PSI

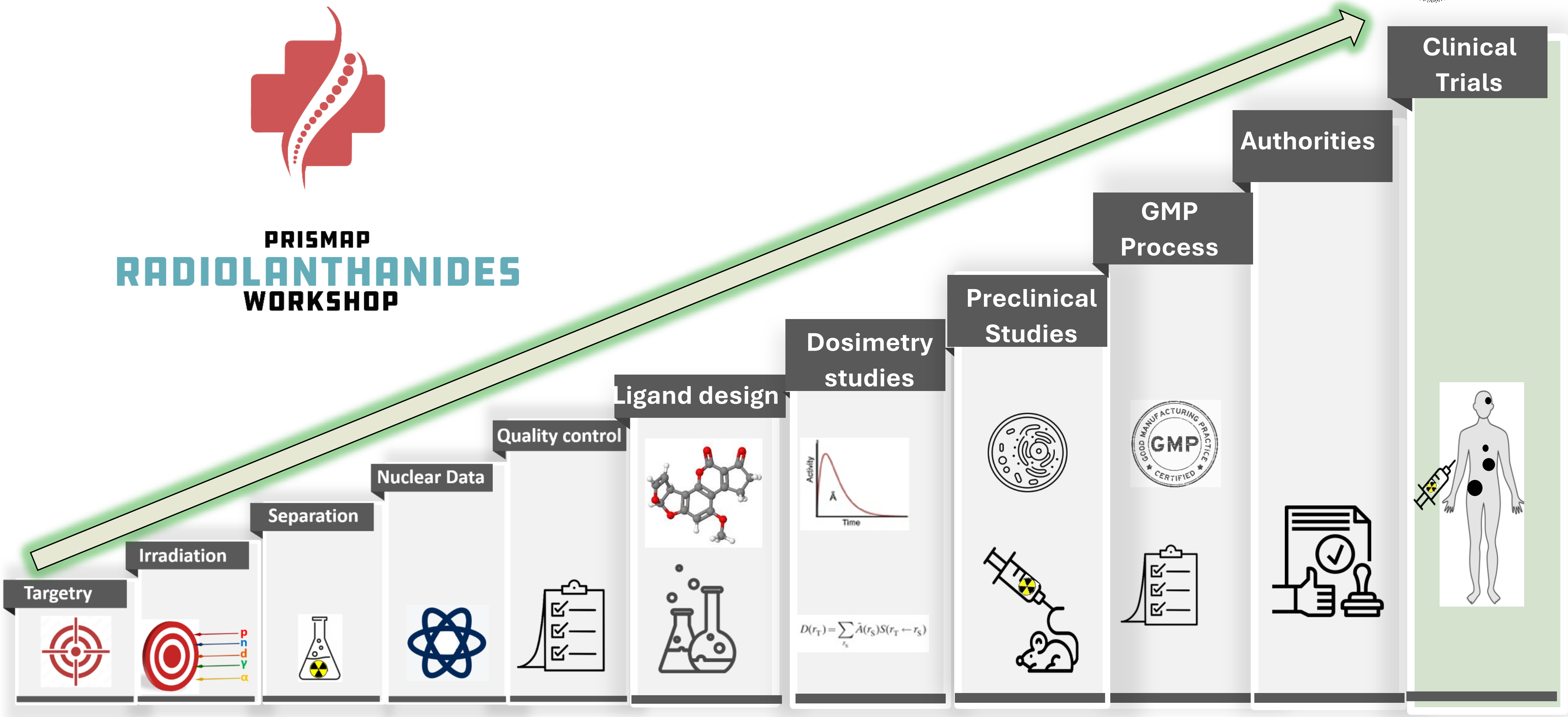
Production of novel medically relevant radiolanthanides at Paul Scherrer Institute

Dr. Zeynep Talip

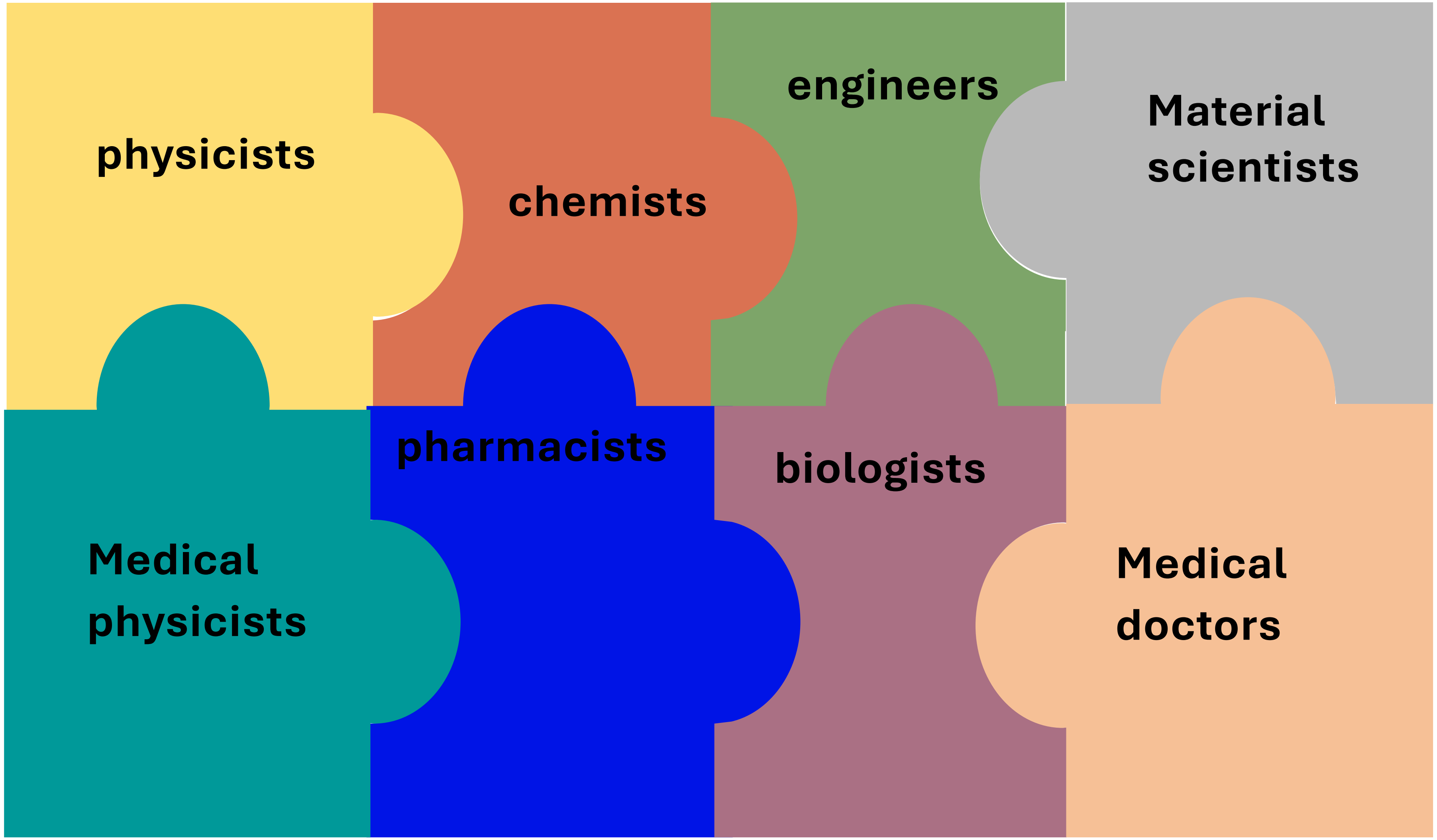
PRISMAP Radiolanthanides Workshop, 3 September 2024

