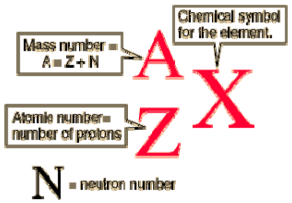
Radioactivity in Medicine

László Smeller

Nuclear radiation

Reminder: basic definitions



mass number (A)
atomic number (Z)
A = Z + N

- Nuclides with equal proton number (Z), but different neutron numbers (N) are called **isotopes** of an element.
- Unstable isotopes (=**radioactive isotopes**) decay:
- **Decay types**: α, β^-, β^+, electron-capture, isomeric transiton
- **Nuclear radiations**: α (He^{2+}), β^-(e^-), β^+ (e^+), γ(electromagn.)

Reminder:comparative properties of nuclear radiations

radiation	**alpha**	**beta**	**gamma**
nature	helium nucleus	electron or positron	high energy photon
charge	+2*e*	+ *e* or - *e*	none
resting mass/mass of proton	4	1/2000	none
ionisation mechanism	frequent collisions with orbital electrons	collision with electrons	photoelectric effect, Compton effect, pair production
number of ion pairs produced per mm of air	1000	10	1

Reminder: Activity

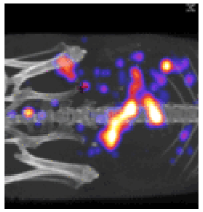
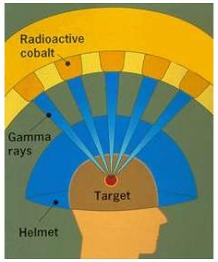
Activity **:** $\Lambda = \left|\frac{dN}{dt}\right|$

N: number of nuclei to be decayed

t: time

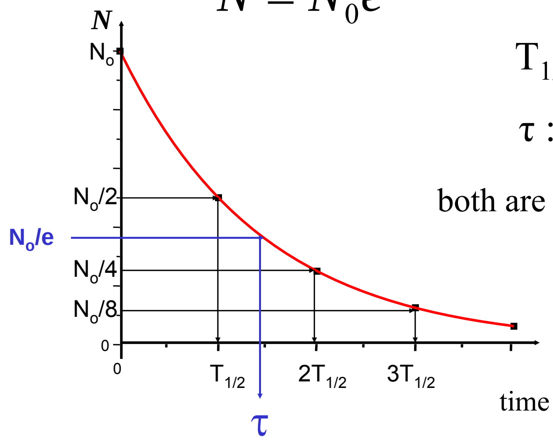
number of nuclei decayed in a unit time

1Bq = 1 decay/sec

natural background	*in vivo* diagnostics	laboratory practice	therapy
			
kBq,	***MBq,***	***GBq,***	***TBq***

Reminder: decay law

$$N = N_0 e^{-\lambda t}$$



$T_{1/2}$: the half-life time

τ : the mean life time

both are characteristic to the nuclei

Interaction with atoms

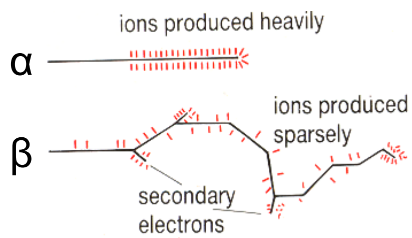
Interaction with matter => Energy loss
=> absorption (and/or detection) of the radiation.

α, β charged particles => direct ionization

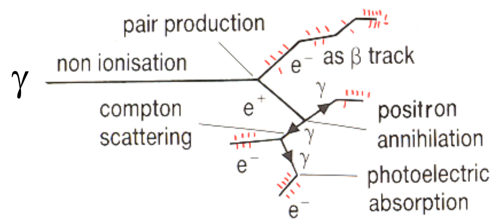
γ uncharged (el.magn.) => indirect ionization

Interaction with atoms

Directly ionizing



Indirectly ionizing



Effective range of charged particles

for α radiation:
in air ~ 3-4 cm, in soft tissue ~ 10-100 μm

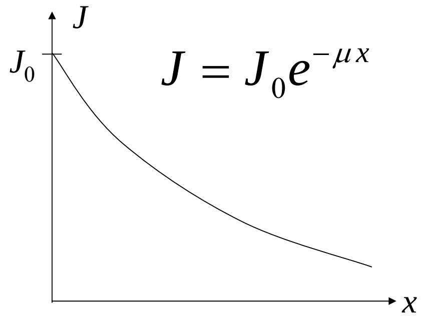
for β radiation:
in air ~several m, in soft tissue ~ few cm

Absorption of the γ-rays

same as for X-ray

Interaction with matter:

- Photoeffect
- Compton effect
- Pair production



$$J = J_0 e^{-\mu x}$$

see practical exercise !

Detection of nuclear radiations

Detection of nuclear radiations:

