Radiation Protection Aspects Related to Lutetium-177 Use in Hospitals

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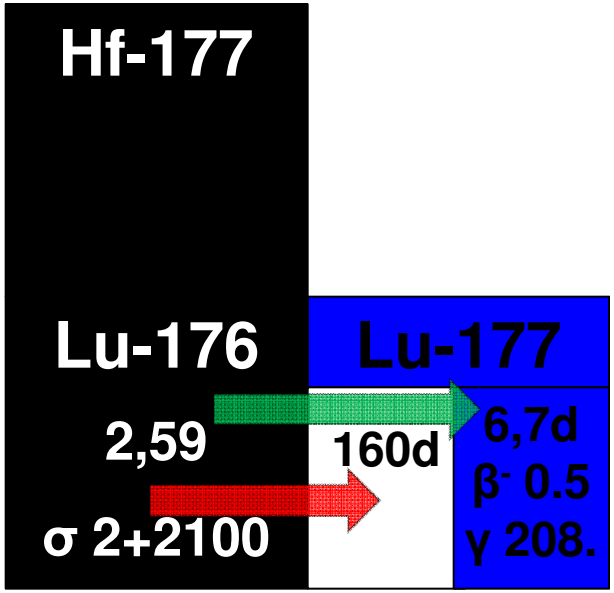
PRRT for neuroendrocrine tumors

- **Peptide Receptor Radionuclide Therapy – PRRT**
- How is it performed?
- Choice of **peptide**: DOTA-TATE, DOTA-TOC
- Choice of **radionuclide**: **^{177}Lu, ^{90}Y**
- Aspects: kidney protection, tumor and organ dosimetry, monitoring of toxicity

Nuclide	Half-life	beta energy	path length(mm)	gamma (keV)
^{177}Lu	**6.7 d**	**133 keV**	**2**	**208, 113**
^{90}Y	**2.7 d**	**935 keV**	**12**	**no**

Direct production: (easy) route
$^{176}Lu(n,\gamma)^{177}Lu$

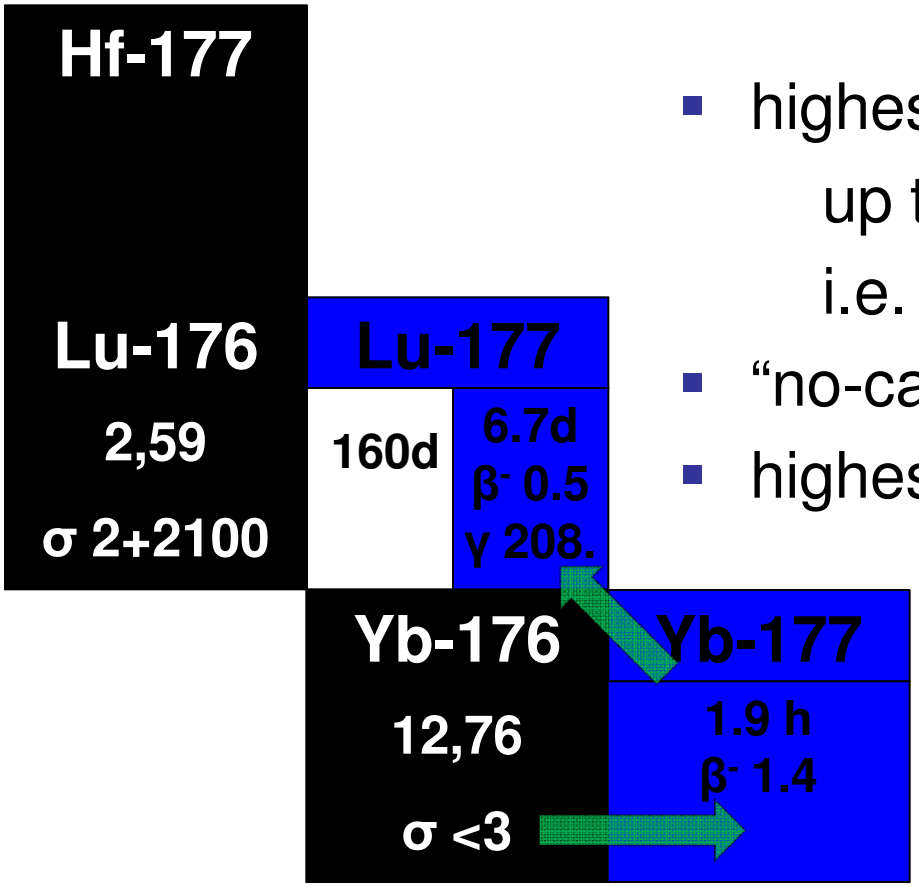
- Irradiate enriched ^{176}Lu sample in typical neutron flux of $(1\text{-}3)\cdot10^{14}$ n./cm^2/s.
- max. specific activity of ^{177}Lu at EOI: 925 – 1220 GBq/mg (*depending on enrichment of target material*), "carrier-added form" more than 3 stable Lu atoms for every ^{177}Lu