Radiopharmaceutical Development Pipeline

PRISMAP RADIOLANTHANIDES WORKSHOP



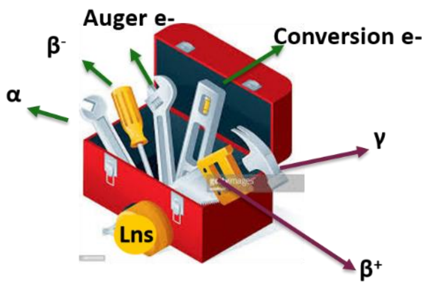
Radiopharmaceutical Development Pipeline



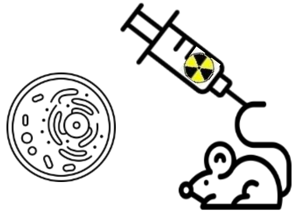
How can **personalized dosimetry** be improved to optimize the therapeutic index of TRT?

How can **Auger electron therapy** be integrated into current treatment protocols to improve overall treatment efficacy?

Availability of a diverse array of radionuclides



Systematic preclinical studies



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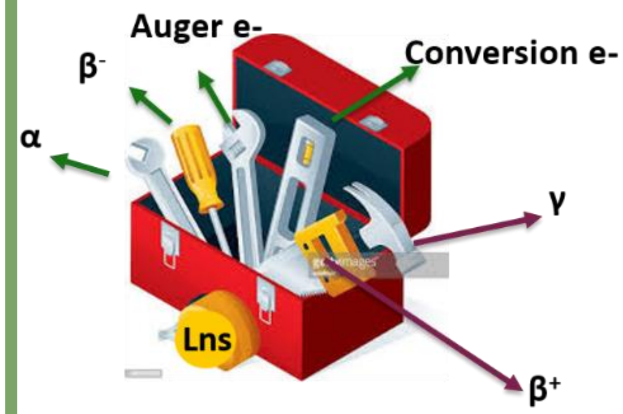


Proper **decay properties** for Nuclear Medicine applications

Analogue coordination chemistry

Clinically approved Lu-177 will shorten the translation period of the other radiolanthanides to the clinics – **Tb-161** is on the way

Radiolanthanides in Nuclear Medicine

PSI

57	58	59	60	61	62	63	64	65	66	67	68	69	70	71
La	Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu
Lanthanum	Cerium	Praseodymium	Neodymium	Promethium	Samarium	Europium	Gadolinium	Terbium	Dysprosium	Holmium	Erbium	Thulium	Ytterbium	Lutetium
138.905	140.116	140.908	144.242	144.913	150.36	151.964	157.25	158.925	162.500	164.930	167.259	168.934	173.055	174.967

- Pr 143 — 13.57 d — β-
- Pm 149 — 53.1 h — β-
- Sm 153 — 46.28 h — β-
- Tb 161 — 6.95 d — β-
- Ho 166 — 26.81 h — β-
- Er 169 — 9.392 d — β-
- Yb 175 — 4.185 d — β-
- Lu 177 — 6.64 d — β-

- Tb 152 — 17.5 h — β^+ ,EC
- Ho 161 — 2.48 h — EC
- Er 165 — 10.36 h — EC
- Tb 155 — 5.32 d — EC
- La 135 — 19.4 h — β^+ EC
- Tm 167 — 9.25 d — EC

- Tb 149 — 4.1 h — β^+ α

Radiolanthanides Portfolio of PSI

Terbium Swiss knife	Tb 149 4.1 h β^+ α	Tb 152 17.5 h β^+ ,EC	Tb 155 5.32 d EC	Tb 161 6.95 d β-
Auger emitting radiolanthanides	Er 165 10.36 h EC	Ho 161 2.48 h EC	Tm 167 9.25 d EC	
Beta emitting radiolanthanides	Pr 143 13.57 d β-	Ho 166 26.81 h β-	Er 169 9.392 d β-	Yb 175 4.185 d β-

Beta emitting radiolanthanides

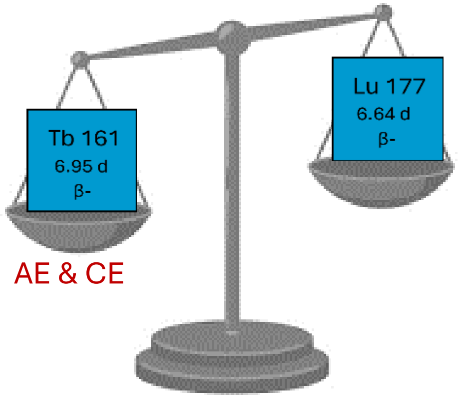
Er 169	Lu 177	Tb 161	Pr 143	Ho 166
9.392 d	6.64 d	6.95 d	13.57 d	26.82 h
β-	β-	β-	β-	β-

Average β$^-$ energies:	**100 keV**	134 keV	154 keV	**315 keV**	**665 keV**

Medium size lesions (315 keV)

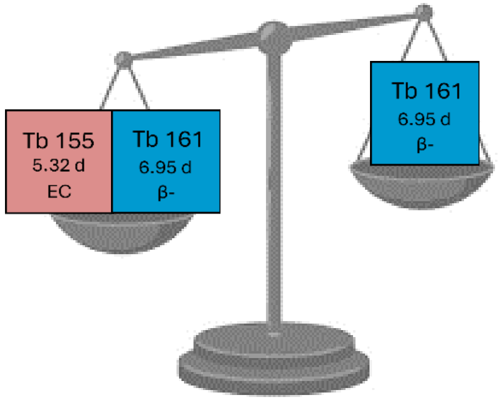
Big size lesions (665 keV)