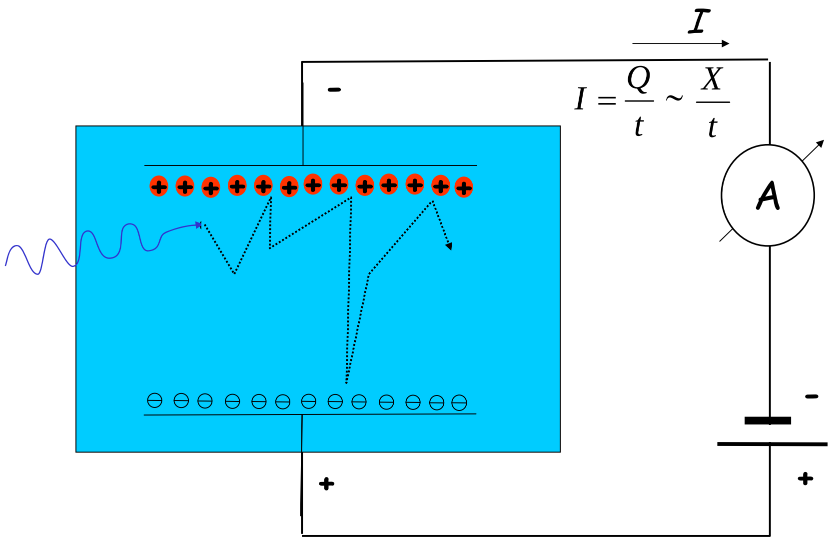
gas ionization

luminescence

photochemical effect

conductivity change

Ionization chamber



Dependence of the gas chamber detectors' current on voltage

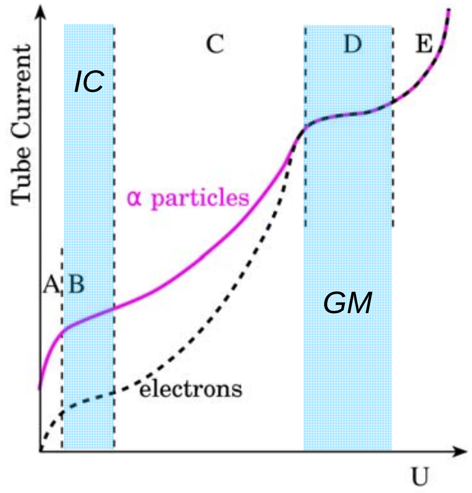
A: slow charge movement, recombination

B: collecting practically all primary ions formed

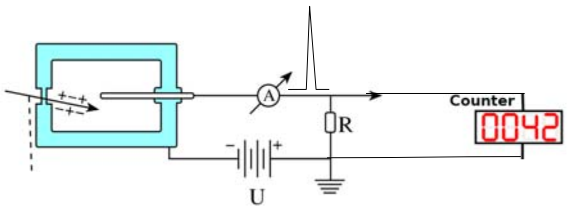
C: secondary ionization

D: discharge after primary ionization

E: discharge without primary ionization



Geiger-Müller counter

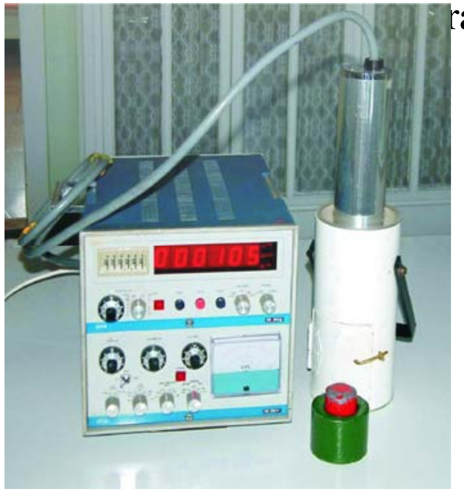


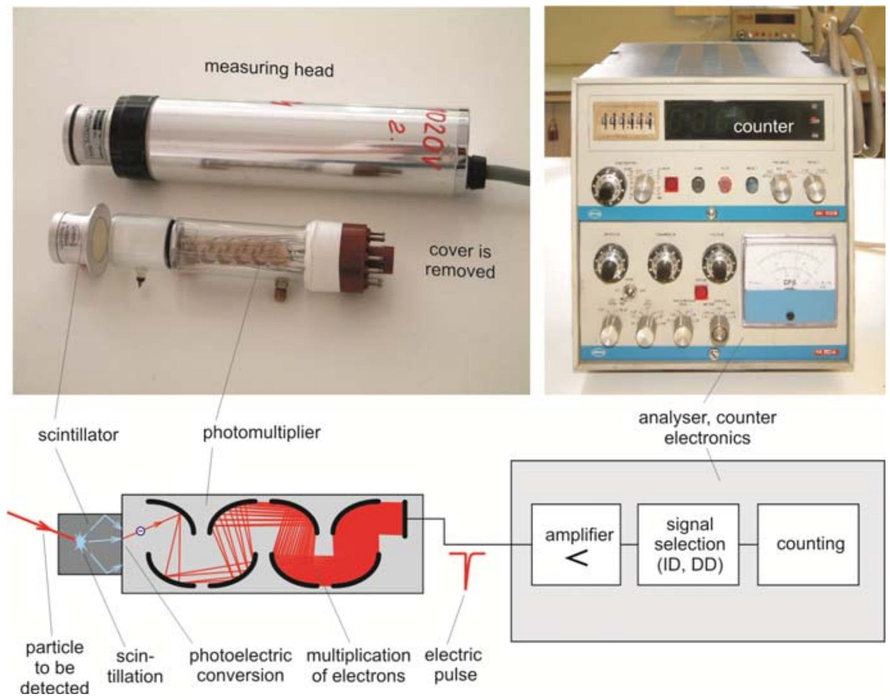
The **strong electric field** bw. the electrodes **accelerates the charges**,
which gain enough energy to **ionize further** creating an **avalanche** of charges.
The resulting current **pulse** can be counted.

advantage: simple construction,
disadvantage: not energyselective, usage: dosimetry

Scintillation counter

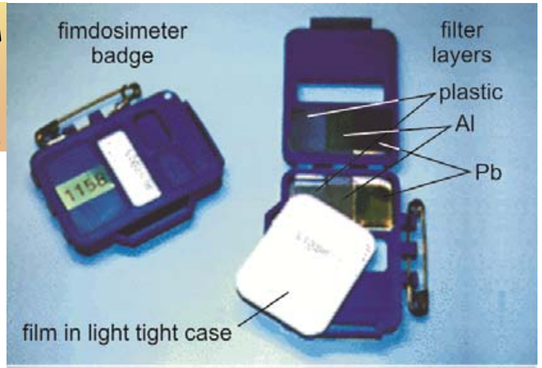
see practical exercise!

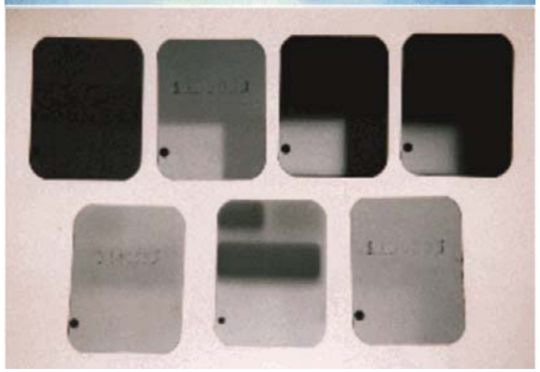




Photochemical detection

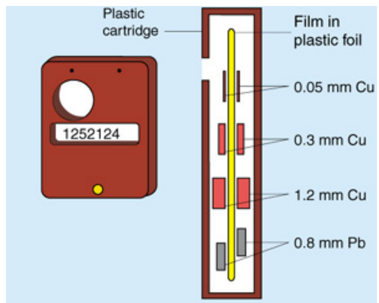
see practical exercise!





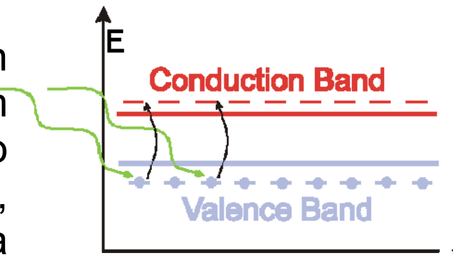
Film dosimeter

The blackening of a photographic film due to radiation is the measure of the dose received. The film cartridge holds various "filters" made of different materials to determine the type and intensity of rays and other factors important to determine the dose.



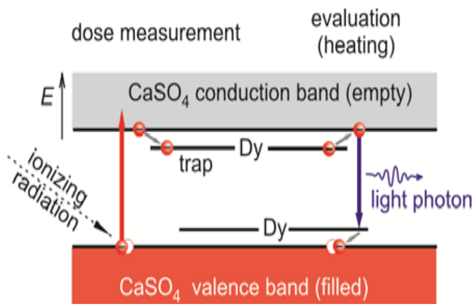
Semiconductor detectors

The ionizing radiation excites electrons from the valence band to the conduction band, which results in a change in the conductance of the crystal.



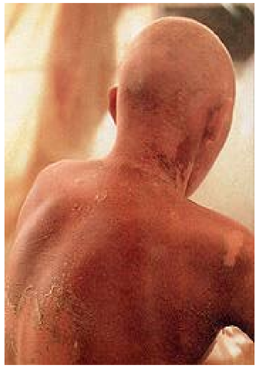
Thermoluminescent detector

Ionizing radiation excites electrons from the valence band to the conductance band. Some part of the electrons is trapped on the inpurity. The dose measurement is evaluated later, by heating the crystal and recording the emitted light.

