27 EU PRISMAP Medical Radionuclides

MEDICALLY RELEVANT RADIOLANTHANIDES: EXPLORING TODAY'S BREAKTHROUGHS AND TOMORROW'S POSSIBILITIES

WP12: Radiolanthanides

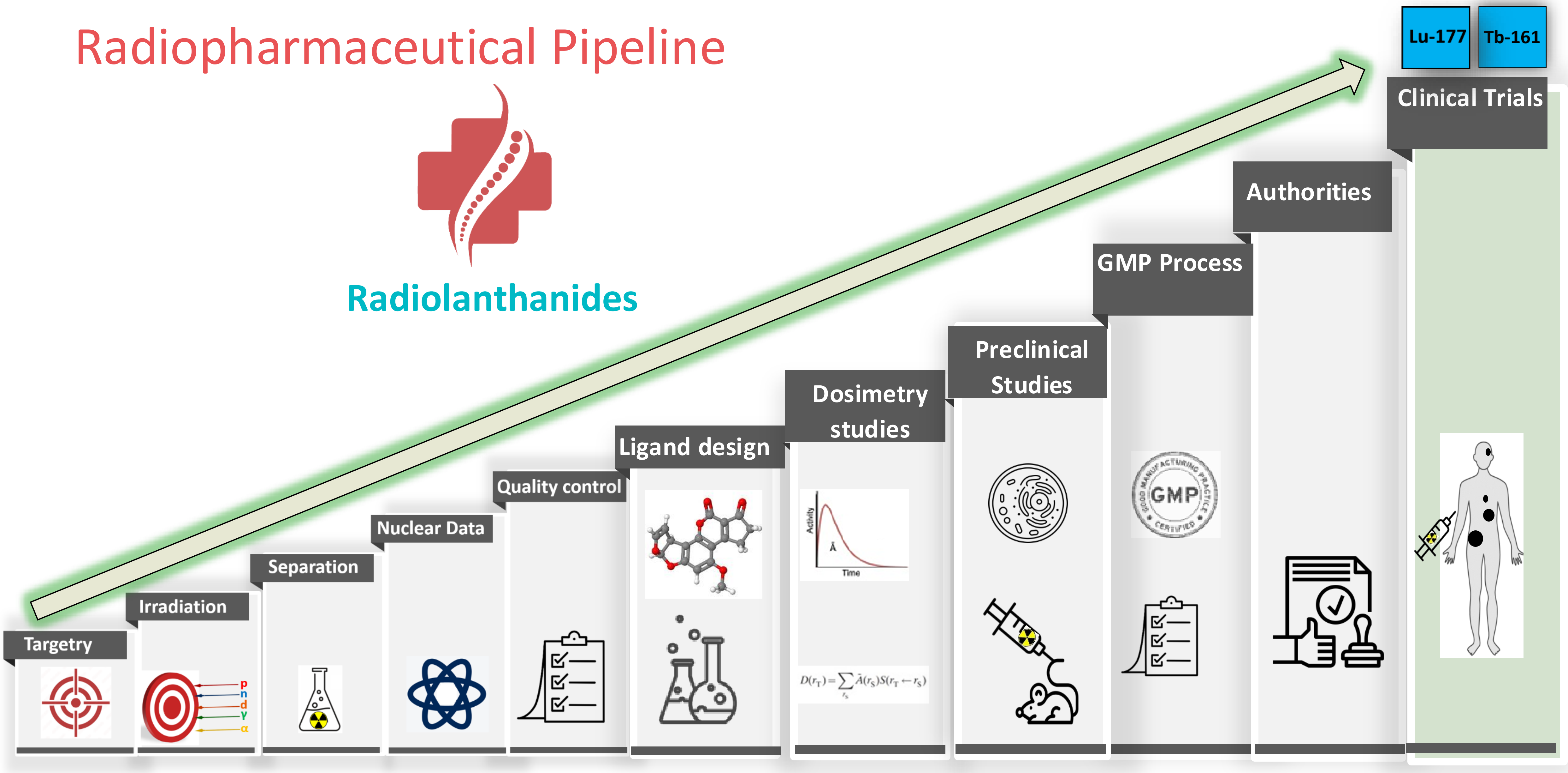
Zeynep Talip

Arronax, DTU, PSI, CERN, SCK CEN, NPL, INFN, IST-ID, KU-Leuven, TUM, CHUV

18 November 2025

Radiopharmaceutical Pipeline

Radiolanthanides



Clinical Trials with Tb-161

EValuation of radIOLigand Treatment in mEn With Metastatic Castration-resistant Prostate Cancer With [^{161}Tb]Tb-PSMA-I&T (VIOLET) **(2022-2026, Phase 1 and Phase 2)**
Peter MacCallum Cancer Centre (Australia)

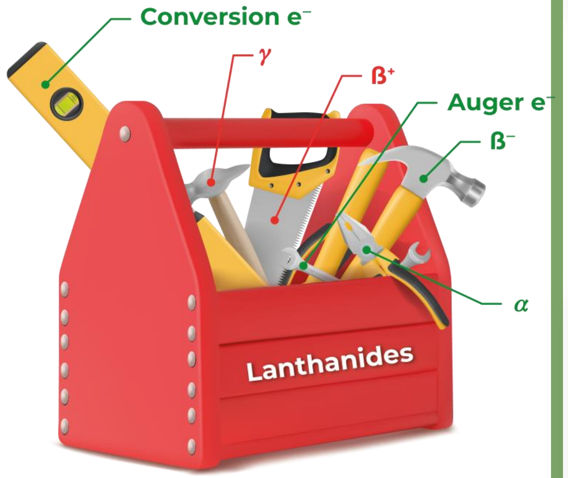
Combined Beta- Plus Auger Electron Therapy Using a Novel Somatostatin Receptor Subtype 2 Antagonist Labelled With Terbium-161 (^{161}Tb-DOTA-LM3) **(Beta plus) (2023-2025-Early Phase 1)**
University Hospital Basel (Switzerland)

Targeted Radionuclide Therapy in Metastatic Prostate Cancer Using a New PSMA Ligand Radiolabelled With Terbium-161 (^{161}Tb-SibuDAB) - Dose Identification/Escalation Phase Ia/b Study (PROGNOSTICS) **(2024-2028 – Phase 1)**
University Hospital Basel (Switzerland)

Tb-PSMA-I&T Radionuclide Before Radical Prostatectomy in Patients With Locally Advanced Prostate Cancer - TbeforePROST Trial **(2025-2028, Phase I and Phase 2)**
Rabin Medical Center (Israel)

Study on the Safety, Tolerability, and Preliminary Efficacy of ^{161}Tb-NYM032 in Patients with Metastatic Castration-Resistant Prostate Cancer **(2025-2026, Phase 1 and Phase 2)**
Mianyang Central Hospital (China)

