

# Biophysics I

## 14. Clinical applications of nuclear radiations

Károly LILIOM

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`liliom.karoly@semmelweis.hu`  
**`karoly.liliom.mta@gmail.com`**

# 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

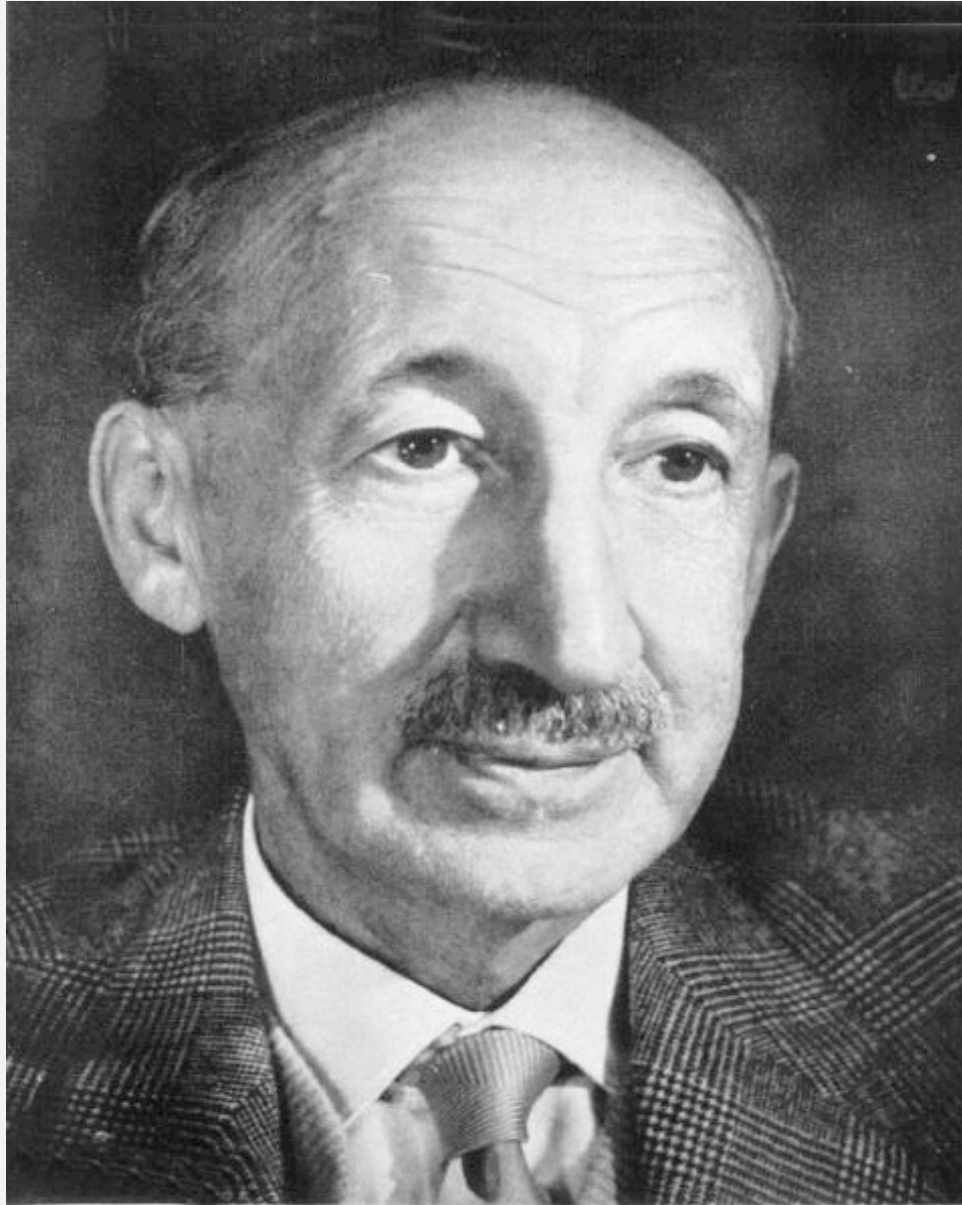


*differences according to the different physical properties of tissues*

**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**

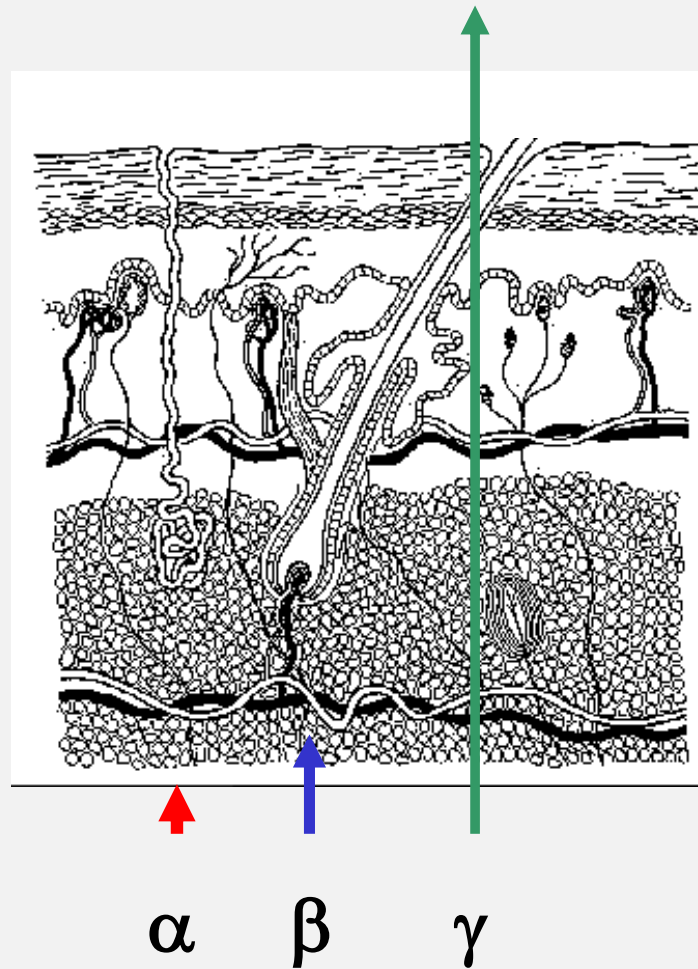
# The choice of the appropriate radioisotope for nuclear imaging

Maximize the information – Minimize the risk

For that find the optimal

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

## Type of radiation



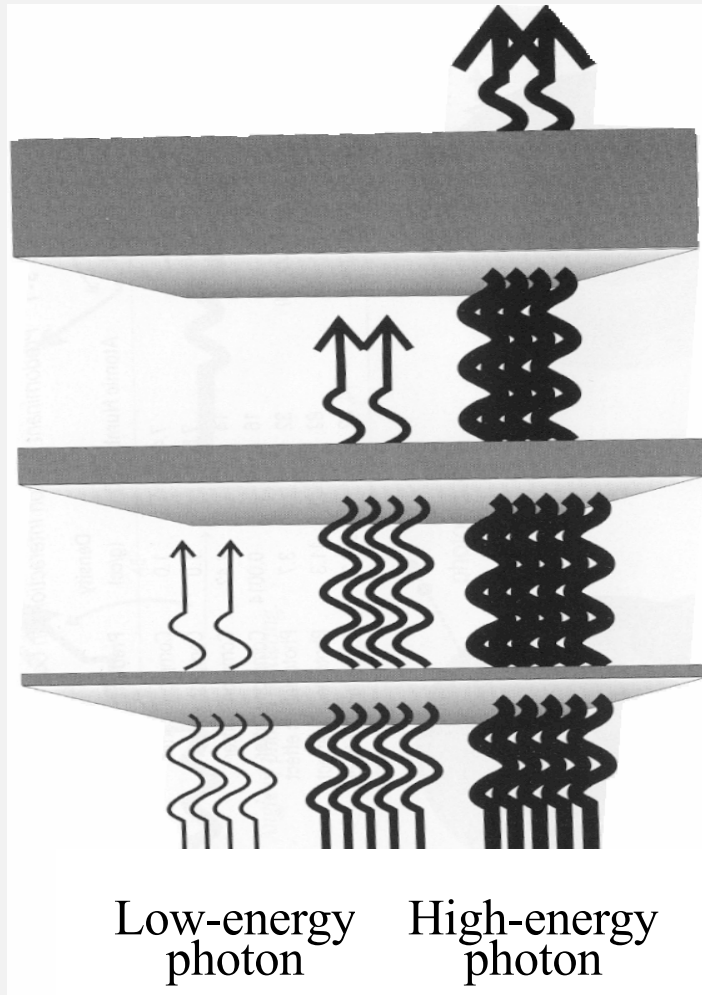
decay via photon emission  
to minimize absorption  
effects in body tissue

only  **$\gamma$ -radiation** has  
sufficient penetration  
depth

*purely gamma-emitting isotope is preferable*

**photon energy**

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



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

BUT

must have not too high energy to be measured 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

