Diagnostic and therapeutic applications of nuclear radiations

- Diagnostics
  - Introduction
  - Selection of isotopes and radiopharmaceuticals
  - Diagnostic equipment and methods
- Therapy

Isotope Diagnostics

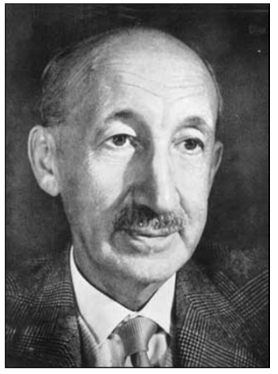
Introduction: basic principles in medical, pharmaceutical applications of radioisotopes

Basis of application: radioisotopes have **identical behavior** in the organism **to corresponding stable atoms**.

- Organ-specific compounds can be labeled with radioisotopes (radiopharmaceuticals)

George Hevesy 1923 – first biological tracing experiment

- Nobel prize in chemistry 1943.)

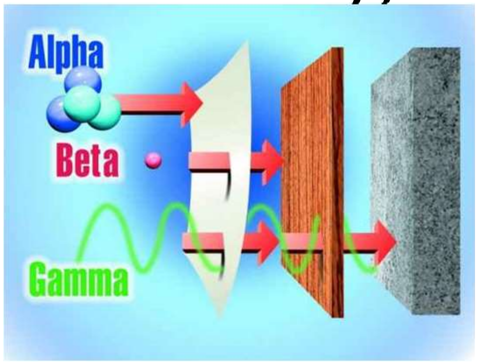


Fields of application: - diagnostics (in vivo, in vitro)
- therapy
- research

If diagnostics + therapy = 100 %, from this 95 % is the diagnostics.

Selection of isotopes for *in vivo* diagnostics

(the radioisotope is introduced into the patient's body)



Viewpoints for selection of isotopes

- **gamma-radiating** (the longest effective range)

- **short half-life** (but not shorter, than the examined process)

  $\Lambda \sim N/T$ $\rightarrow$ for the necessary activity lower amount is enough

- **photon energy should not be too low, and should not be too high** (higher energy $\rightarrow$less absorption in the tissues, but the detection efficiency is lower)

$\rightarrow$ ^{99m}Tc is ideal

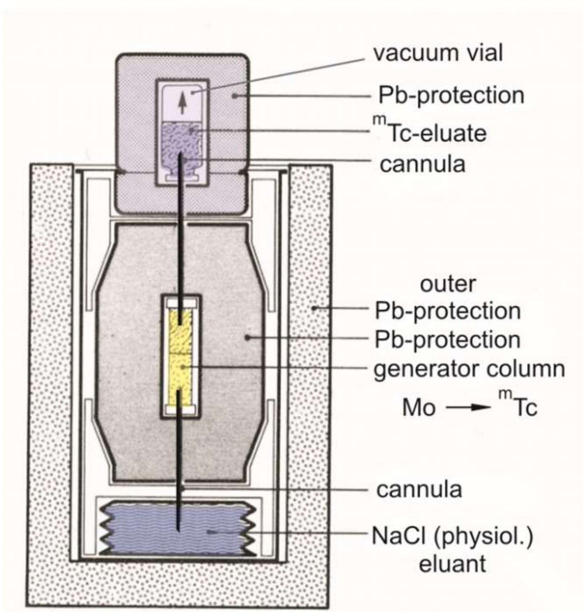
Technetium generator

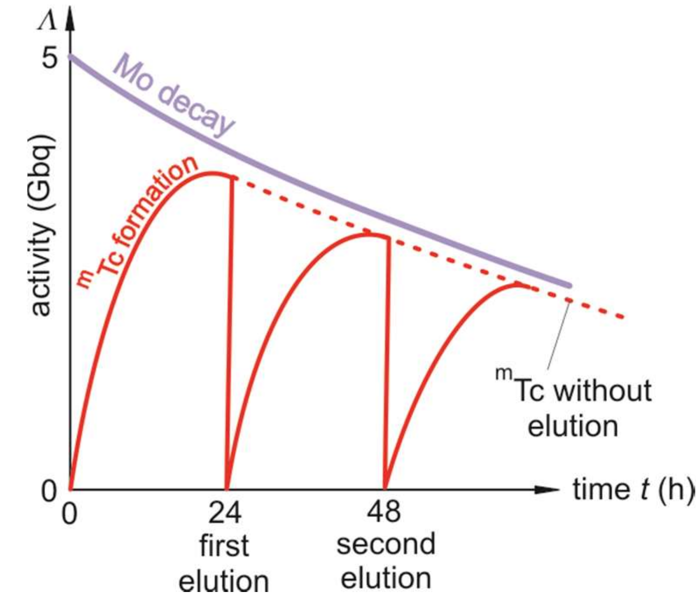
$$ {}^{99}_{42}Mo \xrightarrow[\beta]{} {}^{99m}_{43}Tc \xrightarrow[\gamma]{} {}^{99}_{43}Tc $$

T = 67 hours

T = 6 hours

E_γ = 140 keV





Radiopharmaceuticals

Chemical agents or drugs having radioactivity. Molecules labeled with radioisotopes for diagnostic or therapeutic purposes. During their production the quality and purity requirements of medicines must be fulfilled.

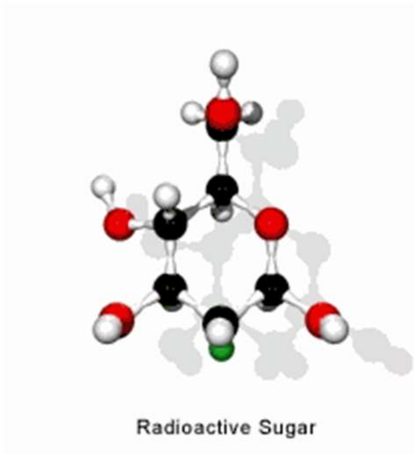
radiopharmaceutical:

drug or organ-specific molecule + radioactive isotope

↑ finds the target organ/tissue ↑ emits radiation

e.g. deoxyglucose + ^{18}F =

= Fluorodeoxyglucose (FDG)



Few examples for radiopharmaceuticals:

At least in **75 %** of the in vivo diagnostic applications **^{99m}Tc** is used to label different organ specific compounds.

e.g. pyrophosphate – bones,
colloids – liver and RES (reticulo-endothelial system), albumin – circulation)

Further γ**-radiating** isotopes that are frequently used: ^{123}I, ^{125}I,
^{131}I (thyroid gland and kidney),
^{67}Ga (inflammations and tumors),
^{201}Tl (heart muscle),
^{81m}Kr, ^{127}Xe, ^{133}Xe (examination of lungs by inhalation)

The most frequently used **positron radiating isotopes** (for PET examinations): ^{18}F, ^{11}C, ^{13}N, ^{15}O

- They have short half-life.
- They are produced in cyclotron.

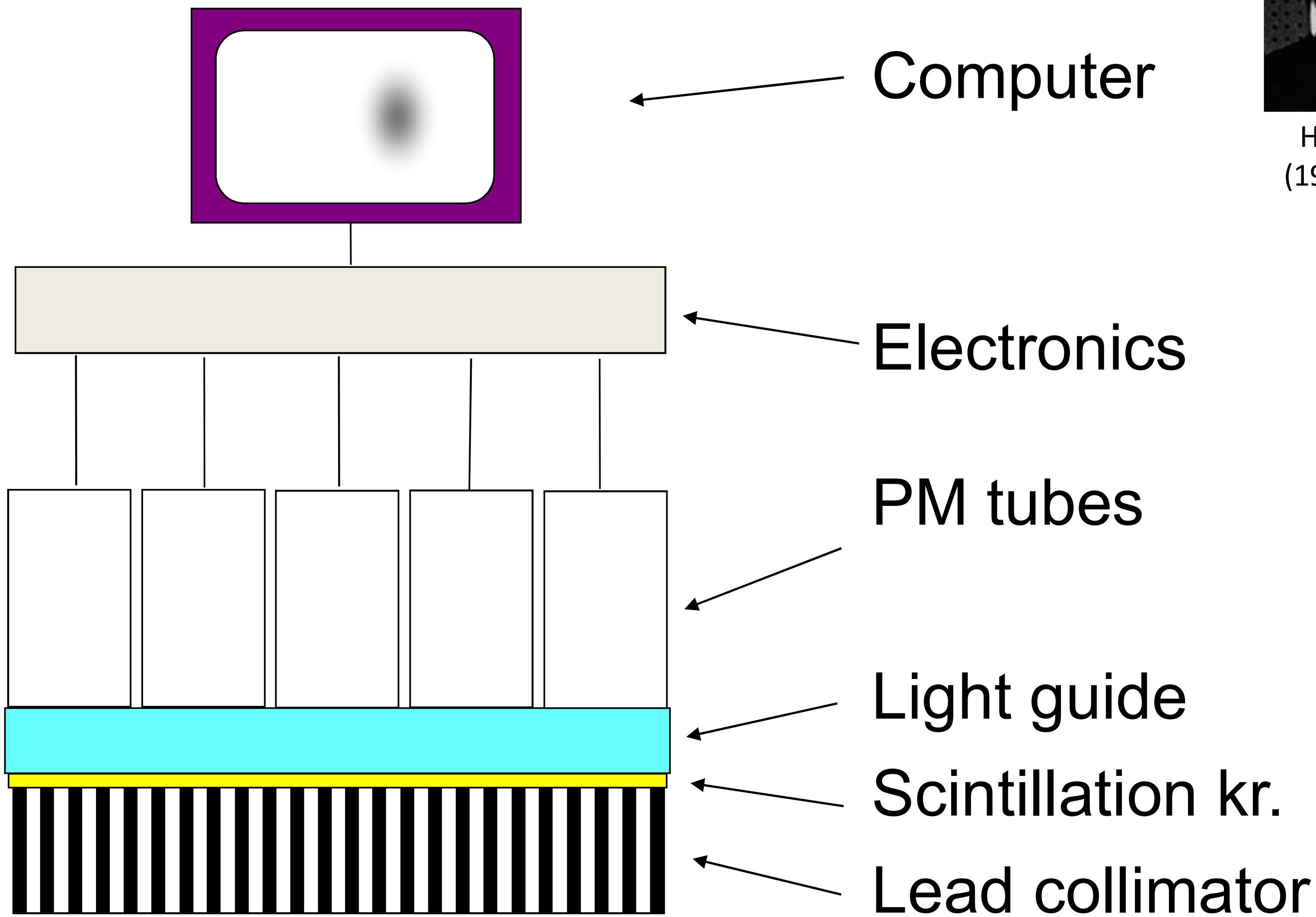
The most frequently used positron radiating radiopharmacon:
fluoro-deoxy-glucose (FDG) – brain activation.