- long-lived radioactive impurities: > 0.01 % of ^{177m}Lu
- easy target processing
- easy chemistry

Indirect production route
$^{176}Yb(n,\gamma)^{177}Yb$ (β^-) ^{177}Lu

- Irradiate highly enriched ^{176}Yb sample in high neutron flux $(1\text{-}20)\cdot10^{14}$ n./cm^2/s, then separate chemically Lu from Yb.



- highest specific activity:
  up to 4000 GBq/mg,
  i.e. nearly every Lu atom is ^{177}Lu
- "no-carrier-added" form
- highest radionuclidic purity

Chemical Separation Yb-Lu

Impurities in the carrier-added Lutetium-177 solution

- During direct irradiation of ^{176}Lu a remarkable amount of ^{177m}Lu ($T_{1/2}$ = 160 d) is produced via $^{176}Lu(n,\gamma)$ (σ= 2 barn).
- It is known that minute amounts of ^{152}Eu ($T_{1/2}$ = 13.3 a), ^{154}Eu ($T_{1/2}$ = 8.8 a), ^{178}Hf ($T_{1/2}$ =31 a), and ^{46}Sc ($T_{1/2}$ = 84 d) are also present in the final product.
- The ^{177m}Lu content in a labelling solution is mainly depending on two factors: irradiation time and time after end of the irradiation (EOI).
- Under the above mentioned conditions reported values for the $^{177m}Lu/^{177}Lu$ ratio from several reactors vary between 0.01% - 0.02% at EOI. The hospitals are using their ^{177}Lu up to one week after EOI when the $^{177m}Lu/^{177}Lu$ ratio has doubled.

Amount of Lutetium-177m

- Lutetium-177 is mainly used for peptide labelling.

  A typical dose is 7 - 9 GBq.

  When the $^{177m}Lu/^{177}Lu$ ratio is 0.02%, it means that a dose includes approximately 1.4 – 1.8 MBq ^{177m}Lu.

Radioactive Material Licence

- To handle radioactive materials, which have more activity than the free limit, it is required to have a radioactive material licence. For ^{177m}Lu the free limit is 1 MBq.
- If the free limit is exceeded the nuclide has to be included in the licence or it should be licenced as a byproduct.
- Hence, hospitals which are using over 5 GBq c.a. ^{177}Lu should have a radioactive material licence also for ^{177m}Lu
- (According to the German Radiation Safety Regulation)

Laboratory Waste

- During the labelling process and treatment the loss of radioactivity is typically 2 to 5% of the activity - that is equal to 28 - 90 kBq ^{177m}Lu.

