



PRISMAP

THE EUROPEAN MEDICAL RADIONUCLIDES PROGRAMME:
AN EMPHASIS ON ALPHA EMITTERS IN THERANOSTICS
APPROACHES

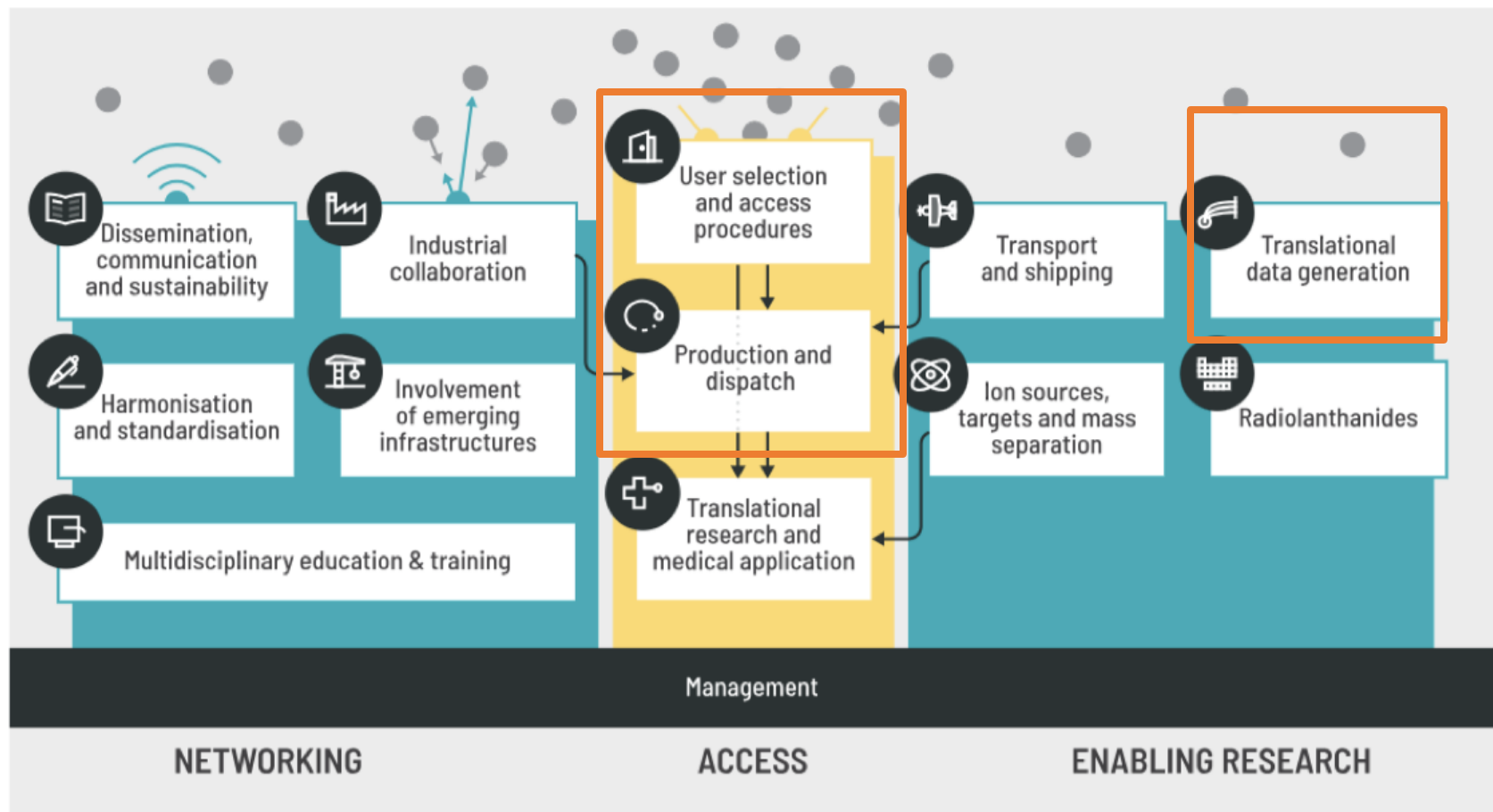
Workshop on Standards and Measurements for Alpha Emitting Nuclides in
Therapeutic Nuclear Medicine