The distribution of isotopes can be detected by diagnostic equipments based on scintillation.

- Scintillation counter (see practice!)

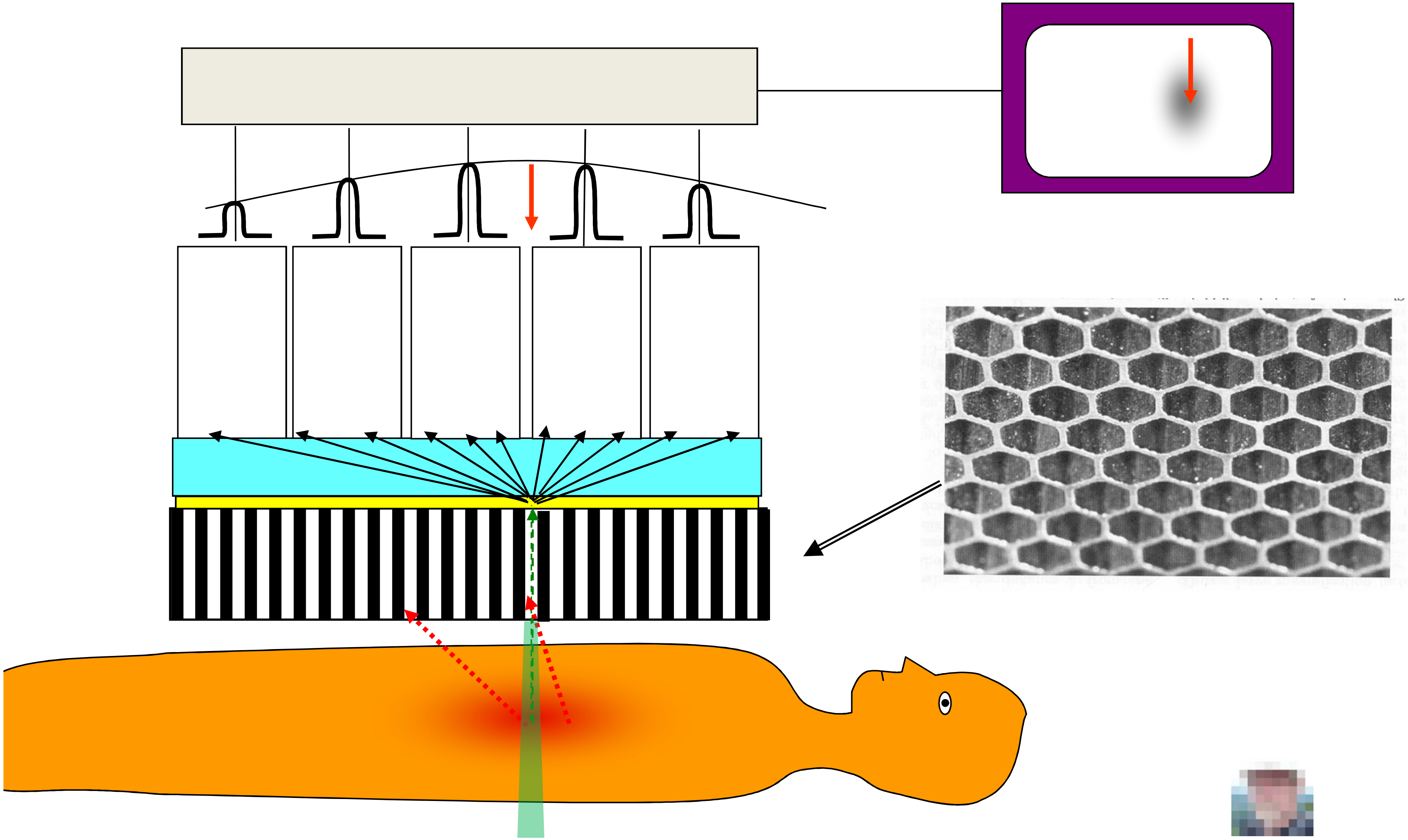
- Gamma camera (Anger camera)
- SPECT (single photon emission computed tomography)
- PET (positron emission tomography)

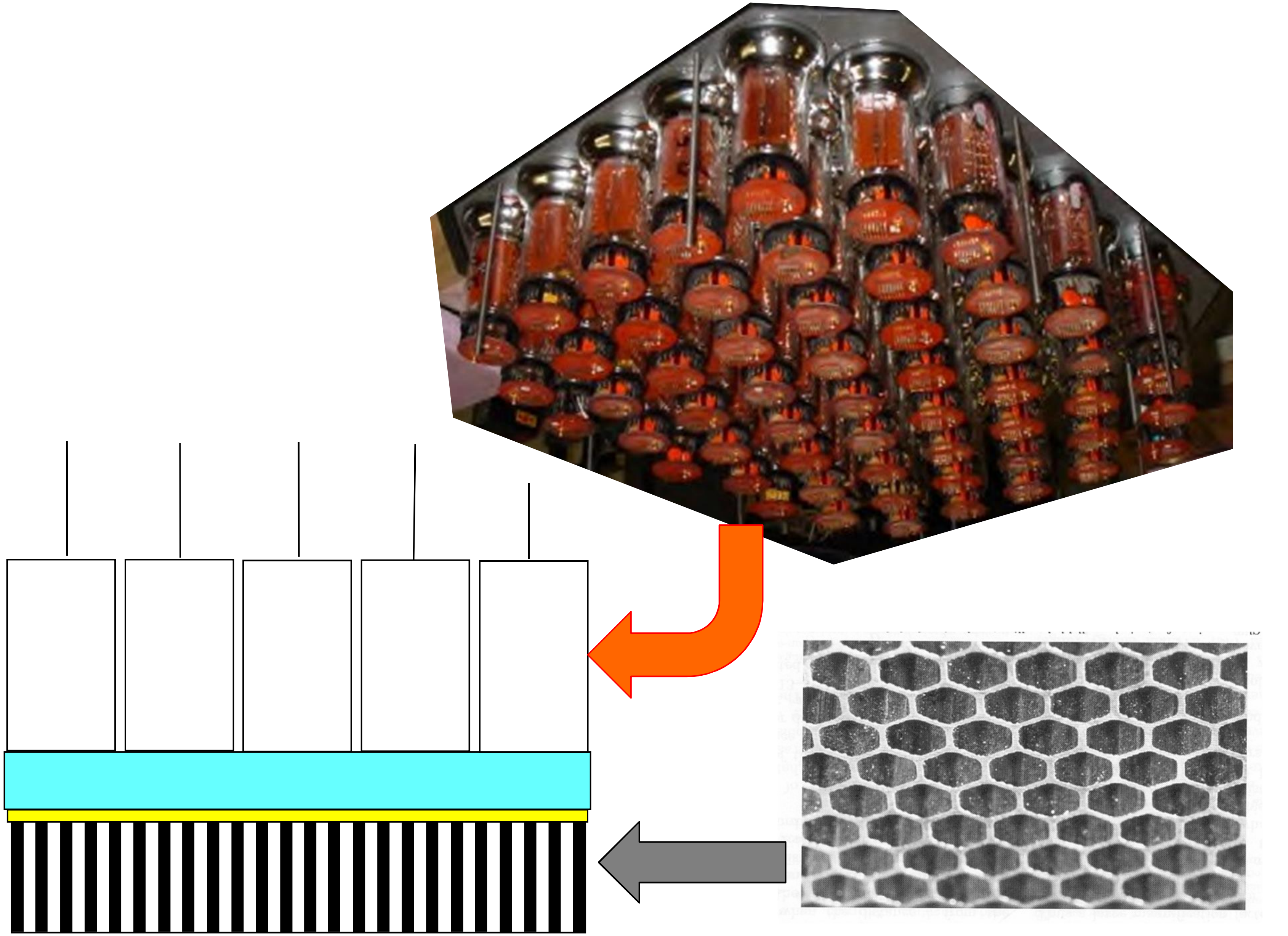
Gamma camera: structure



Hal Anger
(1920-2005)

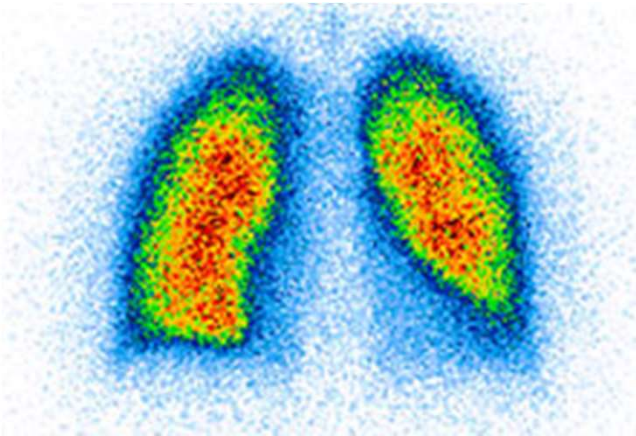
Function of the gamma camera

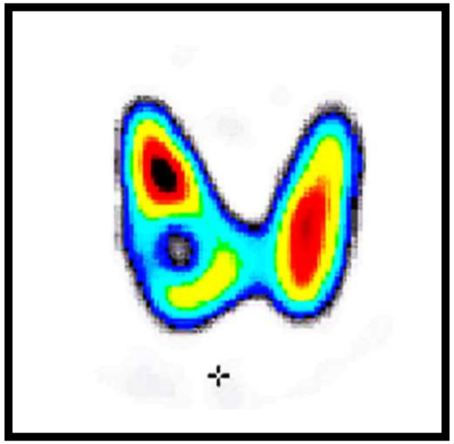


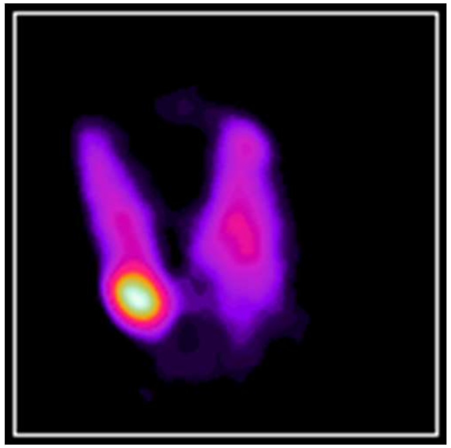



SPEC
IMAGING

Few examples of gamma camera images:





