Bases of radioisotope diagnostic methods

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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 (radiopharmacons)

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.

Radiopharmaceuticals

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

In the pharmacopoeia one can find radiopharmaceuticals in two groups:
- ATC V09 Radiopharmaceuticals used in diagnostics
- ATC V10 Radiopharmaceuticals used in therapy

In vivo diagnostics

Viewpoints for selection of isotopes
- gamma-radiating (the longest effective range)
- short half-life (but not too short)

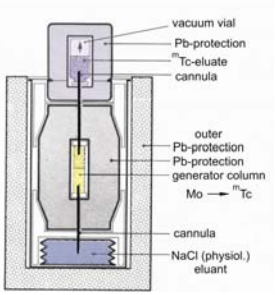
$\Lambda \sim N/T$

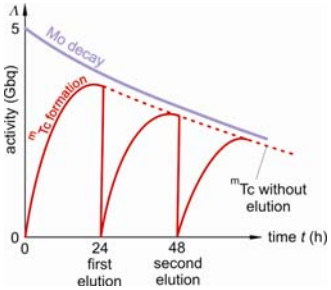
-photon energy should not be too low, and should not be too high (higher energy $\rightarrow$less absorption in the tissues, but the detection efficiency is lower)

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

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

T = 67 hours T = 6 hours

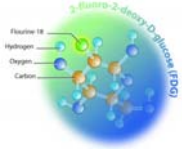




At least in 75 % of the in vivo diagnostic applications ^{99m}Tc is used to label different organ specific compounds.
(e.g. pyrophosphate – bones, colloids – liver and RES, albumin – circulation)

Further gamma-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.



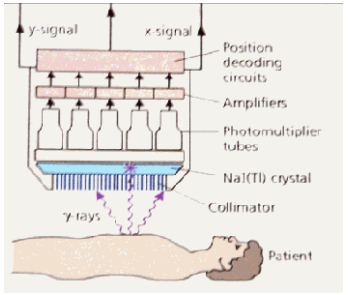
The distribution of isotopes can be detected by diagnostic equipments based on scintillation.

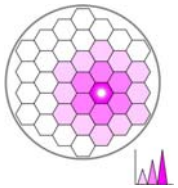
- Scintillation counter (see practice!)

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

Gamma camera

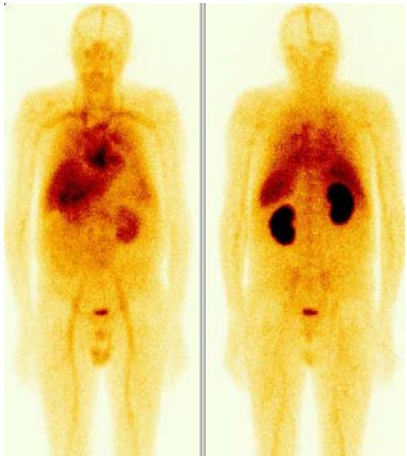
Hal Anger
(1920-2005)





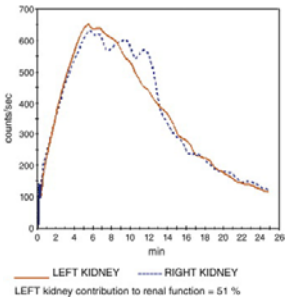
Static examination (scintigram)

