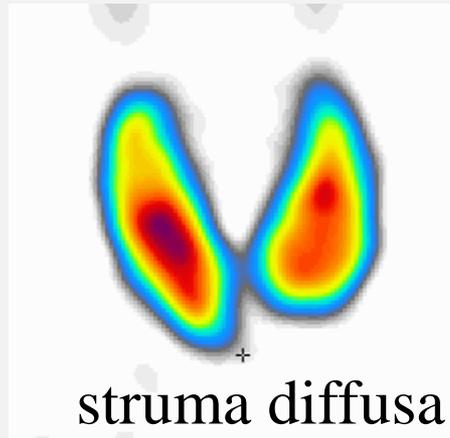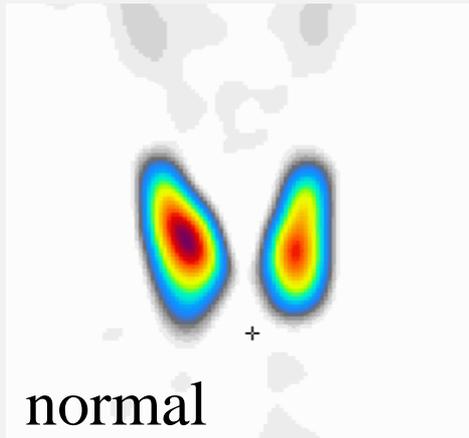
Cold nodules

