PAUL SCHERRER INSTITUT

PSI

RADIONUCLIDE DEVELOPMENT

CRS

CENTER FOR RADIOPHARMACEUTICAL SCIENCES

ETH PSI USZ

^{149}Tb for Targeted Alpha Therapy

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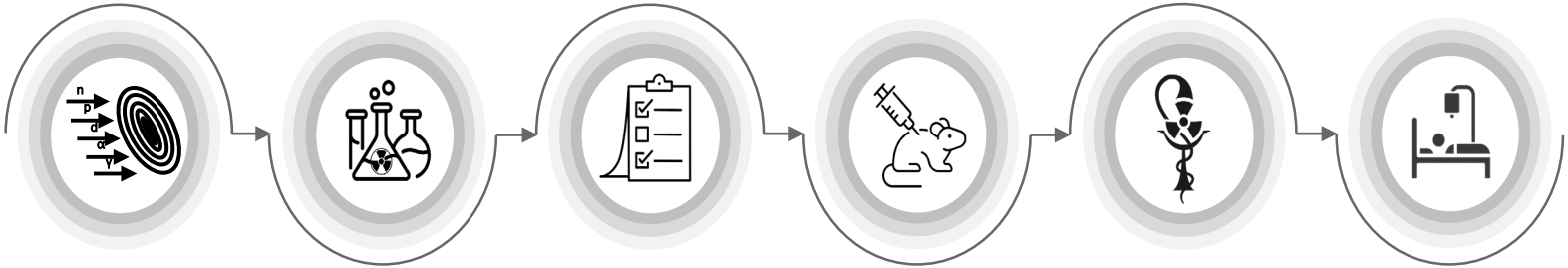
ISOLDE IS688

Process of Radionuclide Development: a multidisciplinary affair



TARGET IRRADIATION

Target development and optimization of irradiation conditions

RADIOCHEMISTRY

Radiochemical separation from target material

QUALITY CONTROL

Chemical purity, radiochemical purity, radionuclidic purity, pH, identity, bacterial endotoxins

PRECLINCAL STUDIES

In-vitro and in-vivo imaging studies

GMP PROCESS DEVELOPMENT

Introduction into the GMP concept for radiopharmaceutical production

CLINICAL STUDIES

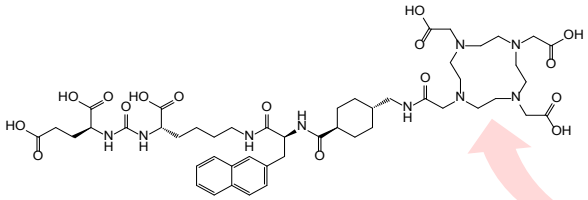
Clinical trials to confirm preclinical results

RADIONUCLIDE DEVELOPMENT

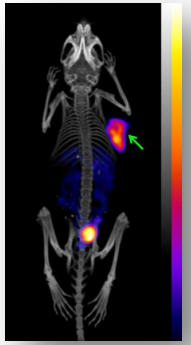
Importance of Product Purity for Preclinical Application

Biomolecule

- Chemical synthesis: metal-free working environment
- Preparation of stock solution: in metal free environment (no metal spatula)

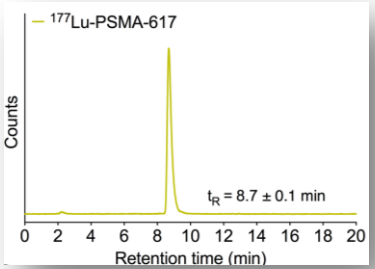


The macrocyclic Chelator is NOT selective for the Radiometal of interest, but will coordinate other (cold) metal ions.



Radionuclide

- **Radionuclidic purity:** >99.9%
- **Chemical purity:** no metal ions (i.e. absence of Fe, Co, Cu, Zn, Gd, Pb etc.)