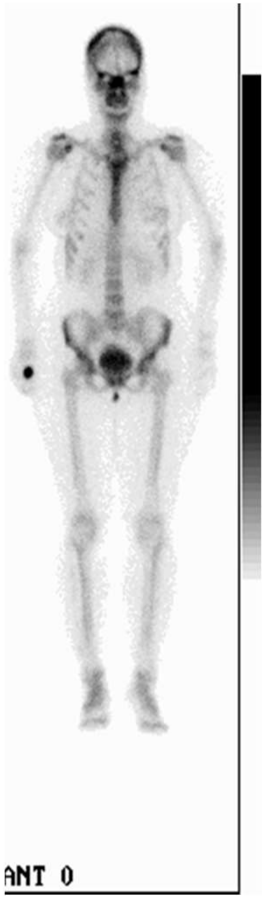


Lung Thyroid gland

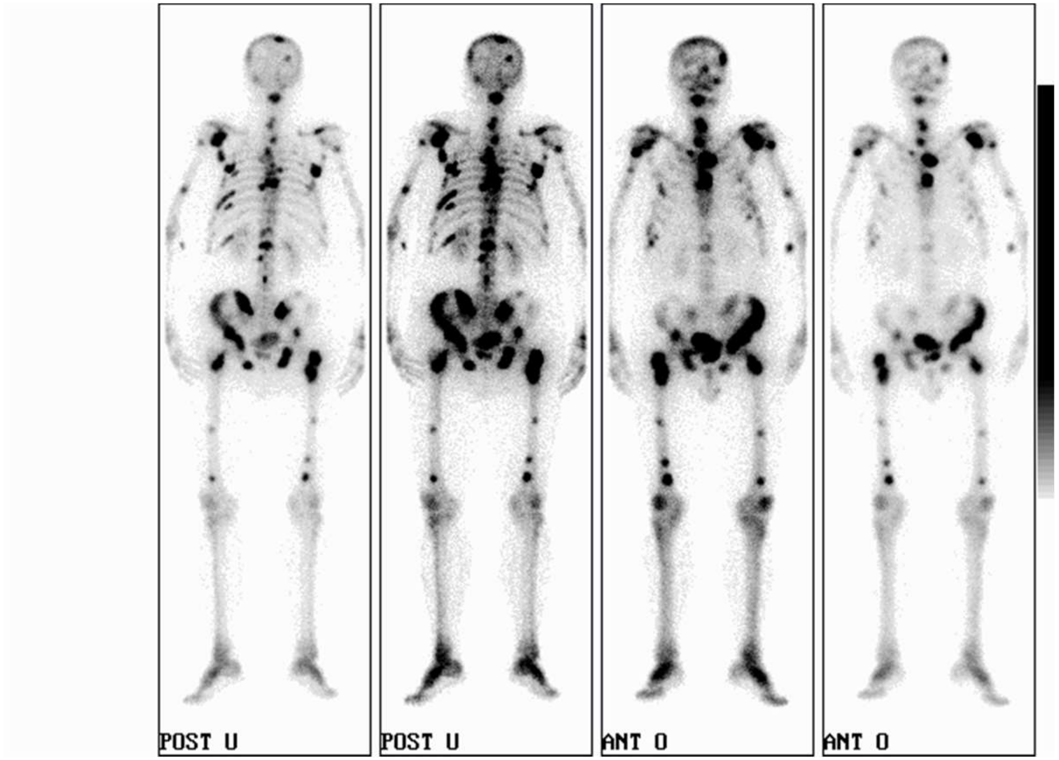
cold nodule hot nodule

Bone scintigraphy

^{99m}Tc-MDP (^{99m}Tc-methyl diphosphonate): 600 MBq



normal



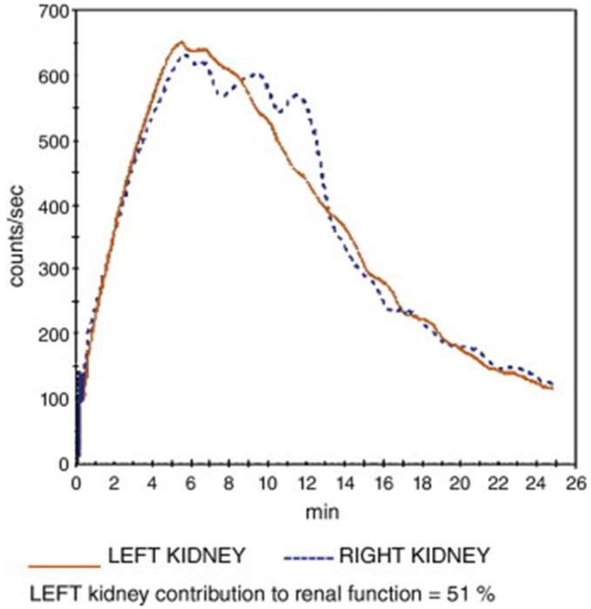
metastase

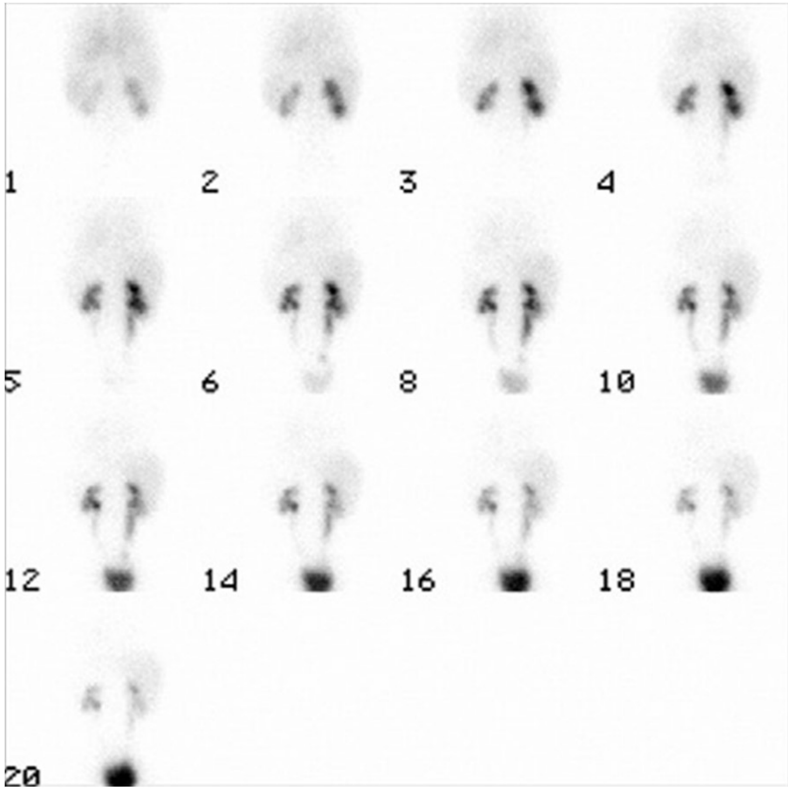
Static examination (scintigram)

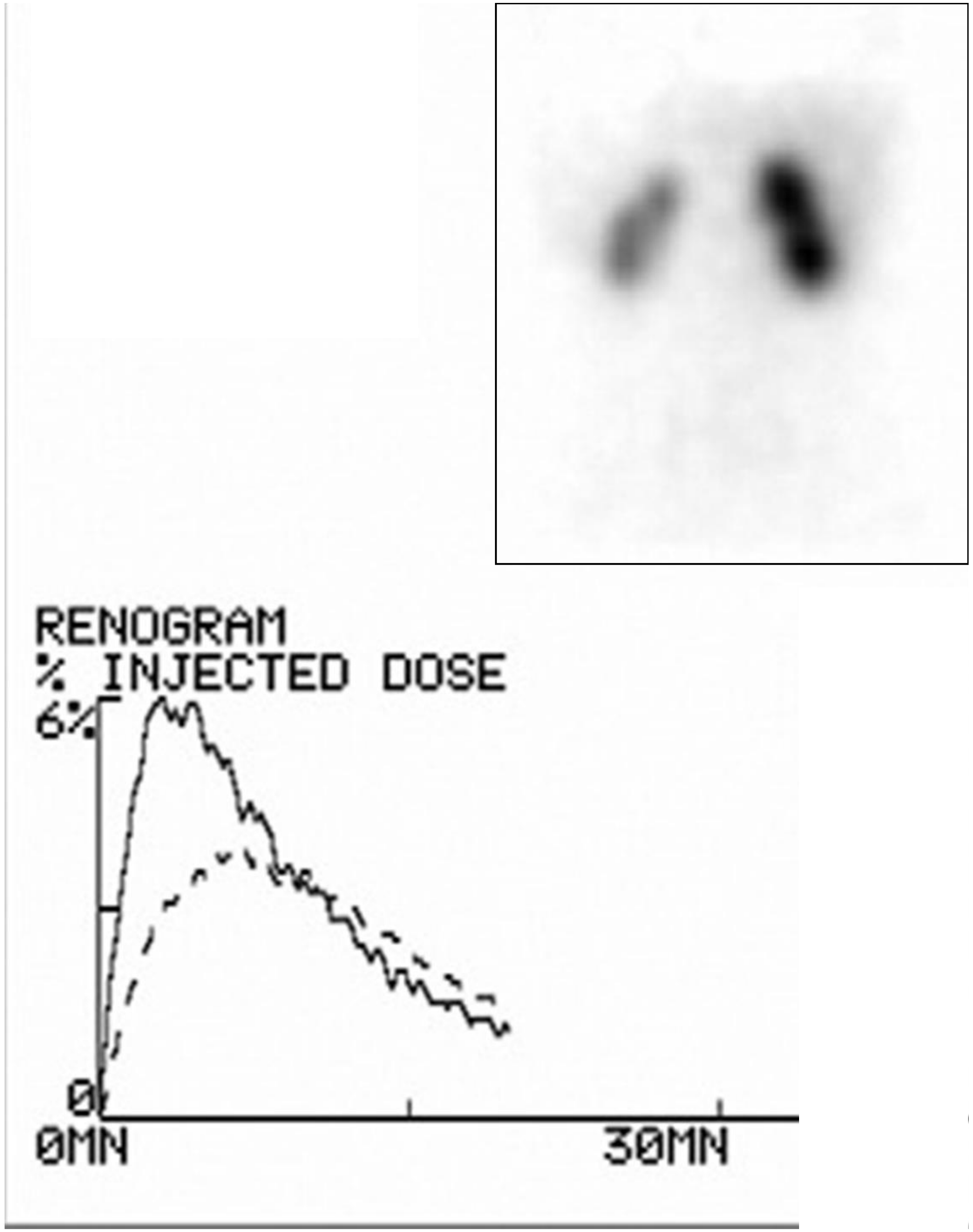
- the distribution of isotope in the space can be examined