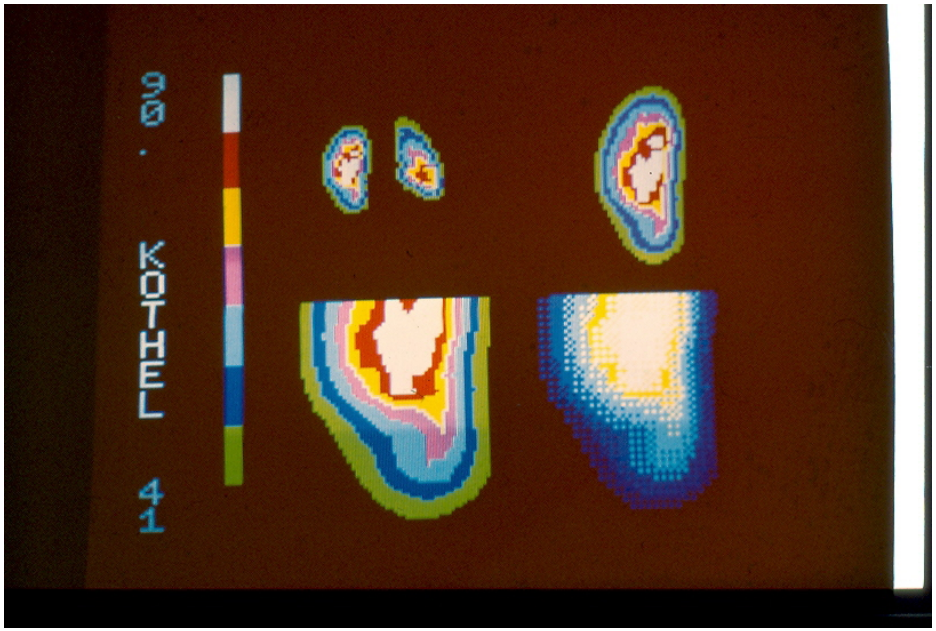
- the distribution of isotope in the space can be examined