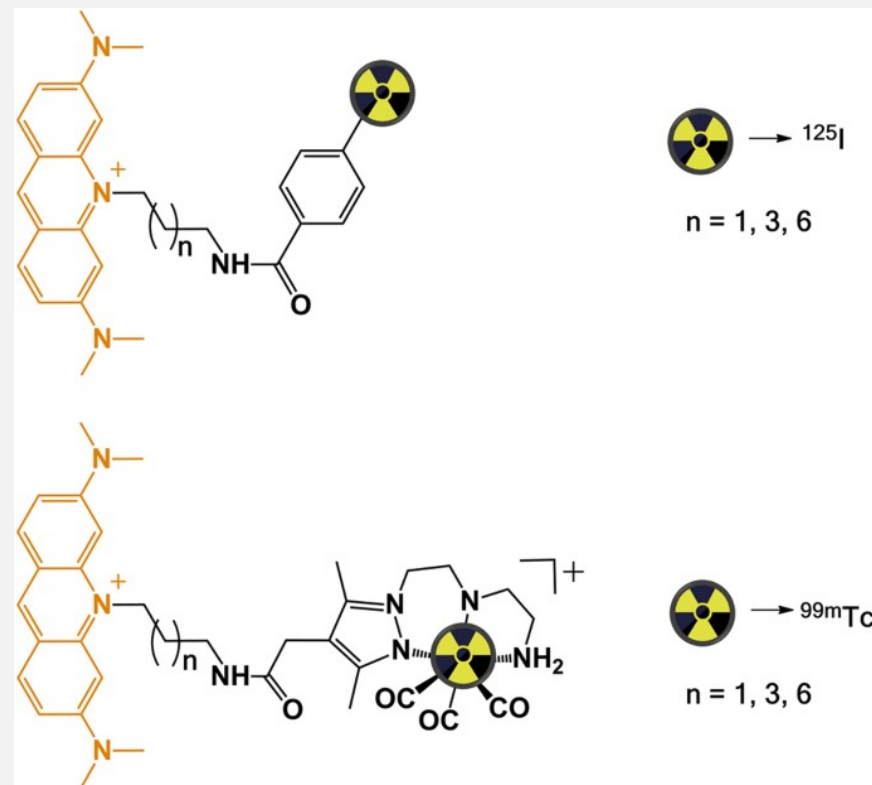
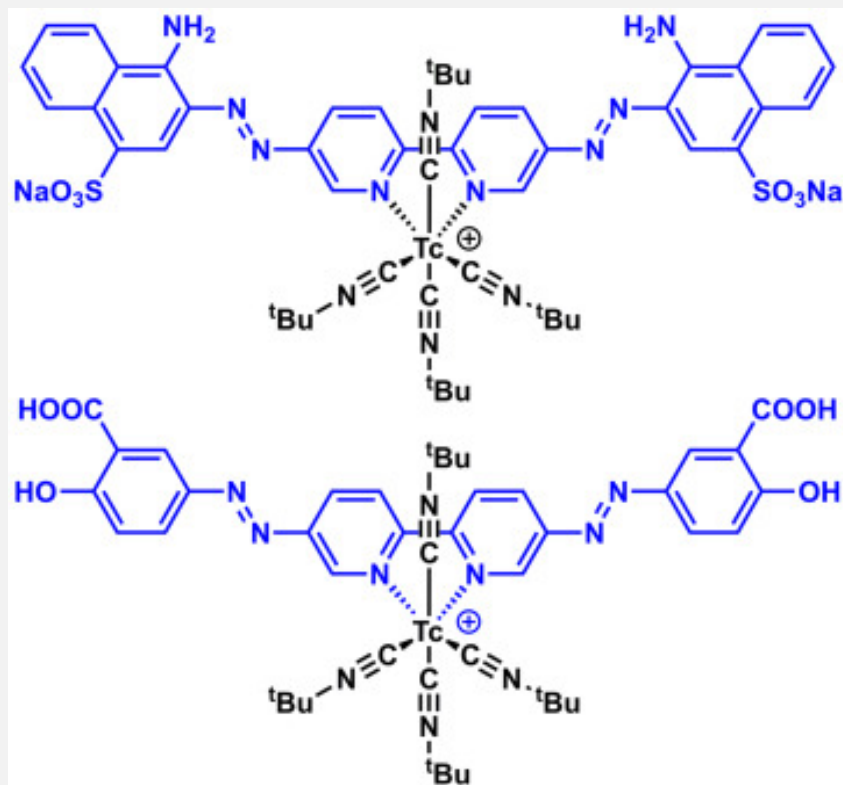
smaller is better  
dose considerations for  
patients

**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.

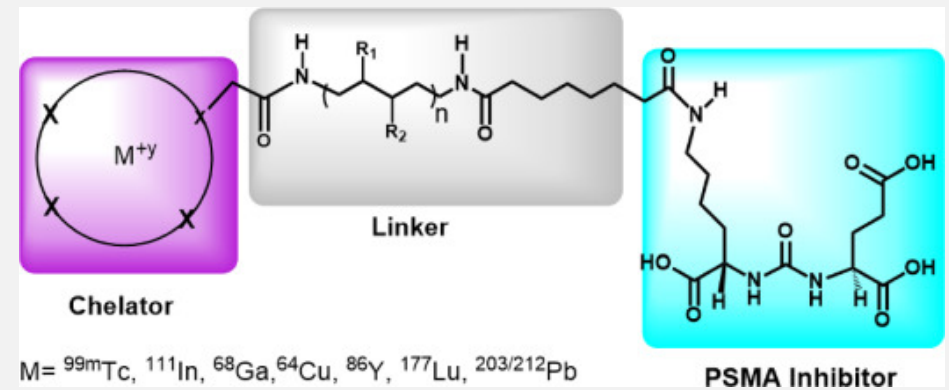


Basic requirements:

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

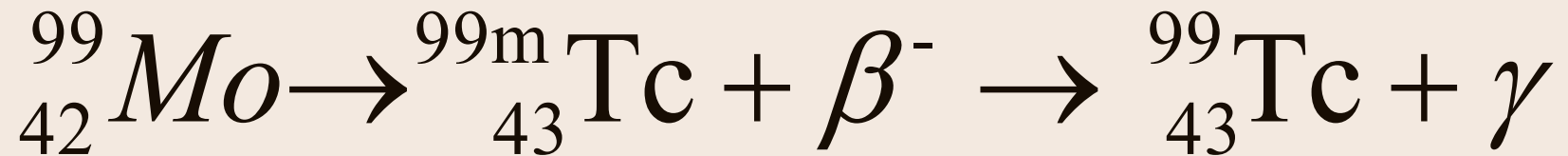
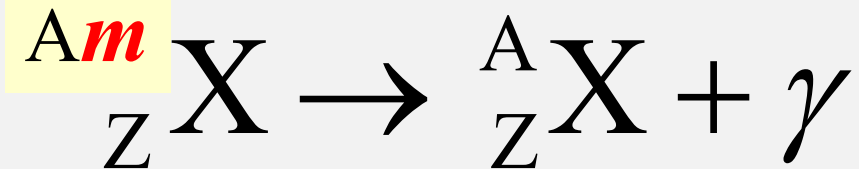
# Factors responsible for ADME-TOX

- 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, charge, hydrophobicity, etc...



# Gamma-emitting isotopes

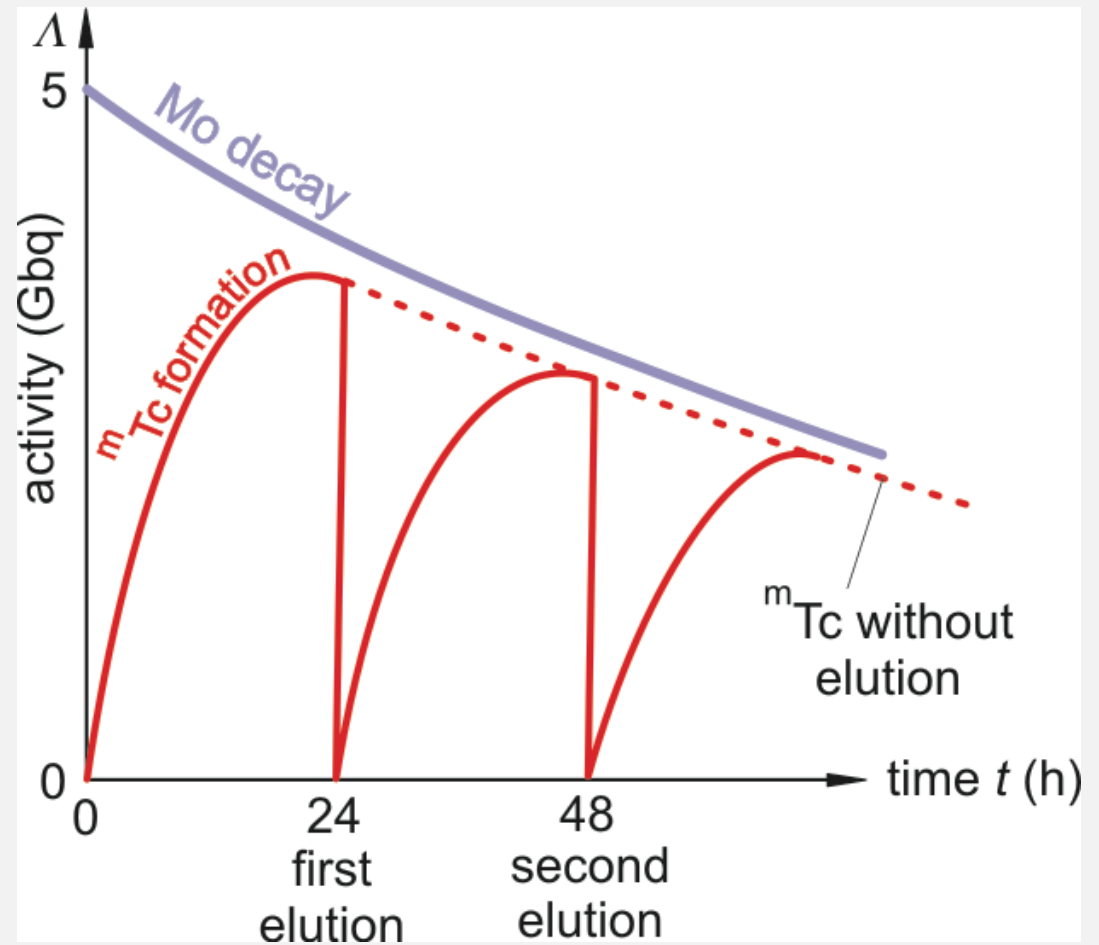
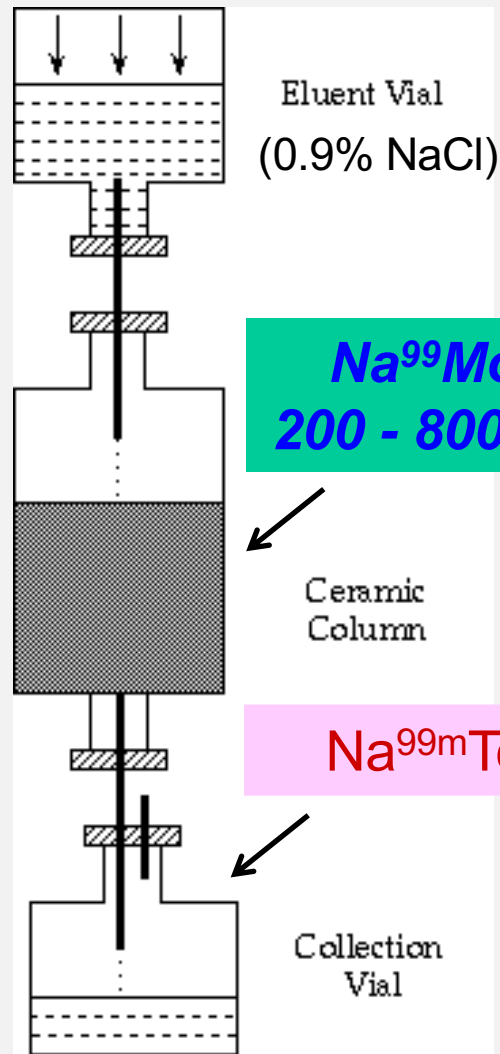
Isomeric transition: some excited states may have half-life ranging from hours up to more than 600 years



$T_{1/2}=67$  hours

$T_{1/2}=6$  hours

# Technetium-99m generator



## examples

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

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# 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 over time