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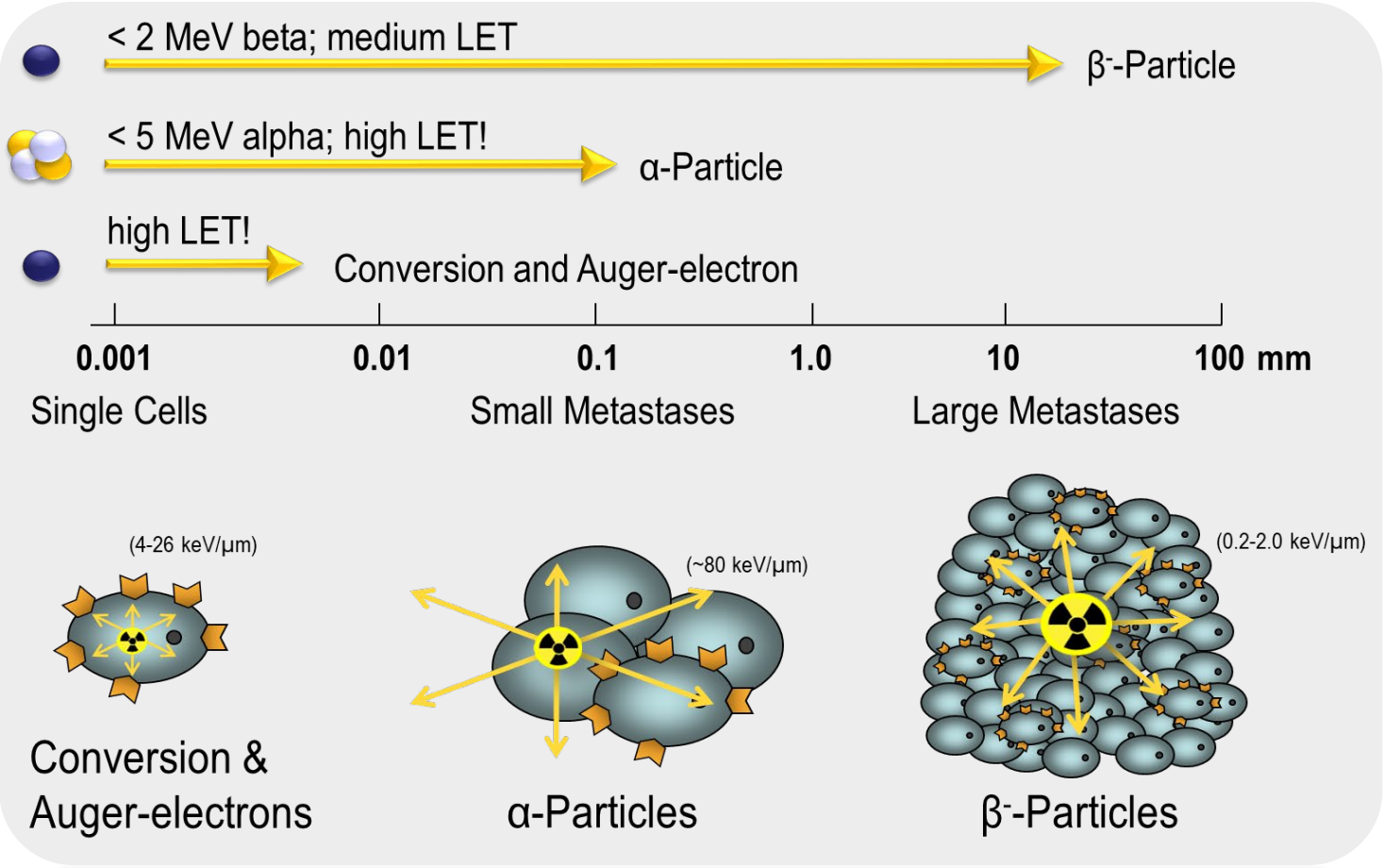
Tissue Range of Therapeutic Radiation