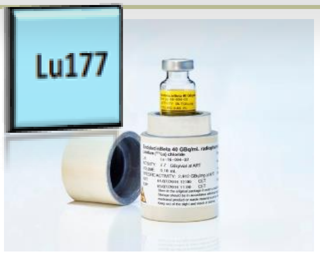
Radionuclides in Nuclear Medicine



Proper **decay properties** for Nuclear Medicine applications

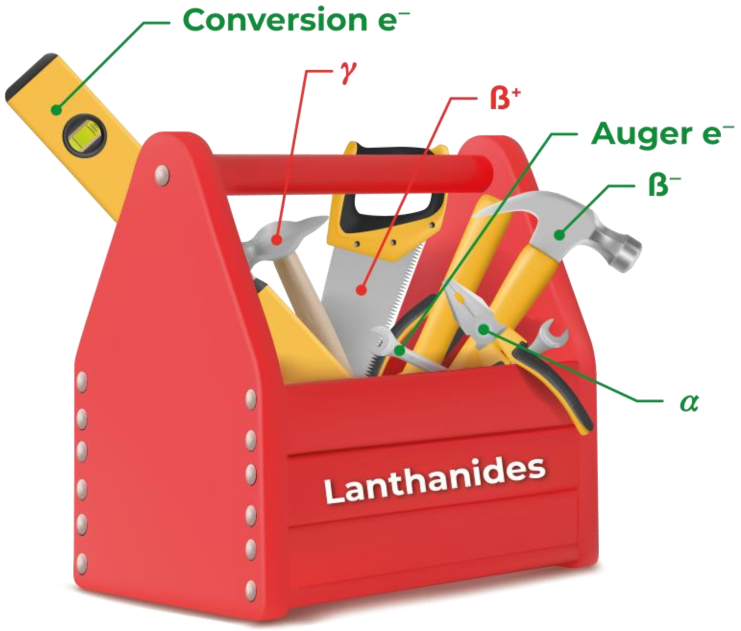
Analogue coordination chemistry

Allow us to perform **systematic preclinical studies**



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

PRISMAP Radiolanthanides Toolbox



β^-		AE		AE/CE
Yb-175	Er-169	La-135	Er-165	Tm-167
Ho-166	Sm-153	Ho-161		

β^-,AE/CE	SPECT	AE, SPECT	α,PET
Tb-161	Tb-152	Tb-155	Tb-149

PRISMAP W12 Deliverables

Cross section measurements

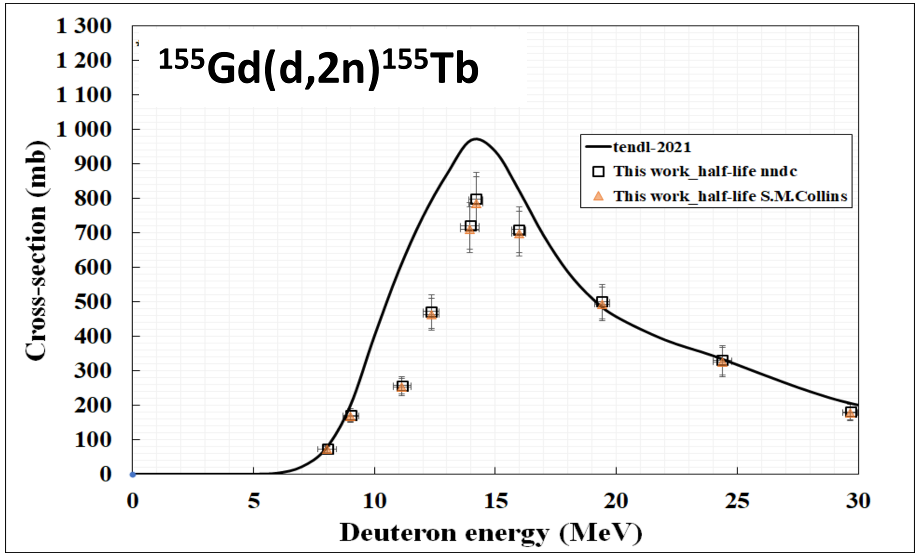
Separation Chemistry

Preclinical Studies

- [ ] Tb-149
- [ ] Tb-155
- [ ] Tb-161
- [ ] Ho-161
- [ ] Tm-167

Cross section Measurements

Tb-155



Y. Wang et al, Applied Radiation and Isotopes, 20 (2023)110996.

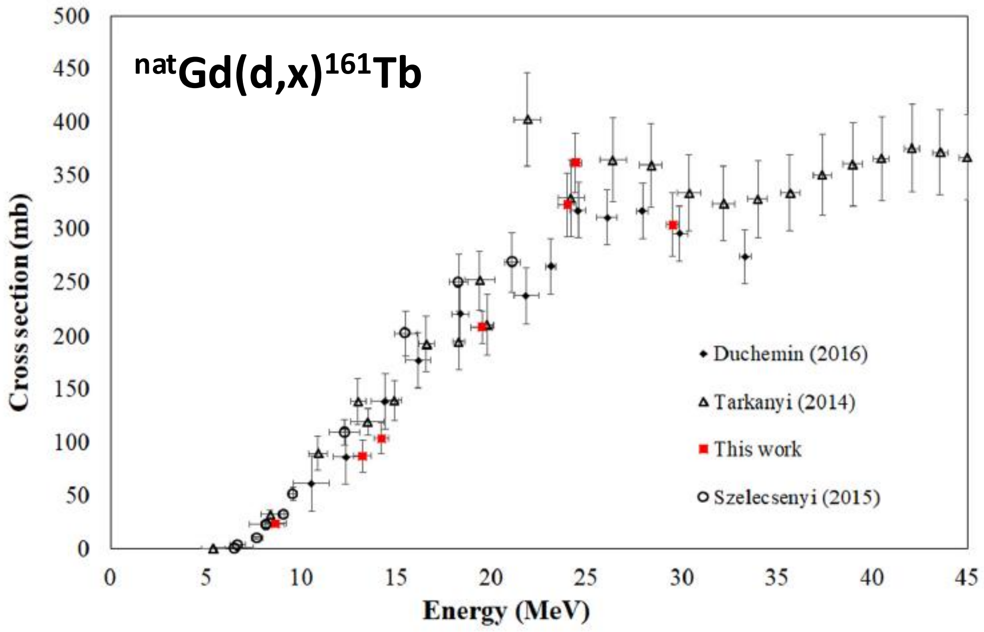
- In general, TENDL-2021 calculations are consistent with measured values.
- TENDL-2021 overestimates the values at lower energy.
- Maximum cross-section = 800 mb at 14.5 MeV.

The production yield of ^{155}Tb is 10.2 MBq/µA/h at End Of Bombardment

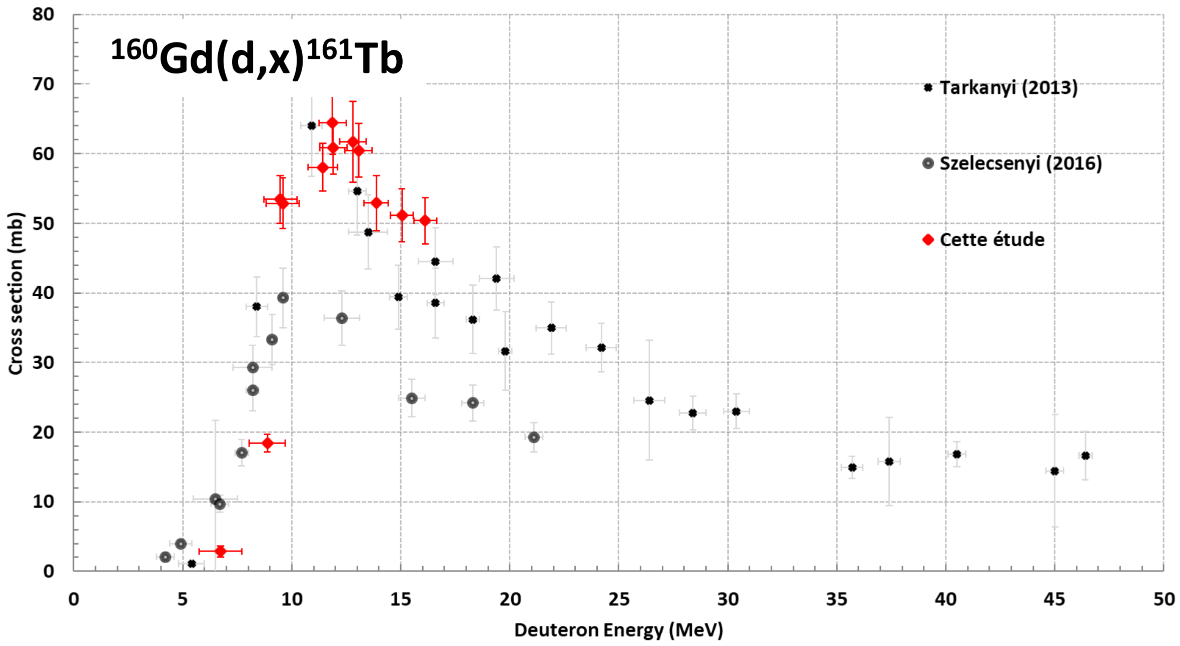
The purity is 89% after 14 days of decay.

Cross section Measurements

Tb-161



Y. Wang et al., Applied Radiation and Isotopes, 186 (2022)110287.



E. Nigron et al., Applied Radiation and Isotopes, 200 (2023) 110927.

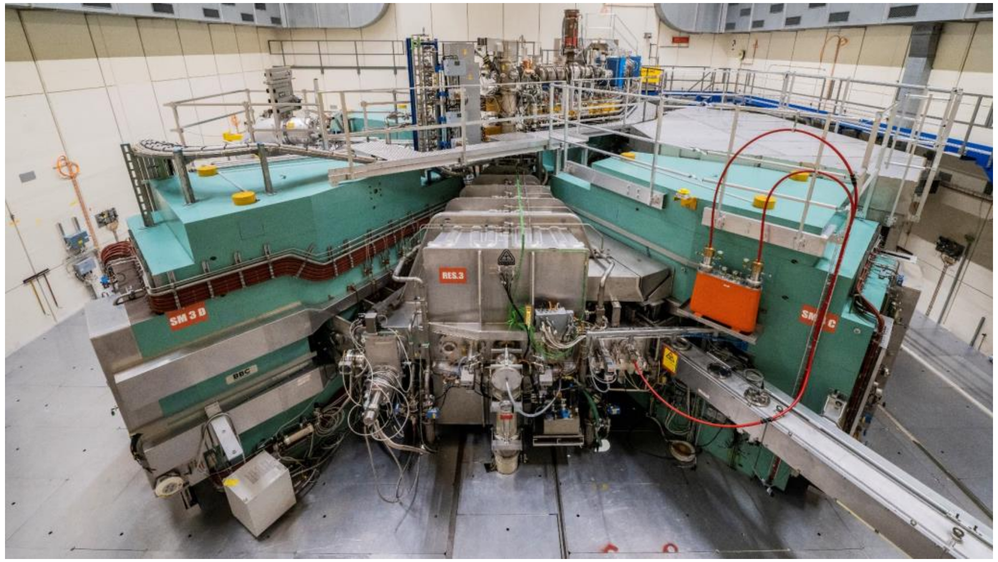
Ho-161 Tm-167

Cross section Measurements

Production cross section and production yield measurements

IBA Cyclone 18/18 HC
Bern University Cyclotron Laboratory

Production yield measurements



Injector II 72 MeV
Paul Scherrer Institute

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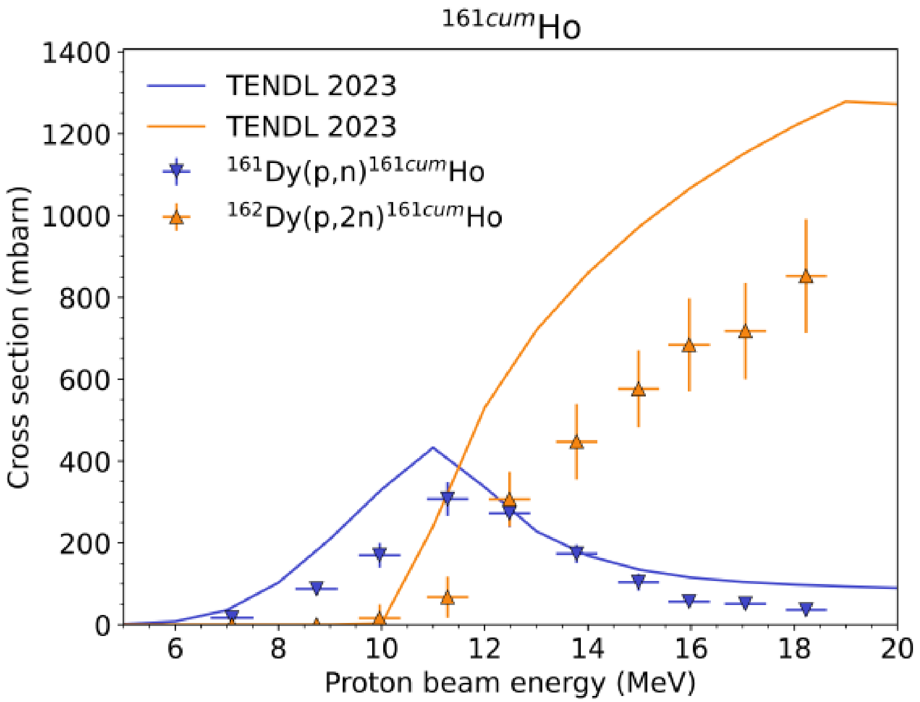
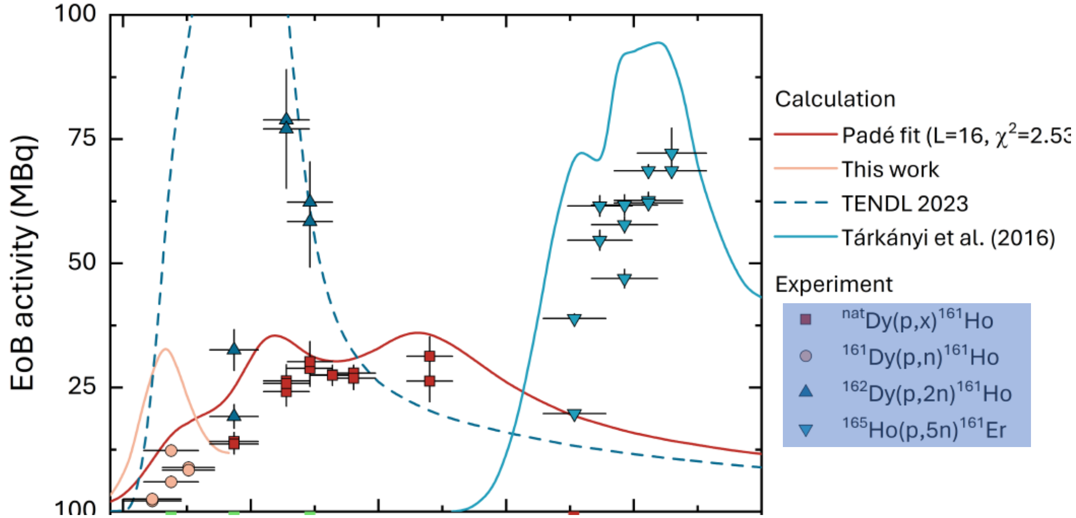
Cross section Measurements