Liver lesion nodules
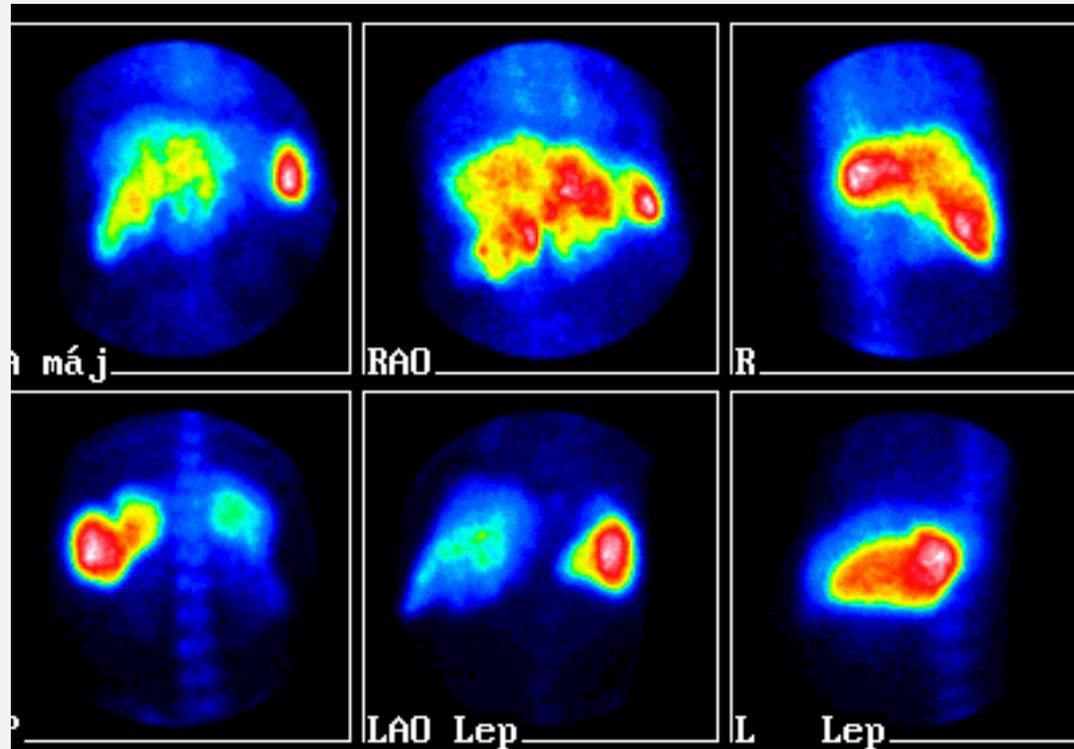
^{99m}Tc- fyton

Bone scintigraphy

^{99m}Tc-MDP: 600 MBq

normal

ANT 0

POST U   POST U   ANT 0   ANT 0
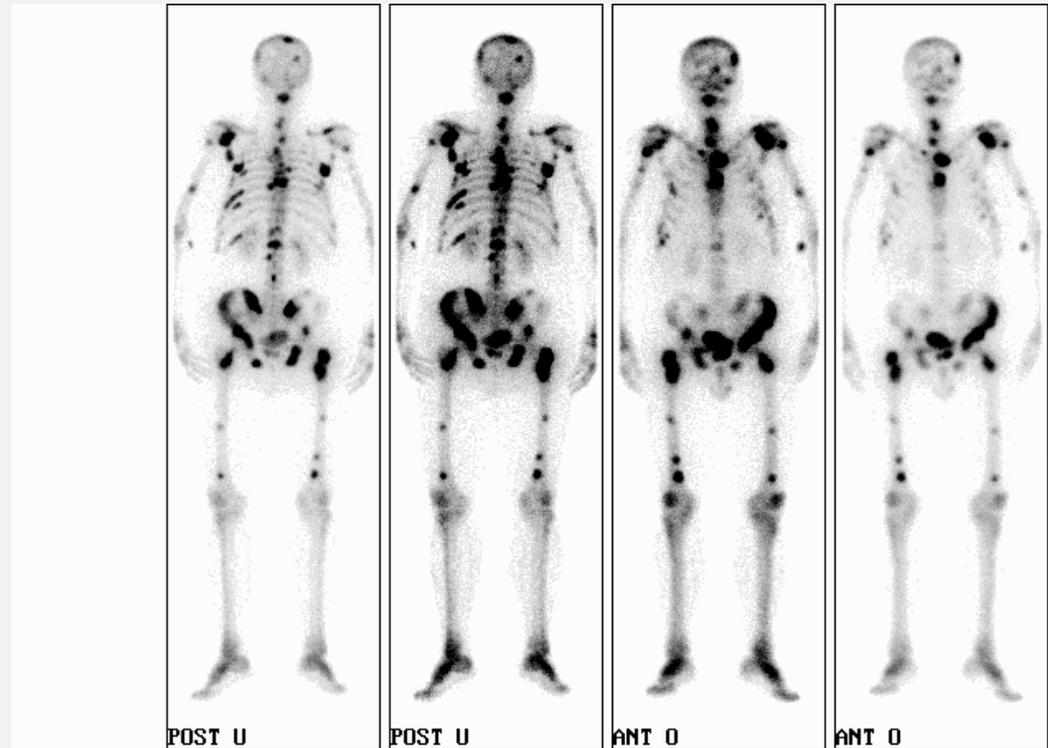
imaging bone metastases

Gamma camera image: summation image (2D)
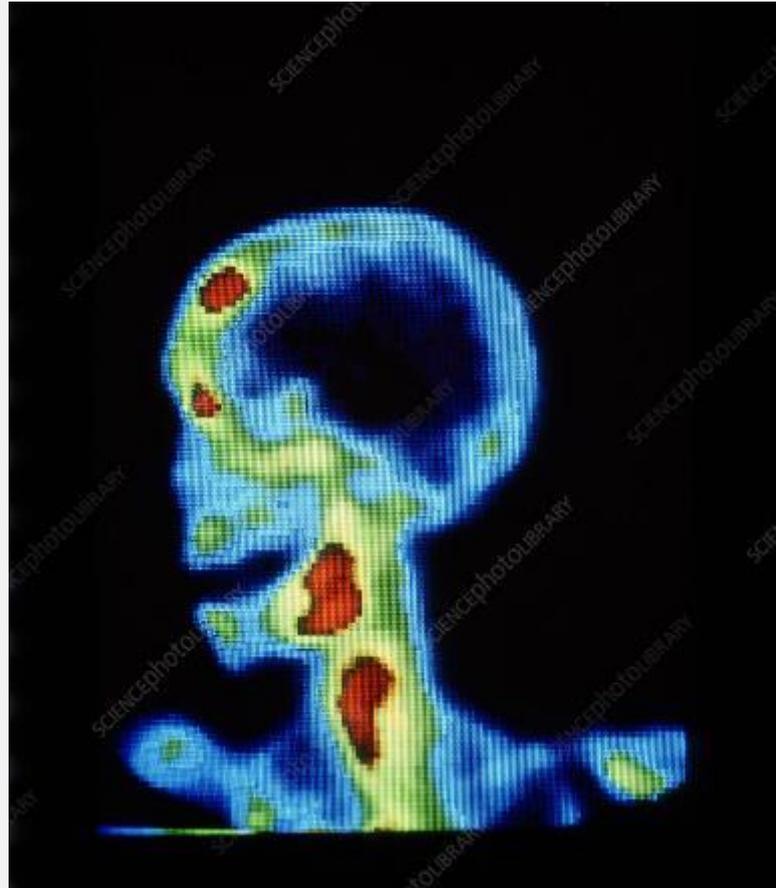
For depth / **3D** resolution: tomographic device is necessary