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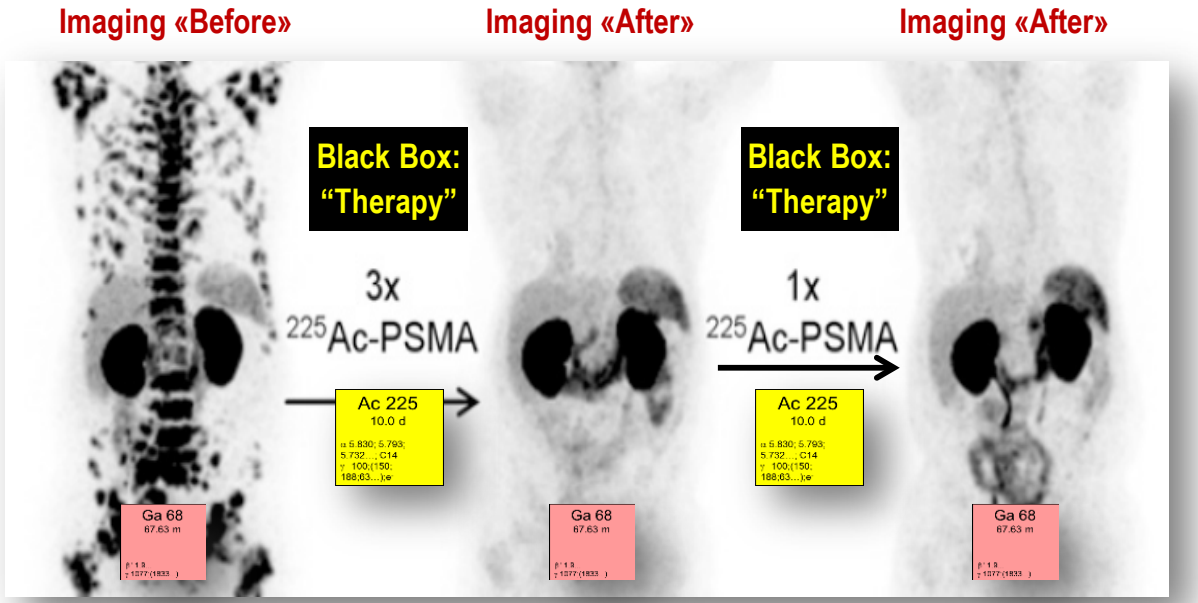
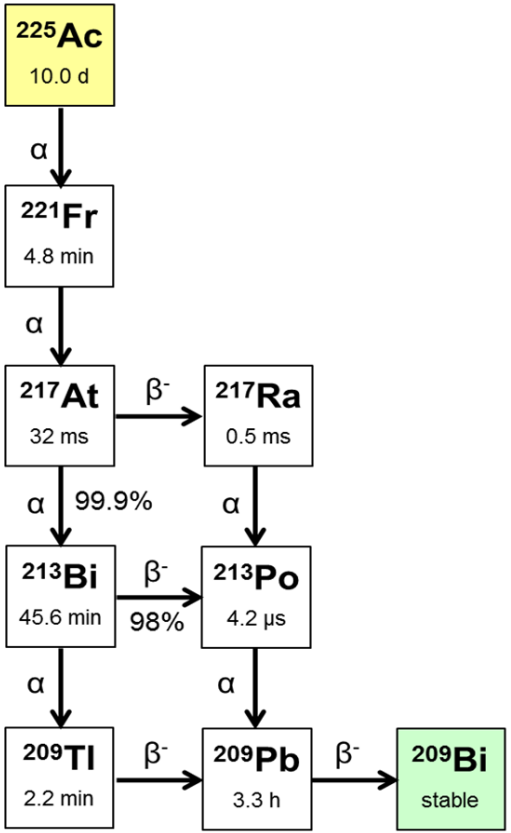
^{225}Ac-PSMA-617: α-Radionuclide Therapy