Time-laps video – series of static recordings

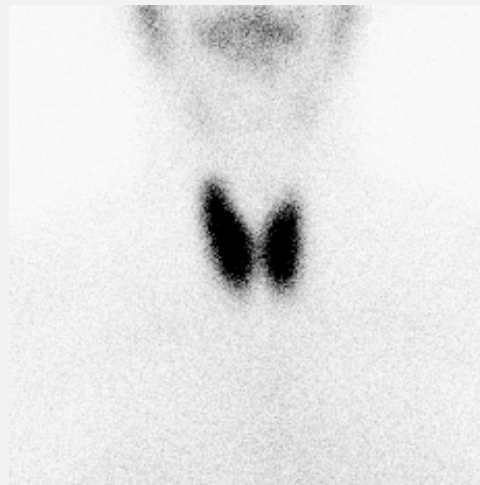
## Emission CT

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

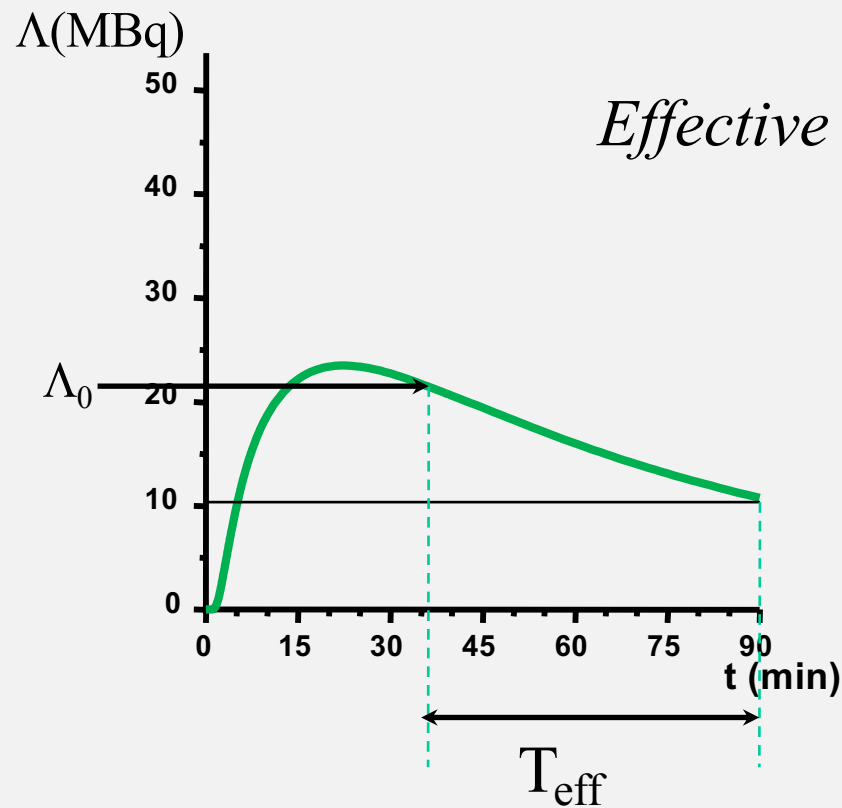


kidneys

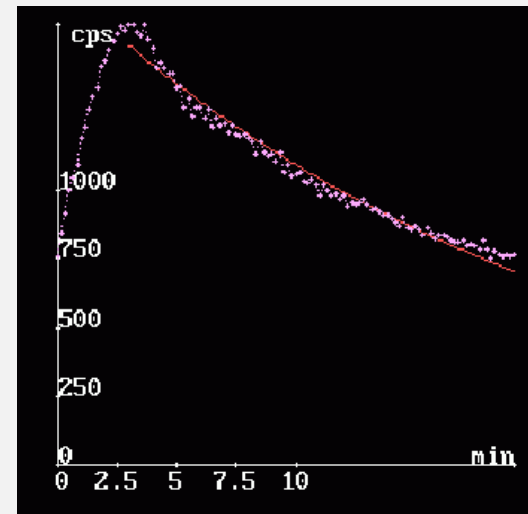
Isotope accumulation in

# Types of images

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

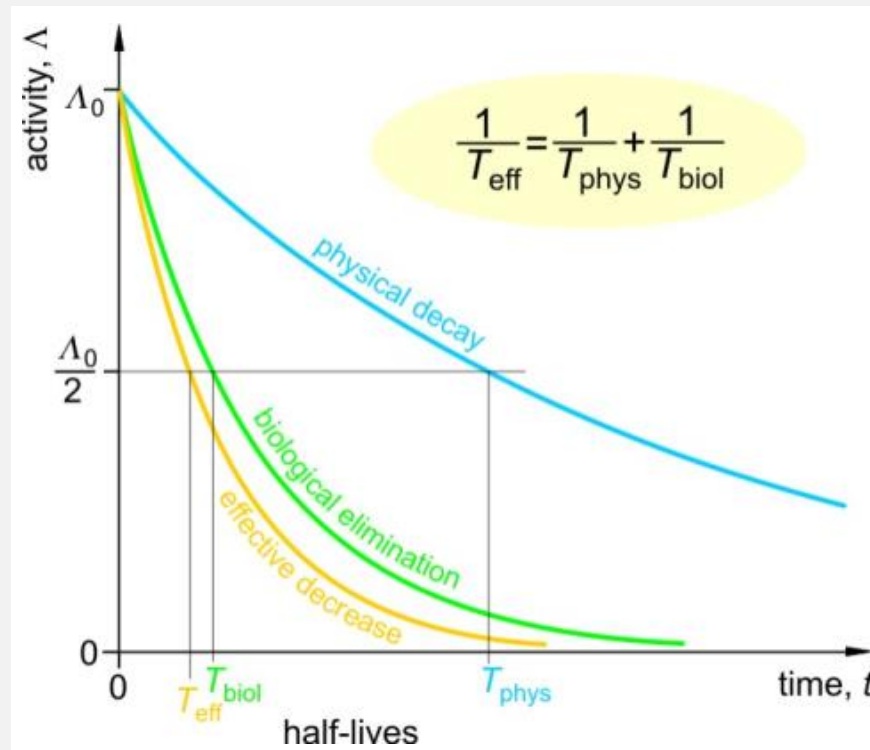


*Effective half-life* – activity decreases by half in the target organ



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

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

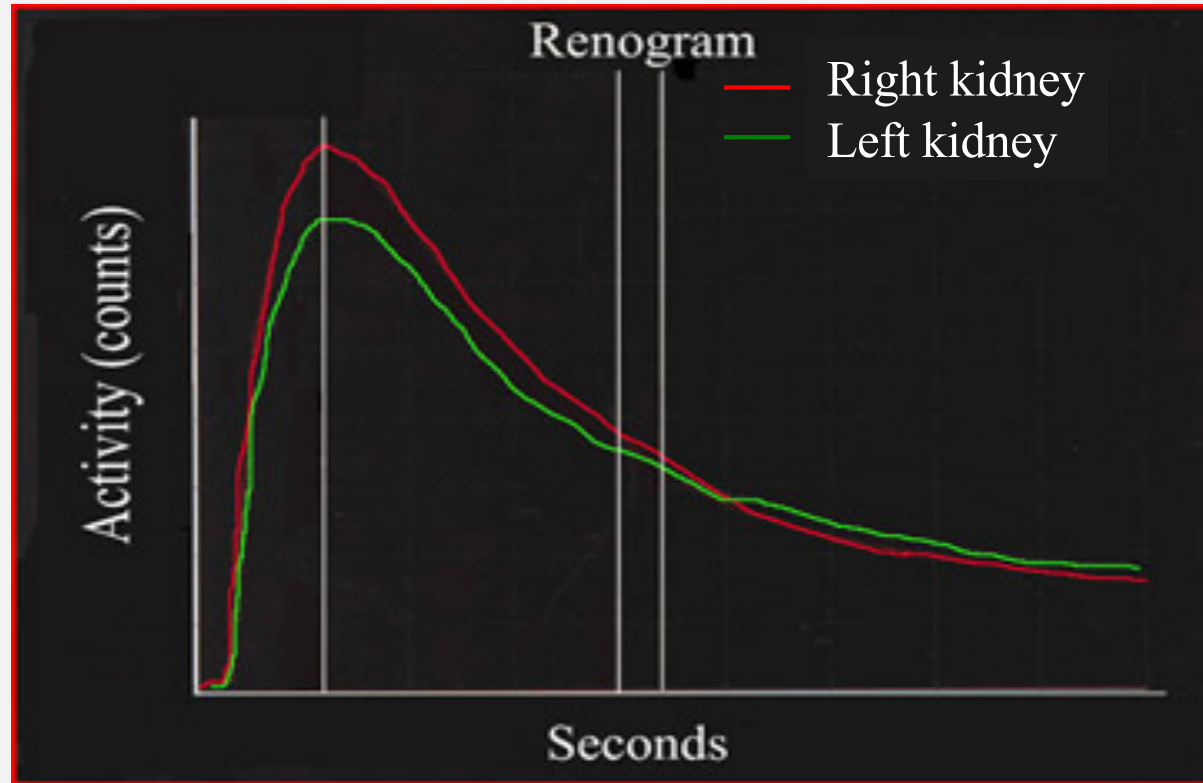


$$\lambda_{\text{effective}} = \lambda_{\text{phys}} + \lambda_{\text{biol}}$$

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

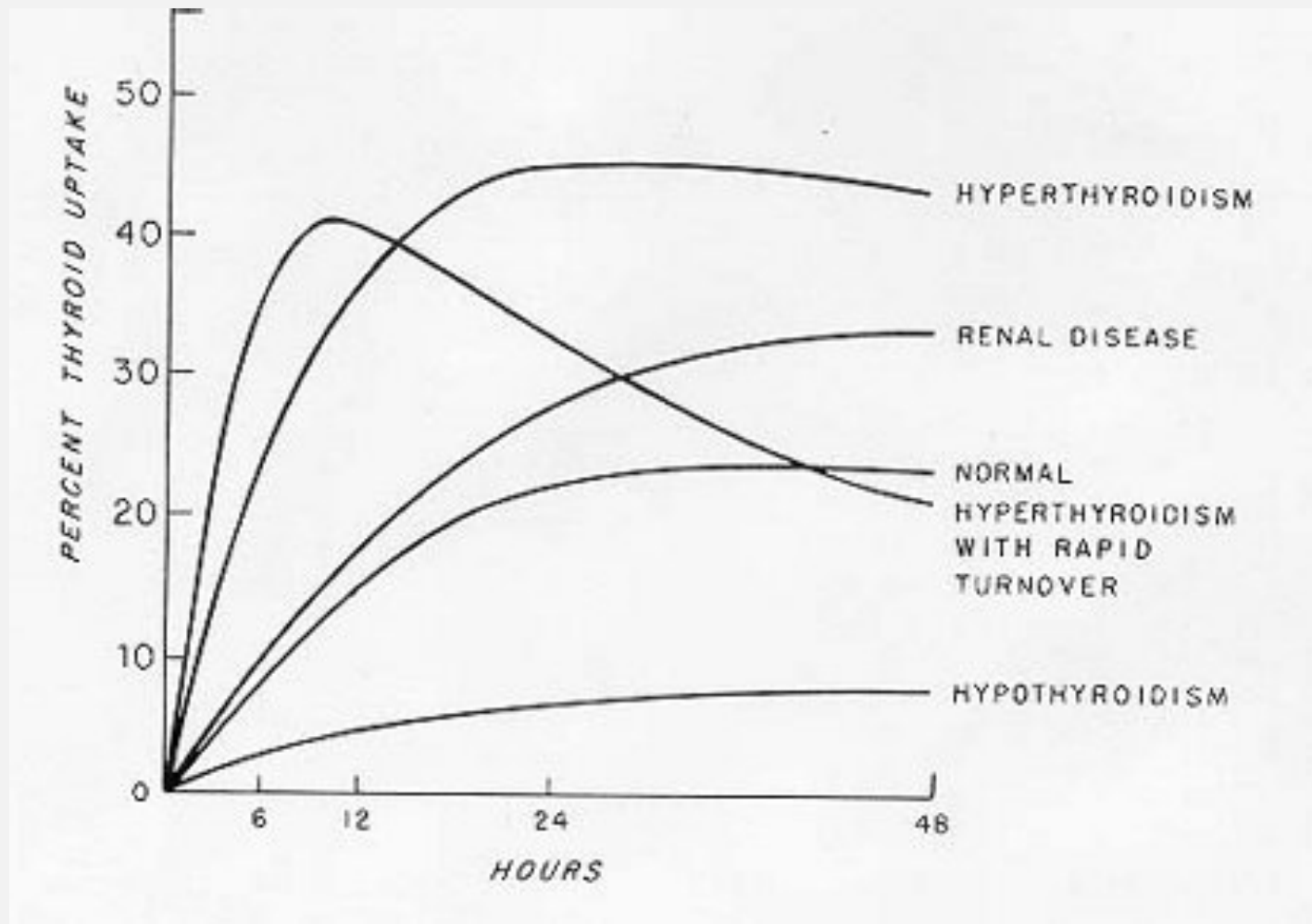