# 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
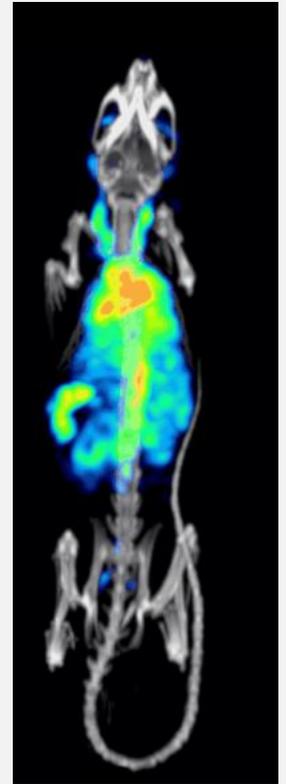
SPECT

SPECT – images of scalp

^{99m}Tc- HMPAO

technetium ^{99m}-hexamethylpropyleneamine oxime

diagnosis of brain death
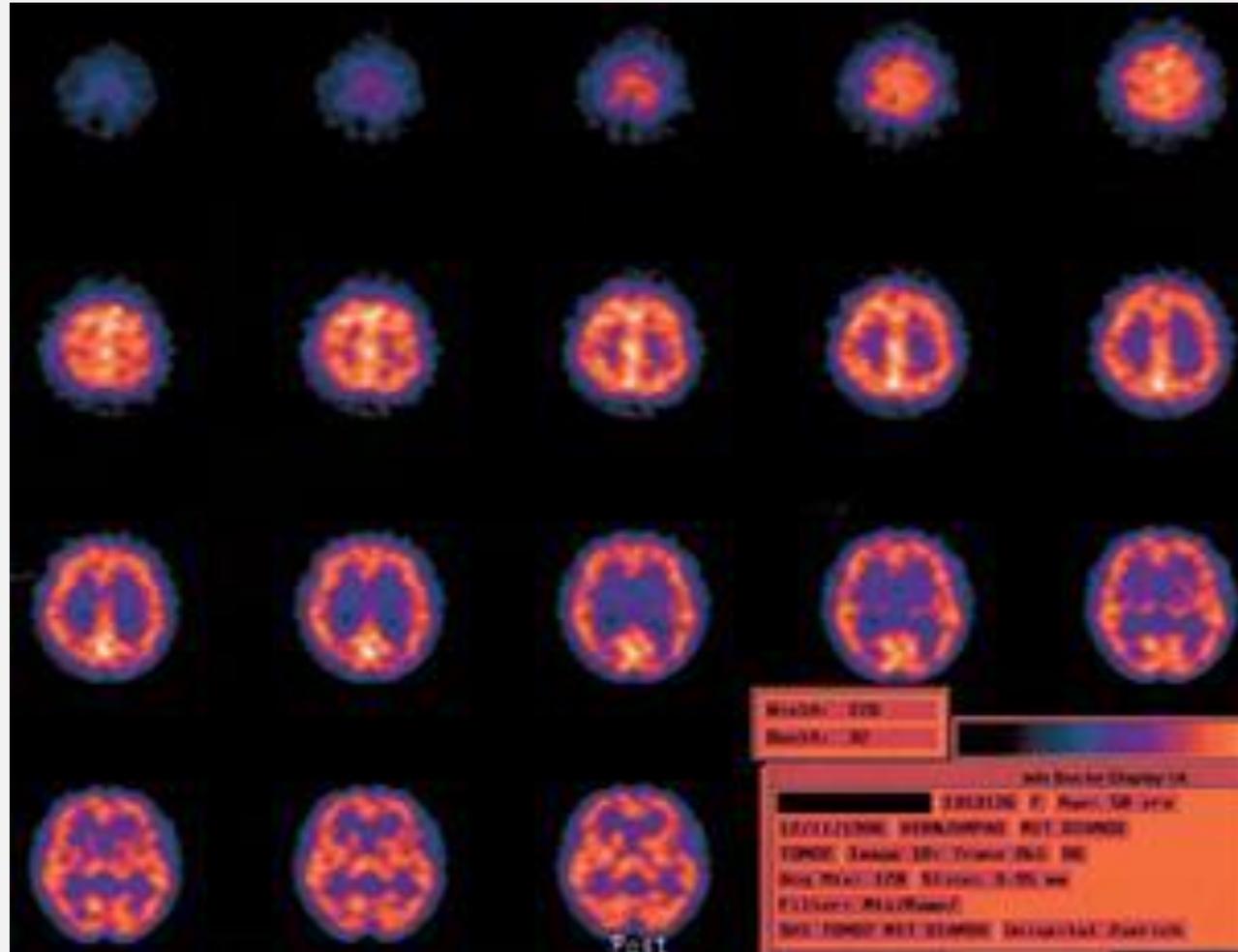
PET – Positron Emission Tomography