Dynamic examination

- the change of activity in the function of time in a certain region can be examined (ROI – region of interest)

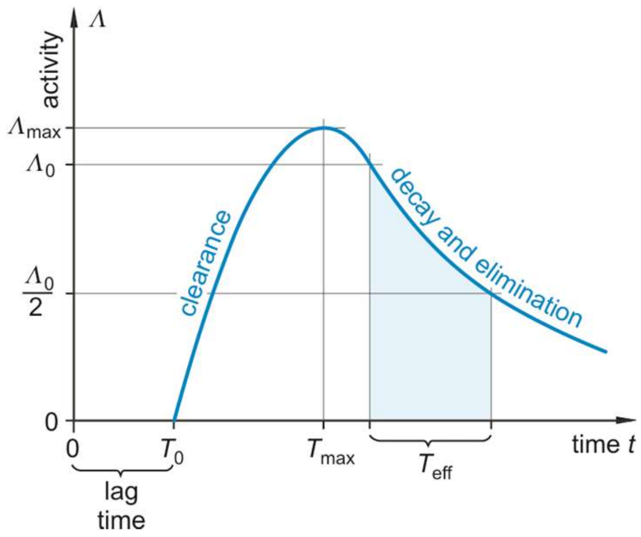


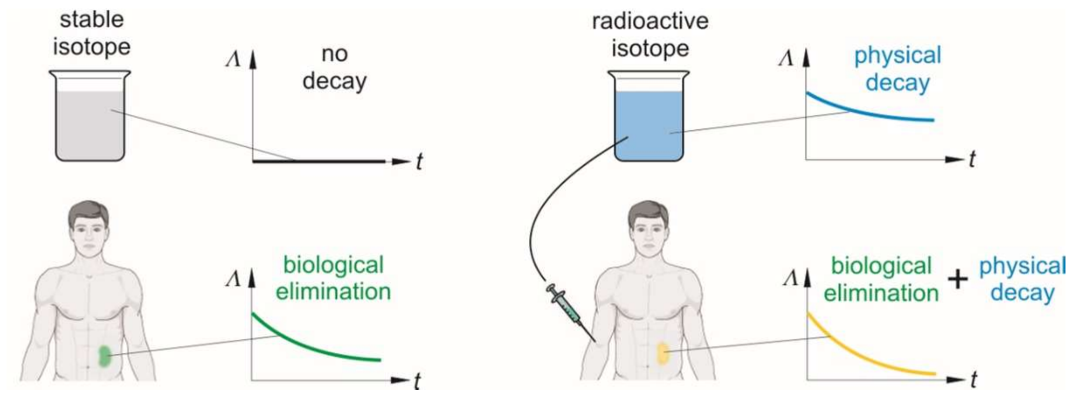




Images from: Biassoni © Chippington: Imaging in Urinary Tract Infections: Current Strategies and New Trends Seminars in Nuclear Medicine Volume 38, Issue 1, January 2008, Pages 56–66

The isotope accumulation curve can be obtained from the measurement of activity in different moments





Connection between half-lives:

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

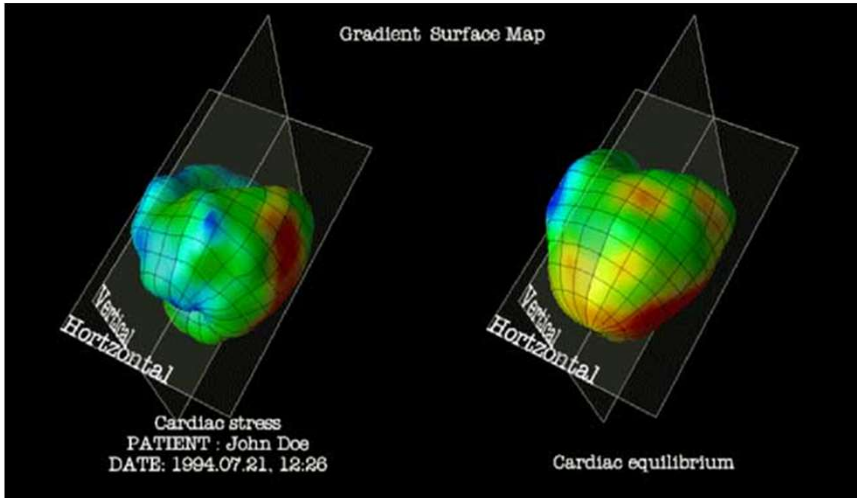
to be measured

known

to be calculated

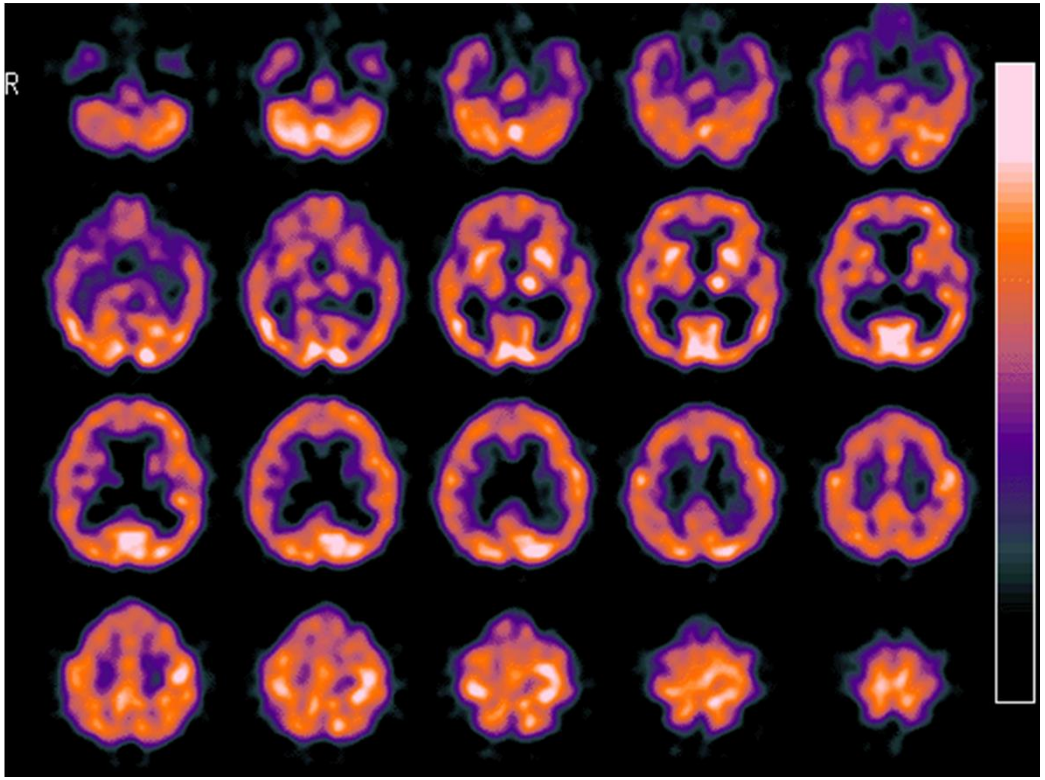
contains diagnostic information about the speed of the metabolic processes!

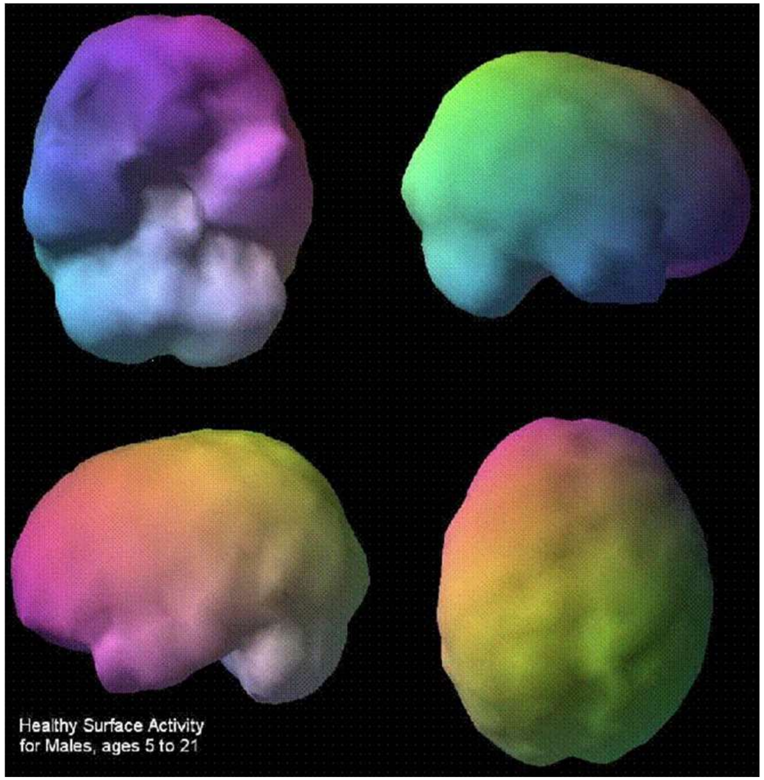
SPECT (single photon emission computed tomography)
the detector of gamma camera is rotated around the body axis $\rightarrow$ three dimensional image