Production cross section measurements



Production yield measurements



40 mg $^{nat}Ho_2O_3$ target **^{165}Ho(p,5n)^{161}Er→^{161}Ho**

25 µA, 45 MeV, 6 h irradiation EOB: **15 GBq ^{161}Er**

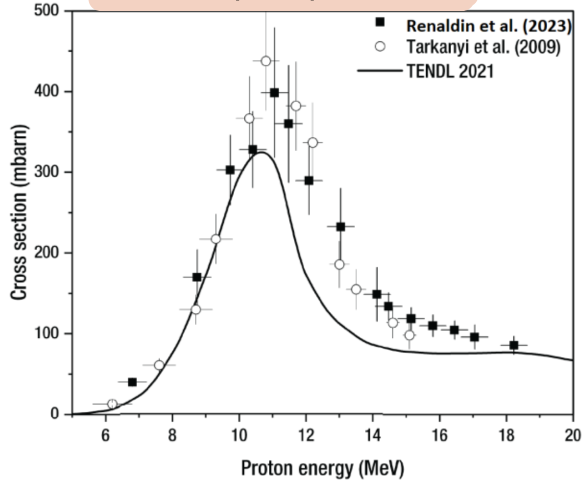
99.98% radionuclidic purity

E. Renaldin et al.,App. Rad. Isot., to be submitted.

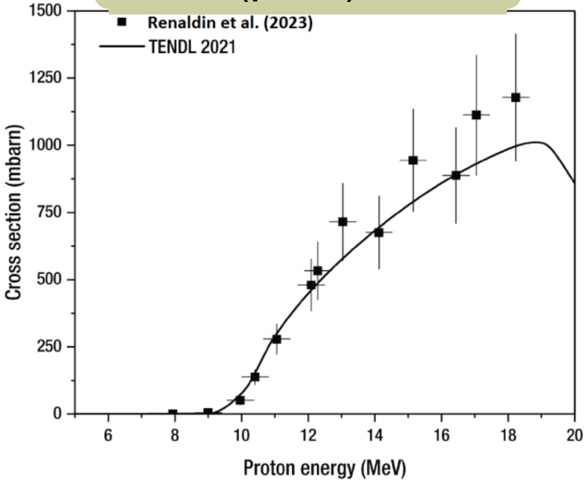
Cross section Measurements

Production cross section measurements

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

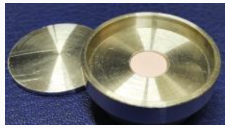


$^{168}Er(p,2n)^{167}Tm$



Production yield measurements

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

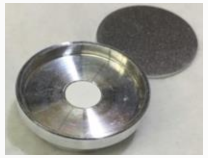


40 mg $^{168}Er_2O_3$ target (^{168}Er: 98.3%)

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**

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

PRISMAP W12 Deliverables

Cross section measurements

- [x] Tb-149
- [x] Tb-155
- [x] Tb-161
- [x] Ho-161
- [x] Tm-167

Separation Chemistry

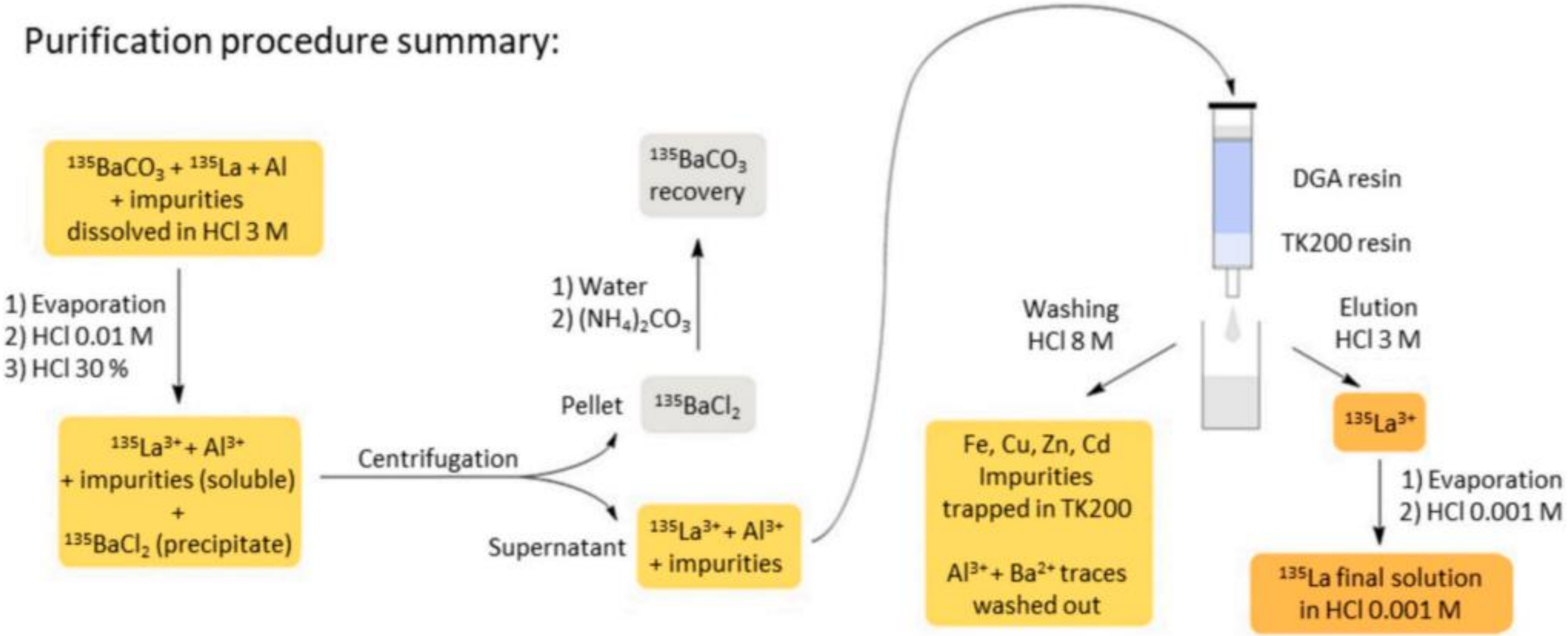
- [ ] La-135
- [ ] Tb-155
- [ ] Er-165
- [ ] Ho-166