coincidence processing unit

dataprocessing

image reconstruction

Annihilation

Coincidence detection

Isotope distribution

annihilation

Channel 1

Channel 2

Summed channel

Coincidence events

Coincidence detection

Ring of detector elements
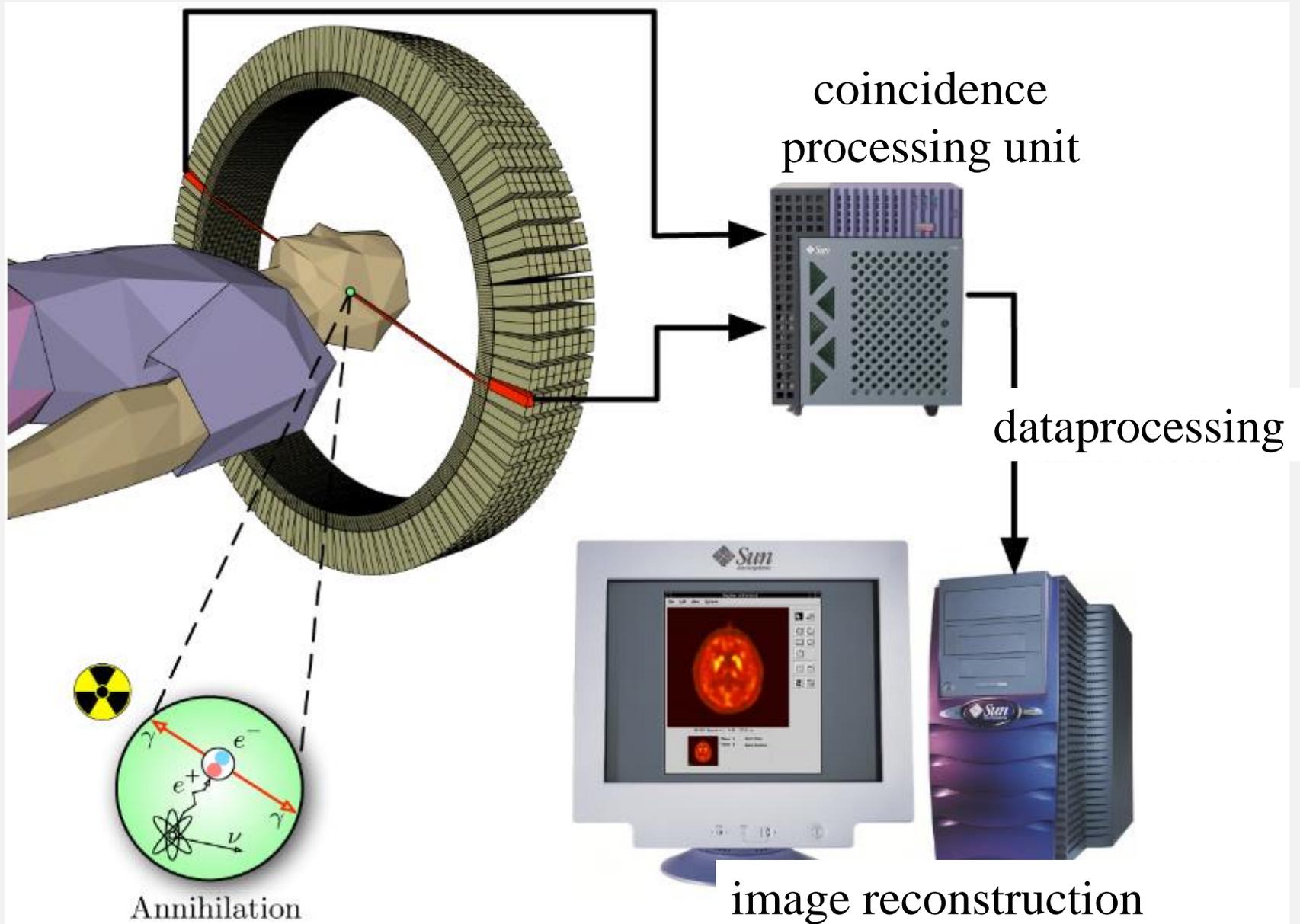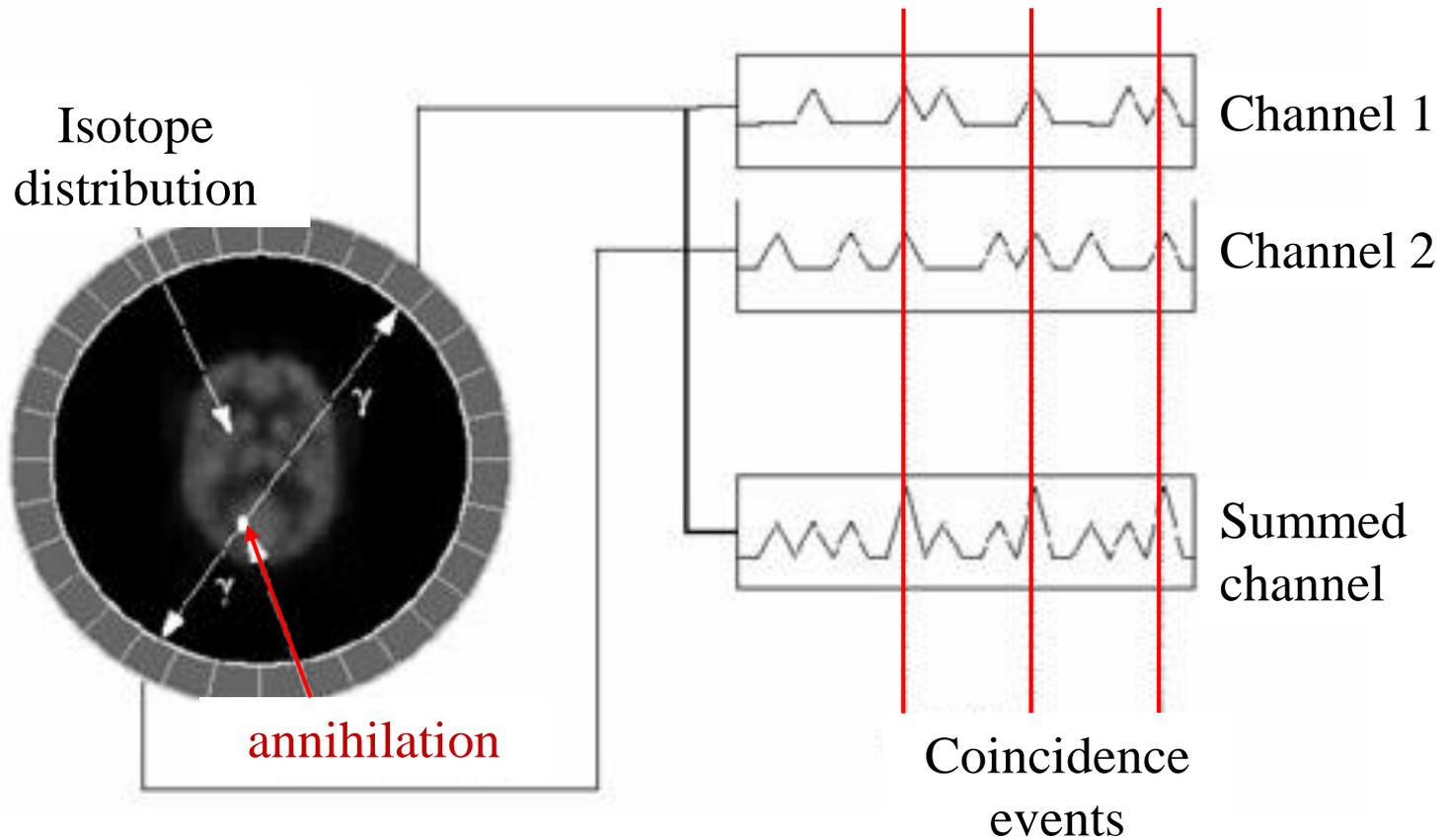
Annihilation event
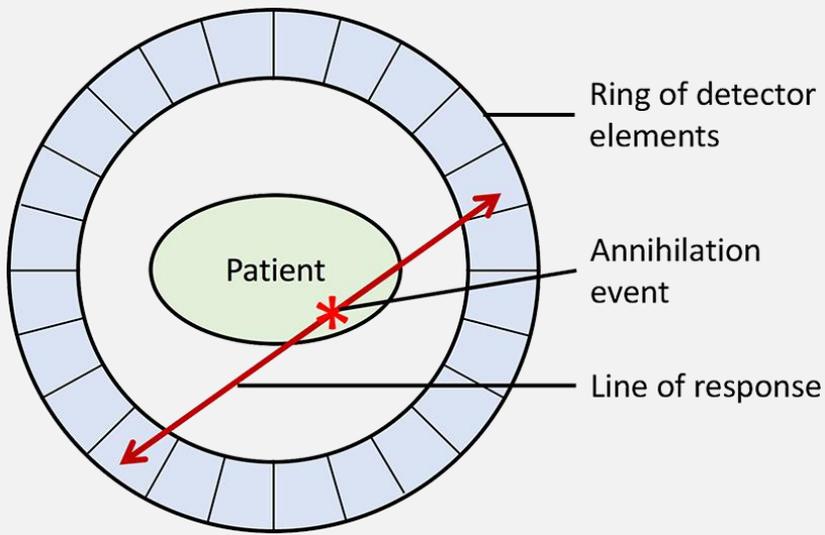
Line of response

