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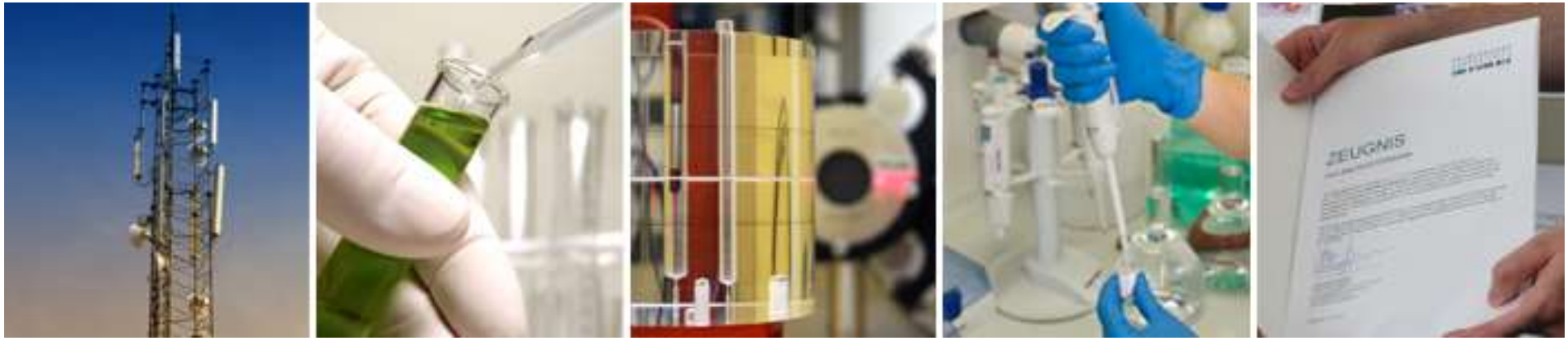
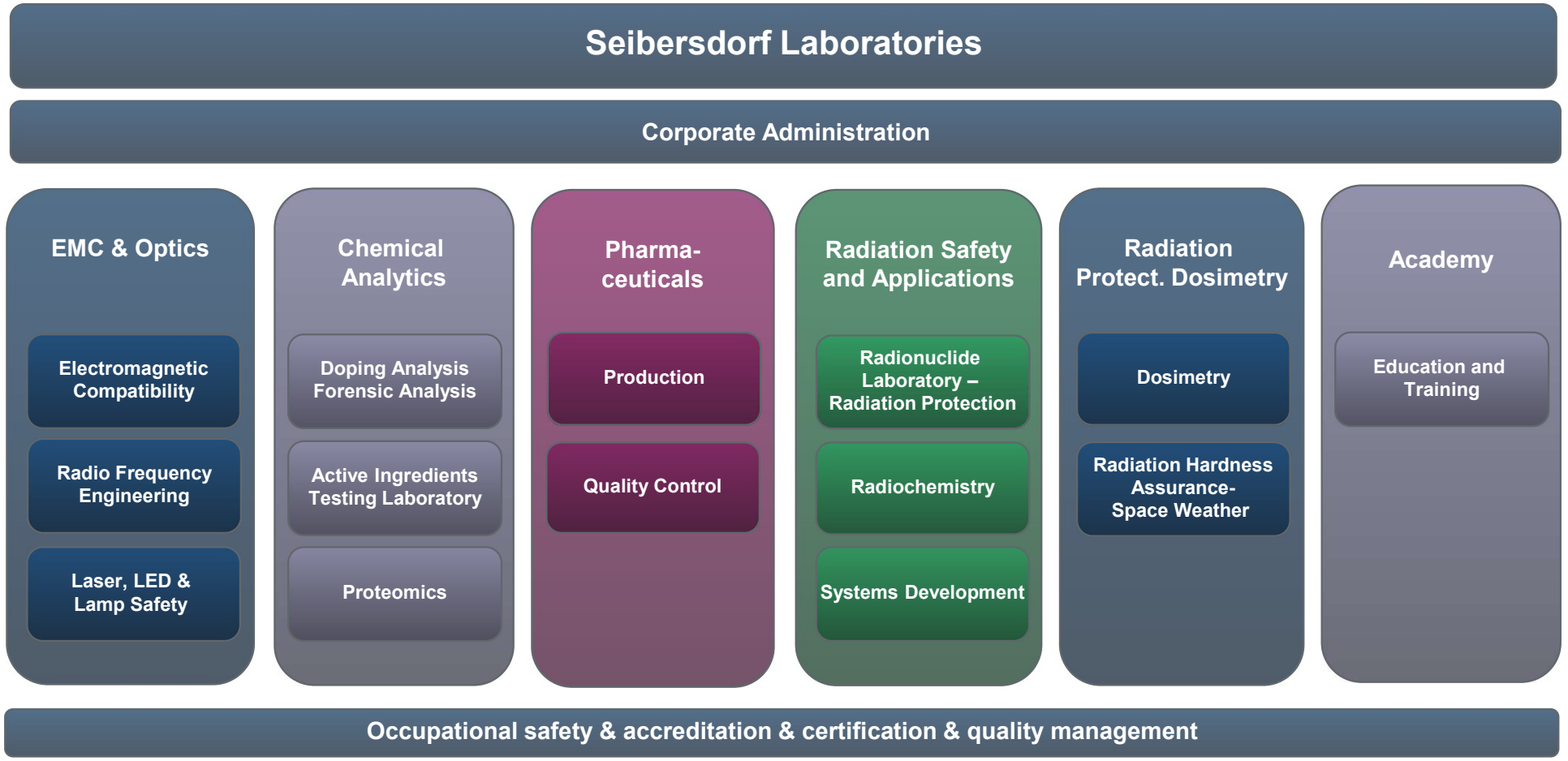
Neue Entwicklungen und Produktion in der kommerziellen Radiopharmazie