The final fate of the radiotracer depends on how the addressed organ deals with the molecule, whether it is absorbed, broken down by intracellular chemical processes or whether it exits from the cells and is removed by kidney or liver. These processes determine the **biological half-life**  $T_{biol}$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

example



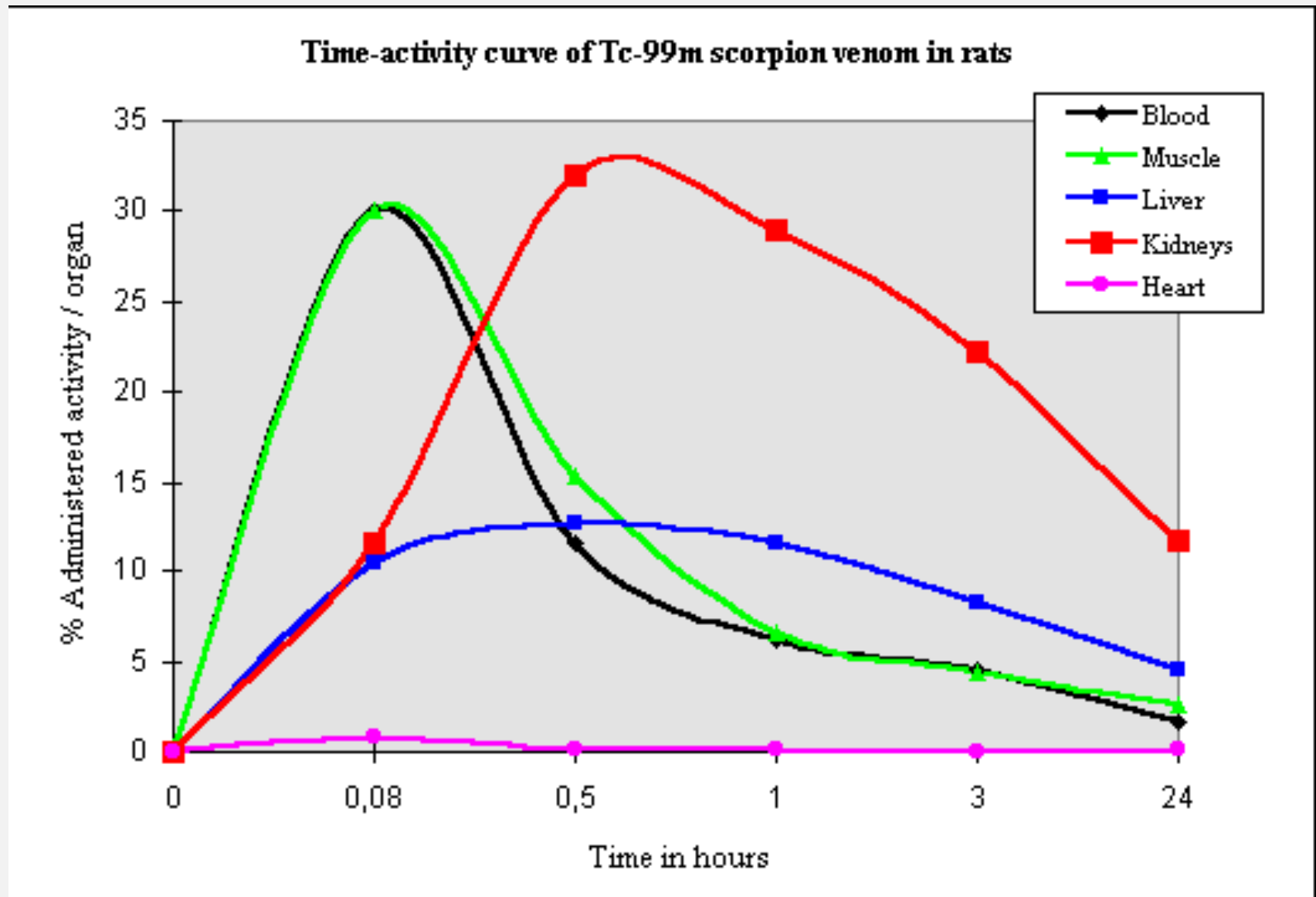
Isotope accumulation traces of kidney.

example



Thyroid glands' isotope accumulation traces

# Pulse-chase experiments



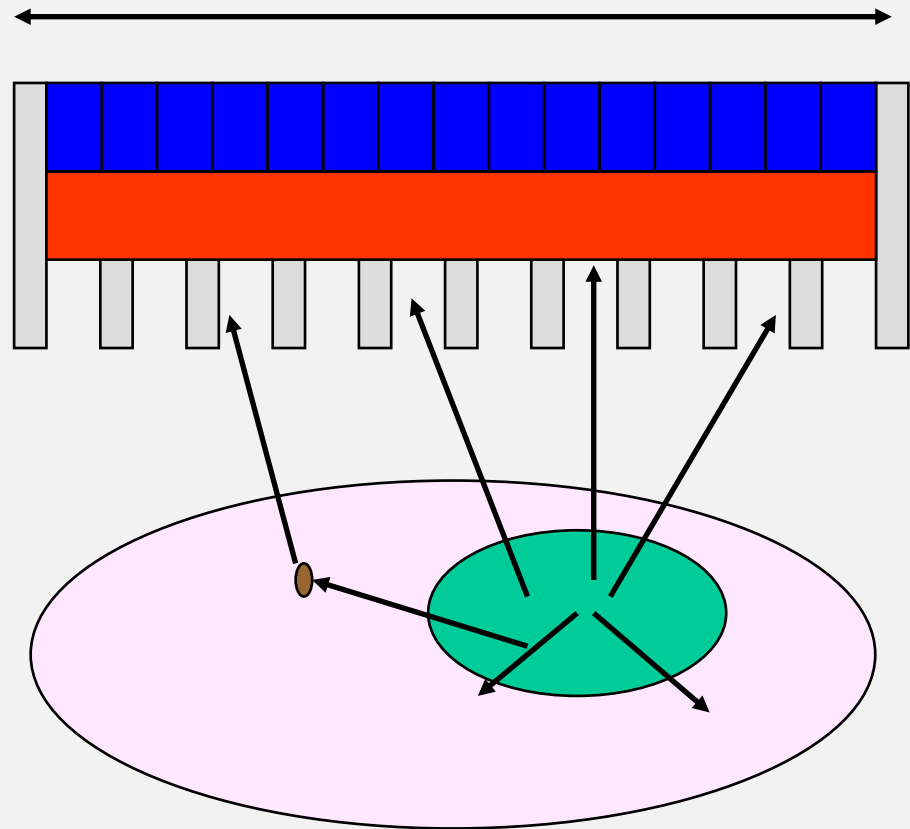


Hal Anger  
1920-2005

# Gamma camera

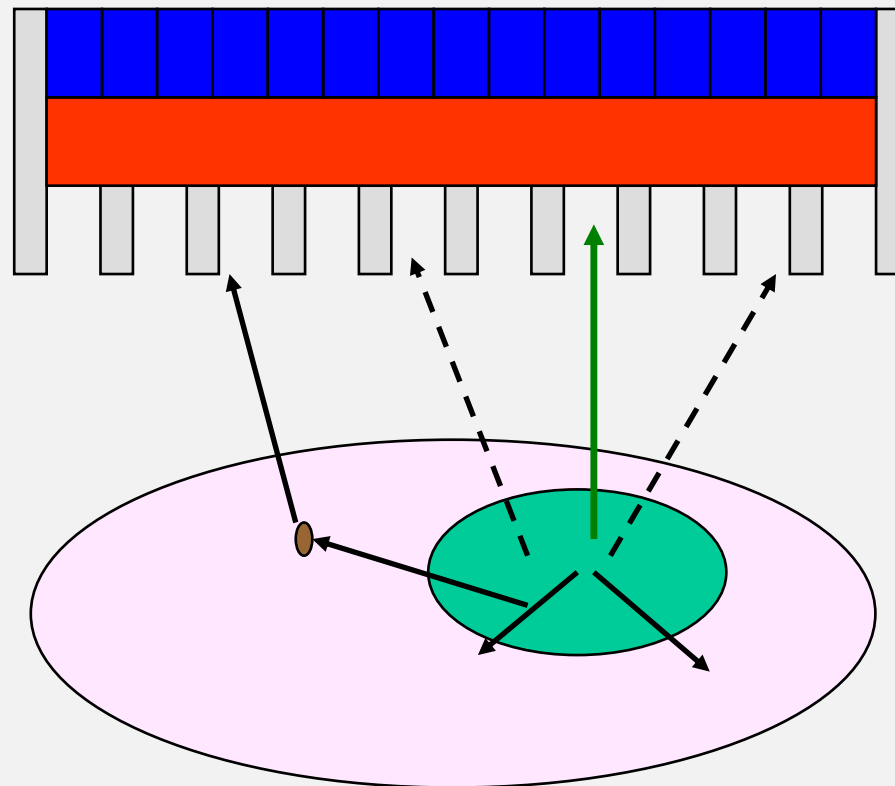
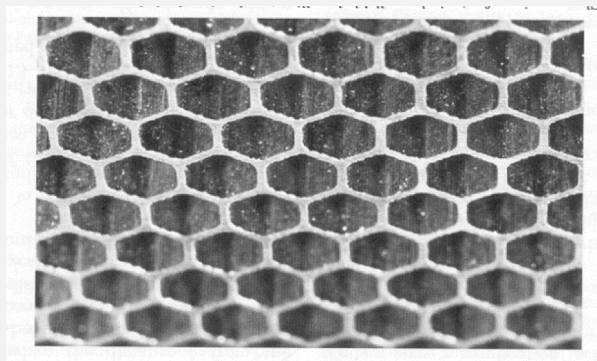
cc 40 cm

Photomultiplier tubes →  
Scintillation crystal →  
Collimator →



A radioactive source emits gamma photons in all directions.

collimator

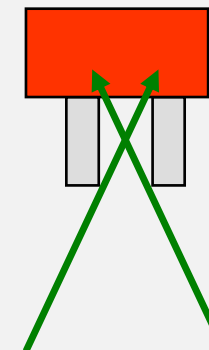


Collimators are composed of thousands of precisely aligned channels made of lead.