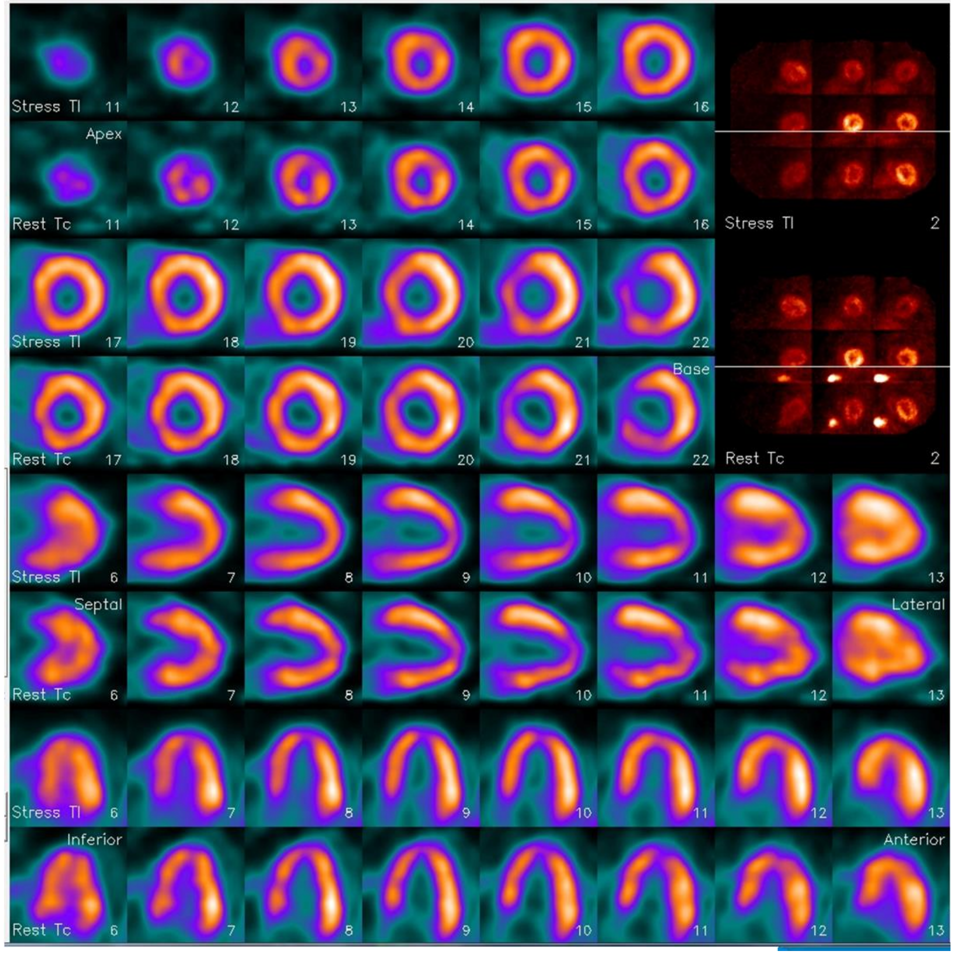
SPECT-images

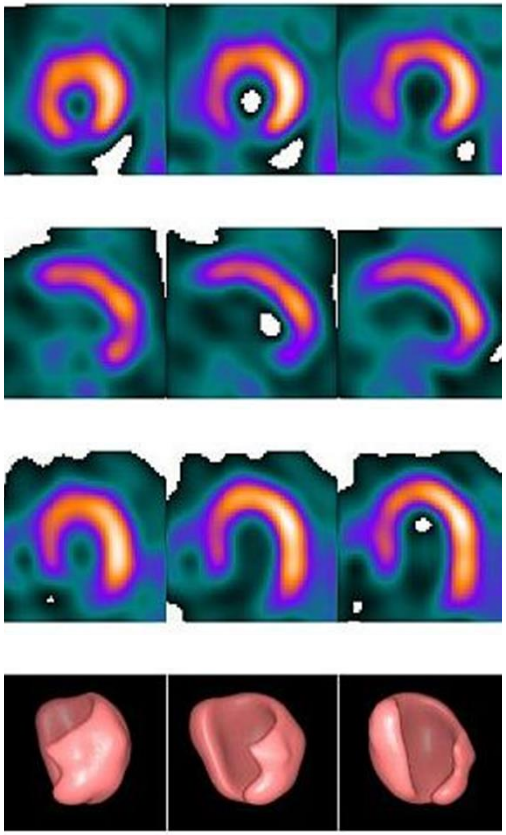
Cross-sectional images are produced showing the layers above each other. From these layers sectional image of any direction or a three dimensional image can be reconstructed.





Heart SPECT

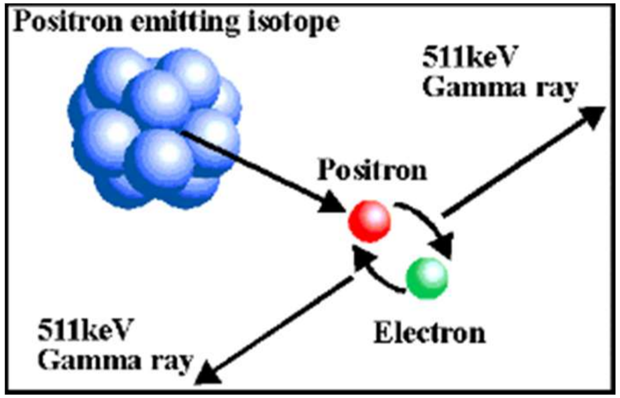

Stress Tl
Rest Tc
Apex
Base
Septal
Lateral
Inferior
Anterior

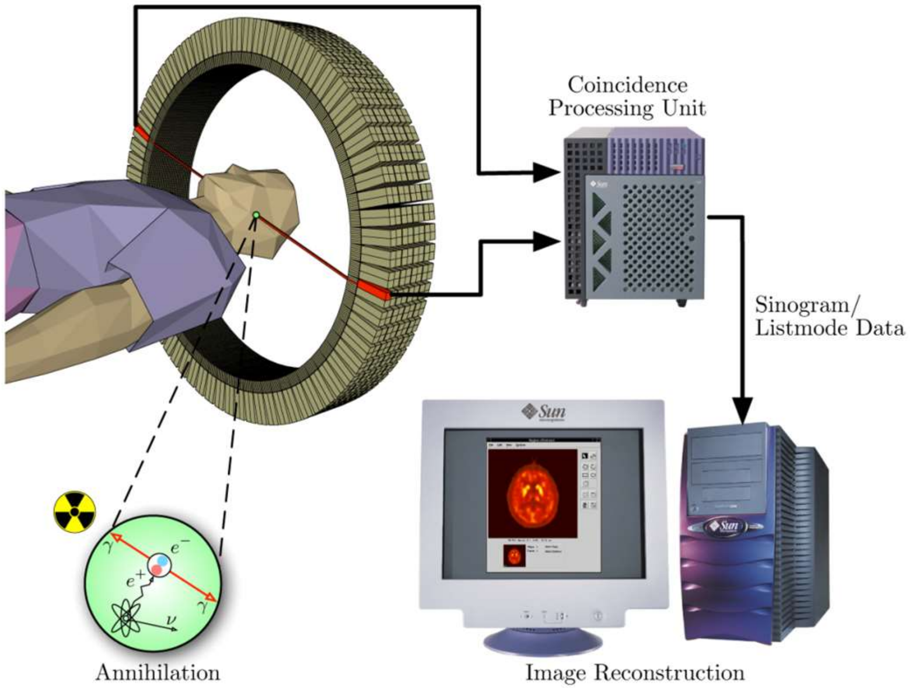


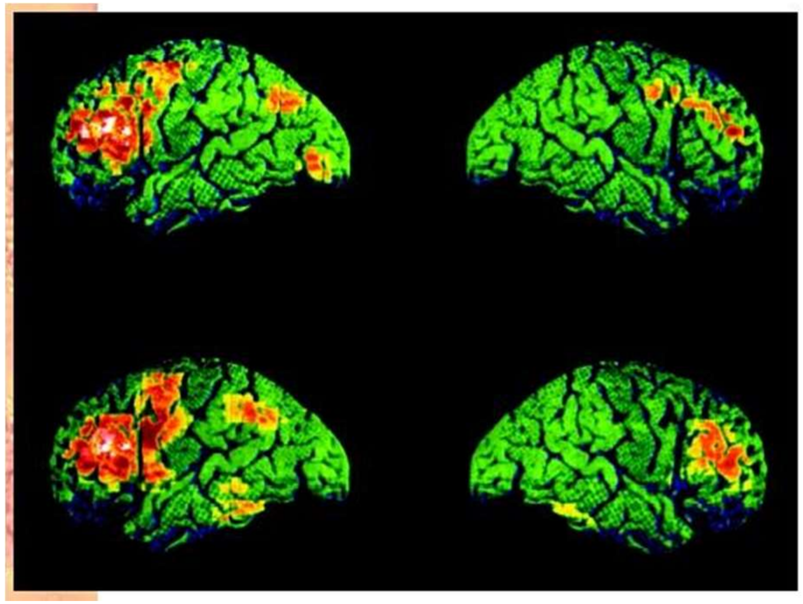
PET examination

positron-radiating isotope – positron-electron meeting → annihilation → 2 gamma photons (511 keV) - these are detected

coincidence: the gamma photons arrive into the two detectors in the same time (within a few ns).