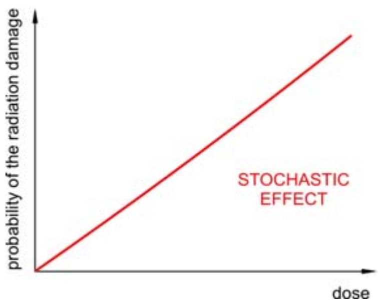


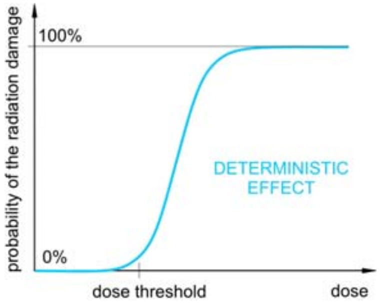
Biological effects of ionizing radiation

Dosimetry



Stochastic and deterministic damages





Deterministic effects

- Large number of cells killed – physiological effect, e.g.
  - **Erythema, epilation, cataracts, "radiation sickness"**
- No risk below threshold doses, e.g.
  - Opacities = 500 mGy
  - Transient erythema = 2 Gy

Stochastic damage

- can be caused by a single photon
- the severity is not effected by the dose
- with increasing dose only the probability increases (somatic cells: cancer, reproductive cells: hereditary effects)

1 gamma photon: the probability to cause cancer is 3 x 10^{-16}
(1: 3,000 billion, but this is the Russian roulette!)

Dosimetry

How can we quantify the effects caused by ionizing radiations?

Pharmacological and radiation dose concepts are different!

Physical doses: absorbed dose

Absorbed dose (D)

$$D = \frac{\Delta E}{\Delta m} = \frac{1}{\rho}\frac{\Delta E}{\Delta V}$$

1 Gy = 1 J/kg

- absorbed energy in unit mass of absorbing medium
- applicable: X-ray, α, β, γ radiations, neutrons, accelerated charged particles etc.
- disadvantage: hard to measure directly

Absorbed dose, typical values

Chest X-ray = 160 μGy skin dose

Background radiation 2.4 mGy/year

Typical 1 minute screening = 20 mGy skin dose

LD_{50} = 4 Gy to whole body (single dose)

Threshold for transient erythema = 2 Gy .

Radiotherapy dose = 40 Gy to tumour (over several weeks)

Absorbed dose is used for prediction of biological consequences in case of **acute irradiation** (i.e. *large* amount of radiation over a *short* period of time). **Deterministic effect!**

Physical doses: Exposure (*X*)

Exposure (*X*):

$$X = \frac{\Delta Q}{\Delta m} = \frac{1}{\rho}\frac{\Delta Q}{\Delta V}$$

(C / kg)

- valid for only X-, γ-rays (< 3 MeV)
- characterizes the ionizing power of radiation in air, instead of the absorbed energy in tissue

Calculation of the absorbed dose

$$D_{air} = f_0 X$$

f_o = 34 Gy / C kg^{-1}

$$D_{tissue} = D_{air}\frac{\mu_{m,tissue}}{\mu_{m,air}}$$

E< 0.6 MeV

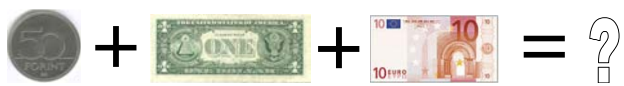
Biological doses: equivalent dose

Equivalent dose (H_T)
Sum of absorbed doses weighted according to type of radiation

$$H_T = \sum_R w_R D_{T,R}$$

Unit: J / kg   with special name: sievert, Sv

$D_{T,R}$ … the absorbed dose averaged over the tissue (T) due to radiation (R)



Radiation weighting factor

represents the effectiveness of radiation inducing stochastic effect at low doses

Weighting factors of different radiations and energies

Radiation and energy range		Radiation weighting factor
Photons, at every energy		1
Electrons, muons, at every energy		1
Neutrons, if the energy is	<10 keV	5
	10 keV–100 keV	10
	100 keV–2 MeV	20
	2 MeV–20 MeV	10
	> 20 MeV	5
Protons, if the energy is	> 2 MeV	5
α-particles, nuclear fission products, heavy nuclei		20

Biological doses: effective dose

Effective dose (E)

the sum of weighted H_T in all tissues and organs in the body

$$E = \sum_T w_T H_T \qquad \sum_T w_T = 1$$

Unit: Sv (J / kg)

provide a basis for estimating the **probability** of **stochastic effects** for doses well below the threshold of deterministic effects

Tissue weighting factors

represent the relative contribution of that organ or tissue to the total damage due to the total of stochastic effects resulting from uniform irradiation of the whole body

Weighting factors of various tissues and organs

Tissue/Organ	Weighting factor, w_T
Gonads	0.20
Red bone marrow	0.12
Large intestine	0.12
Lungs	0.12
Stomach	0.12
Bladder	0.05
Breast	0.05
Liver	0.05
Oesophagus	0.05
Thyroid gland	0.05
Skin	0.01
Surface of the bones	0.01
Other	0.05

Approximate effective doses

Examination	E (mSv)
Chest X-ray	0.04
Chest CT	7.8
Cranial CT	1.8
Abdominal X-ray	1.2
Abdominal CT	7.6 ←
X-ray of the dorsal vertebrae	1.0
X-ray of the lumbar vertebrae	2.1
Barium enema with fluoroscopy	8.7

Risk – loss of life expectancy

Days of average life expectancy
lost due to various causes

Being an unmarried male	3500
Smoking (1 pack/day)	2250
Being an unmarried female	1600
Being a coal miner	1100
25% overweight	777
Alcohol abuse (U.S. average)	365
Being a construction worker	227
Driving a motor vehicle	207
All industries	60
Radiation: 1 mSv/yr x 70 years	10 ⟵
Coffee	6

Relative risk of dying:1 in a million odds

- Smoking 1.4 cigarettes (lung cancer)
- Eating 40 tablespoons of peanut butter
- Eating 100 charcoal broiled steaks
- 2 days in New York City (air pollution)
- Driving 40 miles in a car (accident)
- Flying 2500 miles in a jet (accident)
- Canoeing for 6 miles
- Receiving 0.10 mSv radiation dose (cancer) ⟵

Radiation protection

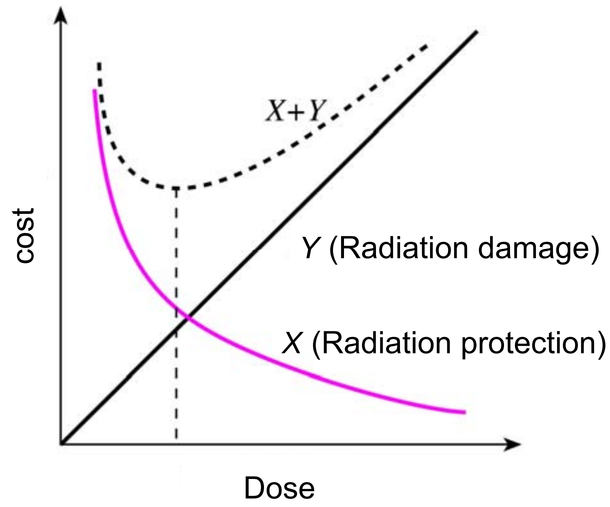
Aim: users of the sources and the members of the public are not irradiated above acceptable risk.