↔ Annihilation path

- - - Calculated line of response

Patient

511 keV photon

Annihilation reaction

β+ + e-

Electron from material in body

Positron decay releases positron

511 keV photon

True coincidence

Patient
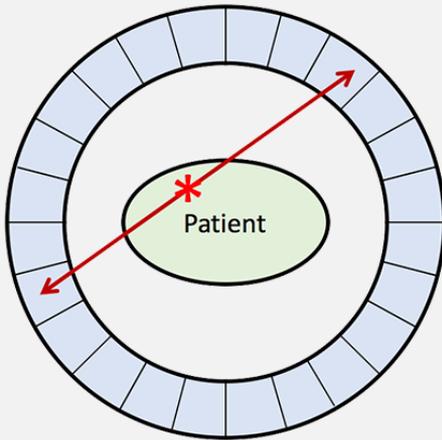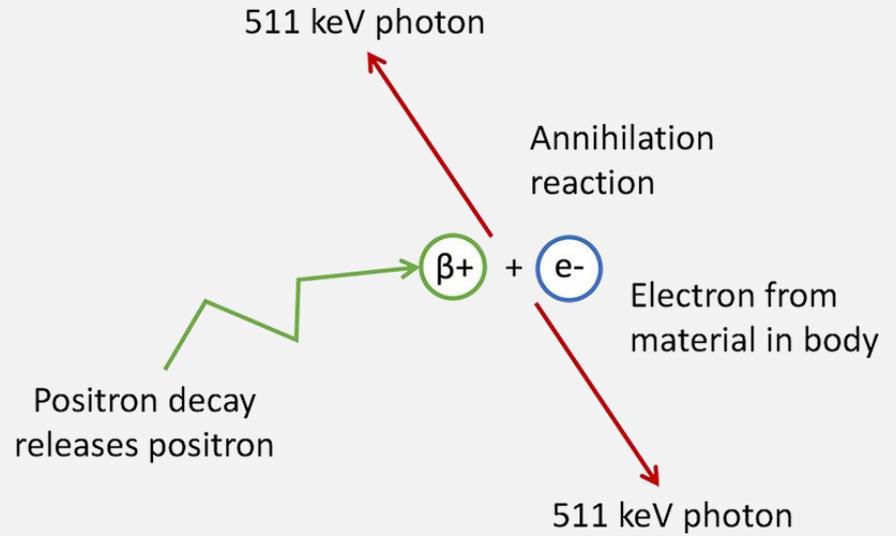
- One annihilation
- Straight path photons in opposite directions
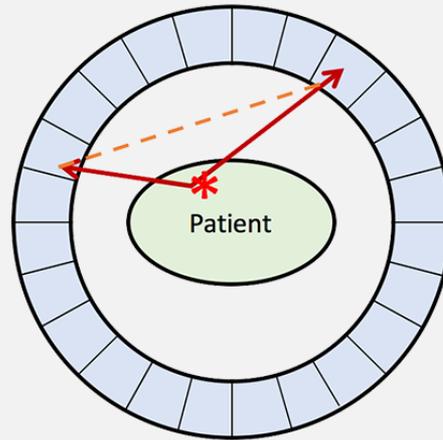
Scatter coincidence

Patient

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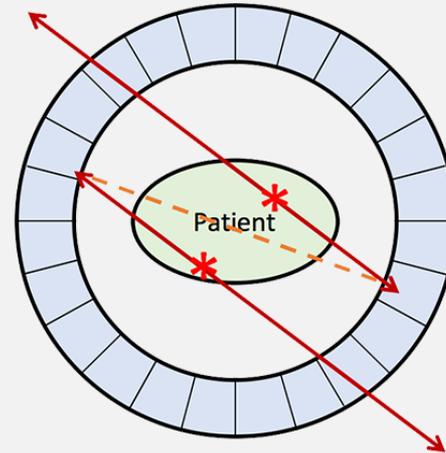
Random coincidence

Patient

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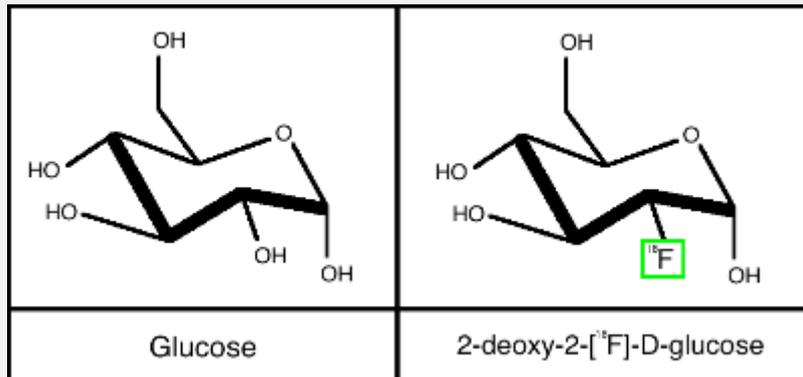
Isotope manufacturing must be nearby the site of application (see half-lives).