Roland Müller



SL Company Organisation



Radiopharmacy Seibersdorf

Our business concept:

Commercial contract manufacturing organisation (CMO) with no own marketing authorizations and no own intellectual properties

Radiopharmacy Seibersdorf

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Our services:

- GMP contract manufacturing of radiopharmaceuticals
- Development, optimization and validation of production lines for radiopharmaceuticals

Radiopharmacy Services

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Our in-house activities include:

- Production
- Quality Control
- Batch release
- Stability testing
- Ordering and transport logistics

We can cover all services from ordering to delivery
(for shipments external couriers are subcontracted)

Radiopharmacy Segments

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Product segments at Seibersdorf:

- Diagnostics (F-18)
- Therapeutics (Lu-177, Ac-225)
- Radionuclide Production (Lu-177)

Radiopharmacy customers

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Our direct customers are:

- Pharmaceutical wholesaler
- Pharmaceutical companies

Our indirect customers are:

- Clinical sites with nuclear medicine

Location

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Radiopharmaceuticals

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- Growing Market/demand
- Personalised medicines (diagnostics & therapy)
- Short shelf life (< 1 week)
- Production on demand only – no warehousing
- Radioactive transports required

Theranostic approach

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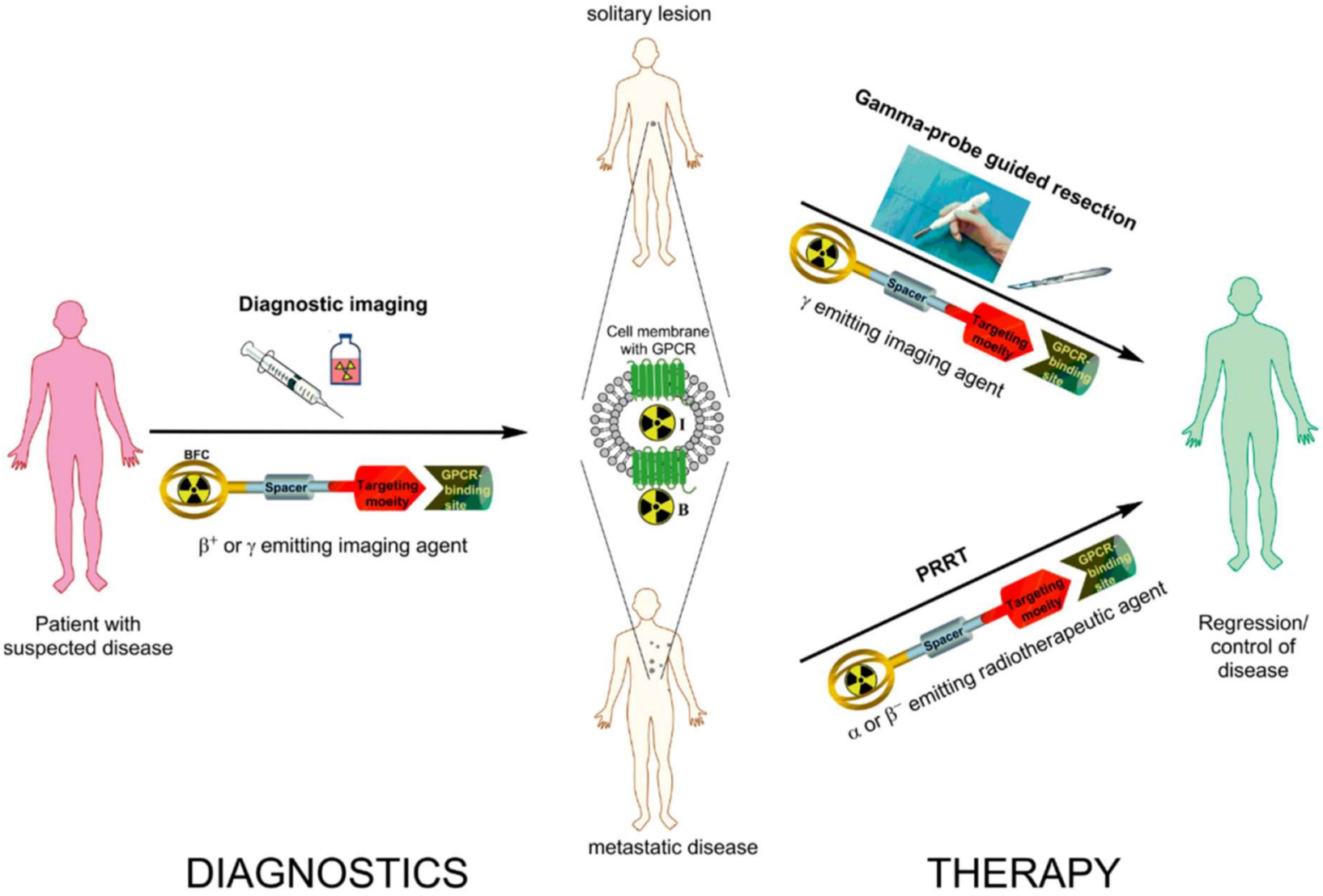