1. Prevention of deterministic effects (except in radiotherapy)
2. Reduction of the probability of stochastic effects

Acceptable risk: radiation illness due to the received ionizing radiation cannot be shown statistically unambiguously.

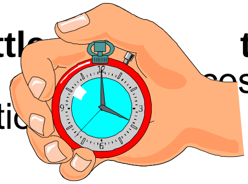
Medicine: cost-benefit

ALARA principle (as low as reasonably achievable)

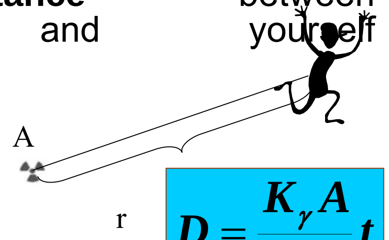


Basic radiation protection strategies

- spend as **little time**, as necessary in the radiation field.



- **keep the distance** between radiation source and yourself as **large** as possible. $D \sim 1/r^2$
- use **shielding**.



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

Imaging using radioactive nuclides

Basic steps of the isotope diagnostics

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

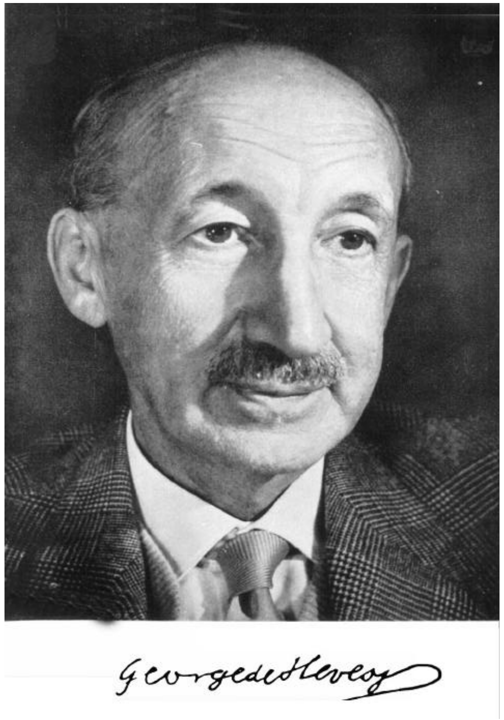
Isotope diagnostics

MRI

dynamic physiological / metabolic processes of different body organs can be followed

X-ray | Isotope diagnostics

Shows the structure | *Reports the metabolic activity*



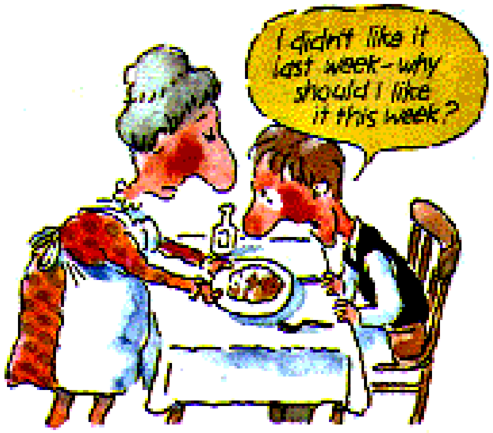
Father of Nuclear Medicine

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

George Hevesy and his landlady



In any event, he became convinced that his landlady had a nasty habit of recycling food. Hevesy secretly spiked the leftovers on his plate with radioactive material. A few days later, the electroscope he smuggled into the dining room revealed the presence of the tracer

The choice of the appropriate radioisotope for nuclear imaging

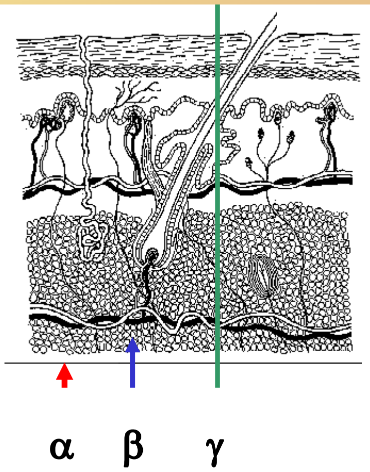
Maximise the information

Minimise 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

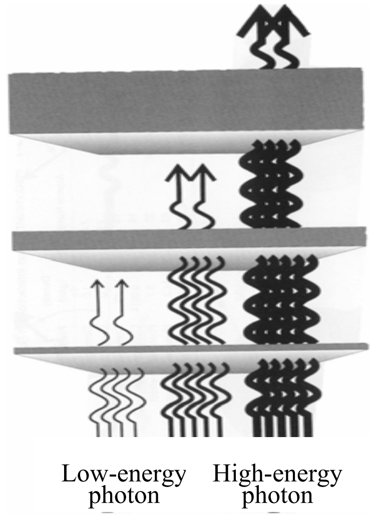
Only **γ-radiation** has

sufficient penetration

distance .

purely gamma-emitting isotope would be preferable

Photon energy



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)

Suitable physical half-life

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

smaller is better (Λ)
but
the value is limited from below
e.g., by the sensitivity of the
detector

smaller is better (N)

dosimetric considerations for patients

shorter is better (T)

but

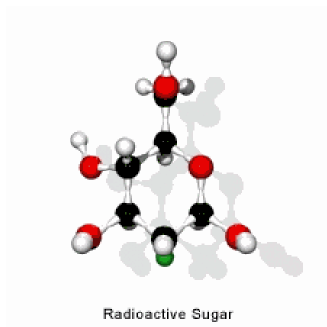
it has to be long enough for monitoring the physiological organ functions to be studied

radiopharmaceutical – is 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 : nontarget* ratio

have no pharmacological or toxicological effects which may interfere with the organ function under study.