BIPM

Thierry Stora, CERN

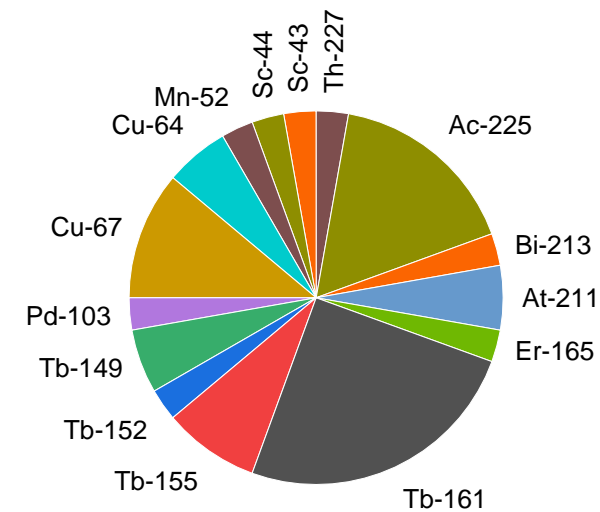
22 Feb 2024

PRISMAP is organised as an INFRA project funded by the European Commission



PRISMAP.EU

- Our web interface : <https://www.prismap.eu/radionuclides/portfolio/>



Interesting alpha emitters, and also some imaging companions*

Disclaimer : I may not only speak of alpha emitting nuclides ?!

PRISMAP in a nutshell

- Provide access to new radionuclides and new purity grades for the medical research → 16 non-conventional radionuclides (amongst the 28)
→ 31 research groups from 12 countries
→ 32 projects covering the different aspects of translational medical research.
- Create a common entry port and web interface to the starting research community

- Enhance clarity and regulatory procedures to foster research with radiopharmaceuticals
- Improve the delivered radionuclide data and regulation along with biomedical research capacity
- Ensure long-term sustainability of PRISMAP

User projects and services

In vivo cellular & molecular imaging lab (ICMI)
 VU Brussels
 Imaging and Pathology
 KU Leuven
 Molecular Imaging Center
 Antwerp

Pharmaceutical Radiochemistry
 TU Munich
 Radiopharmaceutical Cancer Research
 Dresden (/CZ)

UGA – Inserm
 La Tronche
 CEMHTI Radiochemistry
 Orleans
 Inserm
 Montpellier (/PT)

Radiopharmacy
 Bordeaux
 Radiochemistry
 Hopital Frederic Joliot
 Orsay

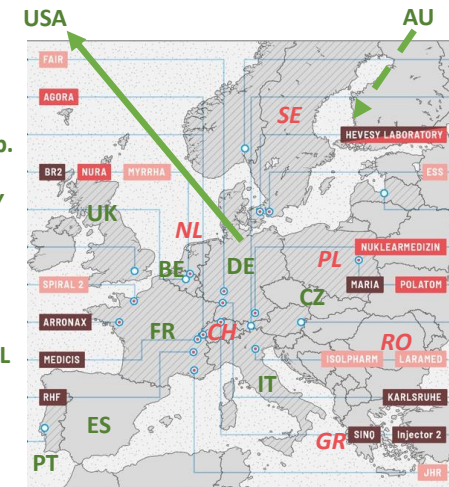
Fondazione IRCCS Istituto Nazionale dei Tumori
 Milano
 Dep Molecular Biotechnology Health Sciences,
 Torino

Radiochemistry unit,
 Hospital Gregorio Marañón
 Madrid

Biomedical Engineering and Imaging Science
 London



T. Stora, CERN – CM6– Nov 2023



<https://www.prismap.eu/access/user-projects/>

After call 4 :
 x2 projects (16 → 33) 1 → US
 +50% countries (8 → 12 UK/CH)
 Southern & Eastern (*) EC country
 (W → W,S,E+ Sweden most N)
 35(*) research teams

Our initial proposal for day-1 radionuclides

Table 1. PRISMAP day-1 radionuclides.