Multiple detector rings
=> 3D image

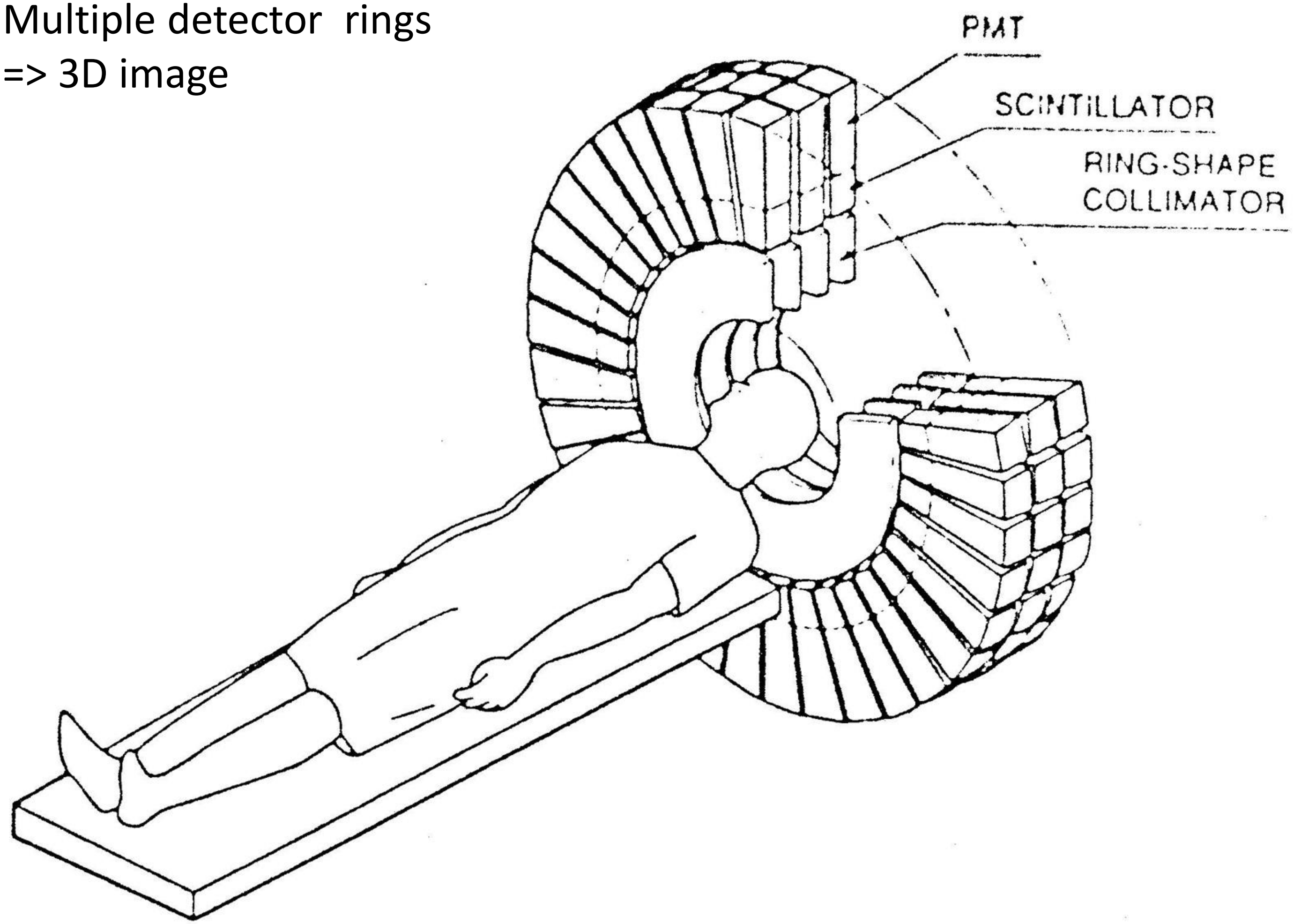
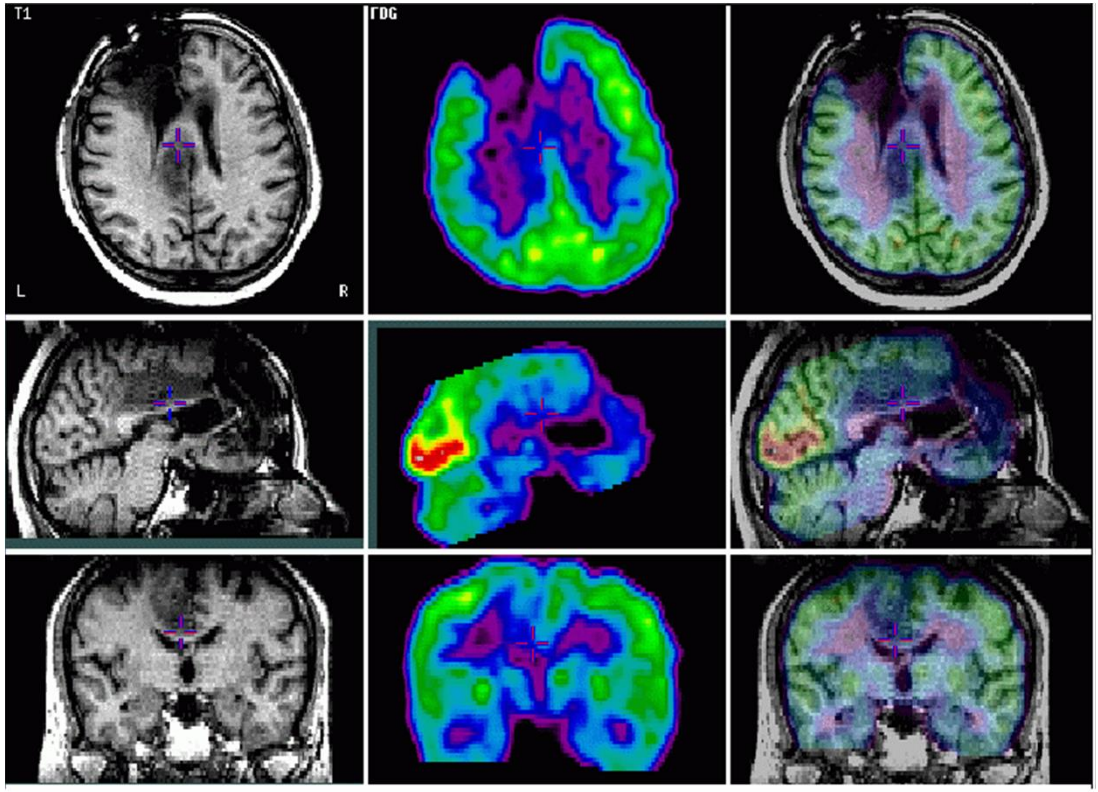


Image fusion

Combination of functional and morphological information

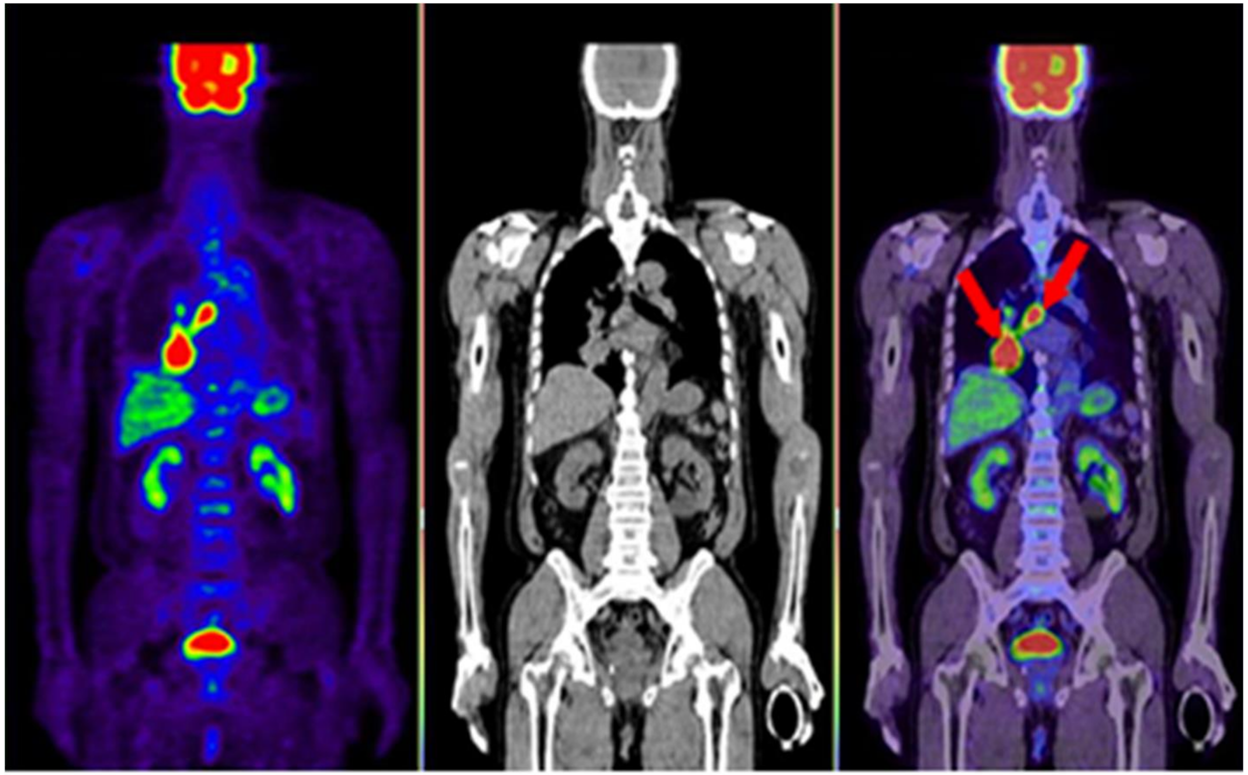
- functional: SPECT and PET
- morphological: CT and MRI



Multimodal equipment

morphological and functional imaging in one equipment

SPECT/CT



PET画像 CT画像 PET/CTフュージョン画像

Combining functional and high resolution morphological information

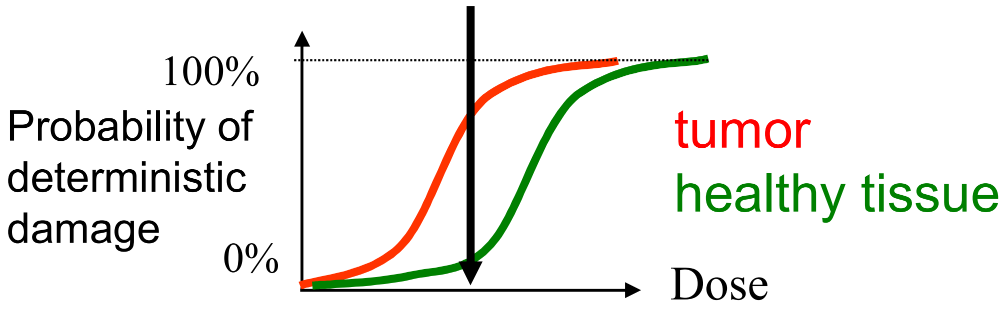
Multimodal equipment
for research purposes

NanoSPECT/CT

NanoPET/MRI

Radiotherapy

Principle: The cell killing effect (radiation damage) of ionizing radiation is used for the treatment.
Most often treated tissues are tumors.
Fast proliferating cells are more sensitive for radiation damage.