Examples

pharmaceutical	radioisoptope	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

Isomeric transition

Metastable excited nuclear state - halfe-life from few hours to 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 $T_{1/2}$=6 hours

hf=140 keV

Isomeric transition

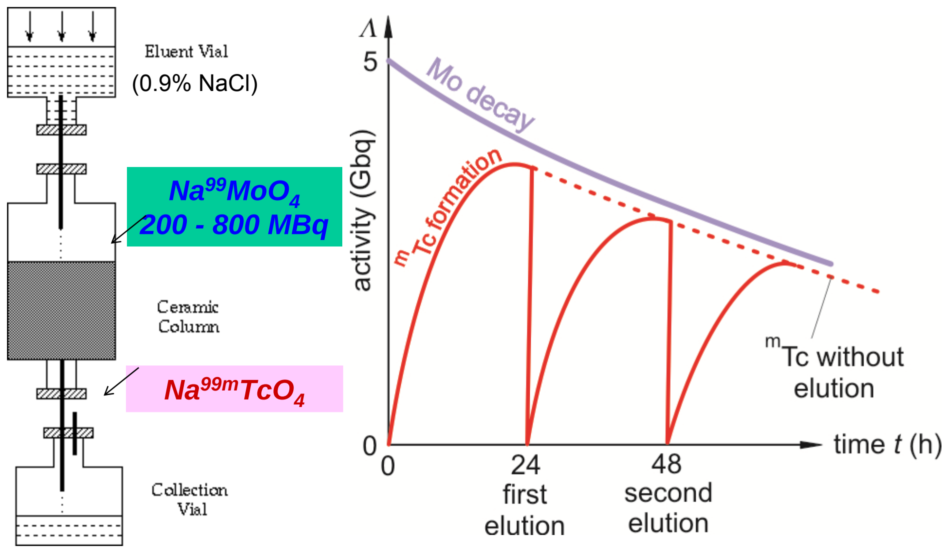
$$^{99}_{42}Mo \rightarrow {}^{99m}_{43}Tc + \beta^- \rightarrow {}^{99}_{43}Tc + \gamma$$

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

hf=140 keV

One of the features that makes **Tc-99m** such an ideal radioisotope for diagnostic imaging is its ability to **readily bind to a wide variety of compounds** under physiological conditions.

Technetium-99m generator



Optimal activity for diagnostic procedure

Maximize the information

Minimize the risk

$$\Lambda \sim 100 \text{ MBq}$$

Types of images

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

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

Static and dynamic picture – series of static recordings

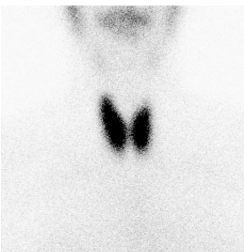
Emission CT

SPECT (Single Photon Emission Computed Tomography)

PET (Positron Emission Tomography)

Types of images

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

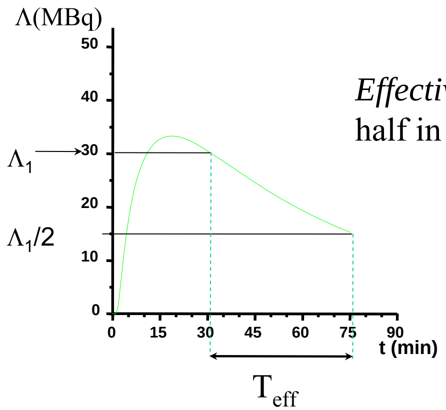


Isotope accumulation in

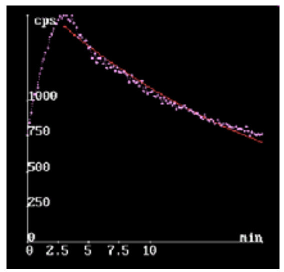
thyroid glands kidneys

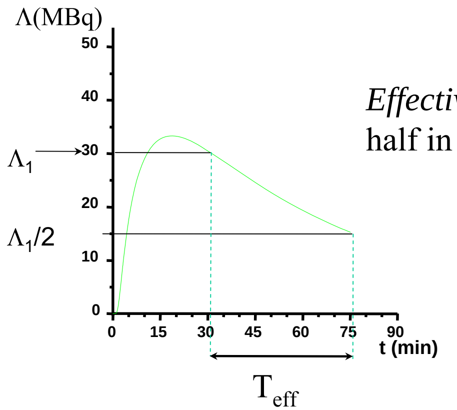
Types of images

Dynamic picture – 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

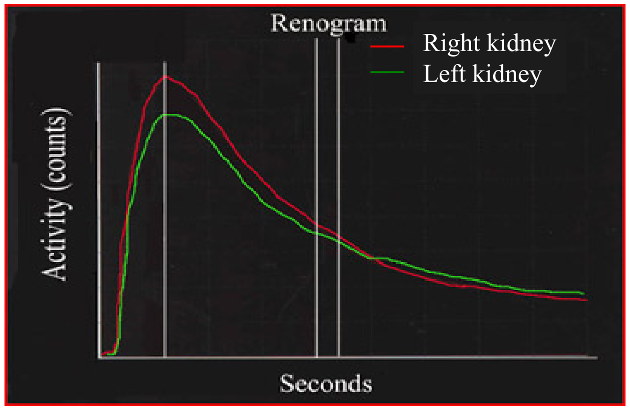
$$\Lambda = \Lambda_0 e^{-(\lambda_{phys}+\lambda_{biol})t}$$

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

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

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.

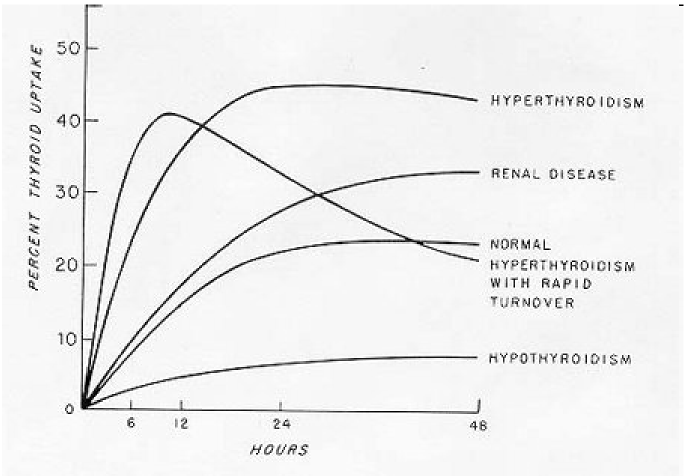
example



kidney

Isotope accumulation

example



Thyroid glands

Isotope accumulation

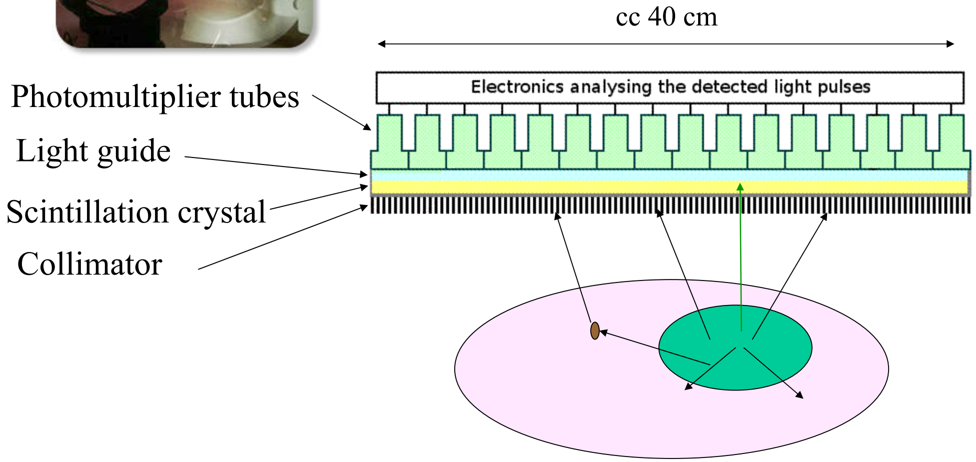
Hal Anger

1920-2005

Hal Anger and coworkers

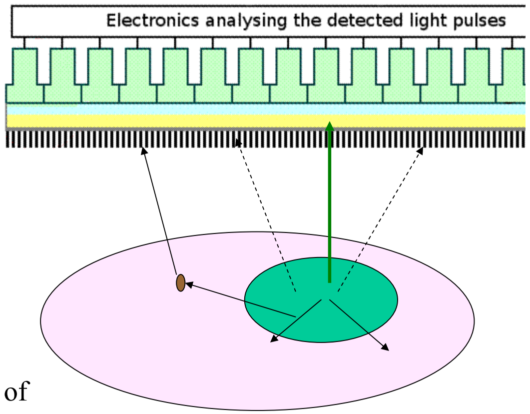
1952

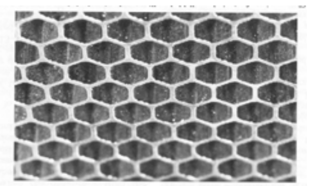
Gamma camera



A radioactive source emits gamma ray photons in all directions.