Preclinical Studies

Development of the Separation Method

La-135

$^{135}Ba(p,n)^{135}La$



5 batches were sent to SCK-CEN for preclinical studies

K. S. Pedersen et al., Appl. Radiat. Isot. (2023), 192, 110612.

Development of the Separation Method

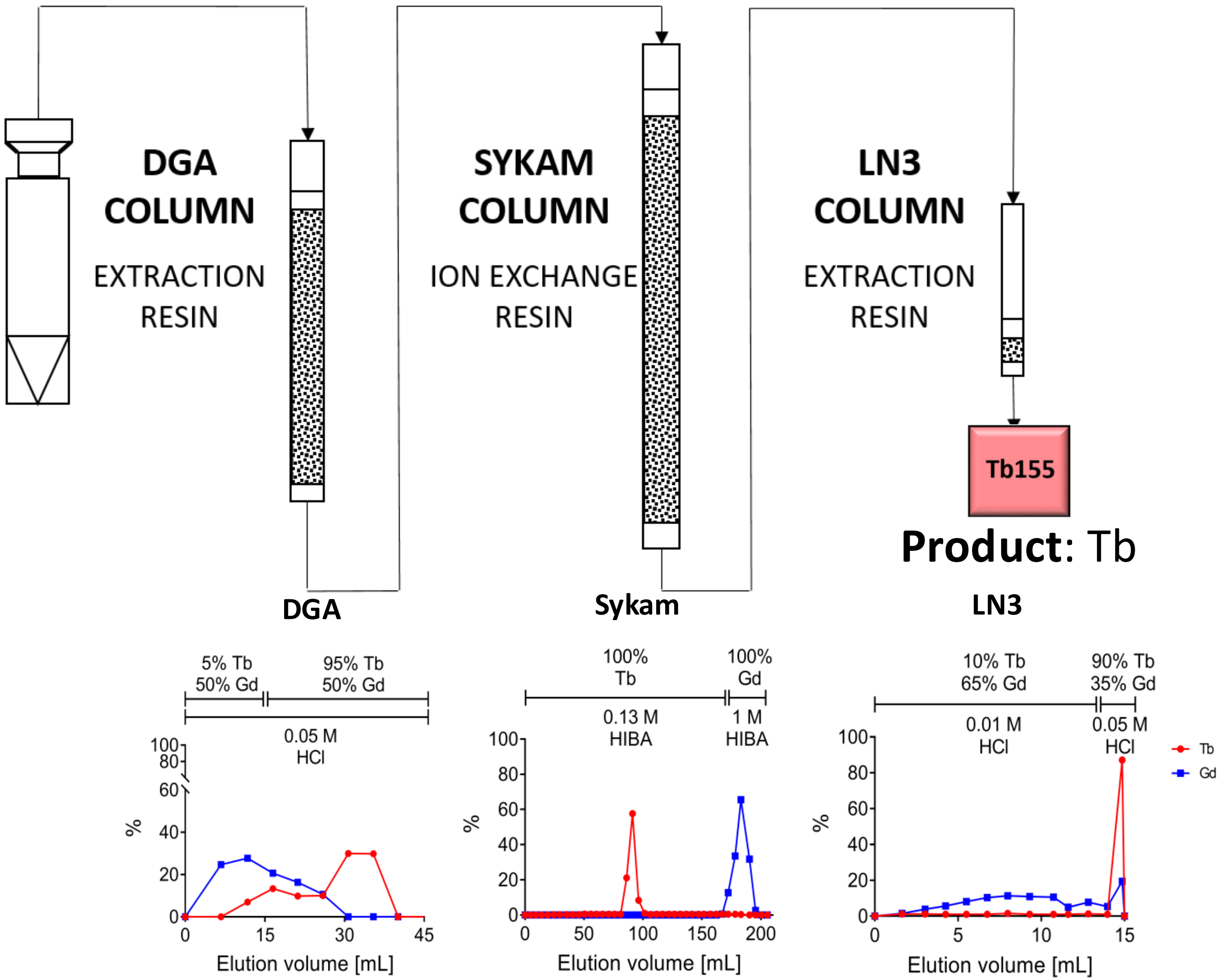
Tb-155

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

Target: enr. $^{156}Gd_2O_3$

100000 µg Gd

0.75 µg ^{155}Tb



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

PRISMAP+

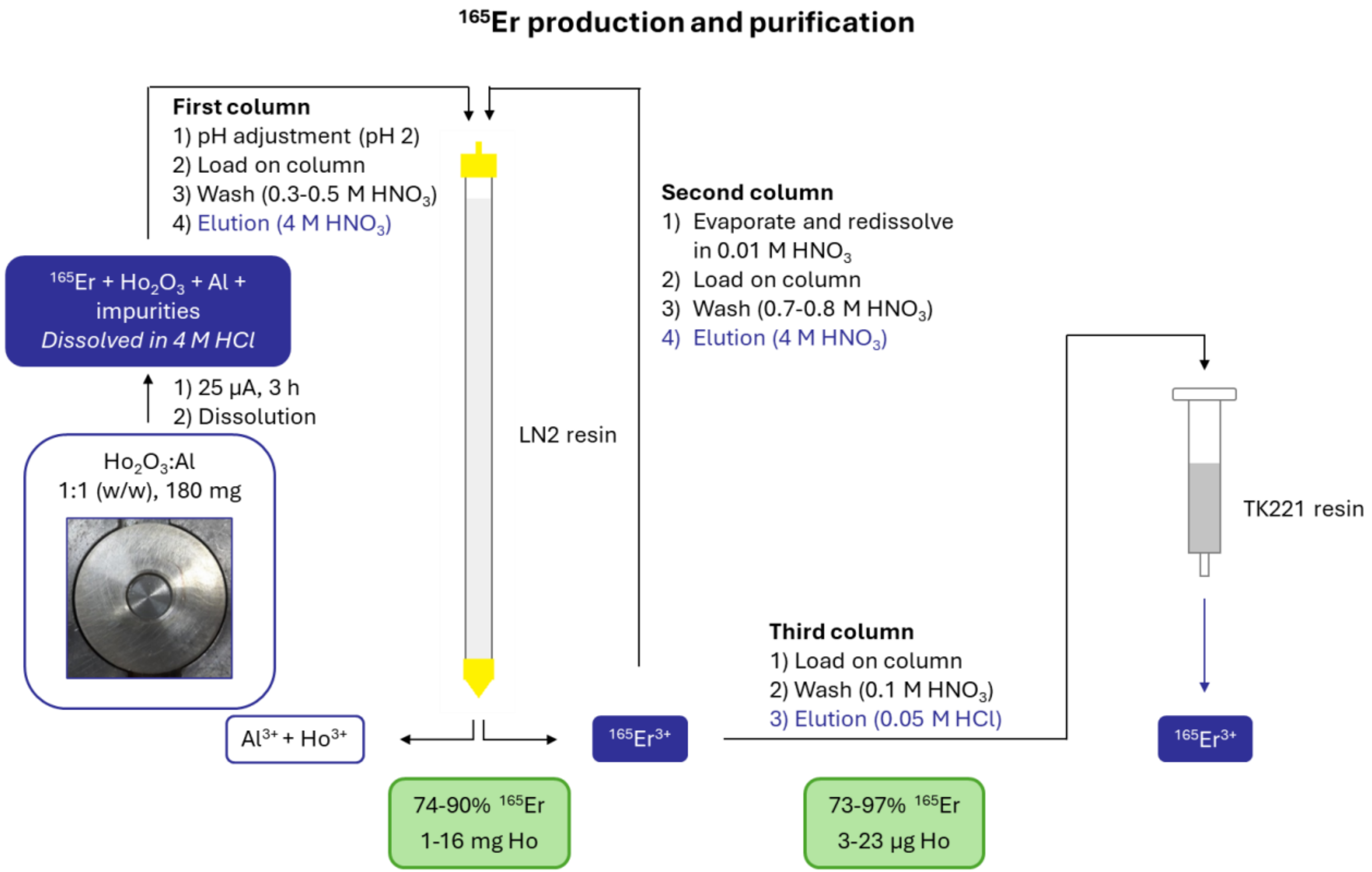
PSI

$^{159}Tb(p,5n)^{155}Dy \rightarrow ^{155}Tb$

Development of the Separation Method

Er-165

$^{165}Ho(p,n)^{165}Er$



Further studies:

- To enhance the efficiency of the procedure
- The quantification of Er-165

PRISMAP+

Danmarks Tekniske Universitet DTU

KU LEUVEN

IST-ID Associação do Instituto Superior Técnico para a Investigação e Desenvolvimento

PRISMAP W12 Deliverables

Cross section measurements

- ☑ Tb-149
- ☑ Tb-155
- ☑ Tb-161
- ☑ Ho-161
- ☑ Tm-167

Separation Chemistry

- ☑ La-135
- ☑ Tb-155
- ☑ Er-165
- ☒ Ho-166

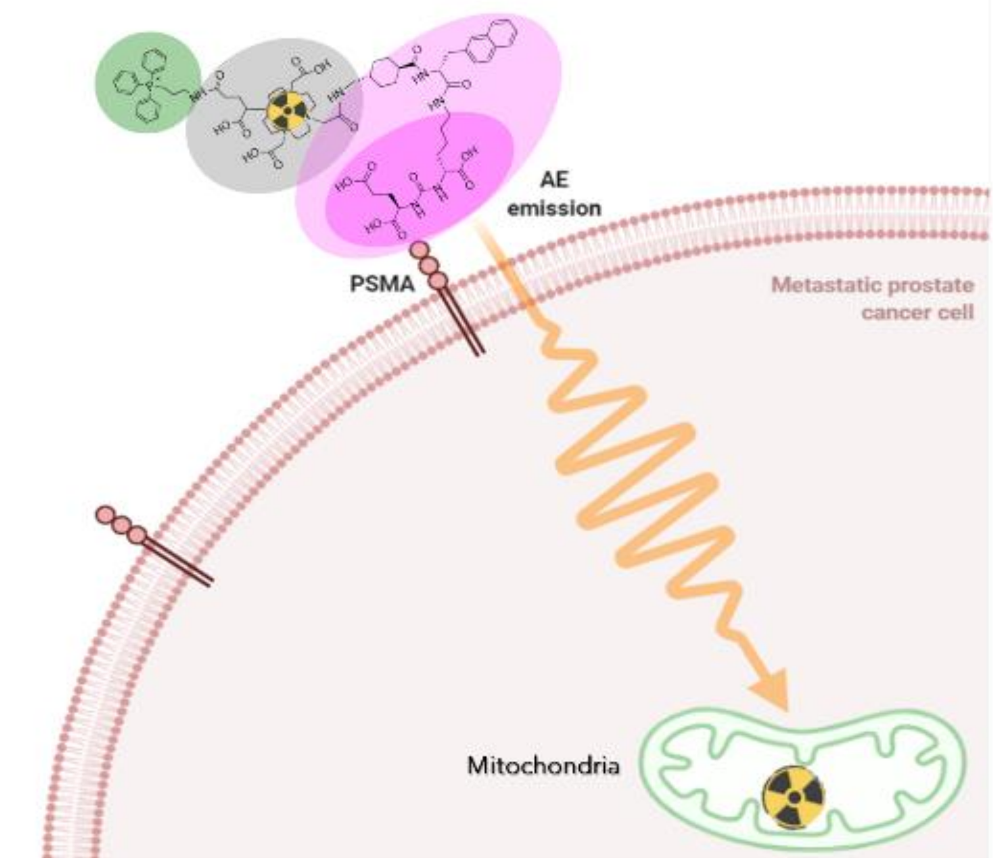
Preclinical Studies

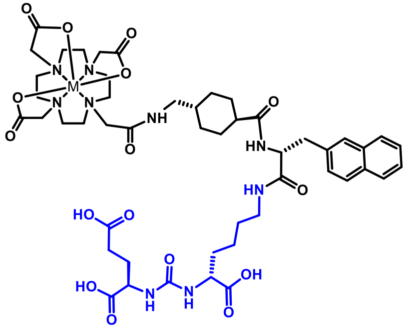
- ☐ Synthesis and characterisation studies of multifunctional chelators
- ☐ Therapeutic efficacy of [Tb-161]Tb-SibuDAB and [Lu-177]Lu-SibuDAB
- ☐ Radiolabeling protocols and quality control procedures for La-135, Sm-153 and Tb-161
- ☐ The role of AEs in TRT (Tb-161 and La-135)
- ☐ AE- and β^--emitting radionuclides to be investigated: Tb-155, Er-165, Er-169, and Yb-175

Preclinical Studies: Dual-Targeted Terbium-161 complexes: Targeting the Mitochondria of PCa Cells

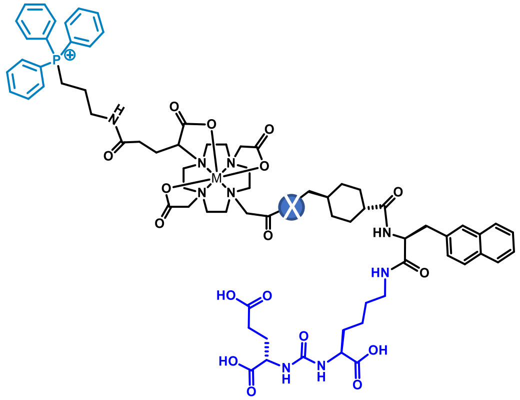
Tb-161

Aim: Specific delivery of Tb-161 to the mitochondria of PSMA-positive PCa cells





^{161}Tb-PSMA-617



X = NH; ^{161}Tb-TPP-DOTA-PSMA-617

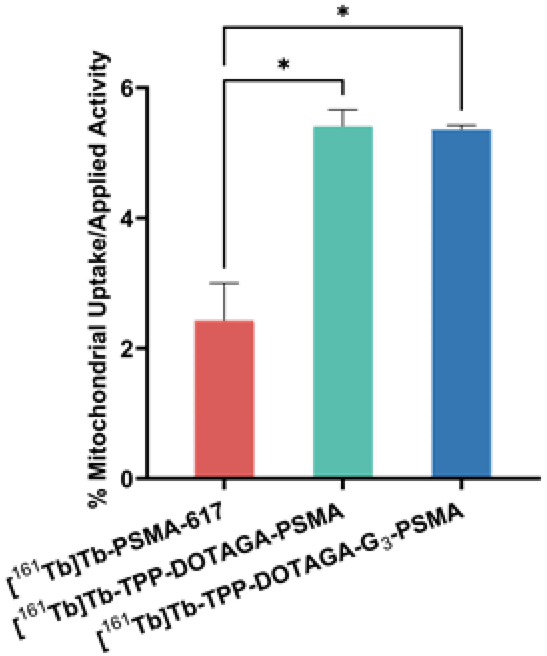
X = GlyGlyGly; ^{161}Tb-TPP-DOTA-G_3-PSMA-617