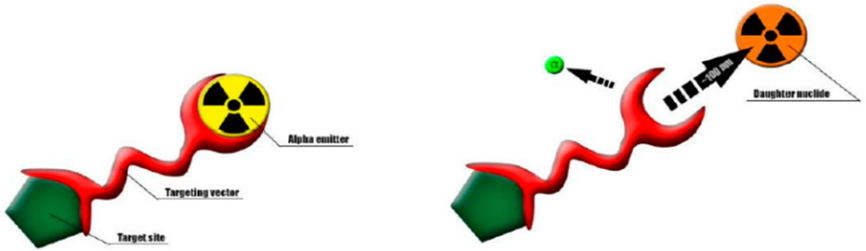


Kratochwil et al. **2016** J Nucl Med 57:1941.

Potential Concern about Actinium-225



Recoiling daughter radionuclide detaching from a targeting agent as a consequence of alpha decay:

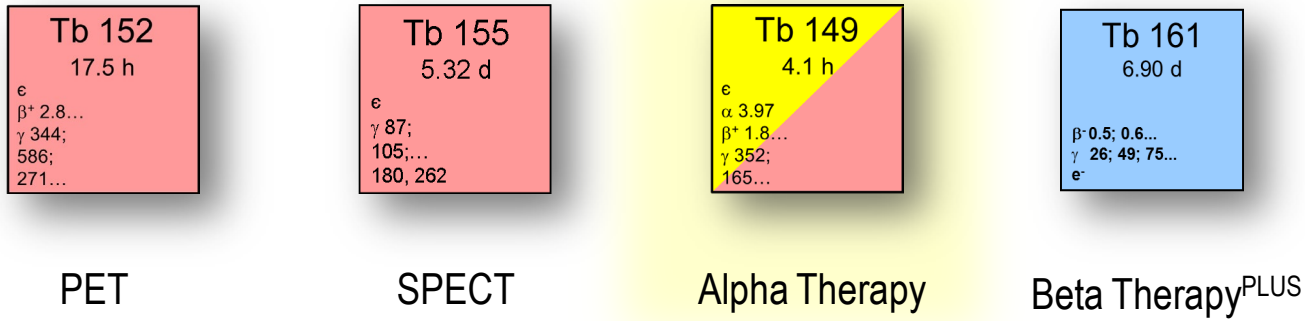


Released daughter nuclides are radioactive!

They accumulate in healthy tissue (bones and kidneys)

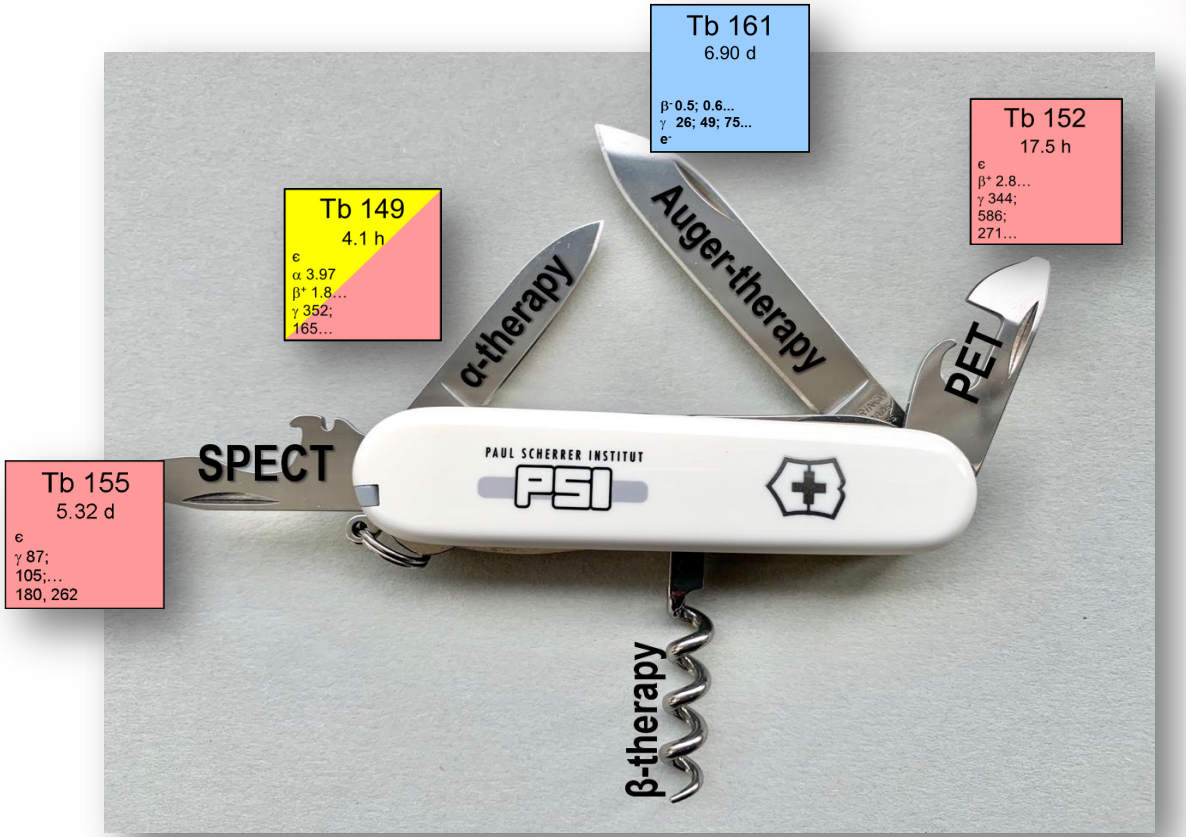
Kruijff et al. **2015** Pharmaceuticals 8:321-336.