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

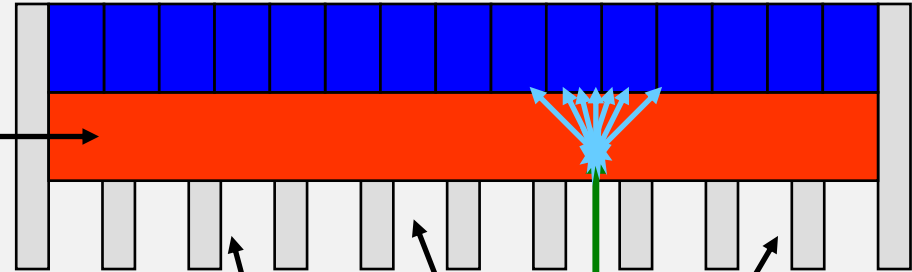
Photons emitted in other directions are absorbed by the septa between the holes.

Size and geometry of holes determine resolution.



# Scintillation crystal

NaI(Tl)



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

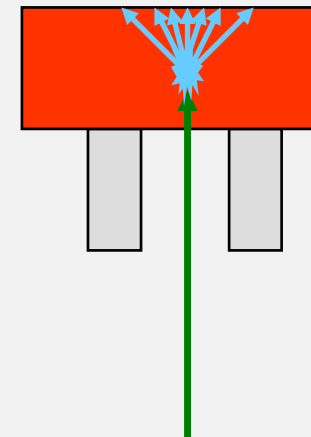
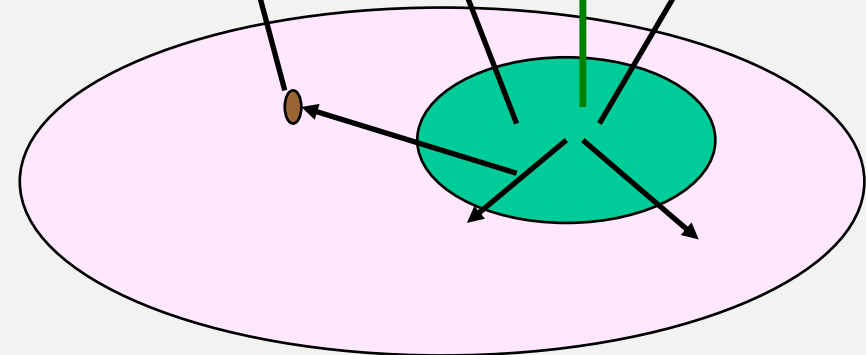
Proper wavelength – 415 nm – for  
PM photocathode

Problems with NaI:

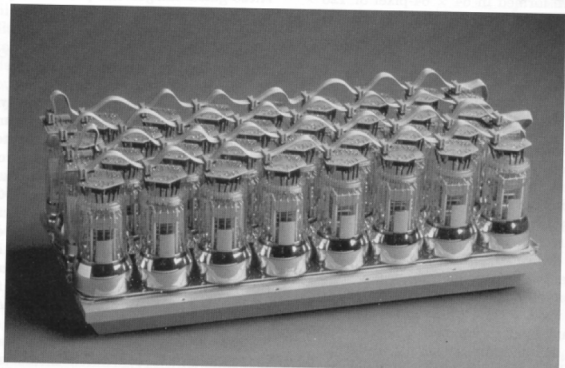
fragile

temperature sensitive

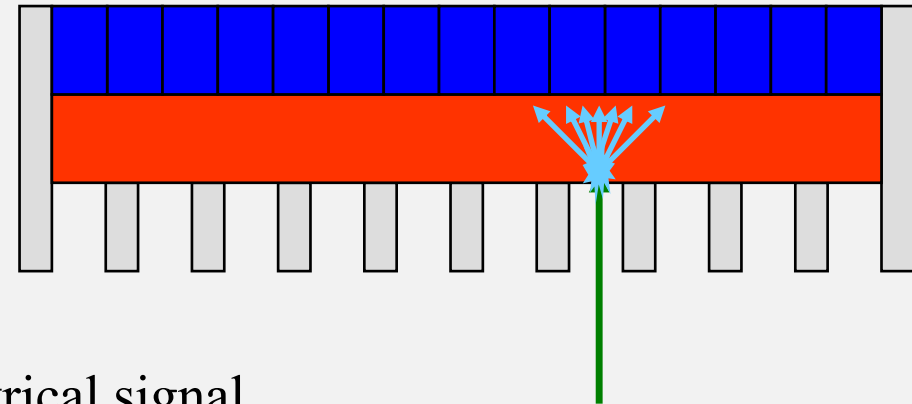
hygroscopic



# Photomultiplier tubes



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

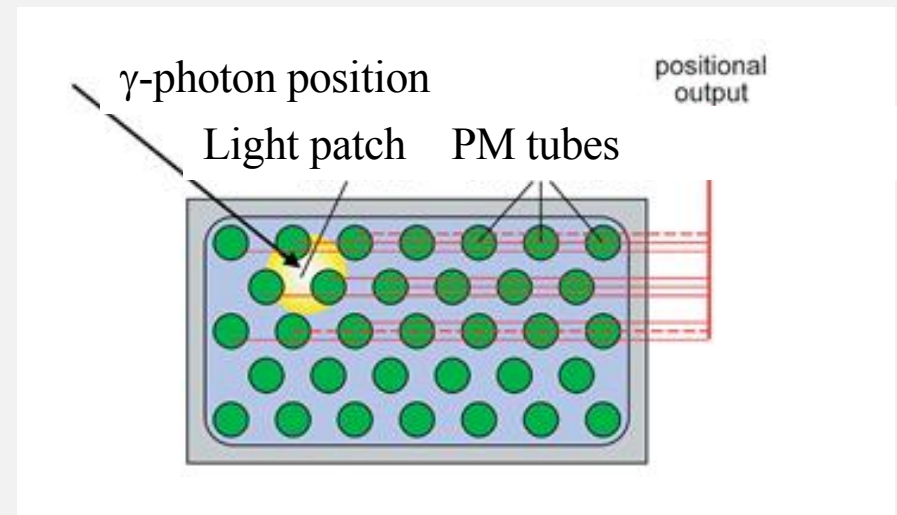


Transformation of light pulses to electrical signal.

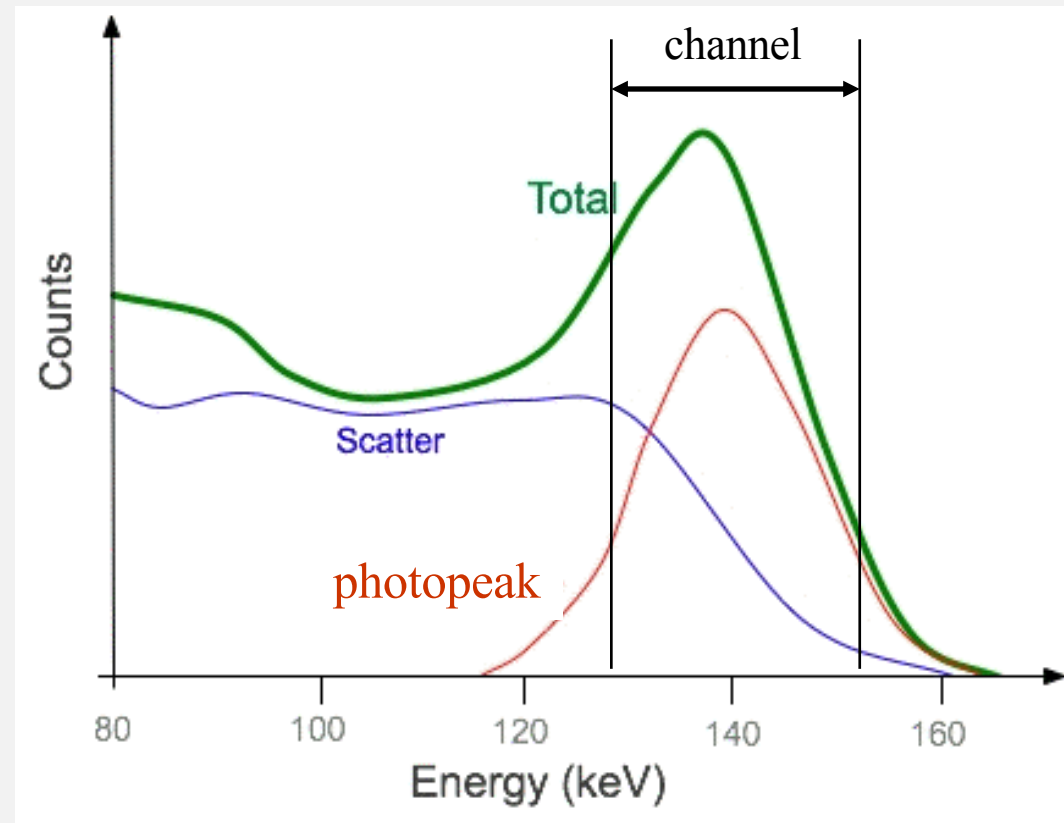
Typically 37-91 tubes, 5.1-7.6 cm diameter each

Amplitude of electric pulses varies in a wide range, because

- absorption of one  $\gamma$ -photon induces electric signals in more than one tubes,
- attenuation mechanism can be photoeffect and Compton-scattering.