Preclinical Studies: Dual-Targeted Terbium-161 complexes: Targeting the Mitochondria of PCa Cells

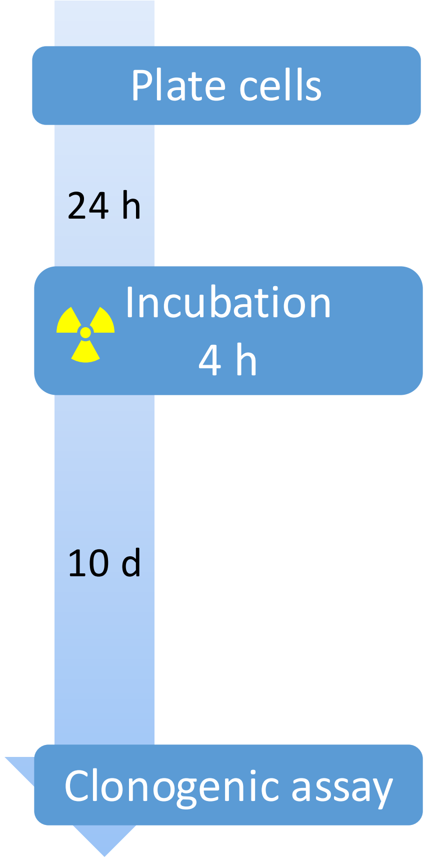
Tb-161

Mitochondrial Uptake

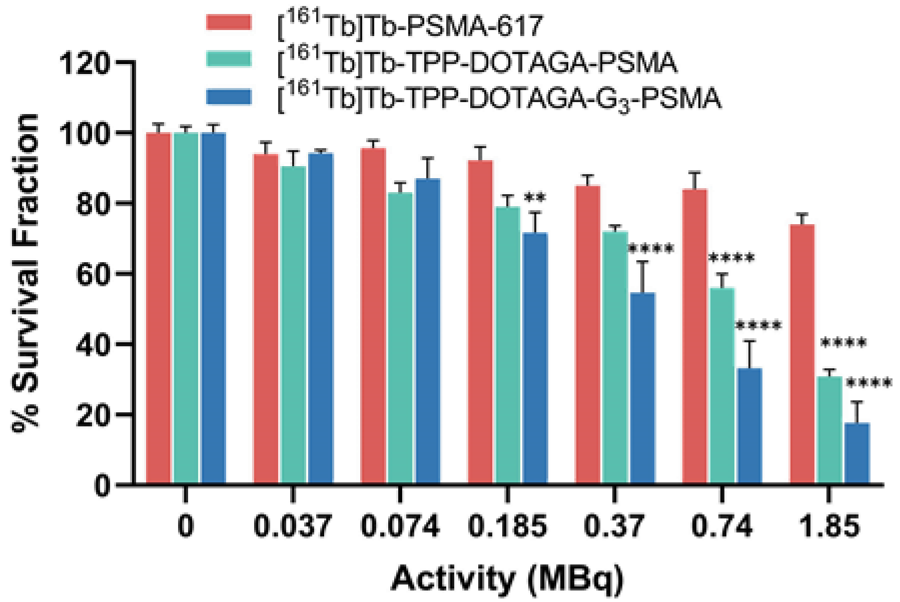
PC3-PIP cells 1 h
Mitochondria Isolation Kit (using magnetic beads) (Miltenyi Biotec)



Clonogenic Assay



PC3 PIP – PSMA (+)

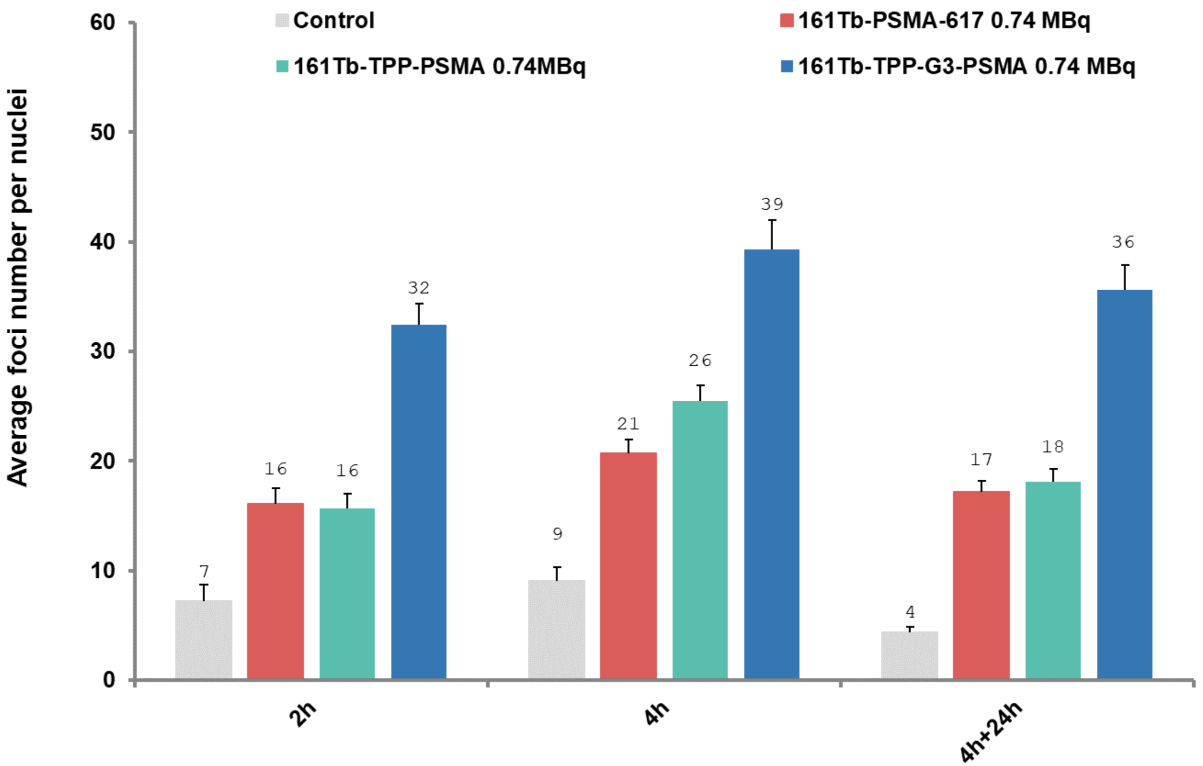


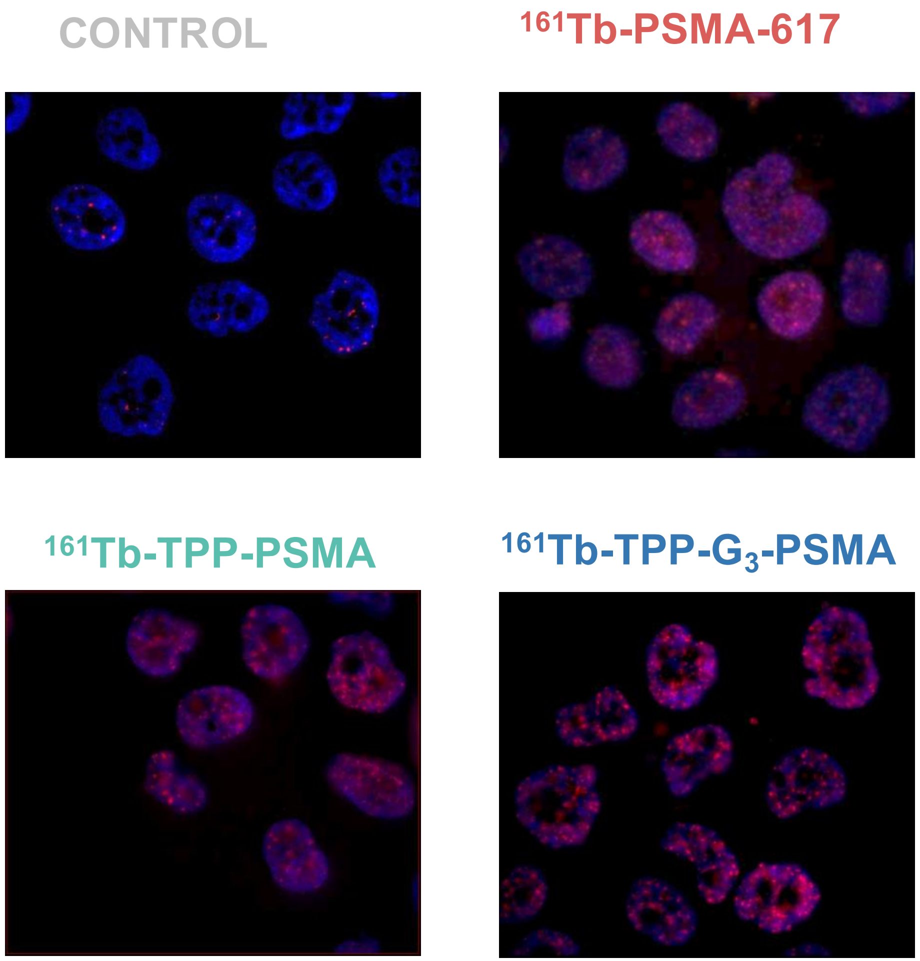
J. F. Santos et al., *EJNMMI Radiopharmacy and Chemistry (2025) 10, 18.*

Preclinical Studies: Dual-Targeted Terbium-161 complexes: Targeting the Mitochondria of PCa Cells