Theragnostics with the four Terbium “Sisters”



Müller et al. **2012** J Nucl Med 53:1951

The Terbium “Sisters”



Collaboration with ISOLDE

History:

- Began with Beyer et al. in late 90's
- Resurrected by PSI members in 2011
- ISOLDE-PSI the only collaboration currently working on ^{149}Tb
- Many groups desire to produce it, but currently do not have the means

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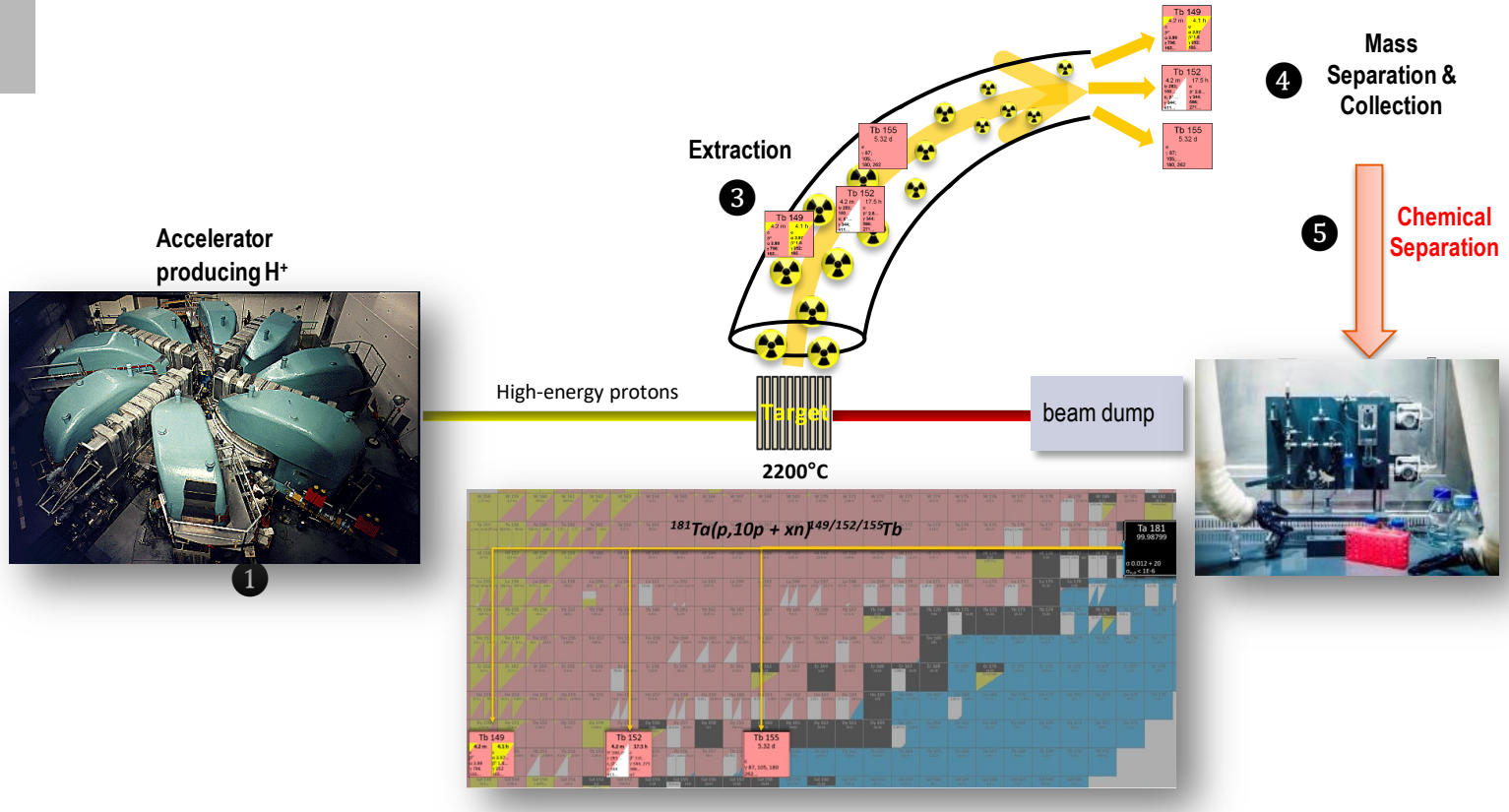
Radionuclide Development using Isotope Separation OnLine (ISOL)