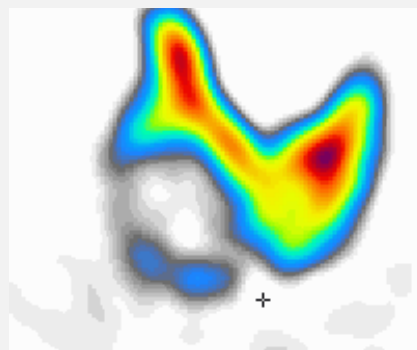
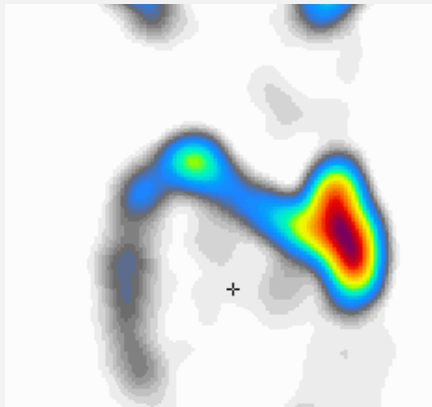
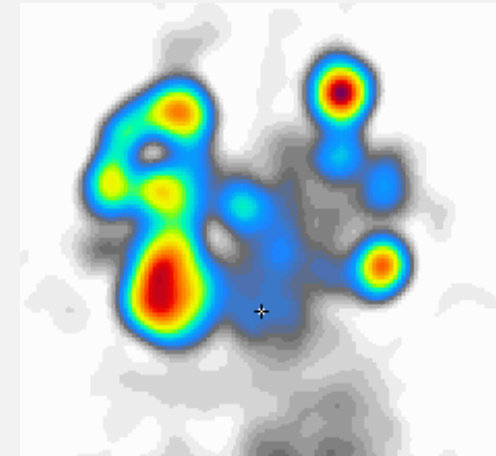
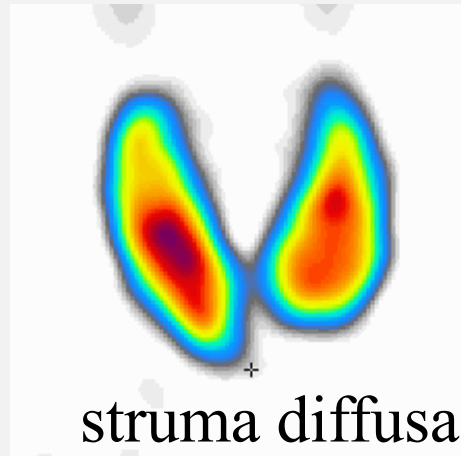
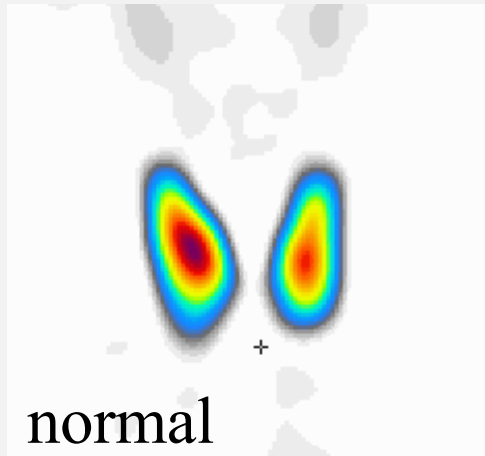


Pulse amplitude spectrum – Amplitude of an electric pulse generated by a  $\gamma$ -photon absorption in photoeffect is proportion to the photon energy.



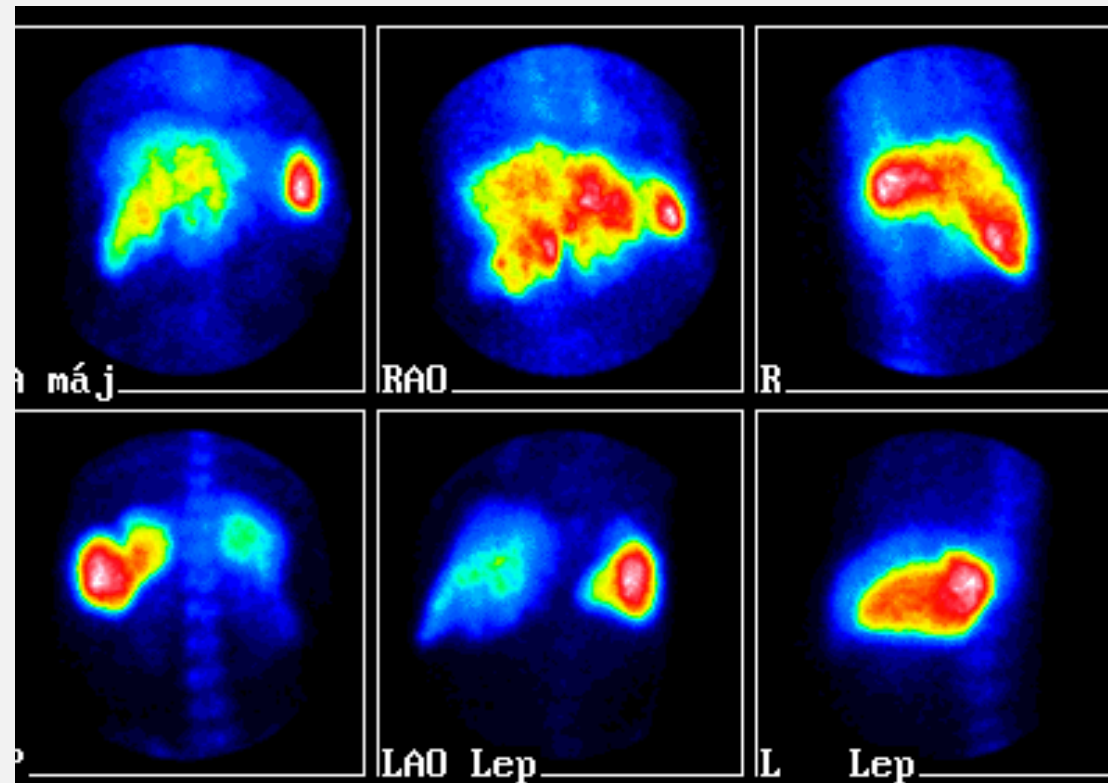
These electric pulses can be distinguished by discrimination (DD).