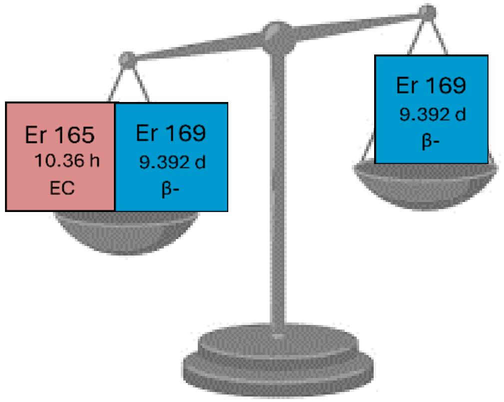
Enhanced therapeutic effects of AEs

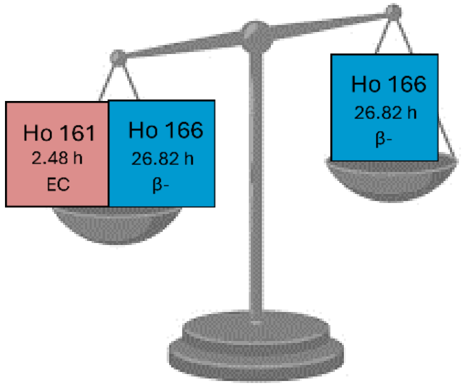


C. Müller et al., Eur. J. Nucl. Med. Mol Imaging, 50, 3181 (2023)

TANDEM Therapy







Thulium-167

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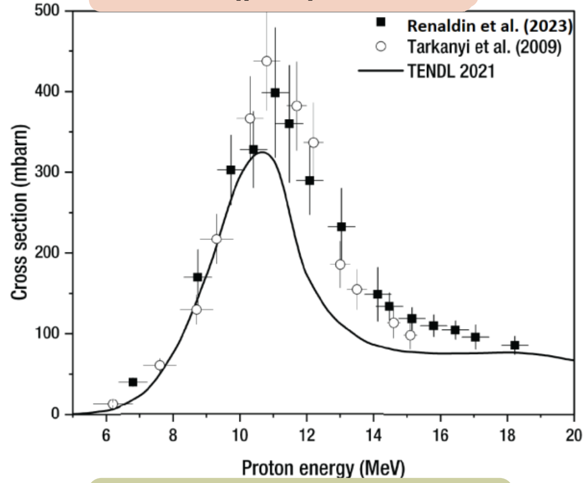
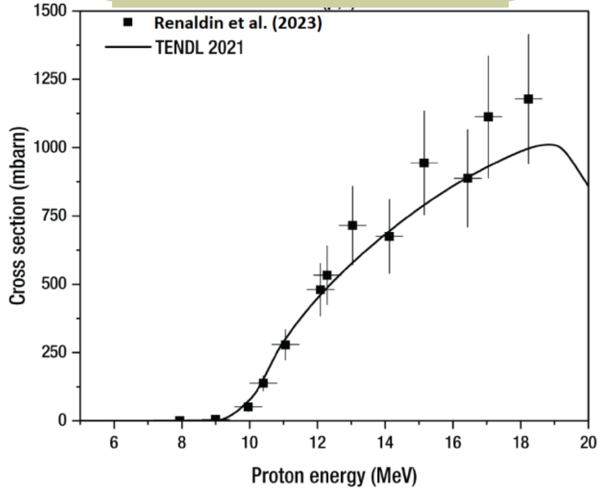
Production cross section measurements

$^{167}Er(p,n)^{167}Tm$



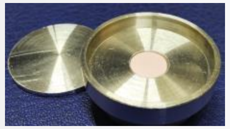
$^{168}Er(p,2n)^{167}Tm$



E. Renaldin et al., Front. Chem., 11, 14 (2023).

Production yield measurements

$^{168}Er(p,2n)^{167}Tm$

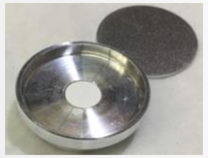


40 mg $^{168}Er_2O_3$ target (^{168}Er: 98.3%)

25 µA, 23 MeV, 8 h irradiation EOB: **1 GBq**

5 days cooling **99.50% radionuclidic purity**

$^{171}Yb(p,5n)^{167}Lu$

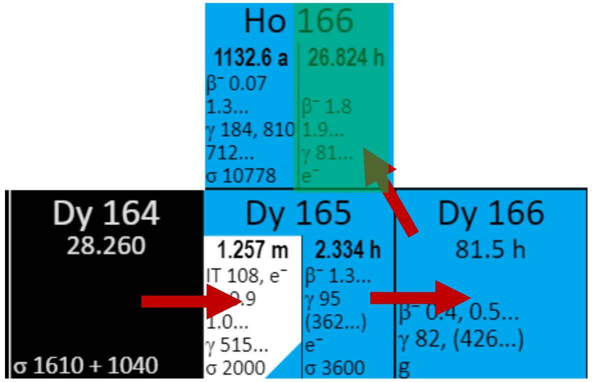


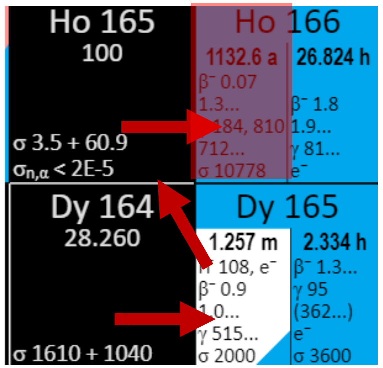
40 mg $^{171}Yb_2O_3$ target (^{171}Yb: 95.5%)