Radiotherapy

Teletherapy

The source of the radiation is **outside** of the body

Brachytherapy

The source of the radiation is **inside** of the body

Teletherapy

Radiations used:

gamma (usually from ^{60}Co isotope) $E_{\gamma} \approx 1,2$ MeV

high energy x-ray $E_{x\text{-}ray}$ =6...20 MeV (higher penetration depth)

accelerated electron E_e =6...20 MeV (few cm penetration depth)

Equipments:

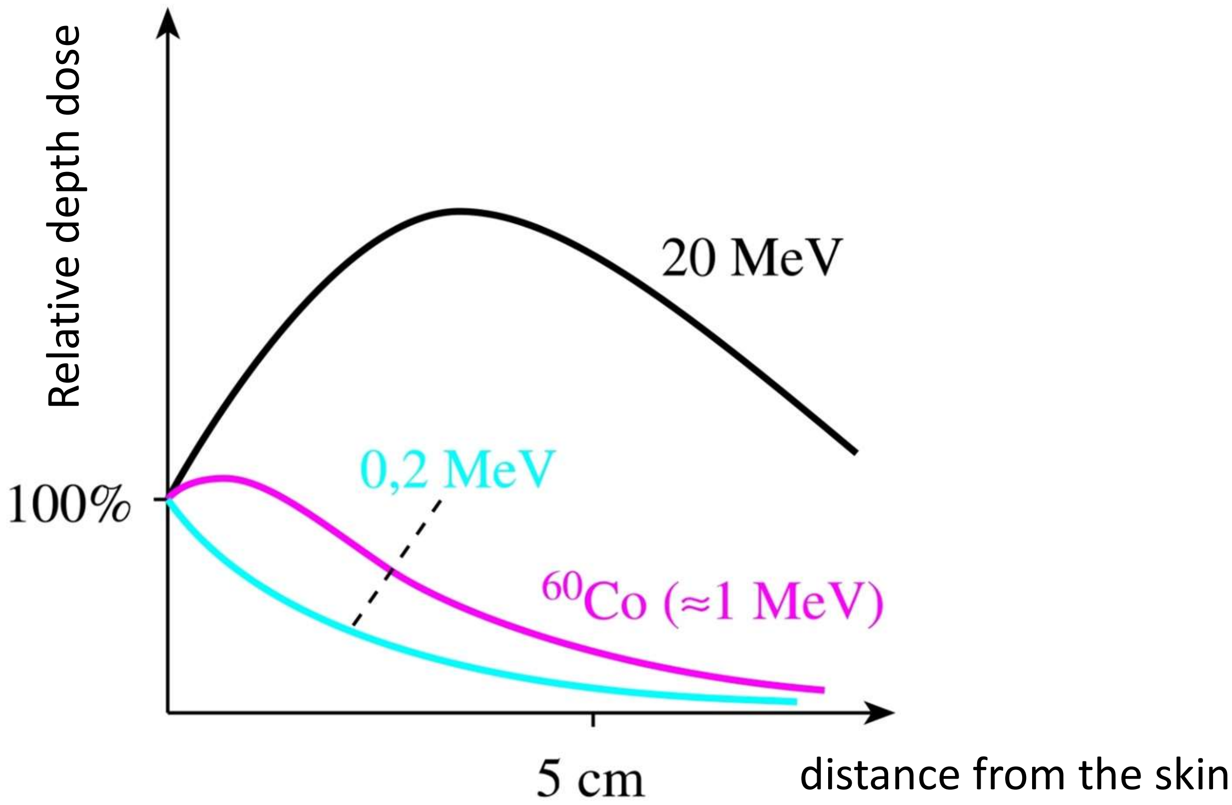
^{60}Co source

linear accelerator to generate electron or x-ray beams

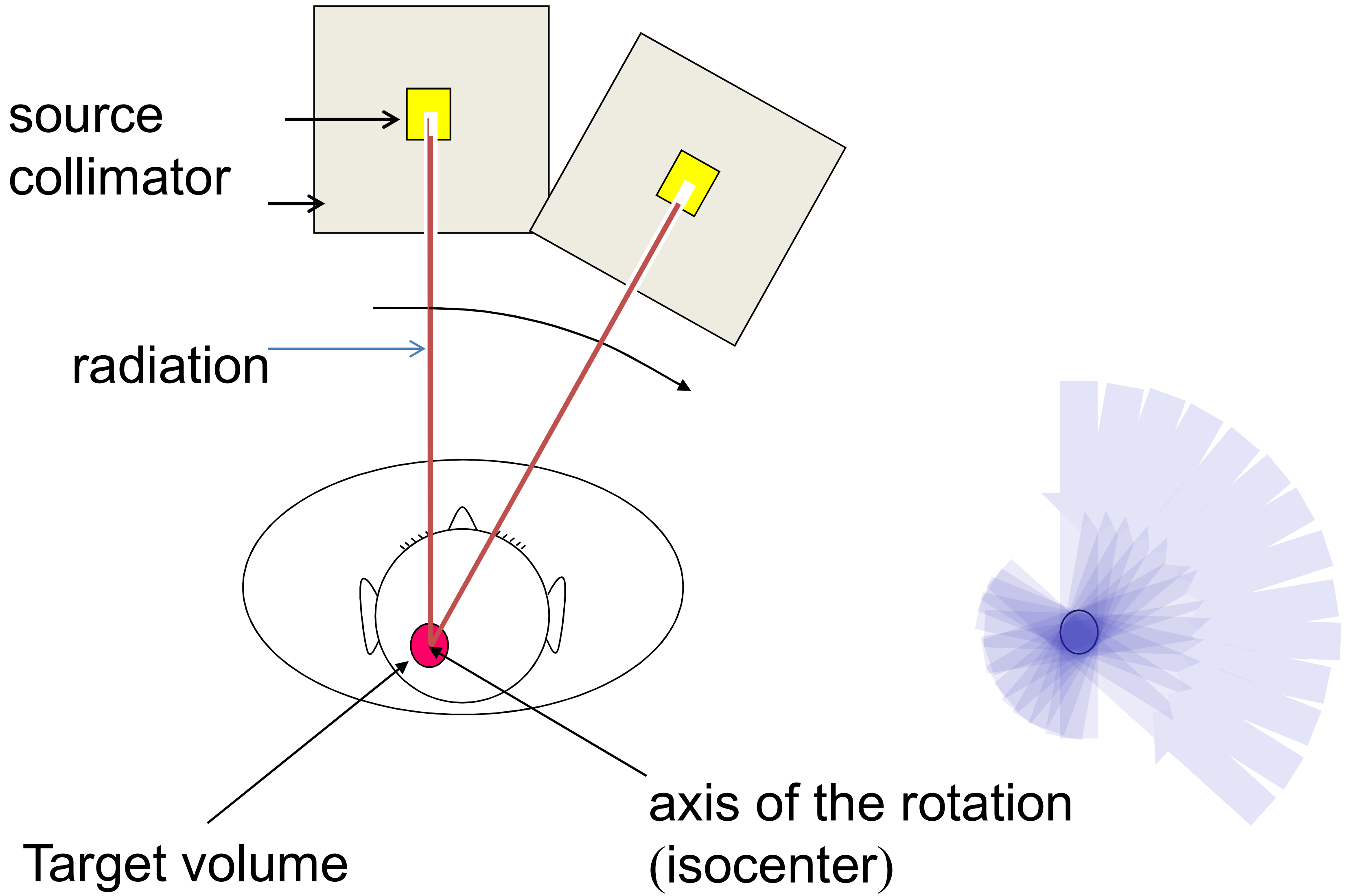
Relative depth dose

The dose at a certain depth related to the dose on the skin surface.

Higher energy radiation and higher distance of radiation source from the body surface results in higher relative depth dose.