collimator



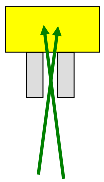


Collimators are composed of thousands of precisely aligned ***channels*** made of lead.

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

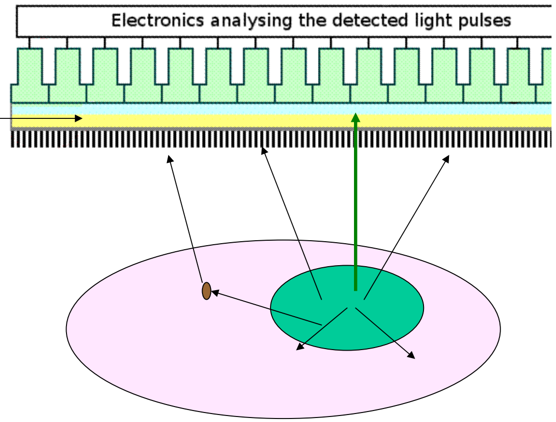
Photons emitted in other directions are absorbed by the septa between the holes.

Size and geometry of holes are essential for the **resolution**.



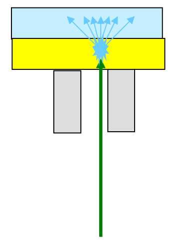
Scintillation crystal

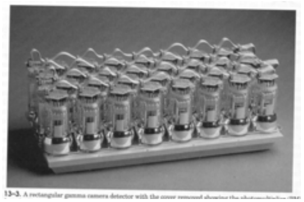
Na(Tl)



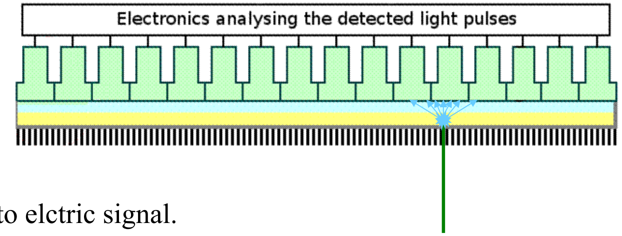
Light guide

Distribution of the ligth for the prhotmultipliers



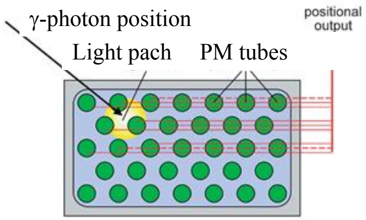


Photomultiplier tubes

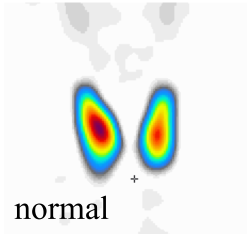


Transformation of light pulses to elctric signal.

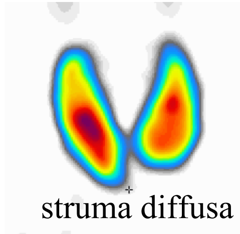
Typically 37-91 tubes,
5-7 cm diameter each



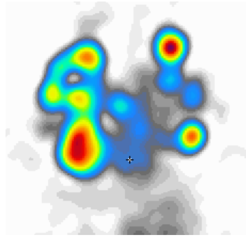
Pertechnetate (intravenous 80 MBq) distribution in thyroid glands