Radionuclide	Application	Imaging(I)/ Treatment(T)/ Generator(G)	Production reaction
Sc-44/Sc-44m	PET	I	$^{44}\text{Ca}(p,n); ^{44}\text{Ca}(d,2n)$
Sc-47	β^- therapy, SPECT	I/T	$^{46}\text{Ca}(n,\gamma)^{47}\text{Ca}(\beta^-)$
Cu-64	PET	I	$^{64}\text{Ni}(p,n); ^{64}\text{Ni}(d,2n)$
Cu-67	β^- therapy, SPECT	I/T	$^{68}\text{Zn}(p,2p); ^{70}\text{Zn}(p,\alpha)$
Ag-111	β^- therapy, SPECT, TDPAC	I/T	$^{110}\text{Pd}(n,\gamma)^{111}\text{Pd}(\beta^-); ^{110}\text{Pd}(d,n)$
La-135	Auger therapy	T	$^{\text{nat}}\text{Ba}(p,X)$
Tb-149	α therapy, PET	I/T	$^{\text{nat}}\text{Ta}(p,\text{spall})$
Tb-152	PET	I	$^{\text{nat}}\text{Ta}(p,\text{spall})$
Tb-155	Auger therapy, SPECT	I	$^{\text{nat}}\text{Ta}(p,\text{spall})$
Tb-161	β^- therapy, SPECT	I/T	$^{160}\text{Gd}(n,\gamma)$
Dy-166	Generator for Ho-166 (β^- therapy, SPECT)	G	$^{164}\text{Dy}(n,\gamma)(n,\gamma)$
Er-165	Auger emitter	T	$^{165}\text{Ho}(p,n)$
Tm-165	Generator for Er-165 (Auger therapy)	G	$^{\text{nat}}\text{Ta}(p,\text{spall})$
Er-169	β^- therapy	T	$^{168}\text{Er}(n,\gamma)$
Yb-175	β^- therapy, (SPECT)	T	$^{174}\text{Yb}(n,\gamma)$
Pt-195m	Auger therapy, SPECT	I/T	$^{194}\text{Pt}(n,\gamma)$
Bi-213	α therapy	T	^{225}Ac generator
At-211	α therapy	T	$^{209}\text{Bi}(\alpha,2n)$
Ac-225	α therapy	T	^{229}Th generator; $^{232}\text{Th}(p,\text{spall})$