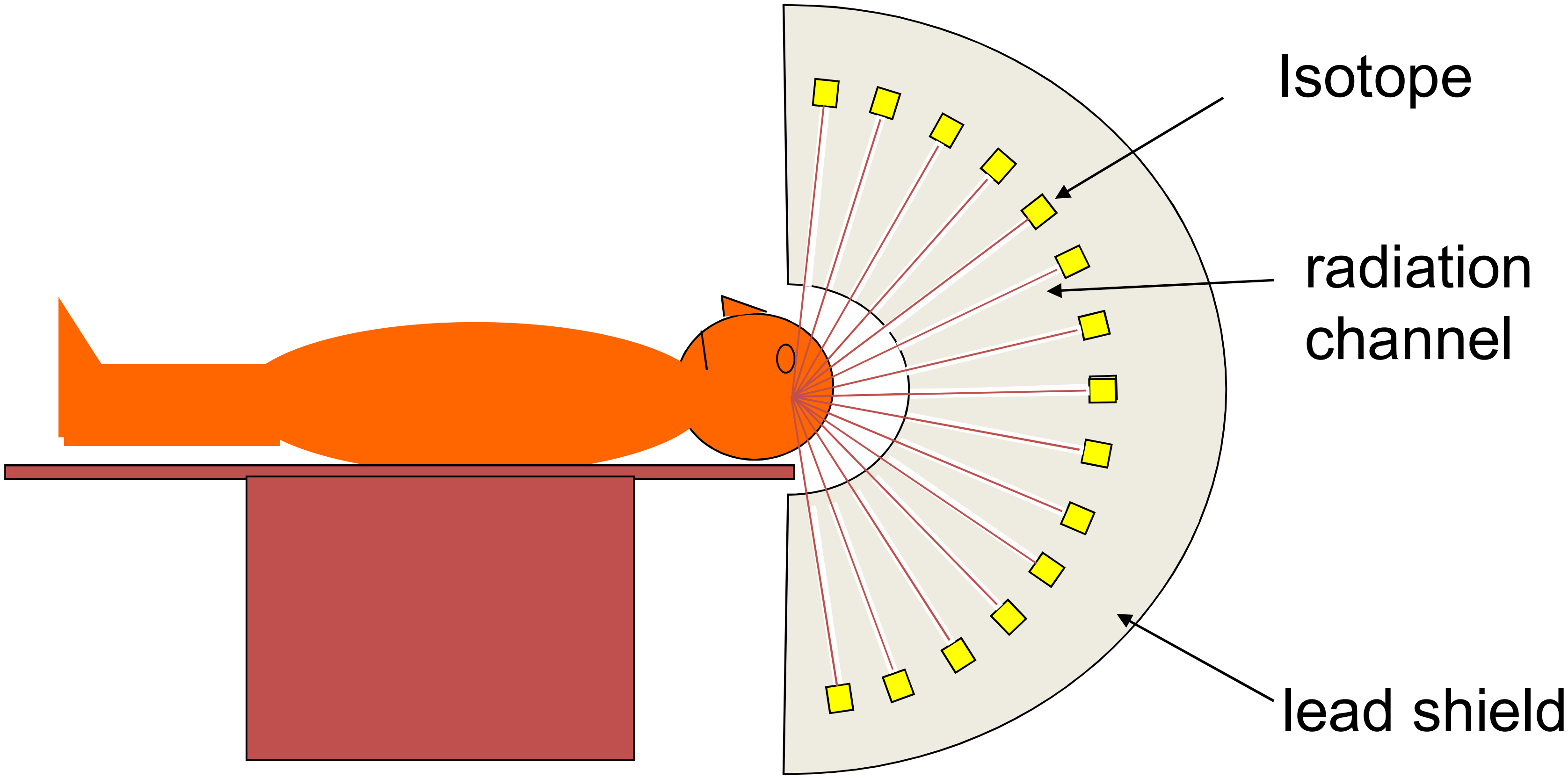


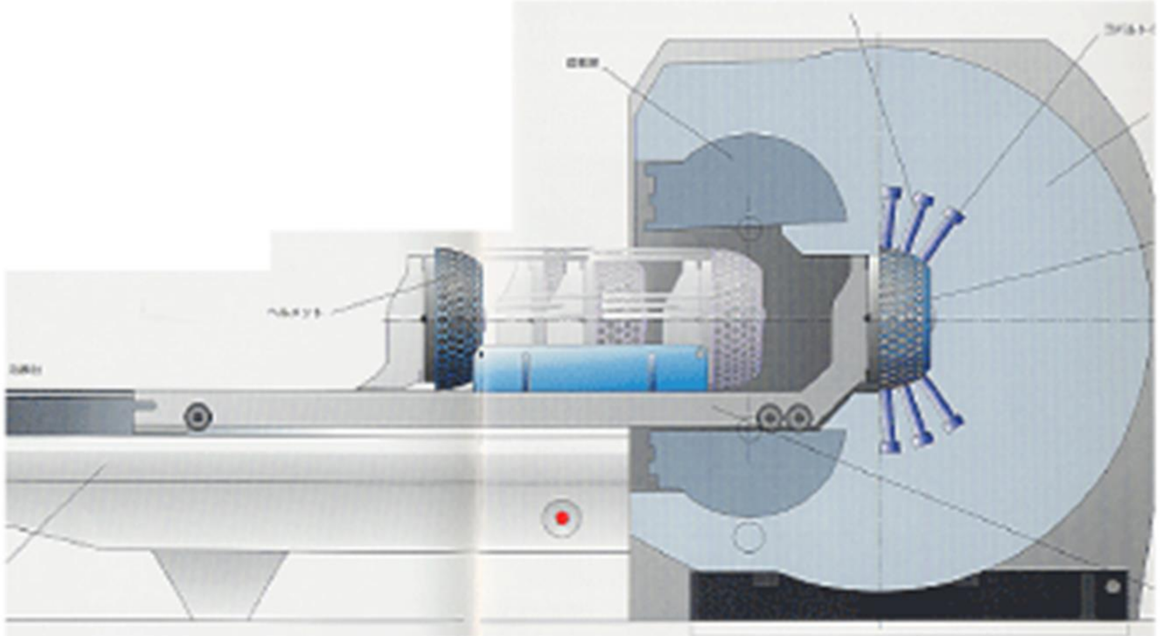
How to reduce the radiation damage in healty tissue?

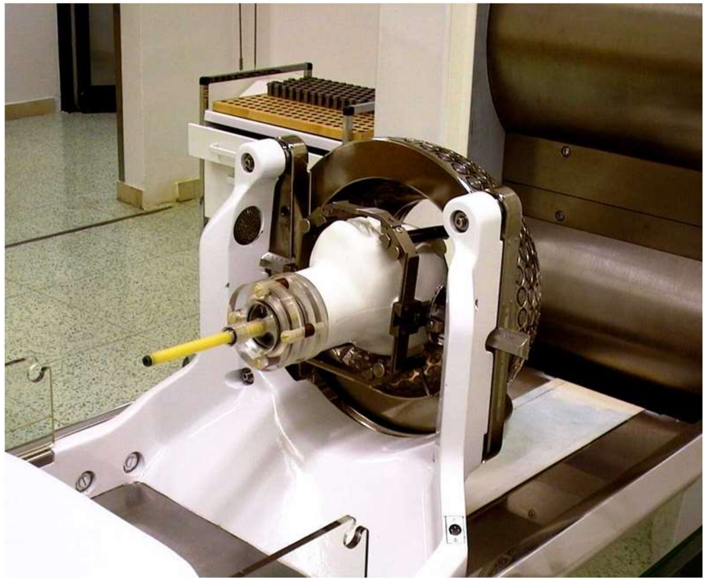


Gamma knife

Several sources (^{60}Co isotopes) arranged around the patient. The channels in the lead shield direct gamma rays to one point, where the dose is extremely high. Designed for brain treatment.



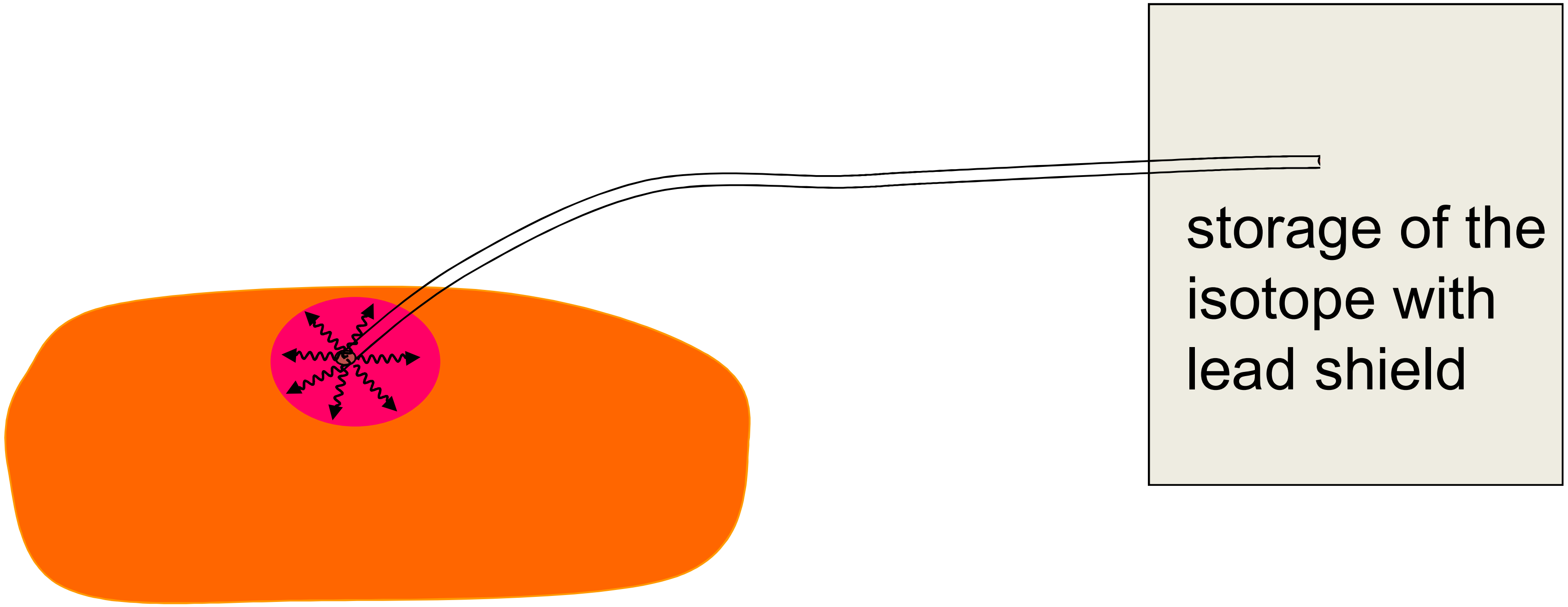

ヘルメット



Brachytherapy

$$D = \frac{K_\gamma A t}{r^2}$$

An applicator can be used to tranfser the isotope into the tumor (after loading technique).



Brachytherapy with implanted isotopes

- Prostate
- ^{125}I „seeds”

  $T_{1/2}$=60 day

Isotope therapy

Targeting of the isotope reached by selective uptake of the isotope in the target organ (e. g. ^{131}I in the thyroid gland in case of hyperthyreosis or by monoclonal antibodies (^{90}Y, ^{153}Sm, ^{186}Re bound to monoclonal antibody)

Alpha-, or beta-radiating isotopes are given to have local effect.

Theranostics: The same object labeled with different isotopes can be used both for diagnostic and therapeutic purposes.