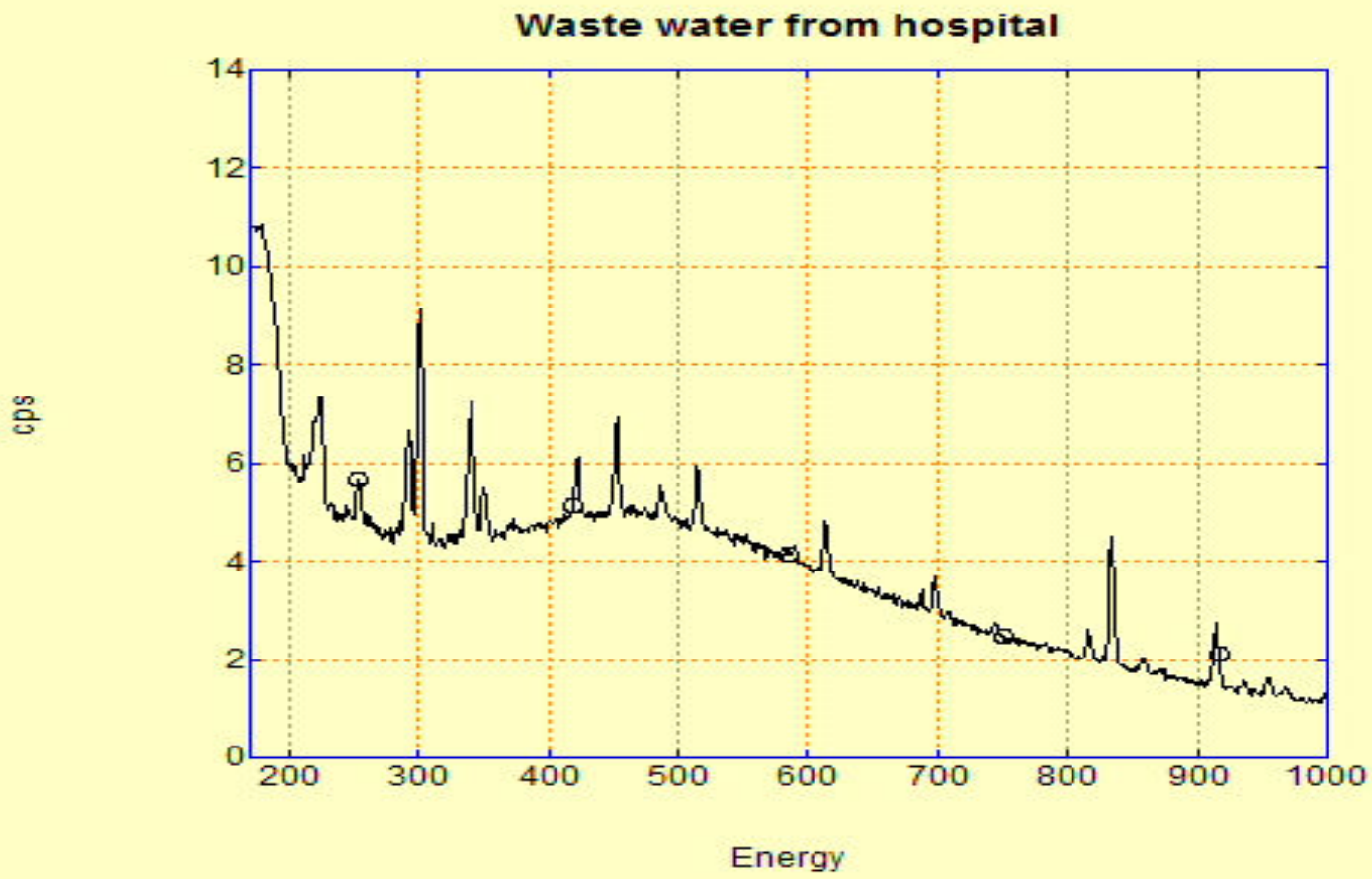
- The release limit for ^{177m}Lu is 10 Bq/g waste. All waste should be collected and shipped to a radioactive deposit or left to decay (if the total waste amount is 0,5 kg per treatment it requires at least 5 half-lives (2 years) to reach the limit).

- (According to the German Radiation Safety Regulation)

Waste Water

- A patient excretes approximately 80% of the dose (1.45 MBq ^{177m}Lu) through the urine relatively fast.
- The highest allowed radioactive concentration in the sewage water canal is 50 kBq/m^3. This means that a patient dose needs to be diluted in 30 m^3 after the cooling time, which is required for ^{177}Lu decay (2.5 months after treatment the total volume should be 60 m^3).
- Great variation how regulatory bodies are calculating the total amount of water that is required and how the radioactive concentration is calculated in a sewage water canal.

Waste Water Gamma-Ray Spectrum



Waste Water in the Tank

- The waste water sample (1 litre) from a nuclear medicine department contained approximately 30 Bq/l of ^{177m}Lu, so the ^{177m}Lu content was under the release limit.
- **BUT**:
- The ^{177m}Lu content was much higher than the estimation of the hospital.
- The sample contained less than 1‰ of solid material. After filtration 50% of the activity was found on the filter.
- How representative was the sample from the waste water tank?
- If the ^{177m}Lu content in the solid residual is estimated from the liquid, it might be underestimated by a factor 1000.

Conclusions

- ^{177}Lu includes a remarkable amount of long-lived ^{177m}Lu when produced from the direct route.
- A radioactive licence might be needed for ^{177m}Lu.
- Laboratory waste should be collected separately and sent to a radioactive deposit.
- In the waste water tanks ^{177m}Lu might exceed the limits alone or with other nuclides (sum activity).
- Indirectly produced n.c.a. ^{177}Lu is the only way to guarantee highest specific activity and best radionuclidic purity, i.e. absence of the ^{177m}Lu problem.
- n.c.a. ^{177}Lu requires high-flux reactors and more involved chemical separation.