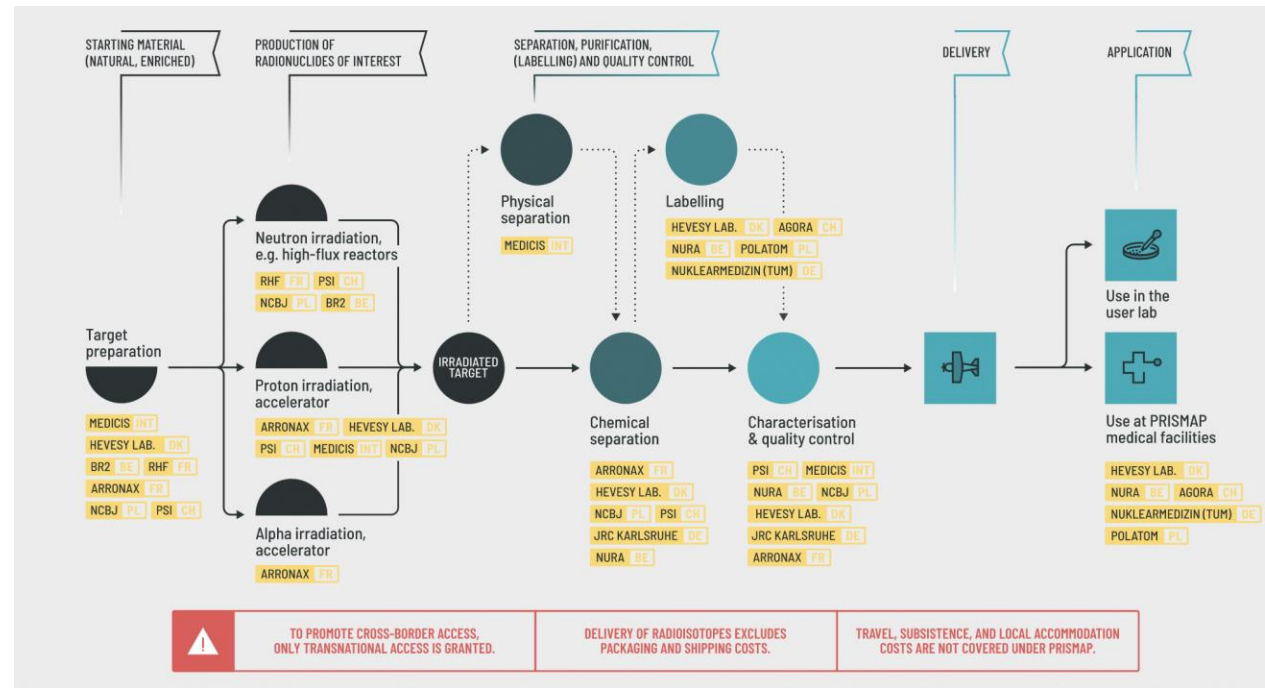
PSI colleagues @ ISOLDE
CERN-MEDICIS

And at call 4 :

→ www.prismap.eu/radionuclides/portfolio/224Ra/
→ www.prismap.eu/radionuclides/portfolio/203Pb/

JRC Karlsruhe
Arronax

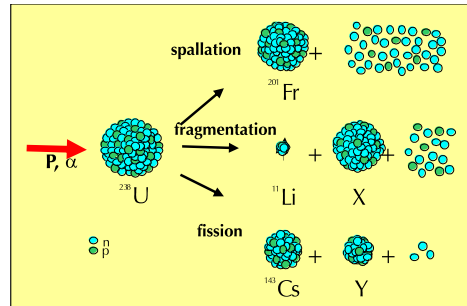
What is in the back of PRISMAP



<p>MEDICIS European organization for nuclear research - CERN</p>	<p>PSI Paul Scherrer Institut – PSI</p>	<p>Hevesy Laboratory Danmarks Tekniske Universitet – DTU</p>	<p>BR2 Belgian Nuclear Research Centre — SCK CEN</p>	<p>ARRONAX Groupement interet public ARRONAX — ARRONAX</p>
<p>RHF Institut Max von Laue - Paul Langevin – ILL</p>	<p>JRC Karlsruhe Joint Research Centre - European Commission – JRC</p>	<p>NCBJ Narodowe Centrum Badań Jądrowych — NCBJ</p>		

Characteristics of the irradiation facilities in PRISMAP

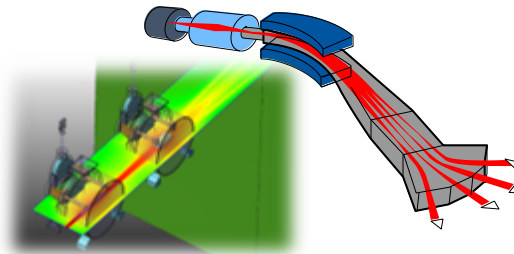
Accelerator



$$I_{[\text{pps}]} \sim F_{[\text{pps}]} S_{[\text{barn}]} N_{[\text{g/cm}^2]} \quad \text{production rate}$$

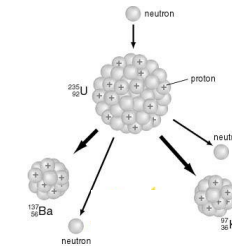
10^{10}pps $100\mu\text{A}$ ($6 \cdot 10^{14}$) 1mbarn 1g/cm^2 for $A_{\text{target}}=30\text{g/mol}$

Isotope mass separation



$$I_{[\text{pps}]} \sim F_{[\text{pps}]} S_{[\text{barn}]} N_{[\text{g/cm}^2]} e \quad [\%]$$

Research reactor



$$\frac{dN'}{dt} = n v \sigma_{\text{act}} N_T$$

Biomedical research projects supplied within PRISMAP

After 4 calls for project and 3 years, we are supporting 23 users projects from across Europe

User projects and services

In vivo cellular & molecular imaging lab (ICMI)
VU Brussels
Imaging and Pathology
KU Leuven
Molecular Imaging Center
Antwerp