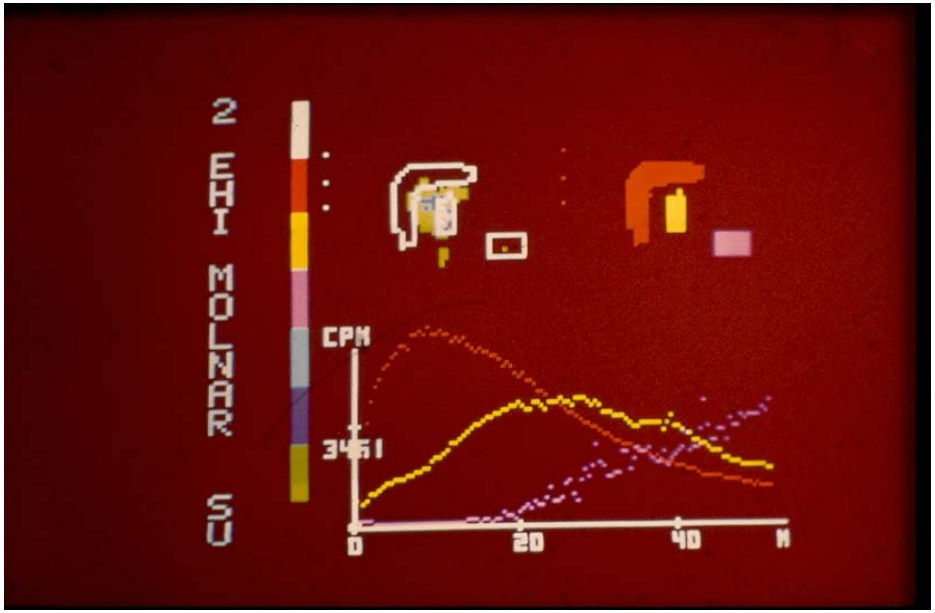


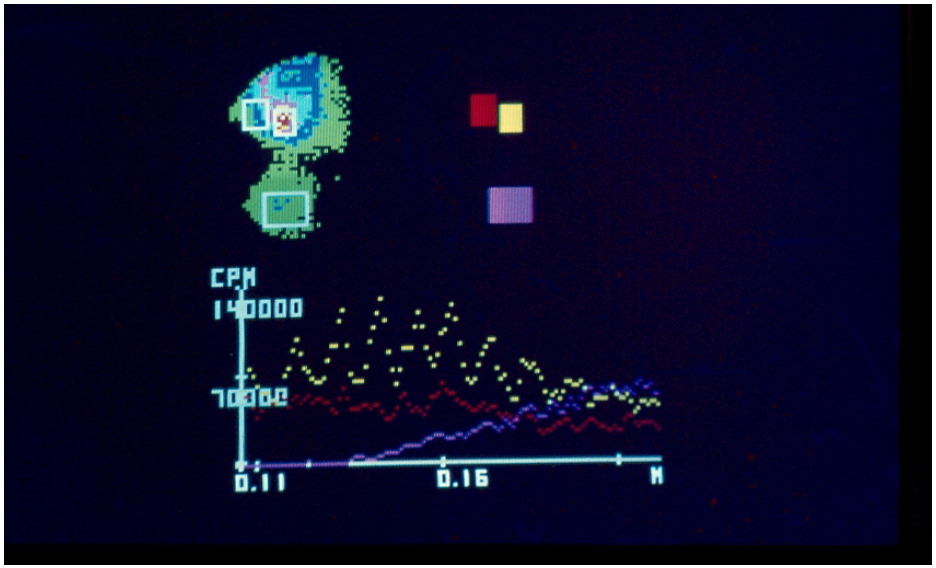
Dynamic examination

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

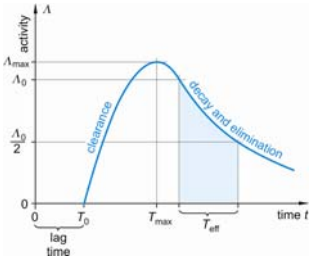


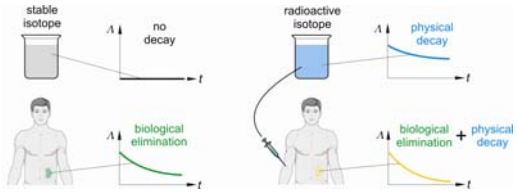






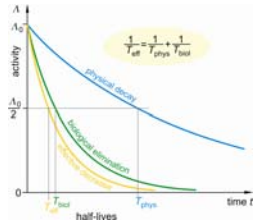
The isotope accumulation curve can be obtained from the measurement of activity in different moments



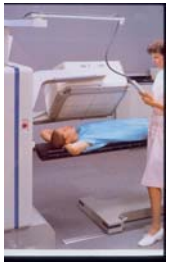


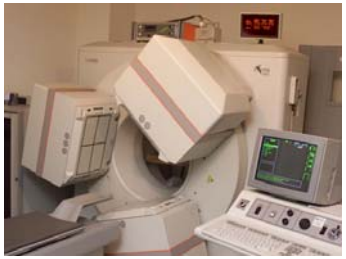
Connection between half-lives:

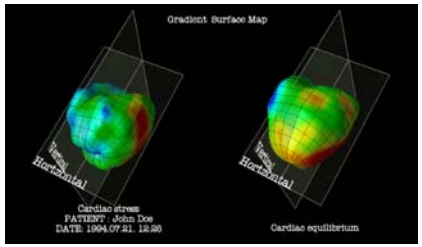
$$\frac{1}{T_{eff}} = \frac{1}{T_{phys}} + \frac{1}{T_{biol}}$$



SPECT (the detector of gamma camera is rotated around the body axis → three dimensional image)