Effect of Ionizing Radiation

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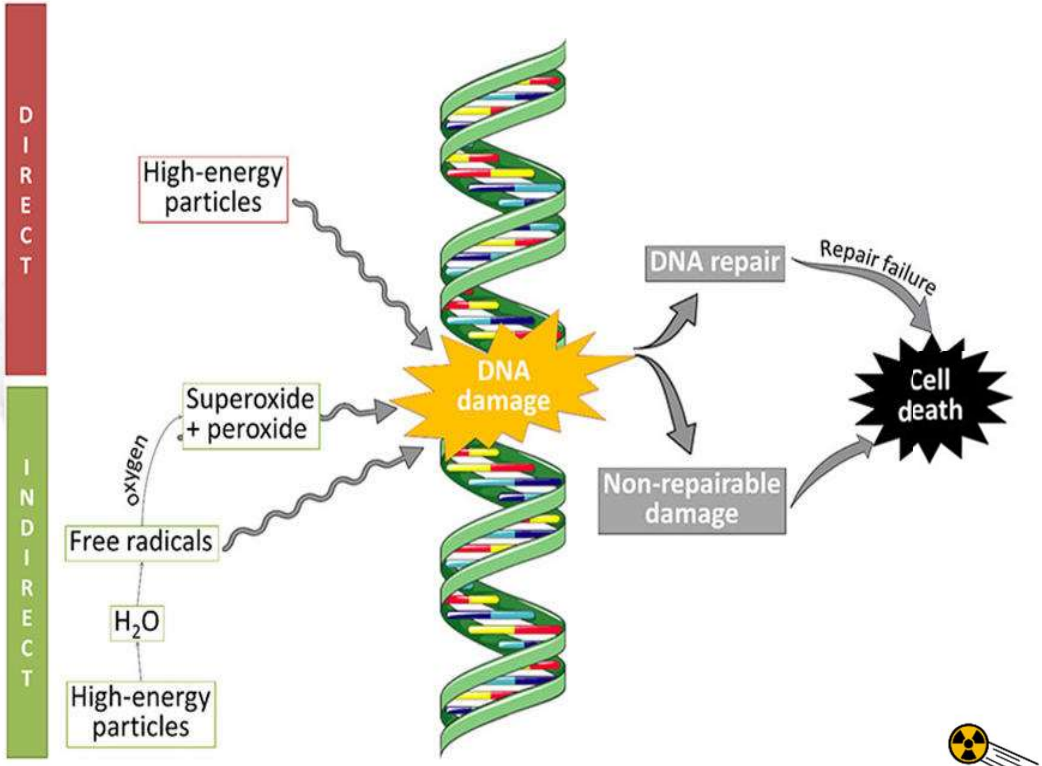