# Pertechnetate (intravenous 80 MBq) distribution in thyroid glands



Cold nodules

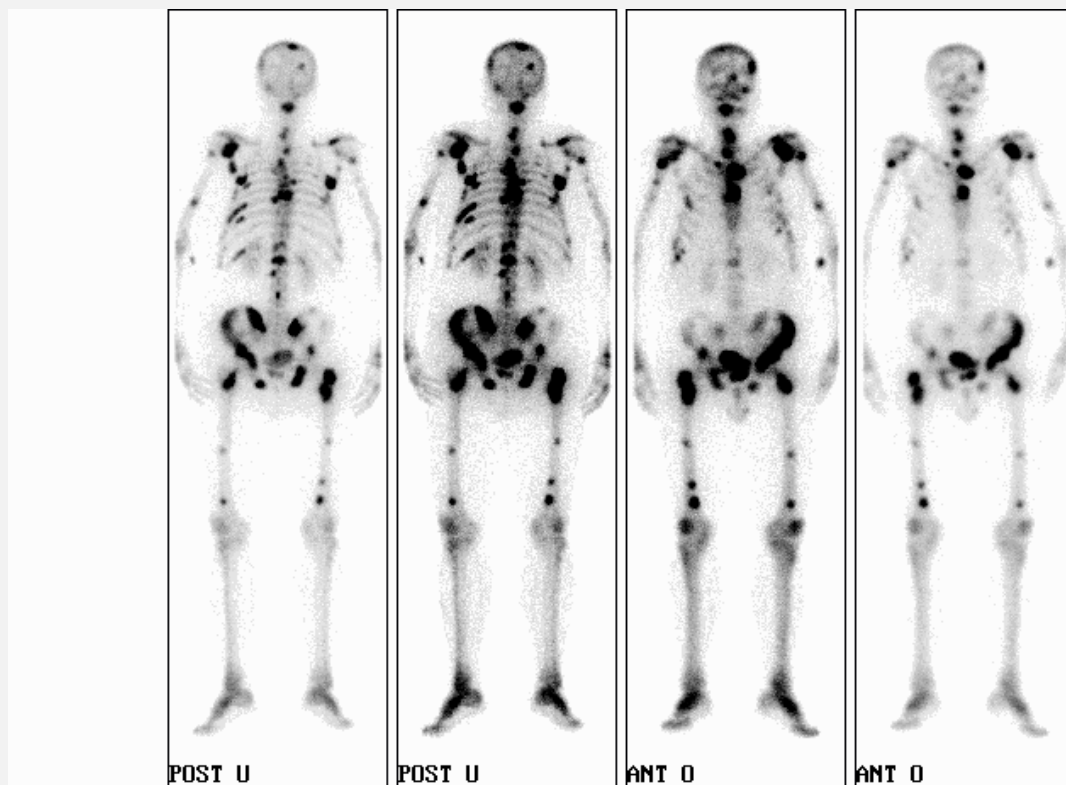
# Liver lesion nodules



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

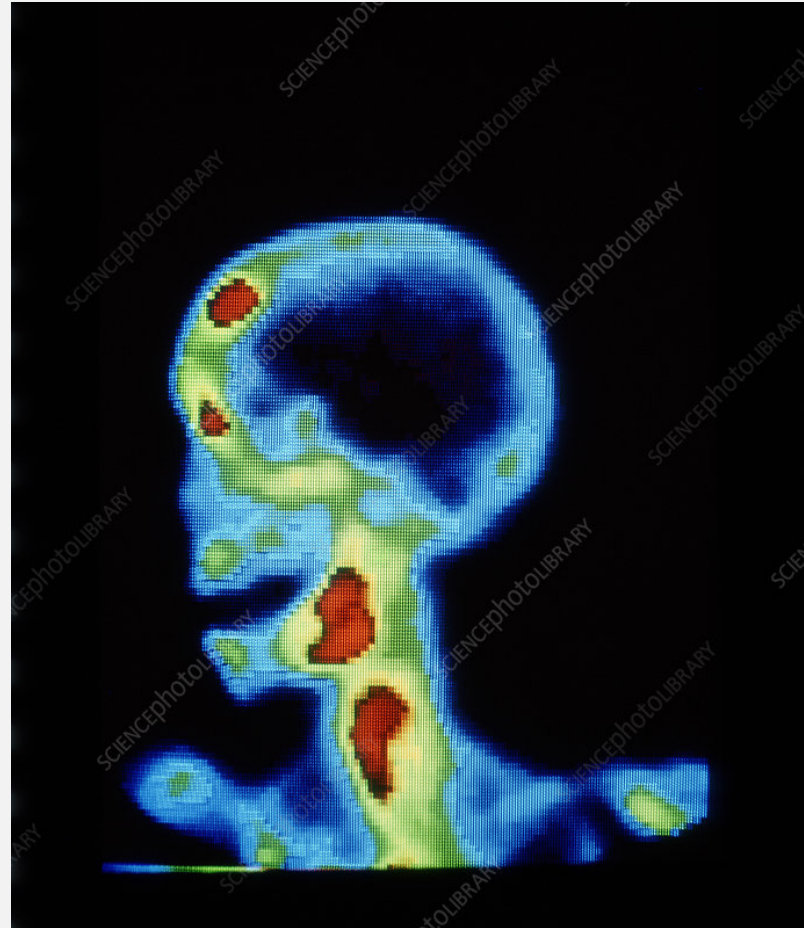
# Bone scintigraphy

$^{99m}\text{Tc}$ -MDP: 600 MBq



imaging bone metastases

# Gamma camera image: summation image



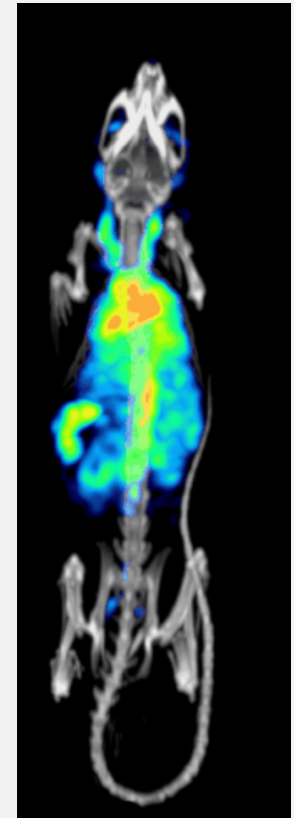
For 3D resolution: tomographic device is necessary

# SPECT – Single Photon Emission Computed Tomography

Tomographic application of  $\gamma$ -cameras – data collection in  $360^\circ$

Measurement of a series of projections.

3D image can be reconstructed from projections.