Tb-161

DNA damage/γH2AX assay

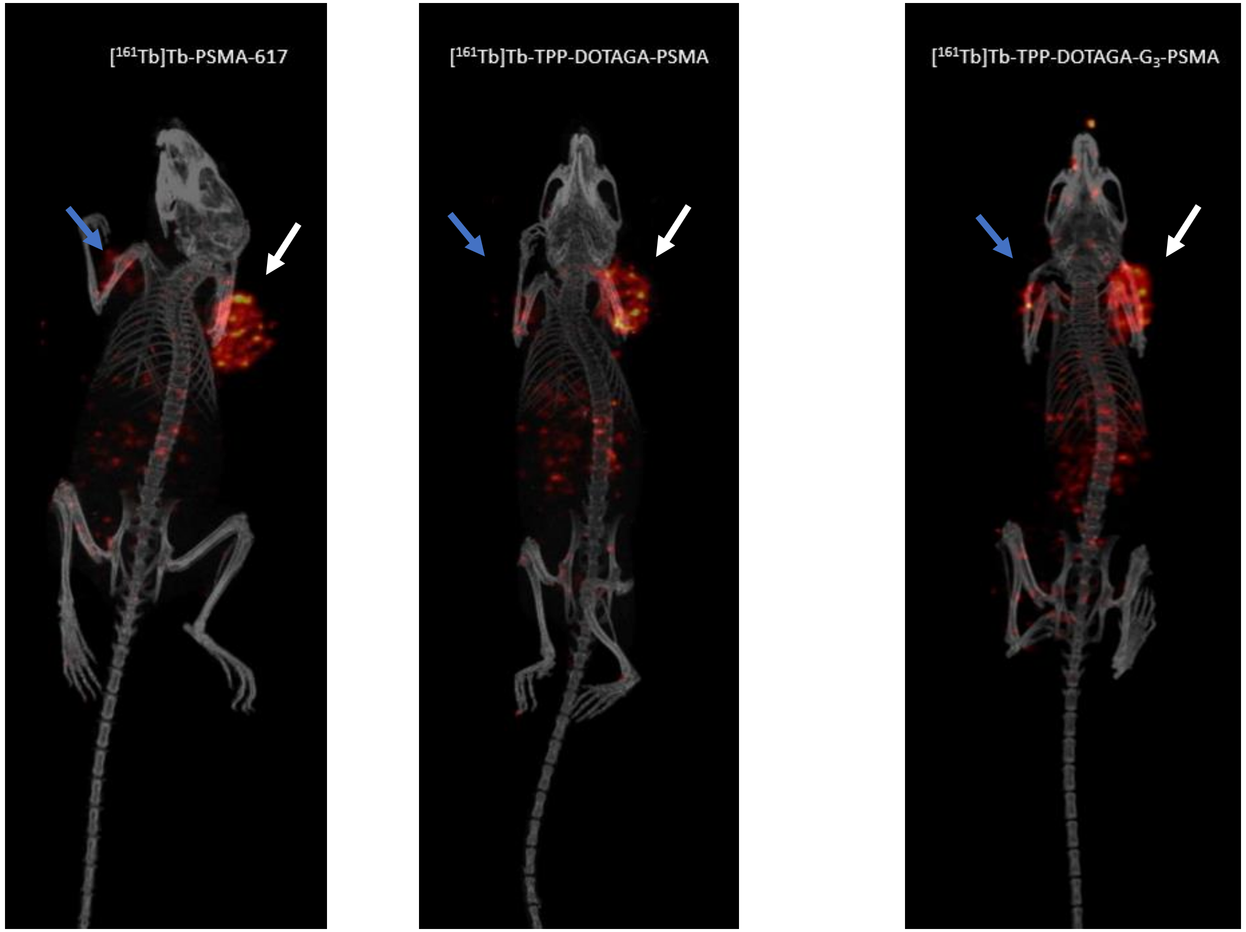




J. F. Santos et al., EJNMMI Radiopharmacy and Chemistry (2025) 10, 18.

Preclinical Studies: µSPECT imaging of the Terbium-161-radioconjugates in PCa xenografts

Tb-161



µSPECT/CT: **24h p.i.**
Right schoulder: PC3.PIP (PSMA$^+$, white arrow)
Left schoulder: PC3.Flu (PSMA$^-$, blue arrow)

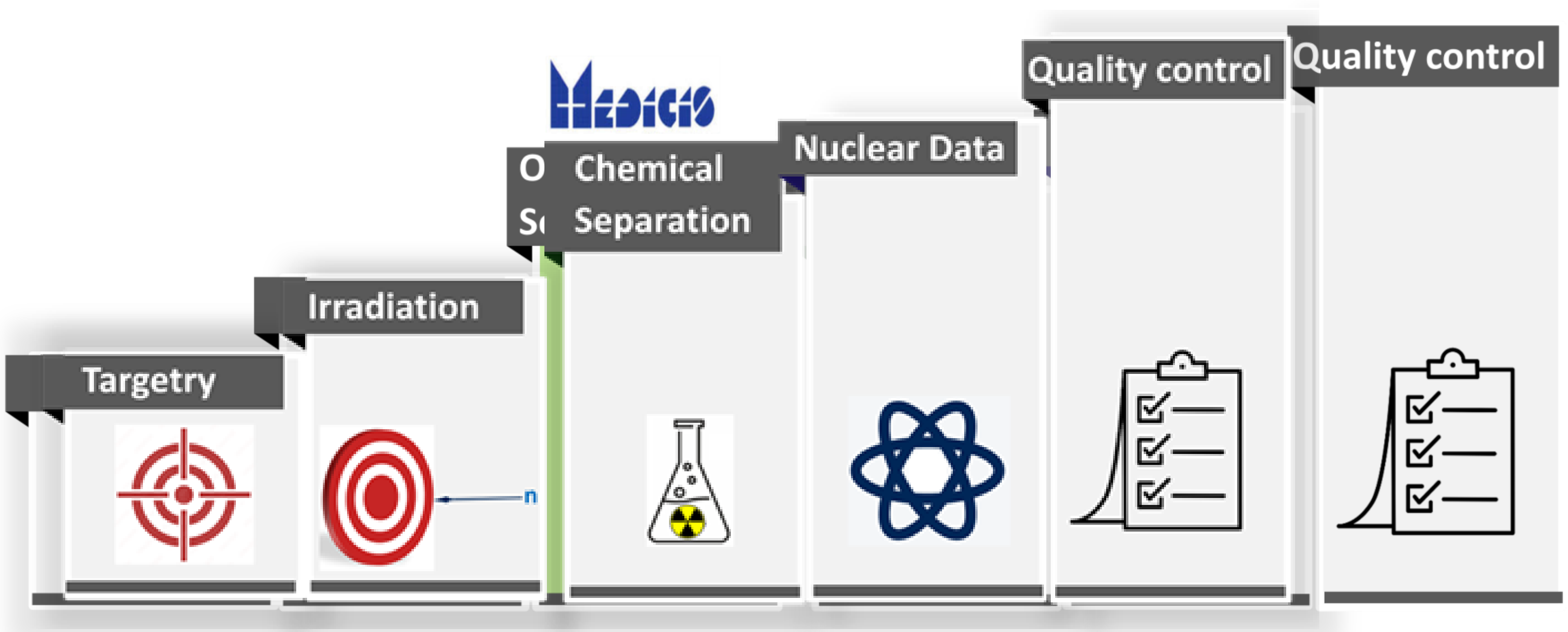
PSMA-specific tumor accumulation and the addition of a TPP-moiety did not have a pronounced effect on the pharmacokinetic profile.

J. F. Santos et al., EJNMMI Radiopharmacy and Chemistry (2025) 10, 18.

Preclinical Studies: Exploring the potential of [^{153}Sm]Sm-DOTA-TATE for TRT

Sm-153

Sm 144	Sm 145	Sm 146	Sm 147	Sm 148	Sm 149	Sm 150	Sm 151	Sm 152	Sm 153	Sm 154	Sm 155
3.08	340 d	$6.8 \cdot 10^{7}$ a	15.00 $1.07 \cdot 10^{11}$ a	11.25 $7 \cdot 10^{15}$ a	13.82	7.37	94.7 a	26.74	46.284 h	22.74	22.18 m
σ 1.64	ε γ 61, (492...) e^- σ 280	α 2.460	α 2.248 σ 57 $\sigma_{n,\alpha}$ 0.00058	α 1.932 σ 2.4	σ 40140 $\sigma_{n,\alpha}$ 0.0307	σ 100	β^- 0.1... γ (22...), e^- σ 15140	σ 206	β^- 0.7, 0.8... γ 103, 70..., e^- σ 420	σ 8.5	β^- 1.5, 1.6... γ 104, 246 141...



The reactor produced ^{153}Sm

7.03 GBq/mg

Mass-separated ^{153}Sm

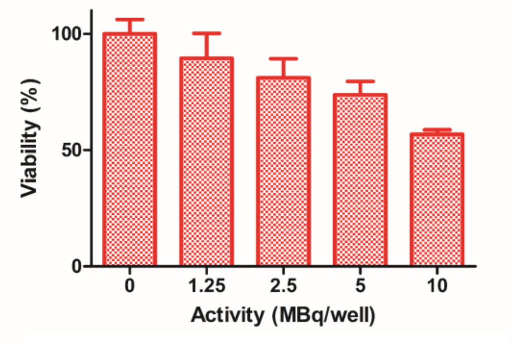
1.5 TBq/mg

Van de Voorde et al., Front. Med. ***2021****, 8, 1153.*

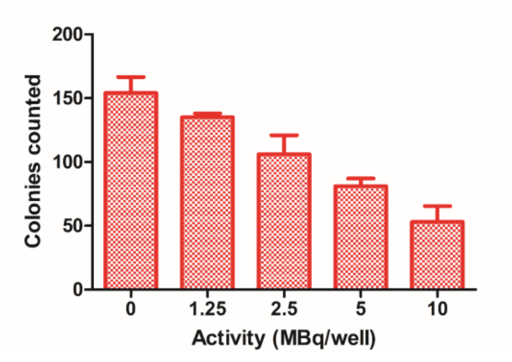
Preclinical Studies: Exploring the potential of [^{153}Sm]Sm-DOTA-TATE for TRT