Pharmaceutical Radiochemistry
TU Munich
Radiopharmaceutical Cancer Research
Dresden (/CZ)

UGA – Inserm
La Tronche
CEMHTI Radiochemistry
Orleans
Inserm
Montpellier (/PT)

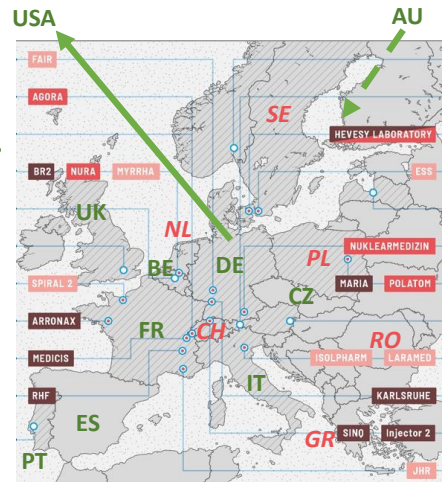
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Milano
Dep Molecular Biotechnology Health Sciences,
Torino

Radiochemistry unit,
Hospital Gregorio Marañón
Madrid

Biomedical Engineering and Imaging Science
London

 T. Stora, CERN – CM6– Nov 2023

BELGIUM
CZECH Rep.
GERMANY
FRANCE
PORTUGAL
ITALY
SPAIN
UK



<https://www.prismap.eu/access/user-projects/>

After call 4 :

x2 projects (16 → 33) 1 → US

+50% countries (8 → 12 UK/CH)

Southern & Eastern (*) EC country

(W → W,S,E+ Sweden most N)

35(*) research teams

- Improved FAP-radiotheranostics for personalised cancer treatment (211At)
- Phantom measurements quantitative 225Ac- (micro)SPECT imaging (213Bi)
- Feasibility of increased 211At production by 210Po assessment
- Dual 152Tb/149Tb radiolabeling for diagnostic and theranostic applications
- 203/212Pb-mcp-D-PSMA for an improved tumor therapy: Preclinical evaluation, automatization and translation to clinical application

....

www.prismap.eu/access/user-projects

Need in the precise determination of some long decay chains

Our information PRISMAP web page on Ra-224

Nuclear properties

Ra-224 decays by α decay with a half-life of 3.6316(23) days. Its decay chain involving Rn-220 ($T_{1/2} = 55.6(1)$ s), Po-216 ($T_{1/2} = 145(2)$ ms), Pb-212 ($T_{1/2} = 10.622(7)$ h), Bi-212 ($T_{1/2} = 60.55(6)$ min), either Po-212 ($T_{1/2} = 0.29$ μ s) or Tl-208 ($T_{1/2} = 3.053(4)$ min) leads to stable Pb-208. Including its decay chain, the cumulative α emission is 400% per Ra-224 decay with an average α energy of 6.75 MeV.

Ra-224 and daughters emit γ -rays and X-rays. Notable emissions are from Ra-224 at 241.0 keV (4.10(5)%), Pb-212 at 238.6 keV (43.6(5)%), Bi-212 at 727.3 keV (6.67(9)%) and Tl-208 at 2614.5 keV (99.754(4)%) and 583.2 keV (85.0(3)%).

Ongoing at University of Oslo on Ac-225

The relative biologic effect (RBE) will be estimated by comparing the absorbed radiation dose (Gy) of ^{225}Ac -PSMA-617 and of X-radiation that gave equal surviving fraction (2D model: clonogenic assay) or gave equal growth delay (3D model: multi-cellular spheroids).

Some is done within PRISMAP



Deliverable D11.1

Table 20. Summary of nuclear decay data needs for the PRISMAP day-1 radionuclides.

Radionuclide	Recommendations for future studies
At-211	▪ New half-life determinations with complete uncertainty evaluation are required.
Bi-213	▪ No recommendations.
Ac-225	▪ Extensive gamma-ray emission intensity studies and γ - γ coincidence studies are recommended are required.