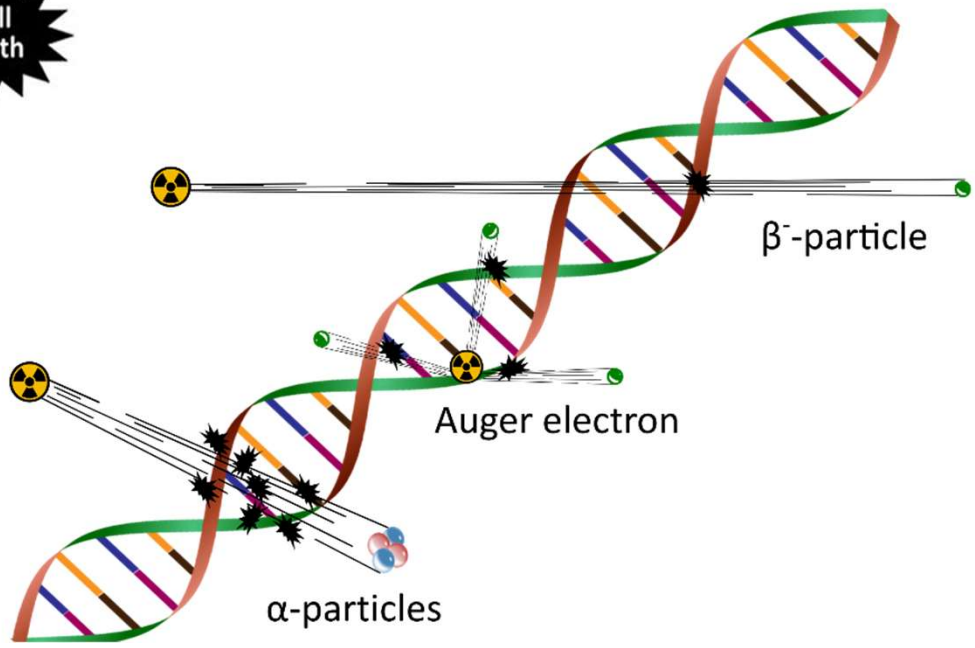

Theranostic pairs (part 1)

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DIAGNOSTIC				THERAPEUTIC		
nuclide	half-life	decay		nuclide	half-life	decay
Cu-64	13 h	PET		Cu-67	2,6 d	beta minus
As-72	1,1 d	PET		As-77	1,6 d	beta minus
Sr-83	1,4 d	PET		Sr-89	2,1 d	beta minus
Y-86	15 h	PET		Y-90	2,7 d	beta minus

Theranostic pairs (part 2)

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DIAGNOSTIC				THERAPEUTIC		
nuclide	half-life	decay		nuclide	half-life	decay
I-124	4 d	PET		I-131	8 d	beta minus
Pb-203	2,2 d	SPECT		Pb-212	11 h	alpha
Ga-68	1 h	PET		Lu-177	7 d	beta minus
In-111	2,8 d	SPECT		Ac-225	10 d	alpha

Alpha particle emitters

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Thorium-226 decay chain:

Th-226->Ra-222->Rn-218->Po-214->Pb-210->Bi-210->Po-210->Pb-206

Thorium-227 decay chain:

Th-227->**Ra-223**->Rn-219->Po-215->Pb-211->Bi-211->Pb-207

Thorium-228 decay chain:

Th-228->Ra-224->Rn-220->Po-216->**Pb-212**->Bi-212->Pb-208

Thorium-229 decay chain:

Th-229->Ra-225->**Ac-225**->Fr-221->At-217->Bi-213->Pb-209->Bi-209

Other alpha emitters: At-211 and Tb-149

Terbium quadruplet

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nuclide	half-life	application
Tb-149	4 h	alpha therapy
Tb-161	7 d	beta minus therapy
Tb-152	18 h	PET
Tb-155	5 d	SPECT

Radionuclides

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All radionuclides commonly administered to patients in nuclear medicine are artificially produced

Most radionuclides for radiopharmaceuticals are produced by

- cyclotrons
- nuclear reactors
- radionuclide generators

Radionuclides

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Considerations for commercial radiopharmaceutical production:

- Availability & number of suppliers (robustness of supply)
- Available Quantity
- Half-life
- Cost
- Technical Quality – Radionuclidic and chemical impurities
- Pharmaceutical Quality
- Types and energies of emitting ionizing radiation
- Decay products
- Chemical properties for synthesis