Sm-153

In vitro evaluation

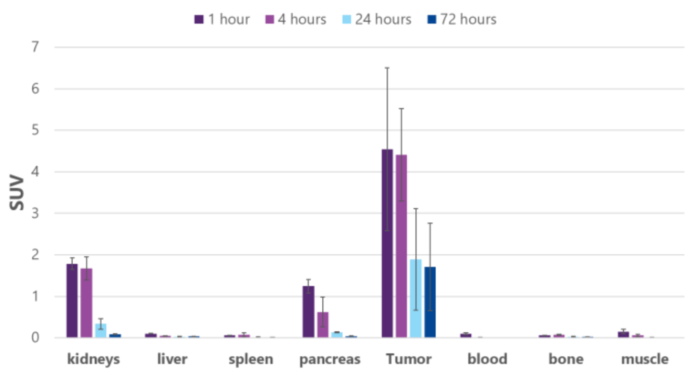


43% reduction in cell viability



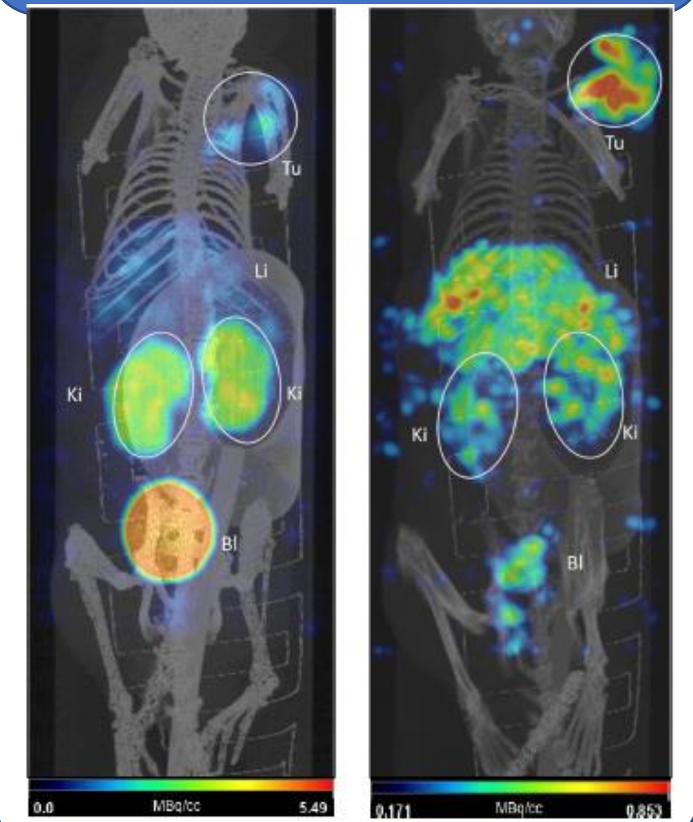
66% reduction in colony formation

In vivo evaluation



High in vivo tumor accumulation

SPECT imaging



K. Vermeulen et al., Pharmaceutics, (2022) 14, 2566.

^{153}**Sm** has strong potential for Targeted Radionuclide Therapy

Preclinical Studies: ^{135}La-labeled 1 SSTR2 agonists and antagonists

Radionuclide quantification

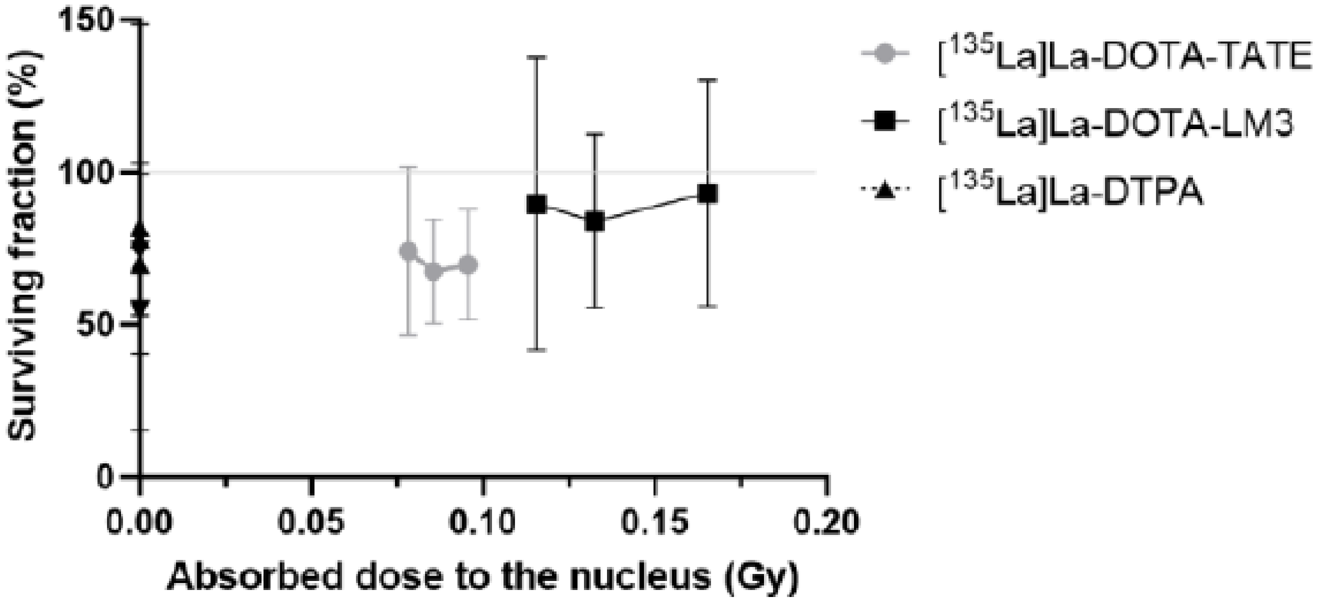
Vector Radiolabeling

Radiolabeling

Biological response

DOTA-TATE (agonist)

DOTA-LM3 (antagonist)



^{135}La offers limited therapeutic potential in combination with the respective internalizing and membrane-bound SSTR2-targeting peptides DOTA-TATE and DOTA-LM3 *in vitro*

M. Crabbe et al., submitted to EJNMMI research.

PRISMAP W12 Deliverables

Cross section measurements

- ✓ Tb-149
- ✓ Tb-155
- ✓ Tb-161
- ✓ Ho-161
- ✓ Tm-167

Separation Chemistry

- ✓ La-135
- ✓ Tb-155
- ✓ Er-165
- ✗ Ho-166

Preclinical Studies

- ✓ Synthesis and characterisation studies of multifunctional chelators and their corresponding radiocomplexes
- ✓ Therapeutic efficacy of [Tb-161]Tb-SibuDAB and [Lu-177]Lu-SibuDAB
- ✓ Radiolabeling protocols and quality control procedures for La-135, Sm-153 and Tb-161
- ✓ The role of AEs in TRT (Tb-161 and La-135)
- ✗ AE- and β^--emitting radionuclides to be investigated: Tb-155, Er-165, Er-169, and Yb-175

Publications

M. Colucci et al, Excitation functions of deuteron induced nuclear reactions on dysprosium targets for the production of the theranostic relevant isotopes of terbium, Eur. Phys. J. Plus (2022), 137, 1180.

E. Nigron et al, Can we reach suitable ^{161}Tb purity for medical applications using the ^{160}Gd(d,n) reaction?, Appl. Radiat. Isot. (2023) 200, 110927.

Y. Wang et al, Study of terbium production from enriched Gd targets via the reaction ^{155}Gd(d,2n)^{155}Tb**.** Appl. Radiat. Isot. (2023), 201, 110996.

E. Renaldin et al., Study of thulium-167 cyclotron production: a potential medically-relevant radionuclide, Front. Chem. (2023), 11, 1.

R. Heinke et al., Efficient Production of High Specific Activity Thulium-167 at Paul Scherrer Institute and CERN-MEDICIS, Front. Med. (2021), 8, 1.

K. S. Pedersen et al., Improved procedures for production and purification of ^{135}La from enriched [^{135}Ba]BaCO$_3$ on a 16.5 MeV cyclotron, Appl. Radiat. Isot. (2023), 192, 110612.

Publications

K. Vermeulen et al., Exploring the Potential of High-Molar-Activity Samarium-153 for Targeted Radionuclide Therapy with [^{153}Sm]Sm-DOTA-TATE, Pharmaceutics, (2022) 14, 2566.

J. F. Santos et al. Synthesis and Preclinical Evaluation of PSMA-Targeted ^{111}In-Radioconjugates Containing a Mitochondria-Tropic Triphenylphosphonium Carrier. Mol Pharm. (2024) 21, 216.

J. F. Santos et al., Mitochondria-tropic radioconjugates to enhance the therapeutic potentialof terbium-161, *EJNMMI Radiopharmacy and Chemistry* (2025) 10, 18.

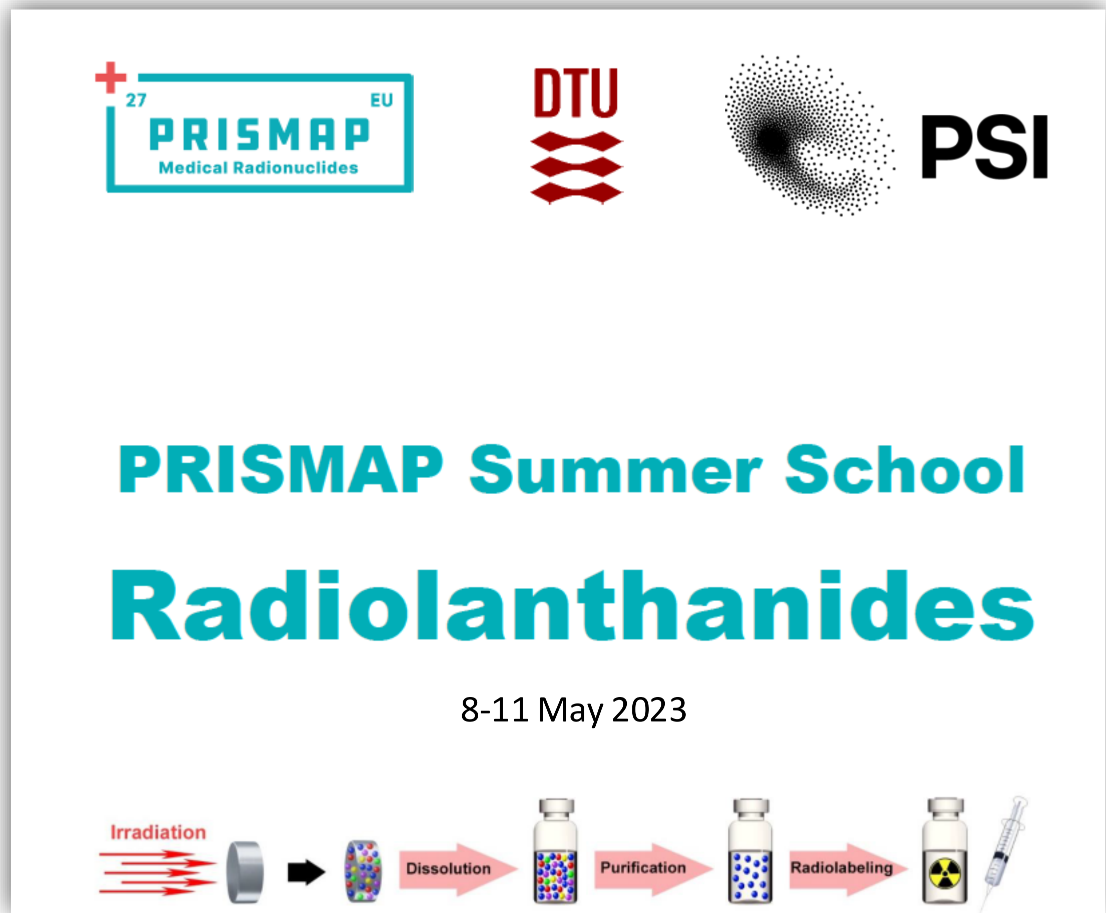
Review paper

C. V. Laere et al., Terbium radionuclides for theranostic applications in nuclear medicine: from atom to bedside, Theranostics (2024), 14, 4.