25 µA, 51 MeV, 8 h irradiation EOB: **420 MBq**

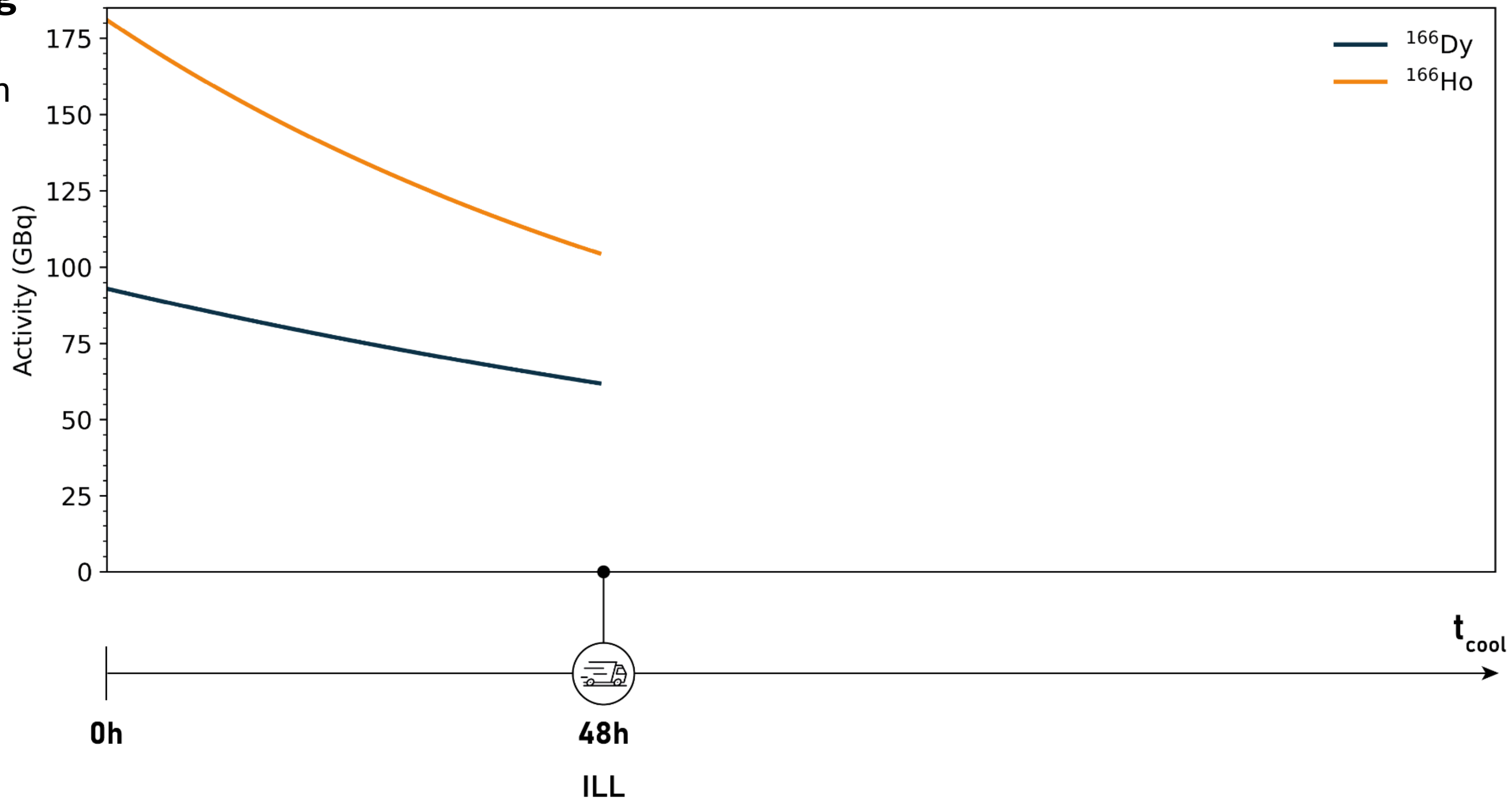
5 days cooling **99.95% radionuclidic purity**