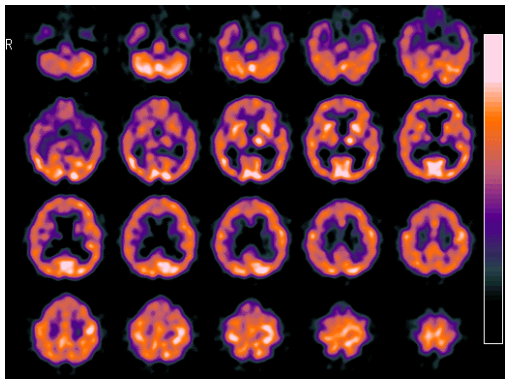


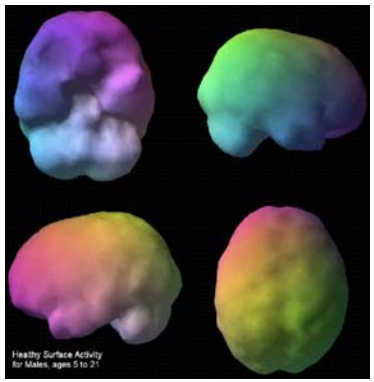




SPECT-images

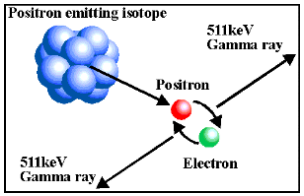
Similarly to CAT-scan cross-sectional images are produced about the layers above each other. From these sectional image of any direction or three dimensional image can be reconstructed.

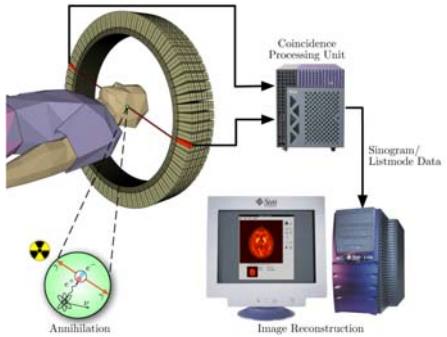


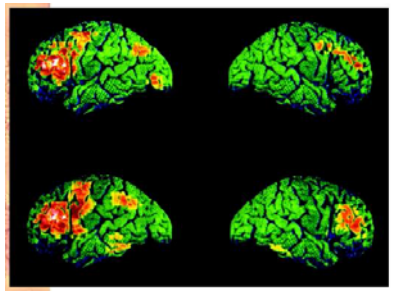


PET examination

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).







PET

The patient is surrounded by circles of scintillation detectors.

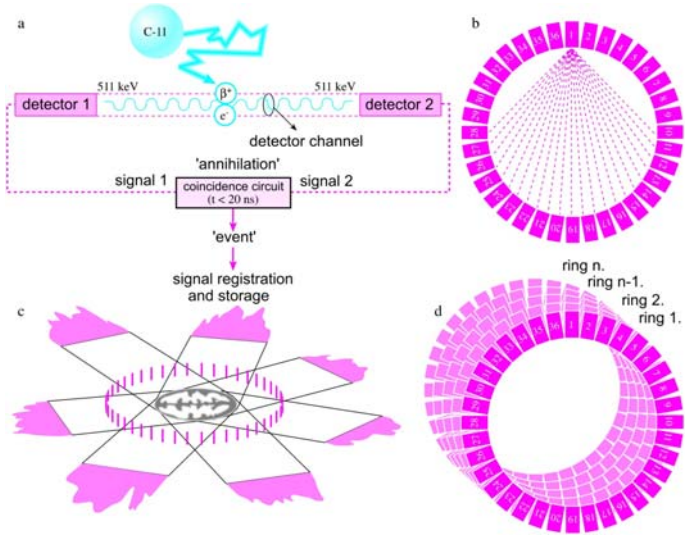
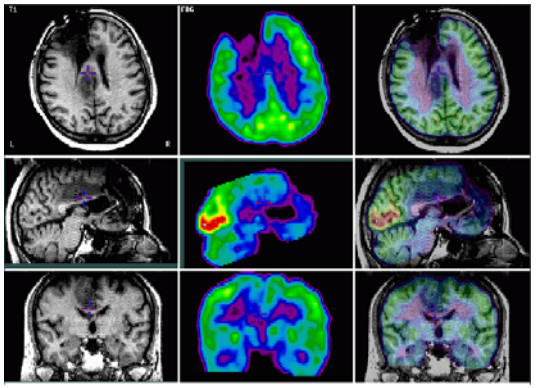


Image fusion

Combination of functional and morphological information

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



Combined equipments (for both diagnostic and research purposes)

NanoSPECT/CT

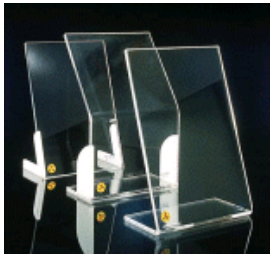
NanoPET/MRI

In vitro isotope diagnostics

- Usually the concentration of a component (e.g. hormone) in body fluid (blood, urine) sample is determined.