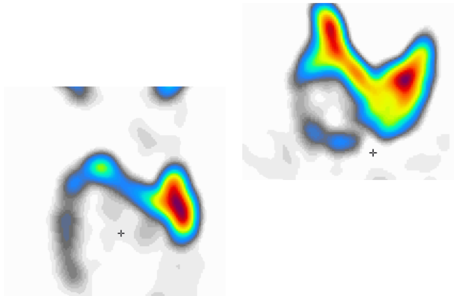
normal



struma diffusa

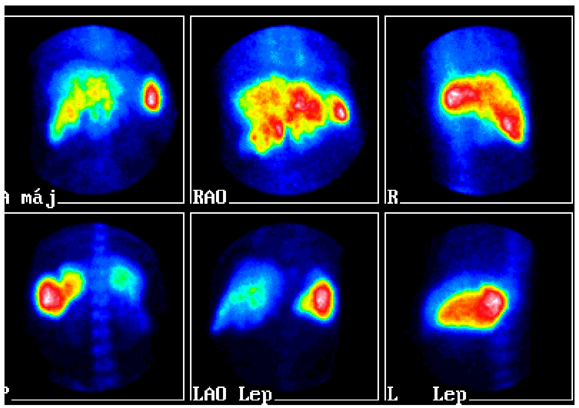


struma multinodularis



Cold nodules

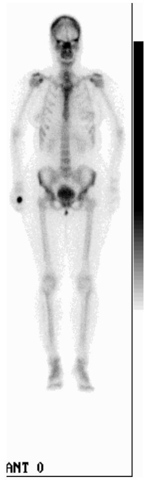
Liver lesion nodules



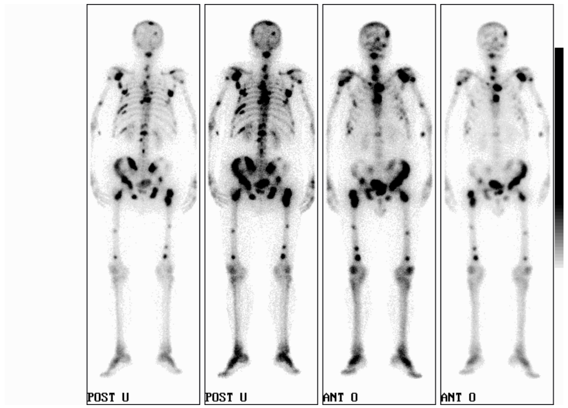
^{99m}Tc- fyton

Bone scintigraphy

^{99m}Tc-MDP: 600 MBq

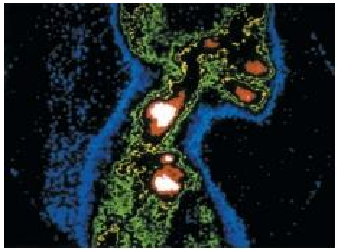


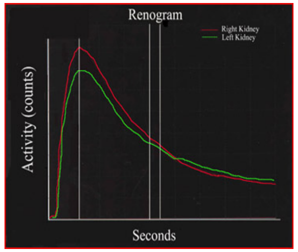
normal



imaging in bone metastases

Gamma camera image:
summation image

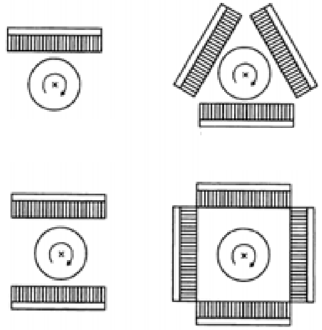




For depth resolution: tomographic device is necessary

SPECT

Single Photon Emission Computed Tomography



Variouos camera arrangements

SPECT

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

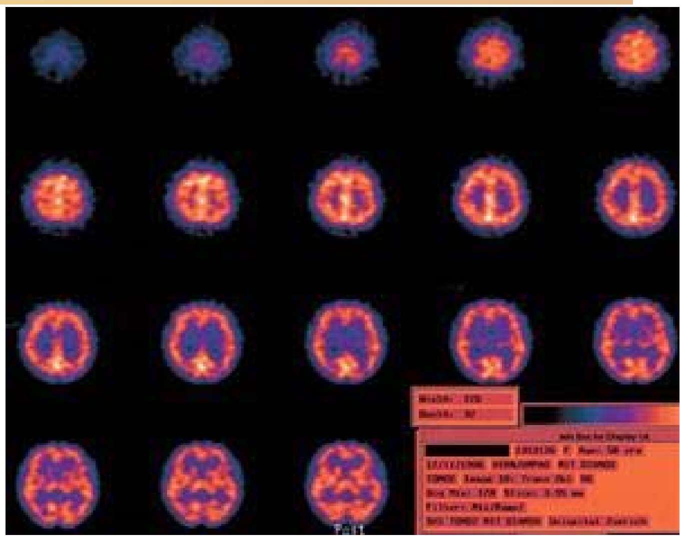
Cross-sectional image can be reconstructed.

Measurement from a series of projections.

Computer directs the movement of the detector, stores the data, reconstruct the cross-sectional image

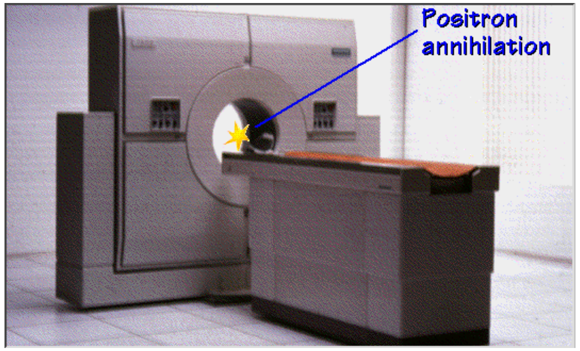
SPECT – images of scalp

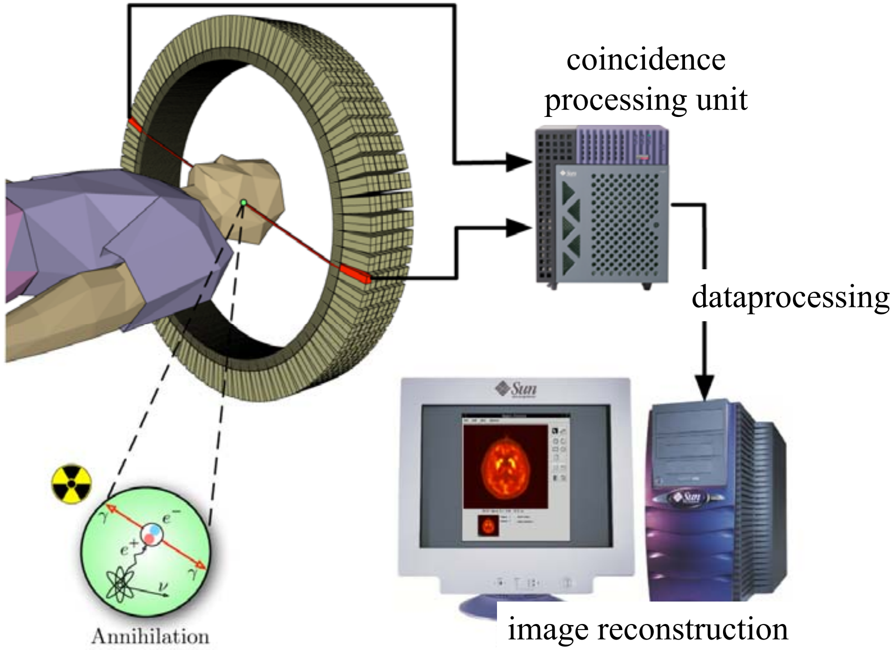
^{99m}Tc- HMPAO



PET

Positron Emission Tomography





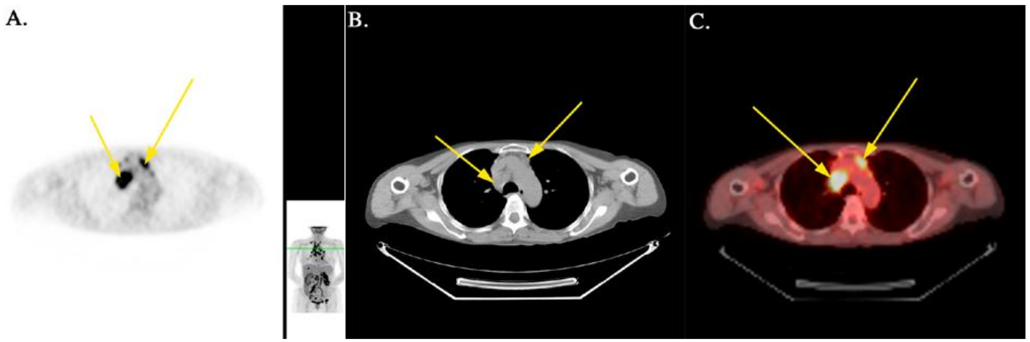
The most frequently used radionuclides in PET are radioisotopes of structural elements of natural organic molecules.