Holmium-166

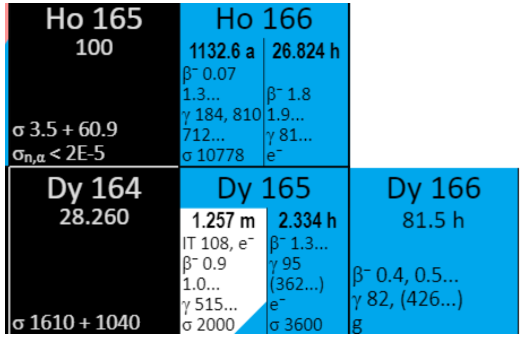




$m_{Dy\text{-}164,0}$ = **650 µg**
96.8 % enriched
6 days irradiation



Holmium-166



$m_{Dy\text{-}164,0}$ = **650 µg**
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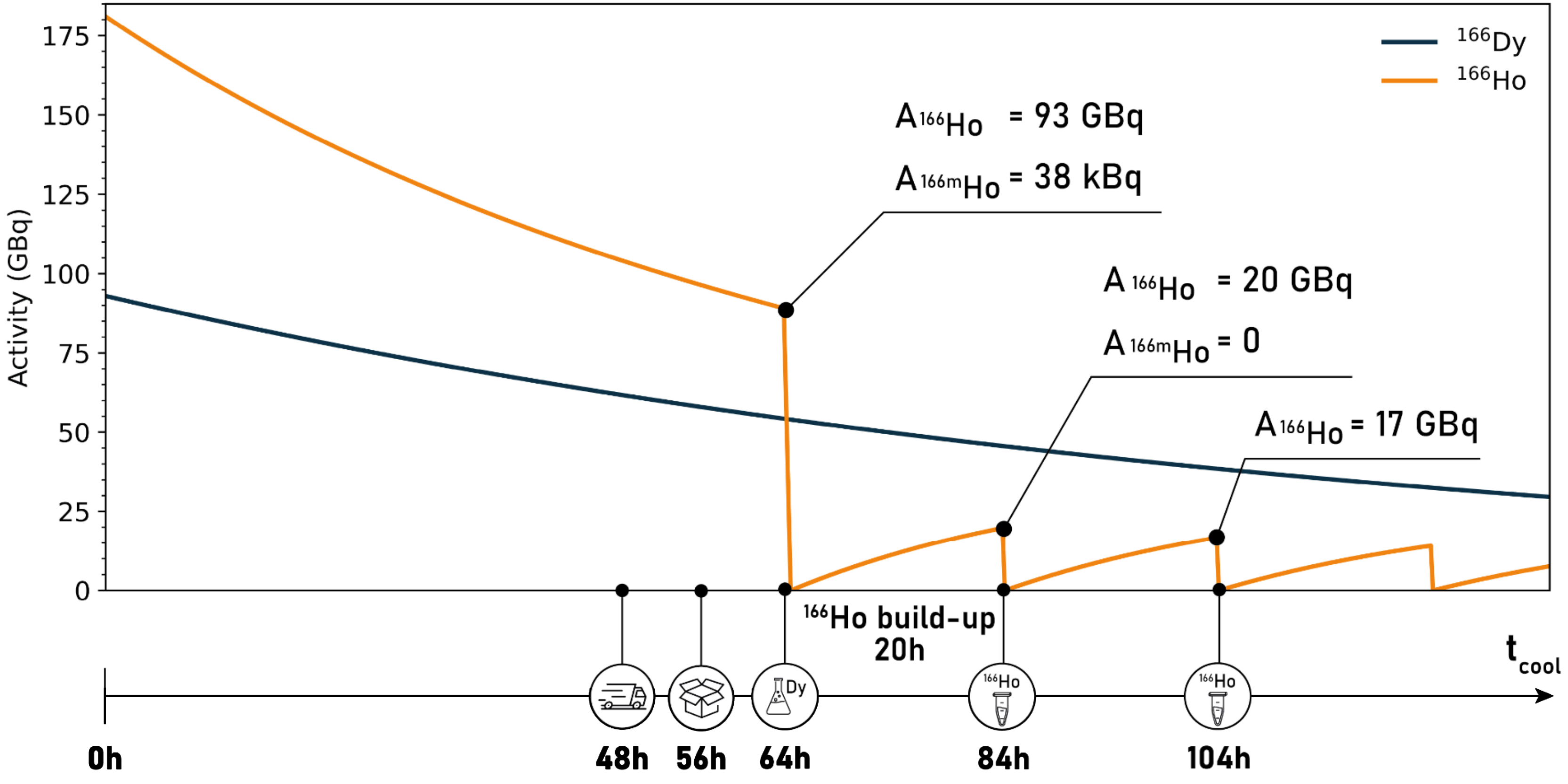
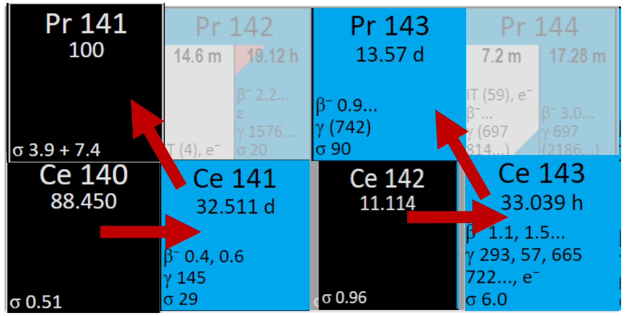
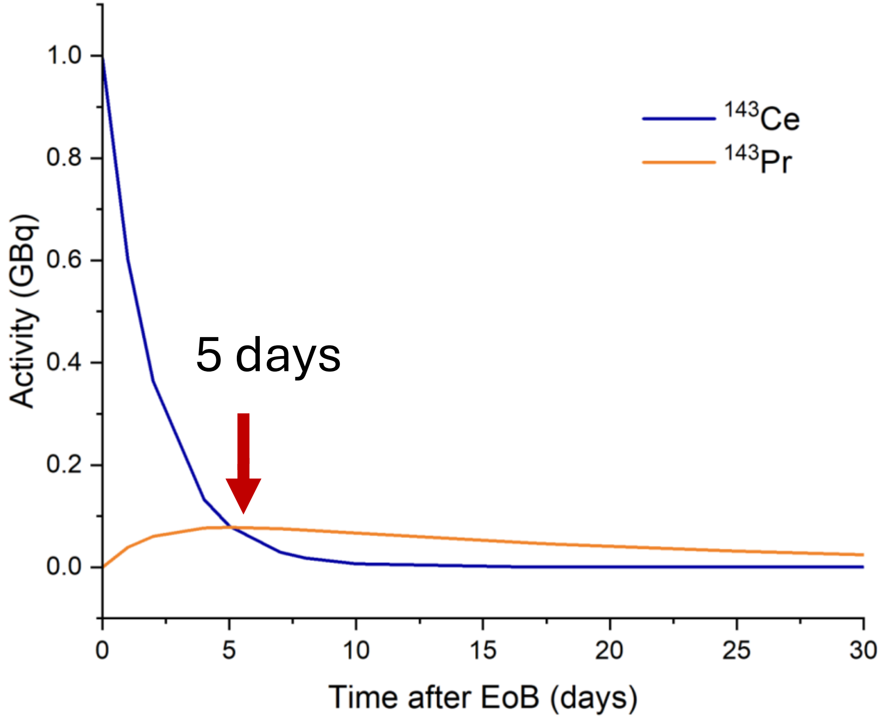
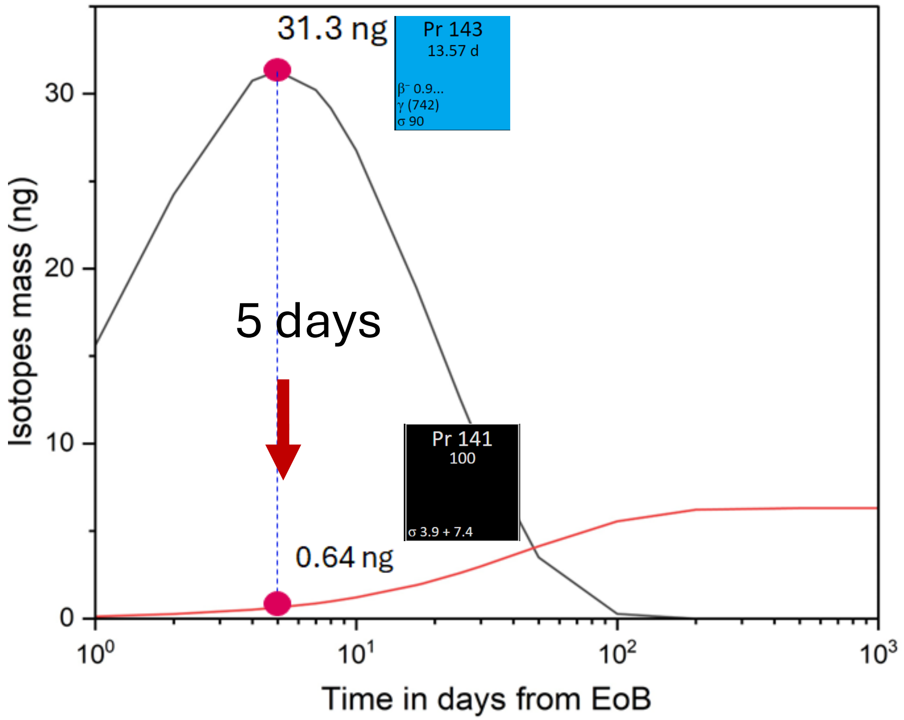


Courtesy: E. Renaldin

Praseodymium-143

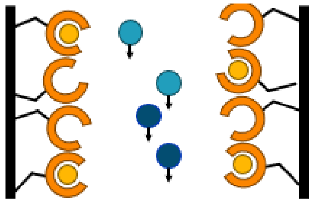
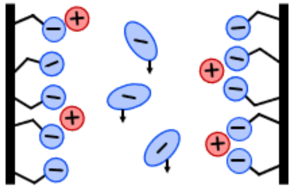






250 MBq of ^{143}Pr per mg of enriched $^{142}CeO_2$

Separation of Radiolanthanides

- Investigation of different **extraction resins (LN Resins, TK resins, DGA)** 
- Investigation of different **cation exchange resins** 
- Investigation of different **complexing agens**, alternative to α-HIB
- **Radiation damage effects** on the extraction resins. 