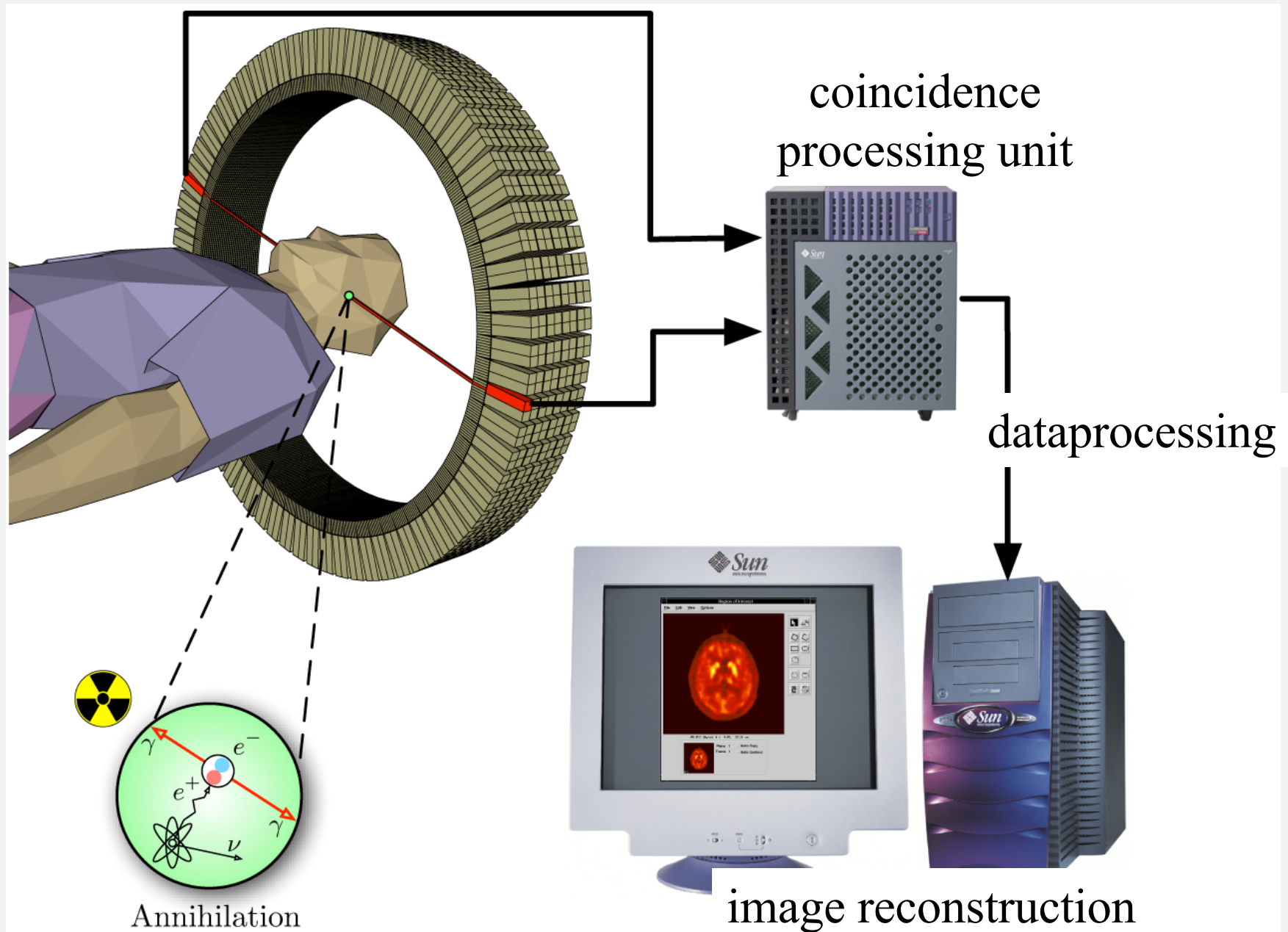


Various camera arrangements

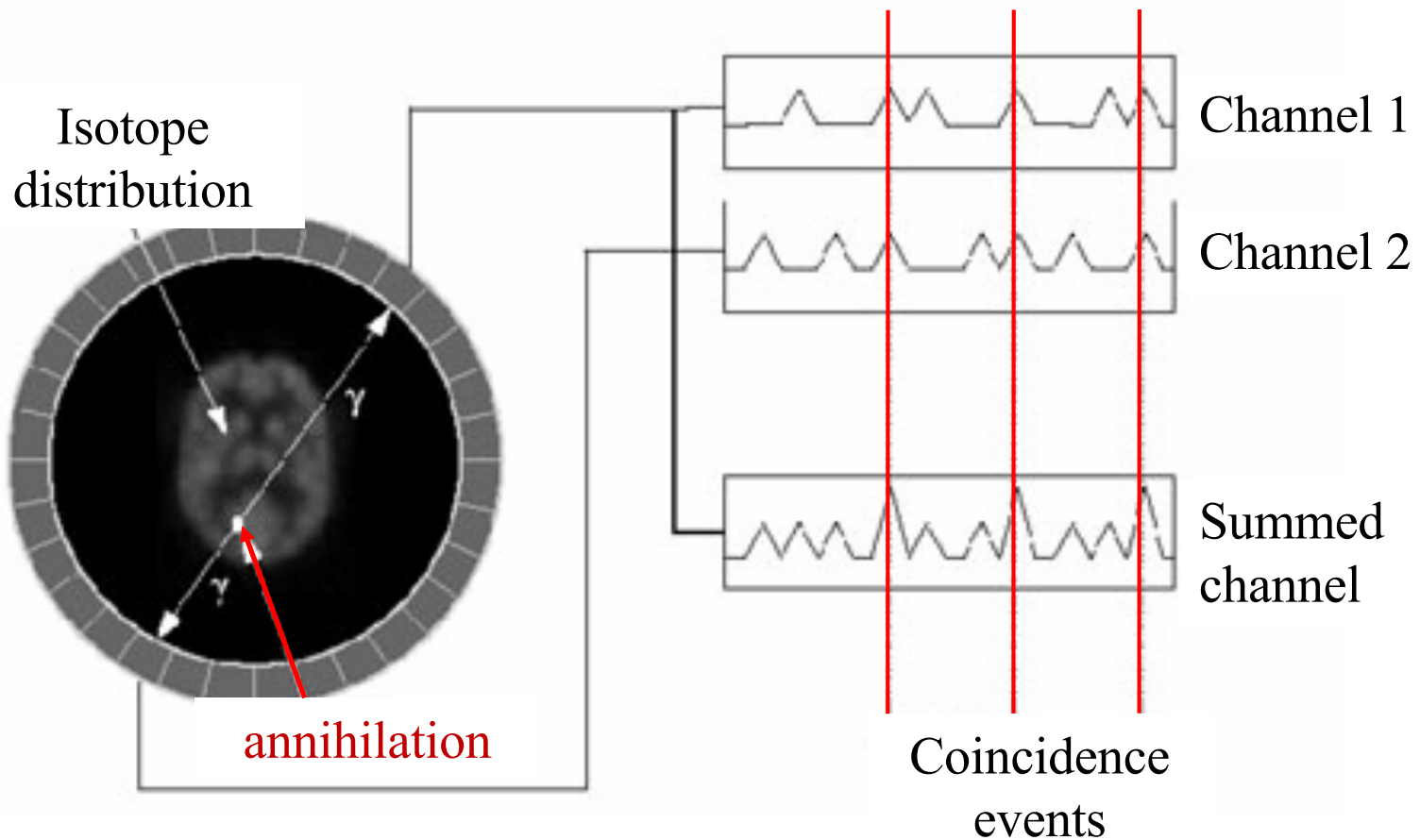
# SPECT



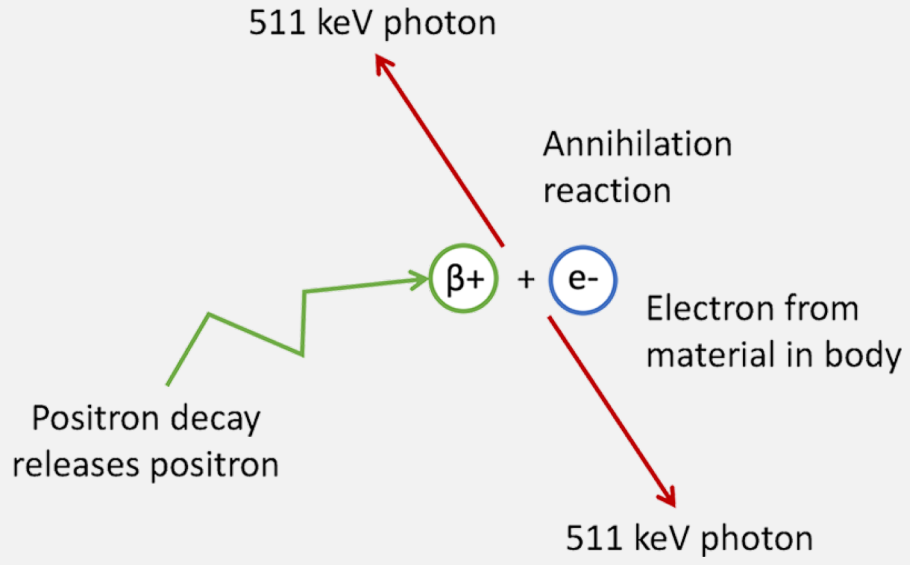
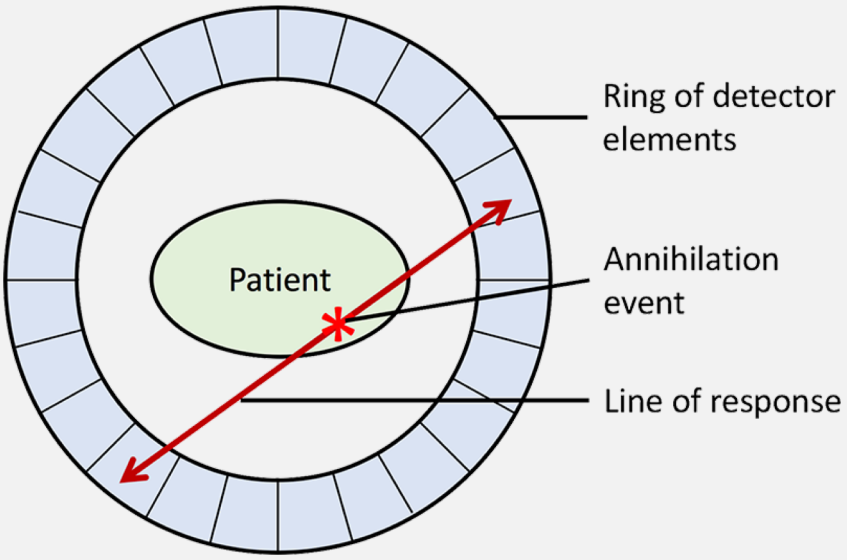
# Positron Emission Tomography PET



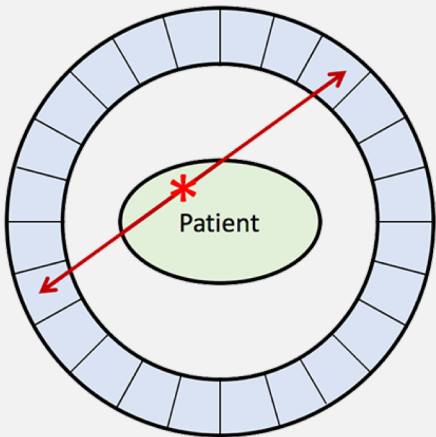
# Coincidence detection



# Coincidence detection

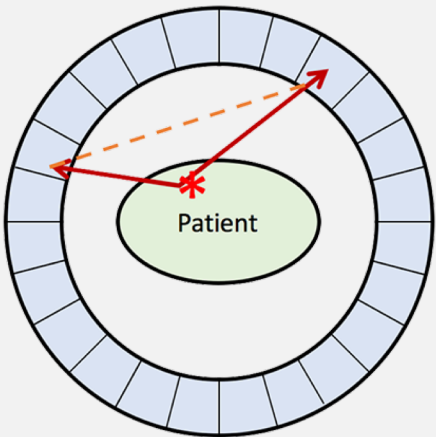


↔ Annihilation path  
 - - - - - Calculated line of response



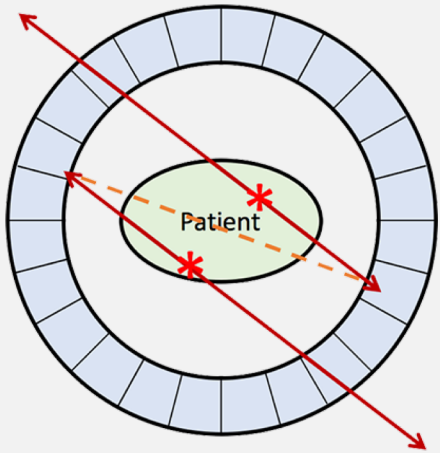
True coincidence

- One annihilation
- Straight path photons in opposite directions



Scatter coincidence

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

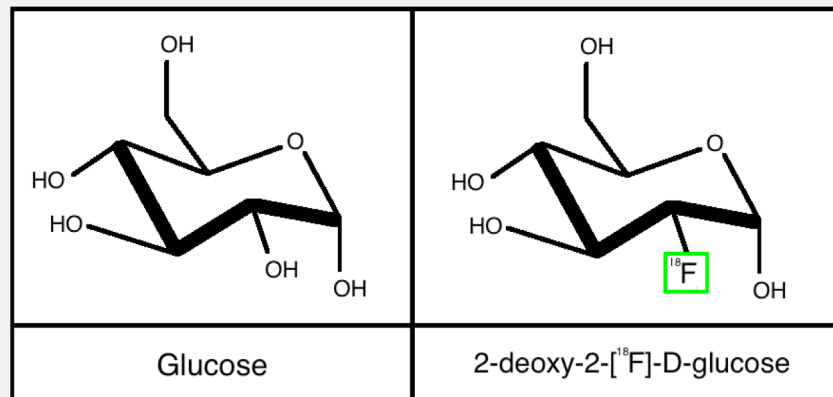


Random coincidence

- 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.

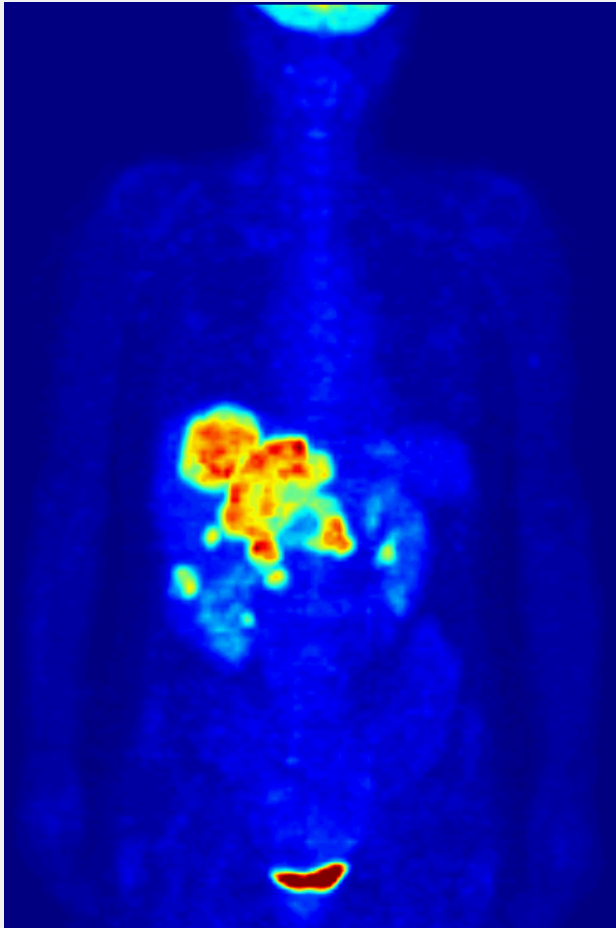
Isotope	$\beta^+$ energy (MeV)	$\beta^+$ range (mm)	1/2-life	Applications
$^{11}\text{C}$	0.96	1.1	20.3 min	receptor studies
$^{15}\text{O}$	1.70	1.5	2.03 min	stroke/activation
$^{18}\text{F}$	0.64	1.0	109.8 min	oncology/neurology
$^{124}\text{I}$	2.1350/1.5323	1.7/1.4	4.5 days	oncology



*Isotope manufacturing must be near at the site of application (half-life).*



## [<sup>18</sup>F]-fluorodeoxyglucose (FDG) – showing glucose metabolism

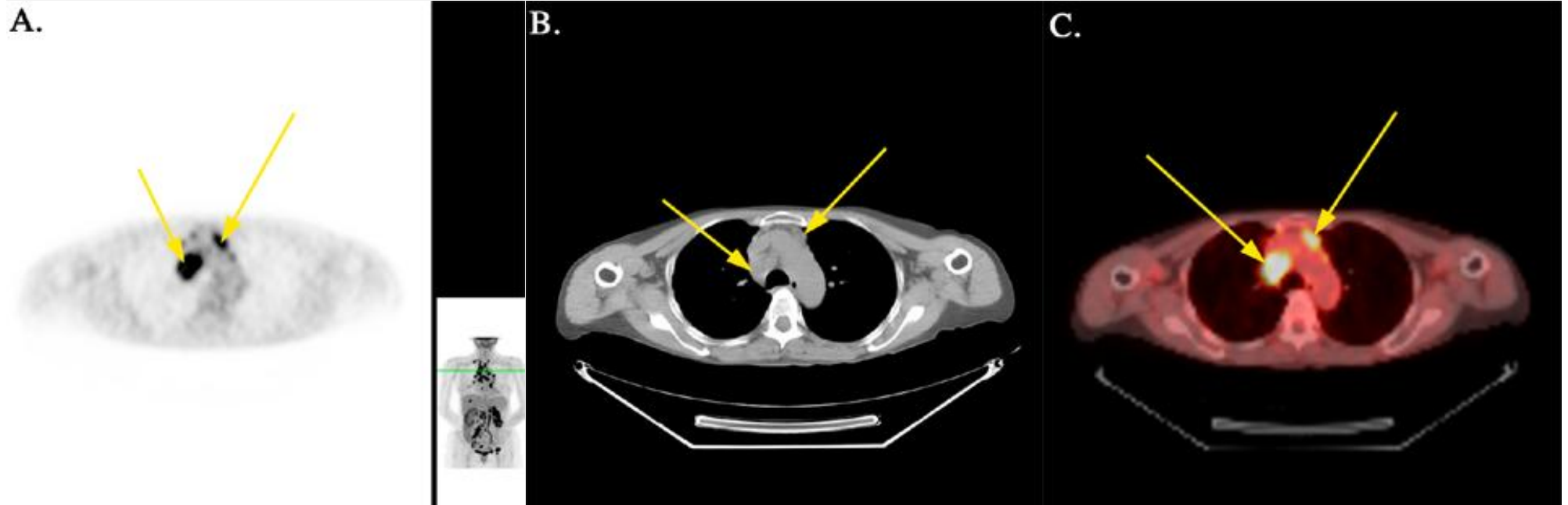


3D reconstruction of tissue metabolic activity from a [<sup>18</sup>F]-FDG PET scan. Notably, we see increased activity along the chest walls, indicating carcinoma, as well as the supraclavicular fossa.

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



# Checklist

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 detection

*Damjanovich, Fidy, Szöllősi: Medical biophysics*

II. 3.2.3

3.2.4

3.2.5

VIII. 3.2

VIII. 4.4

IX.3