Lu-177 production

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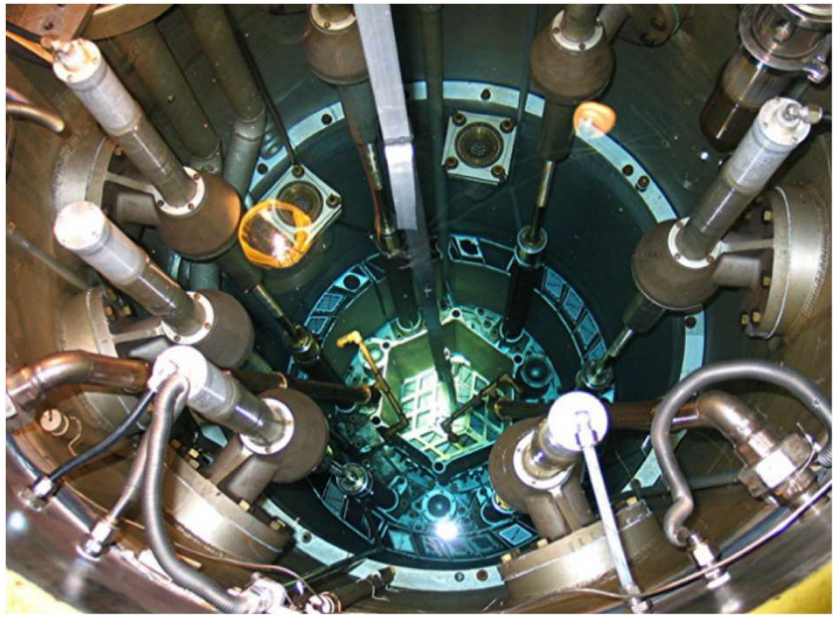
- Uranium-235 undergoes spontaneous fisson by releasing neutrons
- Neutrons normally used to continue the fission
- If other material lowered into ports are irradiated by this neutrons nuclear reaction takes place



Lu-177 production

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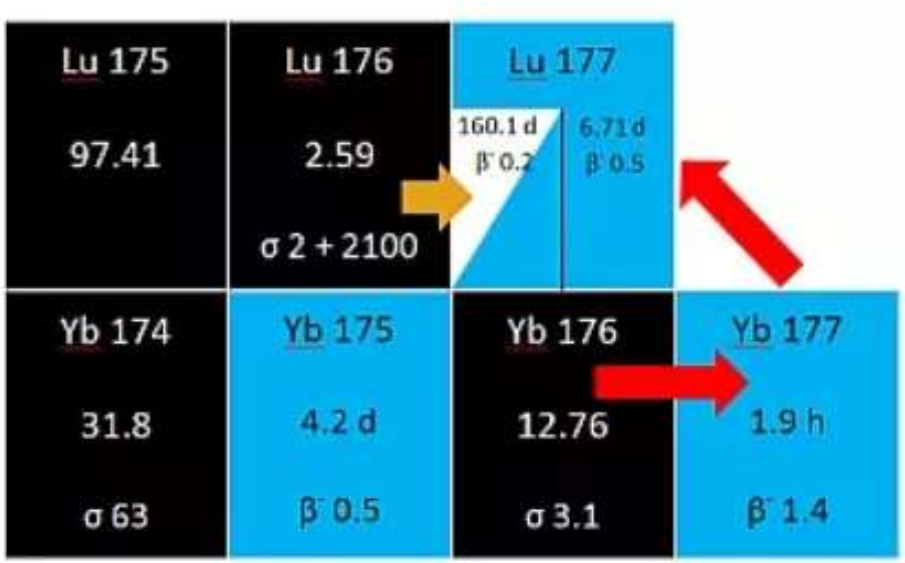

- ***Lu-177 carrier added (c.a.)***

first production route, rather simple production, always contains Lu-177m ($T_{1/2}$: 160 d; < 0,024 %) and has lower specific activity (> 500 GBq/mg)

- ***Lu-177 non carrier added (n.c.a.)***

more complex production, no Lu-177m and higher specific activity (> 3000 GBq/mg)

Lu-177 production

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Lu-177m impurity in Lu-177 carrier added (c.a.)

Example:
a patient dose of 7,5 GBq Lu-177 contains
up to **1,8 MBq** Lu-177m (up to 0,024 %)

Ac-225 production

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Production routes:

- Th-229 Generator
- Spallation of Th-232
  [>100 MeV proton irradiation; contains Ac-227 impurity]
- Cyclotron/Proton irradiation: 226Ra (p,2n) 225Ac
  [proton energies of ~16,8 MeV]
- Rhodotron, Betatron or Linac production route
  226Ra (γ,n) 225Ra -> 225Ac

Measuring of Radioacitivity

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Thermoluminescence dosimeter (TLD)

Probe dosimeter

Personal contamination monitor

Contamination monitor

Dose rate meter SSM-1

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PLEASE FELL FREE TO CONTACT US!

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