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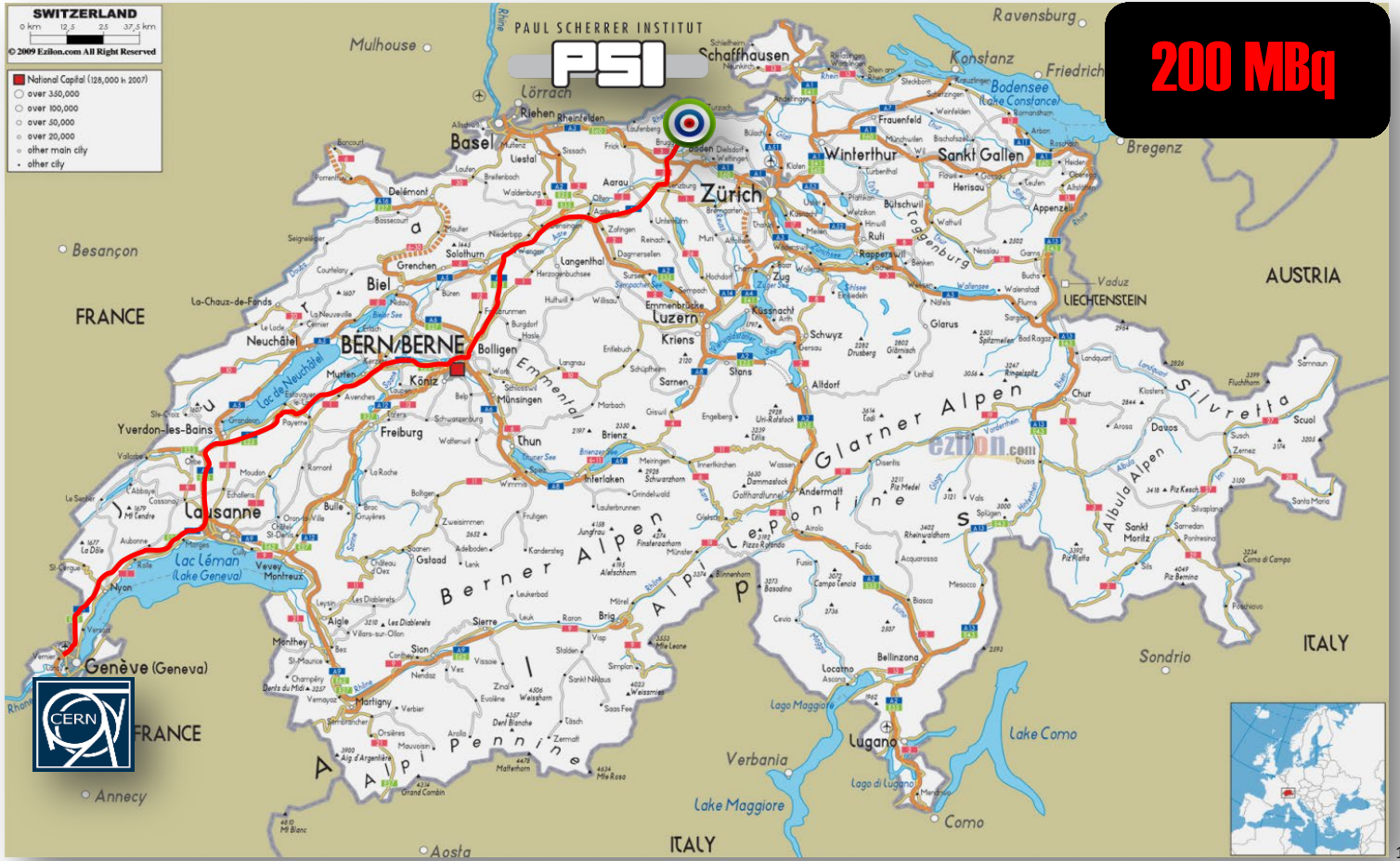
^{149}Tb: The Logistics Challenge



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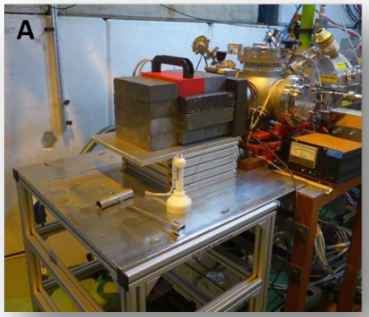
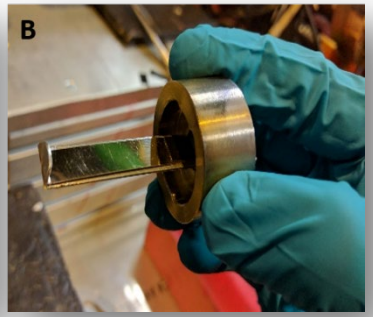
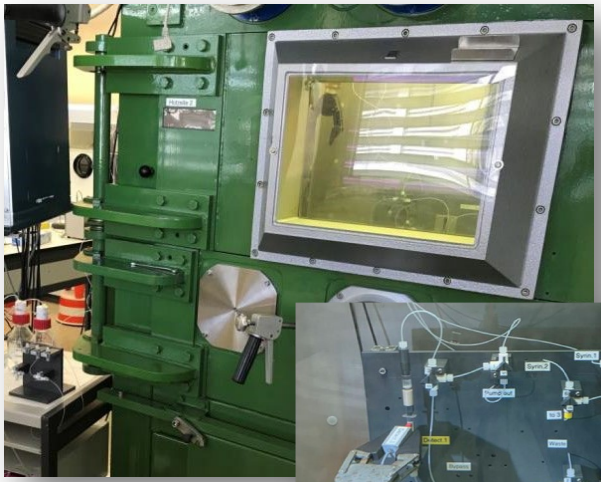
Collection & Separation



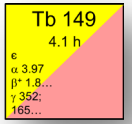




^{149}Tb: *In Vitro* & *In Vivo* Studies

4.1 h

Terbium-149



- Radiolanthanide for α-therapy (easy chelation using DOTA)
- Half-life of 4.1 h
- **Low α-energy of 3.9 MeV → α-Therapy**
- No α-emitting daughters!