[^{18}F]-fluorodeoxyglucose (FDG) – showing glucose metabolism
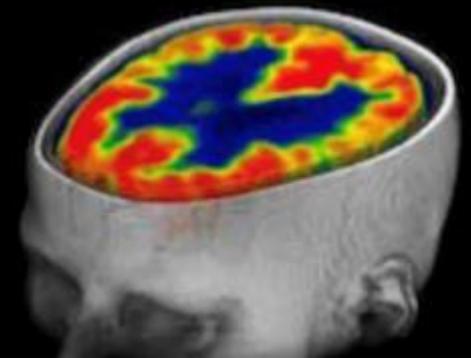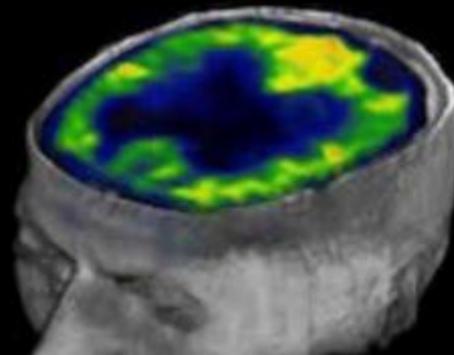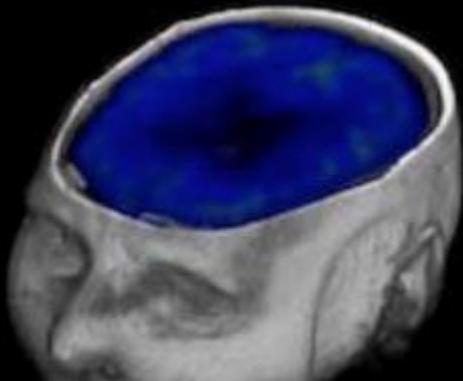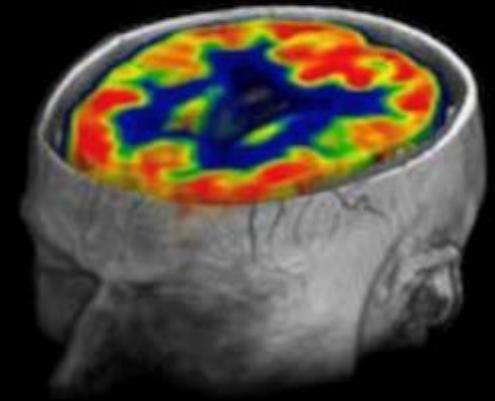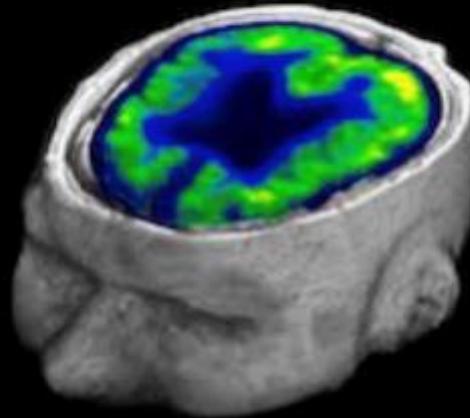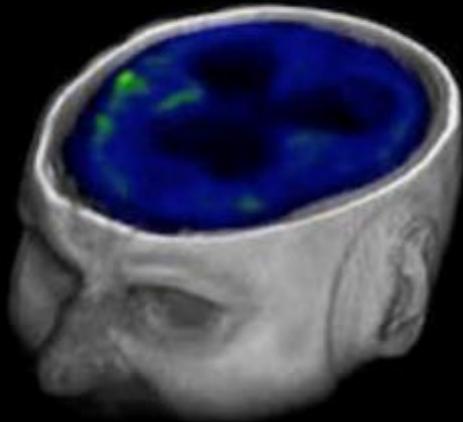
Global cerebral metabolic rate of glucose as an indicator of consciousness. 42% of normal cortical activity represents the minimal energetic requirement for the presence of conscious awareness (middle).