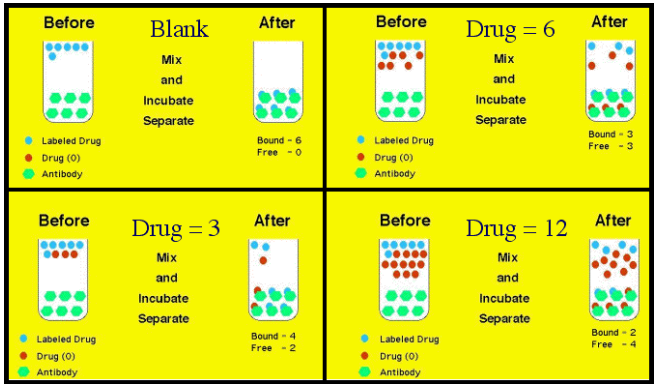
- In the selection of isotopes the measurement technological viewpoints are important. Negative beta-, or soft gamma radiating isotopes are used, e.g. ^{3}H, ^{14}C, ^{125}I.

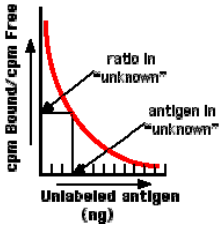
- Working with these preparations plexi plates are used for radiation protection.



Radioimmunoassay (RIA)

- known amount of antibody and radioactive antigen + „cold" antigen in different amounts → calibration curve is made from where the unknown concentration can be read

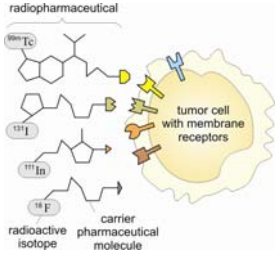


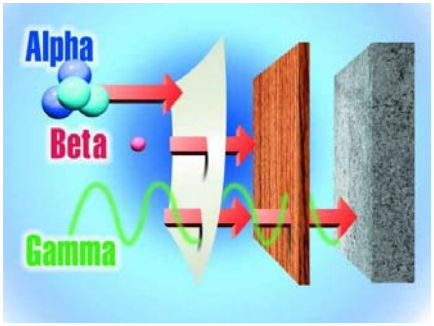


Isotope therapy

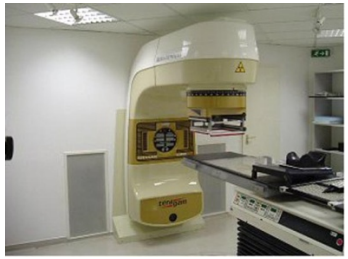
The cell killing effect of ionizing radiation is used for the treatment of e.g. hyperthyreosis (^{131}I) or tumors (^{90}Y, ^{153}Sm, ^{186}Re bound to monoclonal antibody)

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





Therapy with radiation sources outside the body



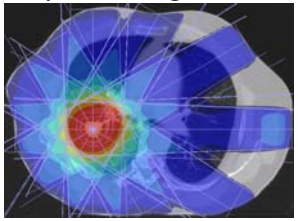
Gamma-radiating isotopes are used (high penetration depth)

Higher photon energy →higher penetration depth.

Mainly for killing of tumors (^{137}Cs, ^{60}Co)

Radiation sources of very high activity are applied, because high dose is necessary to kill the tumor cells.

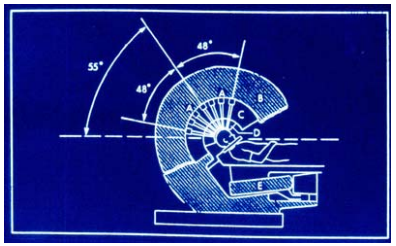
Isotopes of long half-life are useful to keep the activity for a long time.