Chemical Separation

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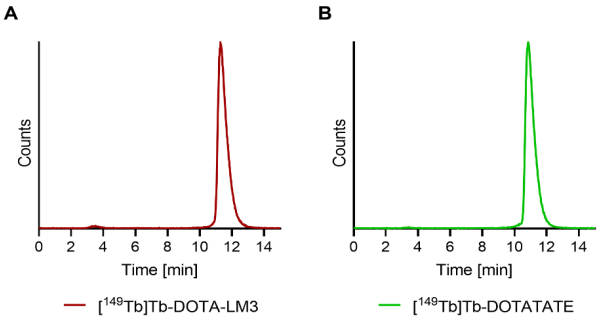
HPLC chromatograms using **Somatostatin Analogues**



Labelling was achievable at **10 MBq/nmol** for the studies (up to 20 MBq/nmol was successfully exemplified)

^{149}Tb *In Vitro* & *In Vivo* Studies: what's next?

Next Campaigns/Desires

- ***Two 1-week campaigns desired in 2023***
- Investigate labelling at **higher molar activity**. (This will determine the quality of ^{149}Tb, requires higher activity).
- Investigate the stability of the ^{149}Tb-radiopeptides.
- Complete the viability assays (further replicates, requires higher activity).

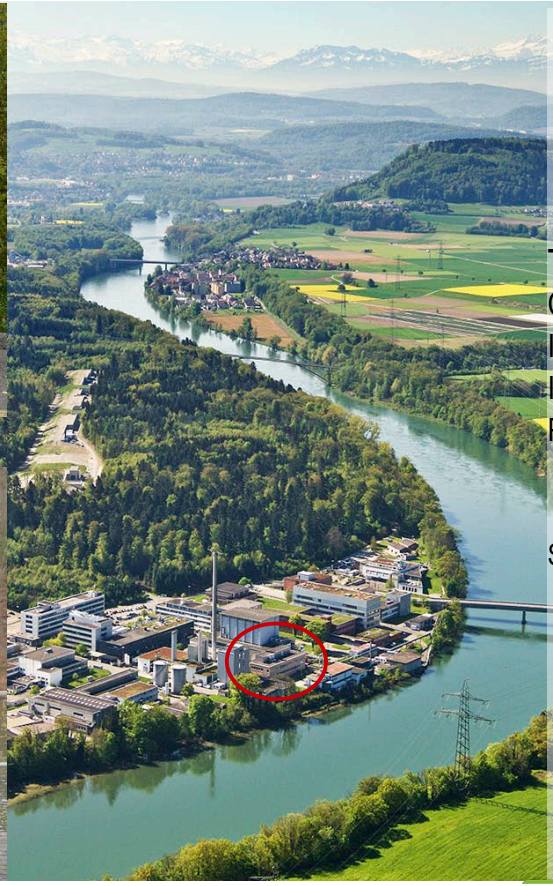
Achieved

- In vitro viability assays using AR42J tumour cells
- In vivo PET/CT imaging of AR42J tumour-bearing mice
- In vivo therapy studies with tumour-bearing mice
- (1 x 5 MBq; 2 x 5 MBq per mouse)
- Investigations of potential undesired side effects

Ongoing

- Data processing, analysis and preparation of images and figures

Thank You For Your Attention!



RADIONUCLIDE DEVELOPMENT

Thanks to:
CERN Radiation Safety & logistics
ISOLDE RILIS
ISOLTRAP-MR-TOF-MS team
PSI Radiation Safety & logistics

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ISOLDE NEUTRONS FOR SOCIETY CERN