Separation of Radiolanthanides

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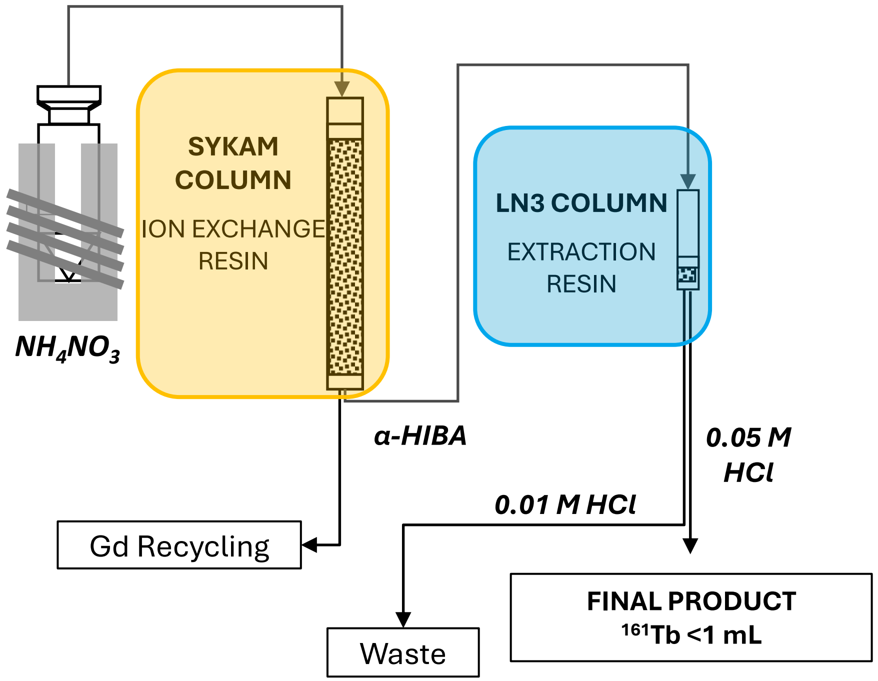
Gd and Tb separation for ^{161}Tb production