20/45 user projects were about radiolanthanides

N. Holzleitner et al., Preclinical Evaluation of Gastrin-Releasing Peptide Receptor Antagonists Labeled with ^{161}Tb and ^{177}Lu: A Comparative Study (2024), 14, 4.

WP12 PRISMAP Events



Radiolanthanides Summer School

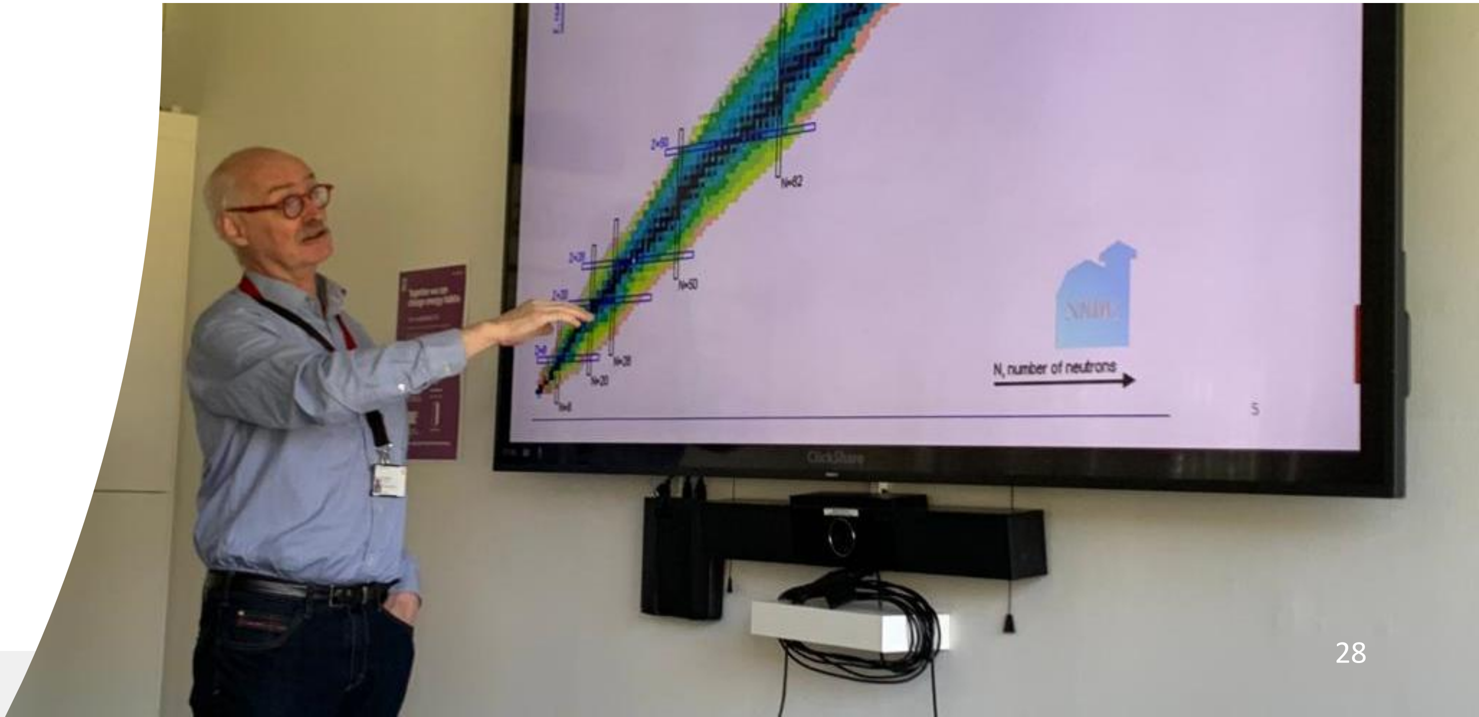
8-11 May 2023

Danmarks Tekniske Universitet DTU

PSI

NEUTRONS FOR SOCIETY

Planned to be reorganized for InnomedRad



PRISMAP Radiolanthanides Workshop (3-5 September 2025)

PRISMAP
RADIOLANTHANIDES
WORKSHOP

80 participants

(Austria, Belgium, Canada, Denmark, France, Germany, Hungary, Italy, Netherlands, Portugal, Sweden, Switzerland, UK and USA)

23 invited speakers and 23 poster presentations

To be continued

Tb-149 | Tb-155 | Ho-161 | Er-165 | Tm-167 | Pr-143 | Ho-166

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PhD Student in Radiochemistry

27.10.2025 • Doctoral • 4702-25173 • 100%

PSI

Apply online now

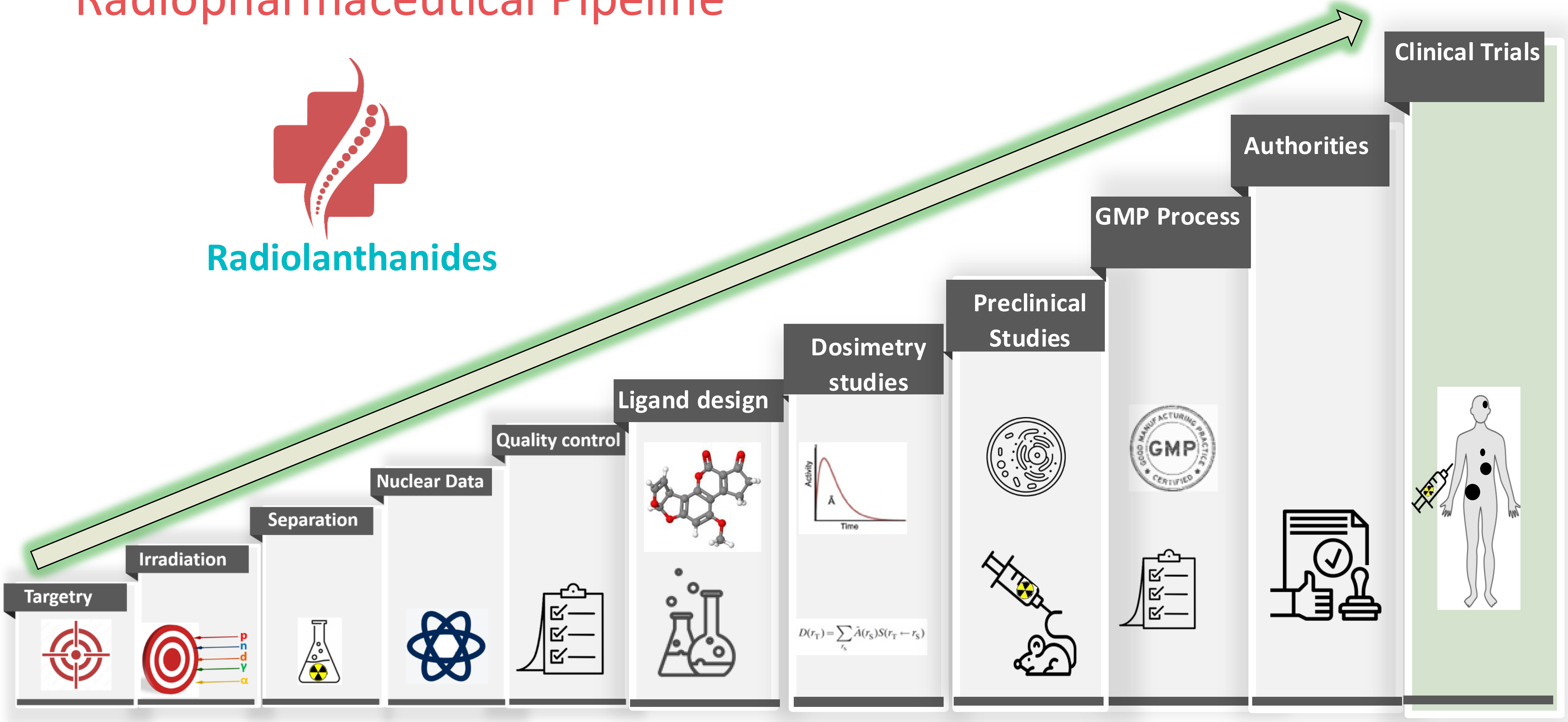
Application deadline: January 5th

Your tasks

The PROACTIVE Project (Production of RadiOlanthanides for Advancing Cancer Therapy, InVestigations through Enhanced Efficacies) will focus on the development and optimization of large-scale production and purification methods for Auger electron- and beta-emitting radiolanthanides, aiming to achieve the quality required for their application in targeted radionuclide therapy. Experimental activities will involve the production of the desired radiolanthanides at the PSI Injector II cyclotron, the Swiss Spallation Neutron Source (SINQ), and facilities of partner institutes such as the Institut Laue-Langevin (ILL), as well as the measurement of production yields and the determination of side products. The work will encompass an in-depth investigation of lanthanide separation methodologies employing a range of complexing agents and chromatographic resins.

The candidate will be enrolled in the Doctoral Program in Chemistry at the University of Bern, with teaching duties, and will have the opportunity to present research at leading national and international conferences, publish results in high-impact, peer-reviewed journals and co-supervise students.

Radiopharmaceutical Pipeline



PRISMAP Pipeline

PRISMAP Radionuclide Production JRAs

PRISMAP Radionuclide Production JRAs

WP8

Generators

WP11

Nobel metal radionuclides

WP12

Radiolanthanides

WP12

Auger electron emitters

THANK YOU!

Arronax, DTU, PSI, CERN, SCK CEN, NPL, INFN,
IST-ID, KU-Leuven, TUM, CHUV

Renata Mikolajczak and her team

WWW.PRISMAP.EU @MEDRADIONUCLIDE PRISMAP PROJECT

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