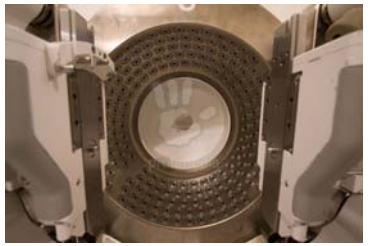


The necessary amount of radiation is given in smaller parts from many direction in order to avoid the injury of the surrounding healthy tissues. The exact distribution in space and time is planned by computer.

Gamma-knife

Used for the treatment of intracranial tumors. Many (approx. 200) ^{60}Co isotopes are put in different directions around the skull. Their radiation is focused to a small volume.





Radiation protectional viewpoints during work with ionizing radiation

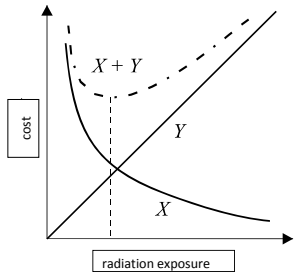
1. Justification – the application of ionizing radiation must be useful: the risk of application should be lower than the risk of not applying the radiation – this must be considered from the viewpoint of the patient.

2. Optimization – the dose caused by the application should be As Low As Reasonably Achievable (ALARA-principle). This must be considered both from the viewpoint of the patient and the personnel.

3. Dose limits – the probable doses should not exceed the individual dose limits that are safe. This must be considered from the viewpoint of the personnel.

Optimization

X – cost of radiation protection
Y – cost of the treatment of radiation injury



Dose limit for employees working with ionizing radiation:

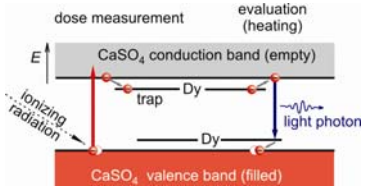
- Whole body dose limit: 20 mSv/ year.

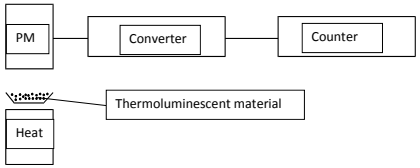
Some dose values obtained during medical application
(dose concepts: see practice and textbook)

In vivo isotope examinations usually: 4 – 5 mSv
Dental X-ray examination: 2 – 16 µSv
Chest X-ray screening: 0.1 mSv
Skull CAT-scan: 1.5 – 2 mSv
Chest or abdominal CAT-scan: 7 -8 mSv
Interventional radiology: several 10 mSv

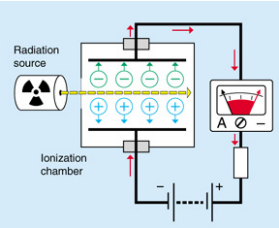
Average background radiation in Hungary: 3.1 mSv/year
Average background radiation in the World: 2.4 mSv/year

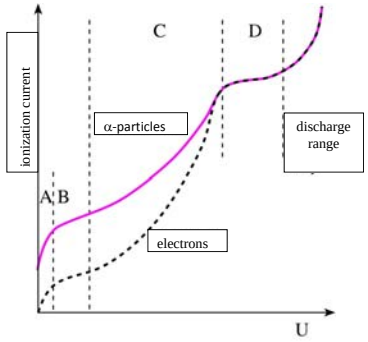
Thermoluminescent dosimeter





Detection of radiation based on gas ionization





A: recombination range
B: ionization chamber range
C: proportional range
D: Geiger – Müller range

The exposure can be measures with ionization chamber, too.

The risk depends on the type of radiation

If the source is **outside the body**, gamma- or X-radiation is the most dangerous. (because of high effective range)

If the isotope is **incorporated** (by inhalation or by swallowing), alpha-Radiating isotopes are the most dangerous. (All the radiation is absorbed in the body tissues.)

Possibilities to decrease the exposure from radiation source outside the body

- Increase the distance
- Decrease the exposition time
- Application of shielding