reactor produced

$^{160}Gd(n,\gamma)^{161}Gd \rightarrow ^{161}Tb$



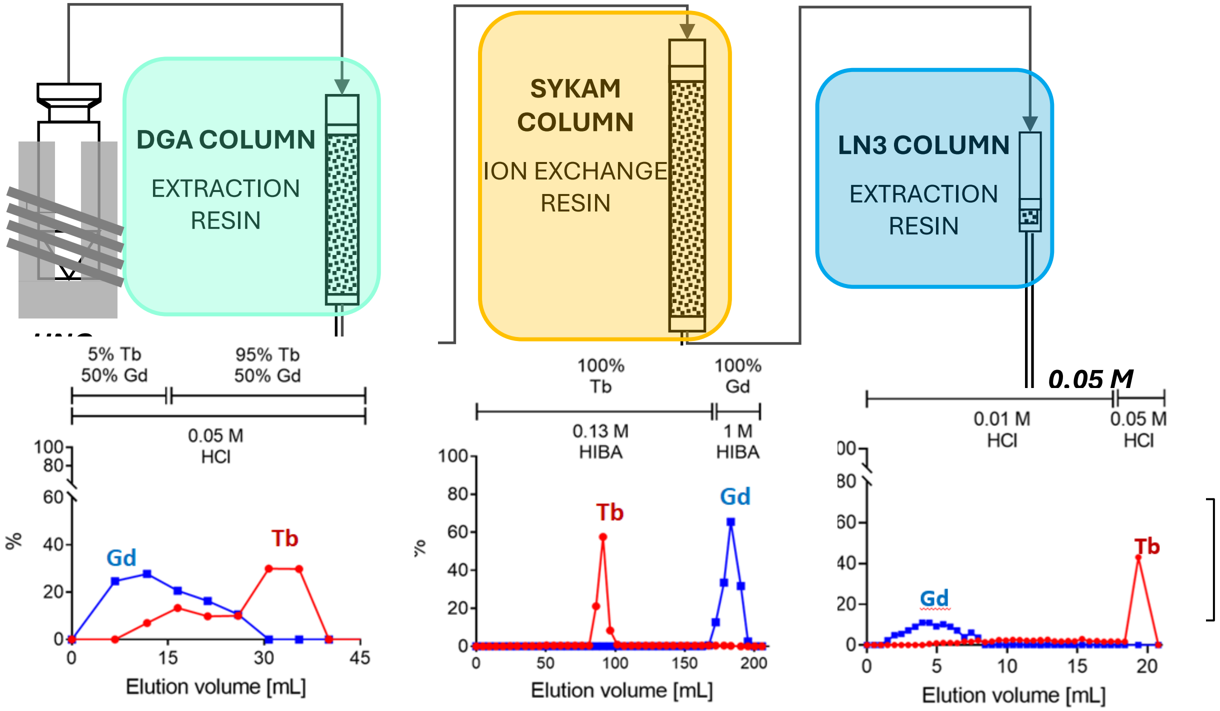
Separation: 1.5 days

N. Gracheva et al., EJNMMI Radiopharmacy and Chemistry, 159, 109085 (2020).

Gd and Tb separation for ^{155}Tb production

cyclotron-produced

$^{156}Gd(p,2n)^{155}Tb$



Separation: 6 - 7 hours

C. Favaretto et al., EJNMMI Radiopharmacy and Chemistry, 6, 37 (2021).

Comparison of Extraction Resins

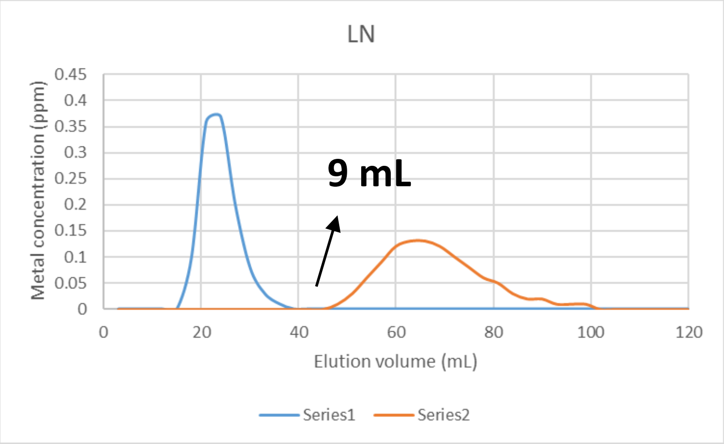
Tm and Er separation

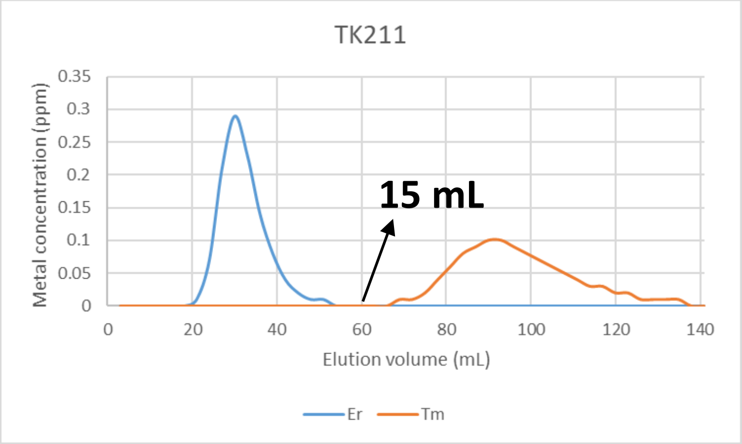
5 µg Er, 5 µg Tm

Loading: 1 mL 0.75 M HNO_3

Eluent: 2 M HNO_3

Column volume: 3 mL column



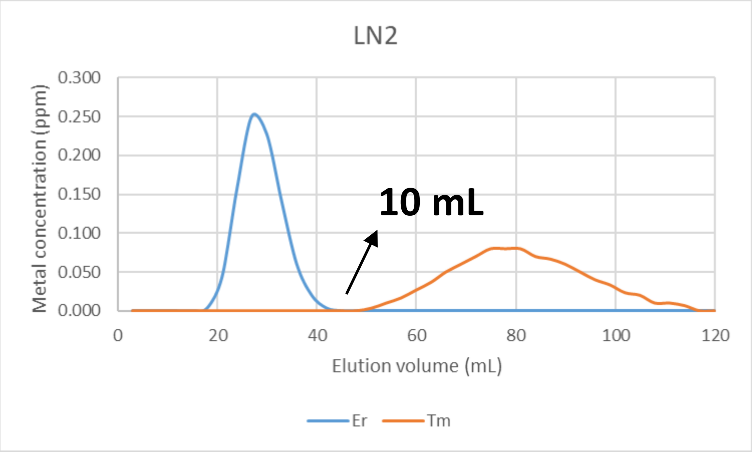


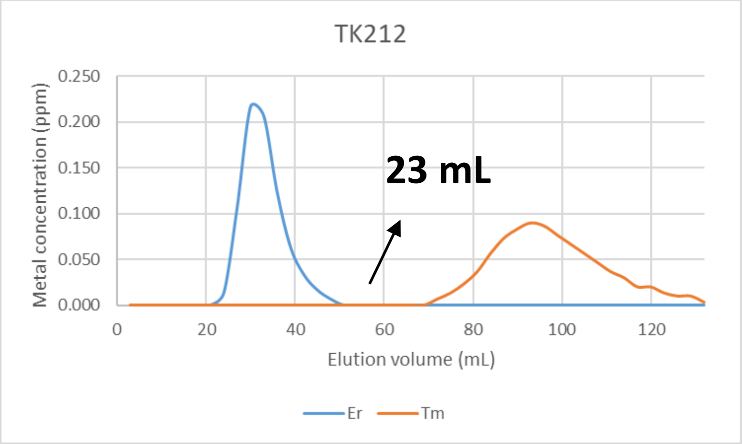
5 µg Er, 5 µg Tm

Loading: 1 mL 0.25 M HNO_3

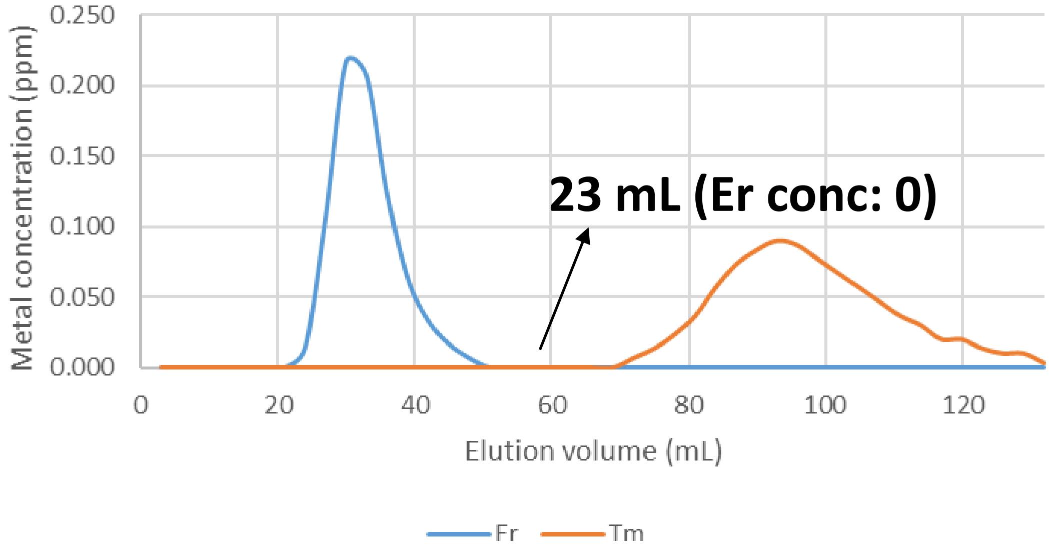
Eluent: 0.75 M HNO_3

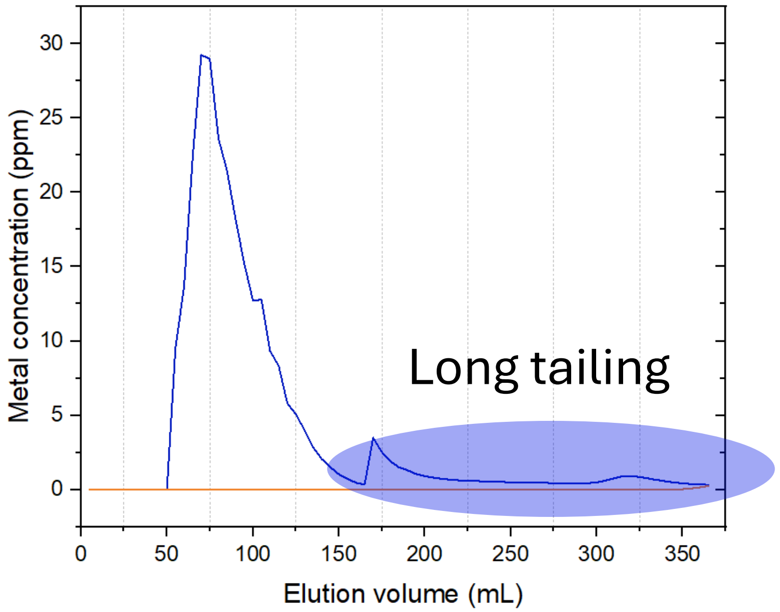
Column volume: 3 mL column





Effect of target mass on TK212 resins





5 µg Er, 5 µg Tm

Loading: 1 mL 0.25 M HNO_3;

Eluent: 0.75 M HNO_3

Column volume: 3 mL column

20 mg Er, 200 µg Tm

Loading: 1 mL 0.25 M HNO_3;