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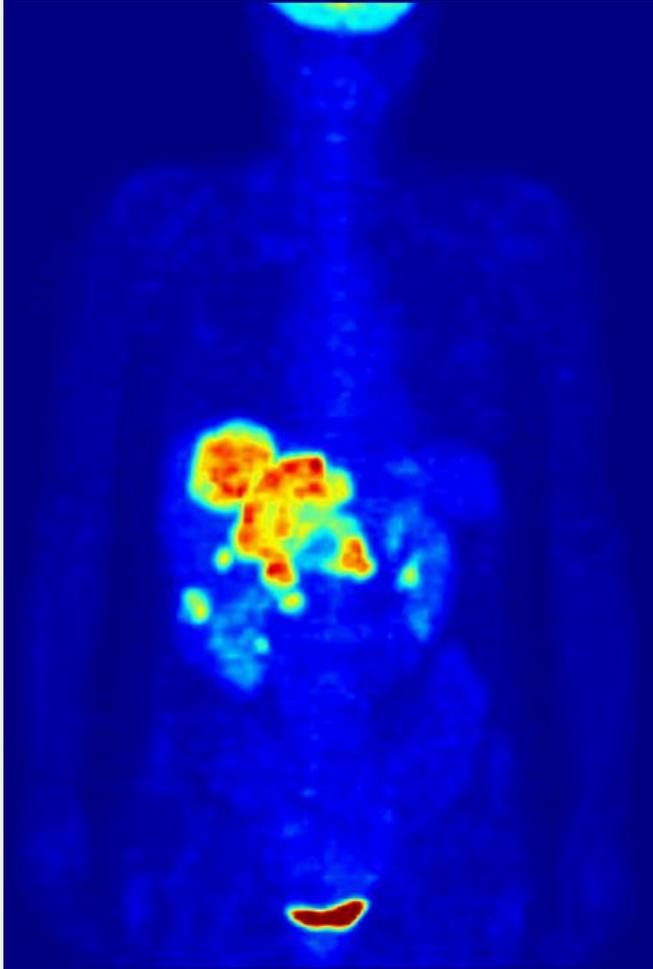
3D reconstruction of tissue metabolic activity from a [^{18}F]-FDG PET scan. Notably, we see increased activity along the chest walls, indicating carcinoma, as well as the supraclavicular fossa.

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

| PET | CT | PET/CT |

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?
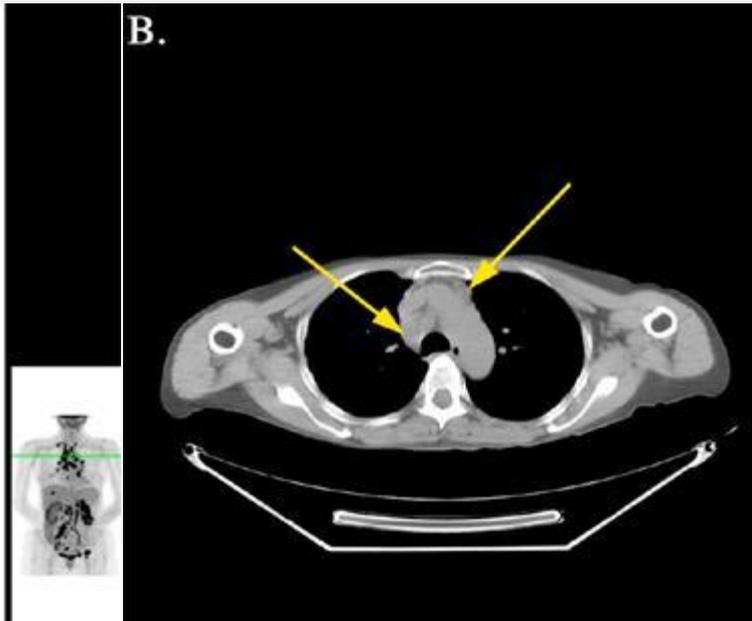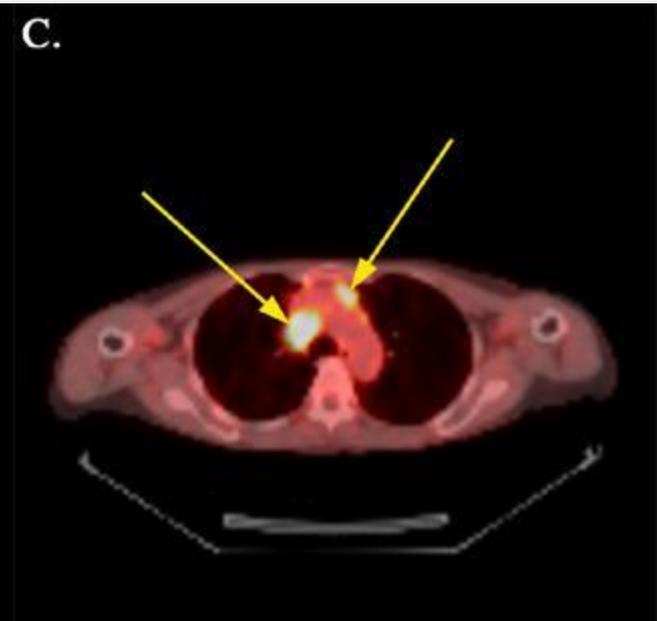
Cheklist

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