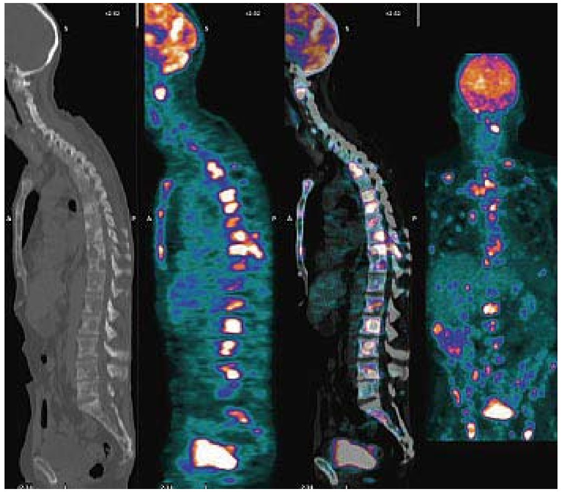
Isotope	β^+ energy (MeV)	β^+ range (mm)	1/2-life	Applications
^{11}C	0.96	1.1	20.3 min	receptor studies
^{15}O	1.70	1.5	2.03 min	stroke/activation
^{18}F	0.64	1.0	109.8 min	oncology/neurology
^{124}I	2.1350/1.5323	1.7/1.4	4.5 days	oncology

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

PET/CT

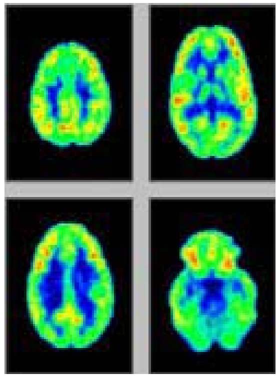
Combination of structural and functional imaging



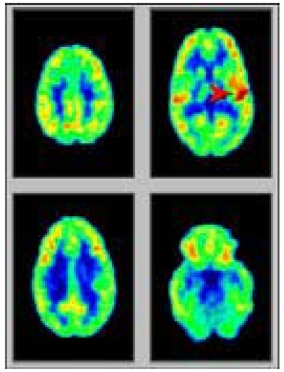


CT PET PET/CT PET

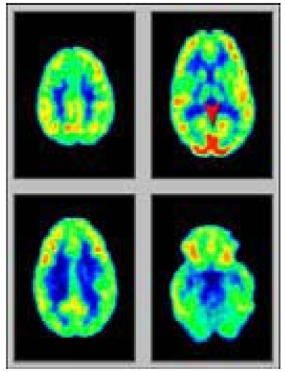
Activity of brain areas



In rest



hearing



vision

Radiation therapy

Radiotherapy : ionizing radiation induces damages at molecular and cellular level. This can be beneficial against tumour tissues

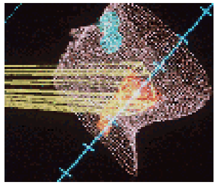
1. Which radiation is the best?
2. What is the optimal dose of radiation?
3. What is the best technique for generation radiation?
4. Irradiation selectivity – protection of healthy structures?

Approaches

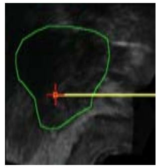
Palliative radiotherapy to reduce pain and address acute symptoms – e.g. bone metastasis, spinal cord compression etc.,

Radical radiotherapy as primary modality for cure – e.g. head and neck

Adjuvant treatment in conjunction with surgery – e.g. breast cancer



α



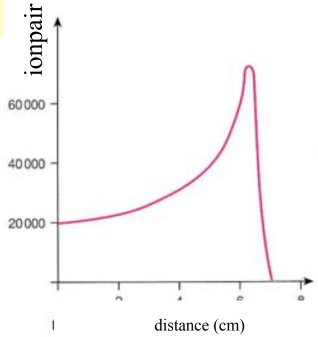
Internally deposited radioactivity

β^-,
e-,
γ,
Rtg,
p
n

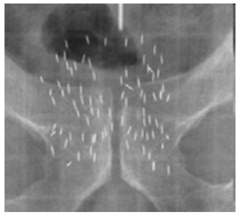
Linear ion density:
the amount of ion pairs in a line generated in a unit distance *(n/l)*

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
production: linear accelerator

γ,
Rtg,
p
n

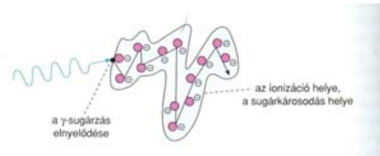
Efficient distance! ≈1cm/3MeV

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

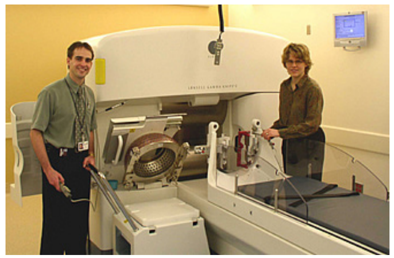
γ : external radiation source

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

Penetration distance is energy dependent



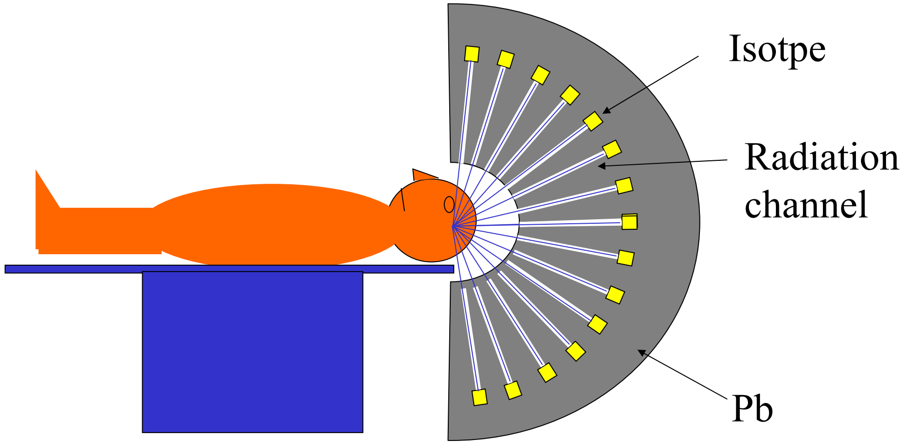
γ-knife: focused dose of radiation

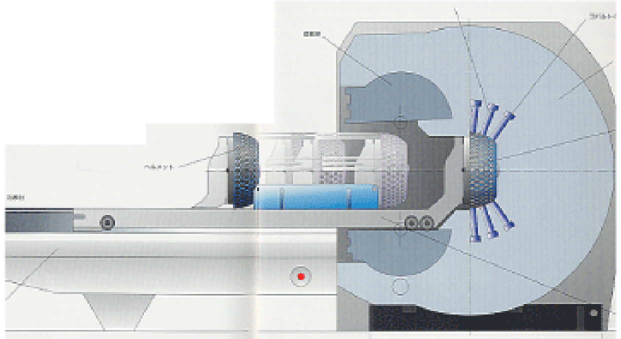


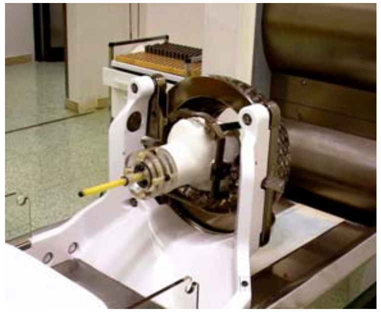
about 200 portals in a specifically designed helmet

e.g., ^{60}Co Eγ≈MeV ,
about TBq activity

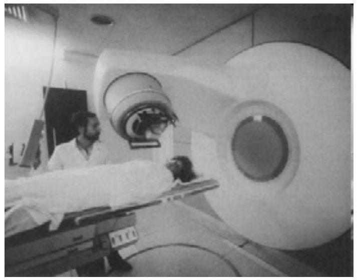
Treat tumors and lesions in the brain







X/ray:



The X-rays are generated by a linear accelerator .

Few MeV photon energy.

Would be ideal, but very expensive!

γ,

Rtg,

p :

n