Eluent: 0.75 M HNO_3

Column volume: 16 mL column

Comparison of cation exchange resins

5 µg Er, 5 µg Tm

Loading: 5 mL water

Eluent: 0.07 M α-HIBA pH 4.5

Column volume: 3 mL column

Sykam

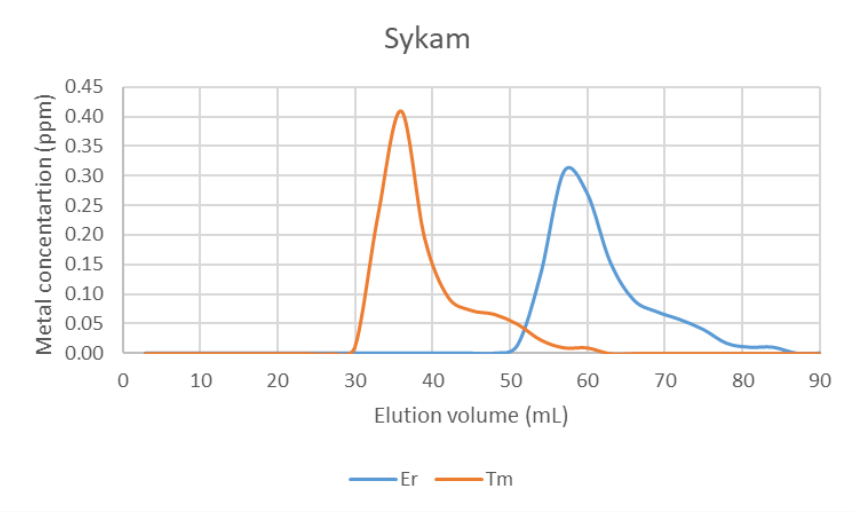
Particle size: 12-22 µM

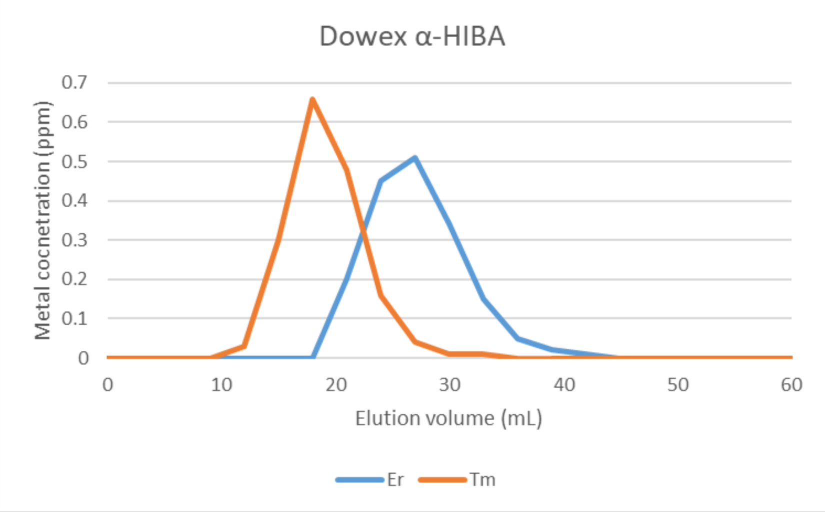
Dowex

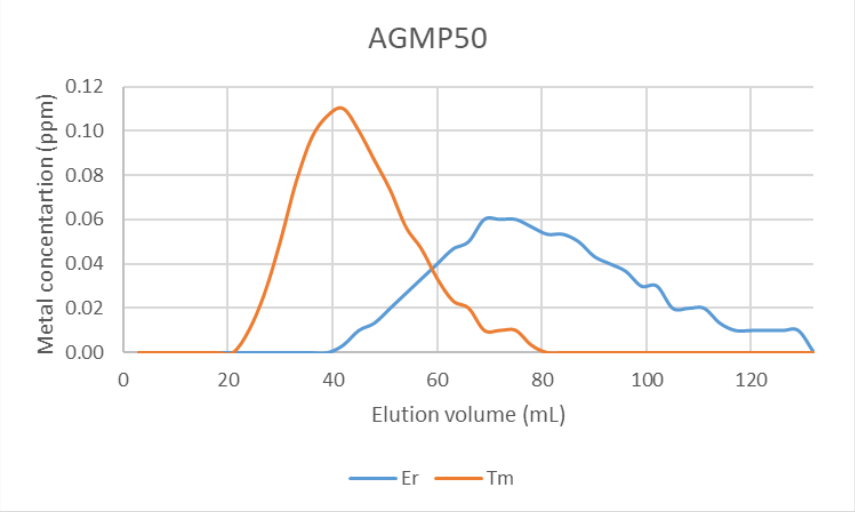
100-200 µM

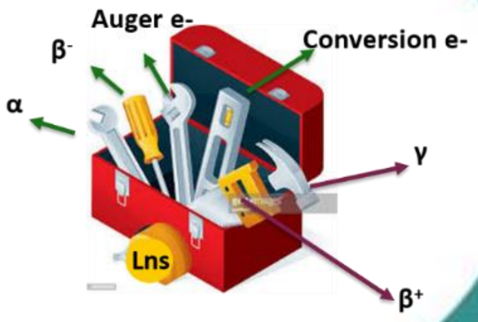
AGMP50

100-200 µM









PSI-Injector 2 cyclotron

^{167}Tm $^{168}Er(p,2n)^{167}Tm$ (1 GBq, 99.5% radionuclidic purity)
$^{171}Yb(p,5n)^{167}Lu$ (420 Mbq, 99.95% radionuclic purity)

ILL nuclear reactor

32 GBq radionuclidically pure **^{166}Ho** per mg of enriched $^{164}Dy_2O_3$

250 MBq of radionuclically pure **^{143}Pr** per mg of enriched $^{142}CeO_2$

Two different lanthanide separation methods were developed, and alternative chemical separation methods for radiolanthanides are in progress.

Acknowledgement

PSI

Wir schaffen Wissen – **heute für morgen**
We create knowledge - **today for tomorrow**

Prof. Dr. Robert Eichler
Prof. Dr. Roger Schibli

Radionuclide Development group
Dr. Nicholas van der Meulen
Dr. Pascal Grundler
Dr. Chiara Favaretto
Edoardo Renaldin
Ramon Zehnder
Sofia Pasolini
Colin Hillhouse

Radionuclide - Production and Maintenance group
Roger Geissmann
Alexander Sommerhalder
Muhamet Djelili

Nuclide Chemistry group
Prof. Dr. Cristina Müller
Dr. Francesca Borgna
Fan Sozzi

PSI GFA
Dr. Hui Zhang

ILL
Prof. Dr. Ulli Koester

Laboratory of High Energy Physics (Unibe)
Prof. Dr. Saverio Braccini
Gaia Dellepiane

IRA-CHUV
Dr. Frederic Juget
Dr. Youcef Nedjadi
Dr. Teresa Duran
Dr. Claude Bailat

CERN MEDICIS
Dr. Thierry Stora
Dr. Charlotte Duchemin
& MEDICIS team

PSI Hot-Lab
Vitor Rodrigues

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CHUV Institut de radiophysique

Thank You For Your Attention!

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