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Phone | **+442089438508**

DOI [10.5281/zenodo.8247128](https://doi.org/10.5281/zenodo.8247128)

Example : Ac-225 case

EUROPEAN ORGANIZATION FOR NUCLEAR RESEARCH

Proposal to the ISOLDE and Neutron Time-of-Flight Committee

Detailed decay spectroscopy of ^{225}Ac and its daughters to support its use in medical applications

September 26, 2023

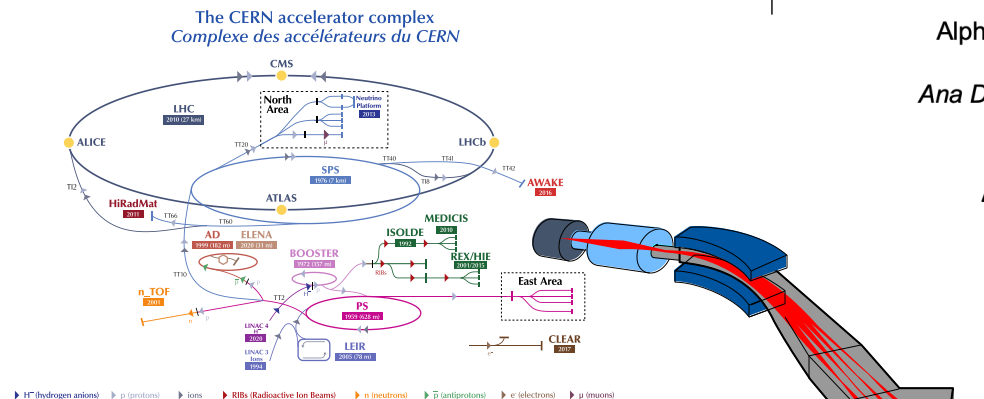
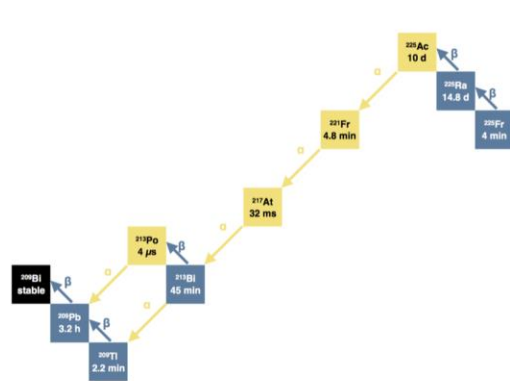
Spokesperson: Thomas Elias Cocolios, thomas.elias.cocolios@cern.ch

Co-spokesperson: Patrick Regan, p.regan@surrey.ac.uk

Co-spokesperson: Sean Collins, sean.collins@npl.co.uk

Co-spokesperson: Razvan Lica, razvan.lica@cern.ch

Contact person: Charlotte Duchemin, charlotte.duchemin@cern.ch



▶ H^+ (hydrogen anions)
 ▶ p (protons)
 ▶ ions
 ▶ RIBs (Radioactive Ion Beams)
 ▶ n (neutrons)
 ▶ \bar{p} (antiprotons)
 ▶ e (electrons)
 ▶ μ (muons)

LHC - Large Hadron Collider // SPS - Super Proton Synchrotron // PS - Proton Synchrotron // AD - Antiproton Decelerator // CLEAR - CERN Linear Electron Accelerator for Research // AWAKE - Advanced WAKEfield Experiment // ISOLDE - Isotope Separator Online // REX/HIE - Radioactive Experiment/High Intensity and Energy // ISOLDE // MEDICIS // LEIR - Low Energy Ion Ring // LINAC - LINear ACcelerator //



Project proposal to the MEDICIS Collaboration board

Determination of ^{227}Ac impurity in ^{225}Ac using alpha spectrometry

¹Ruslan Cusnir, ¹Claude Bailat, ¹Marietta Straub

¹Institute of Radiation Physics, Lausanne University Hospital, Lausanne, Switzerland

Contact of the Principal Investigator: Ruslan Cusnir, PhD, ¹Institute of Radiation Physics, Lausanne University Hospital, Lausanne, Switzerland. Ruslan.Cusnir@chuv.ch



Project proposal to the MEDICIS Collaboration board

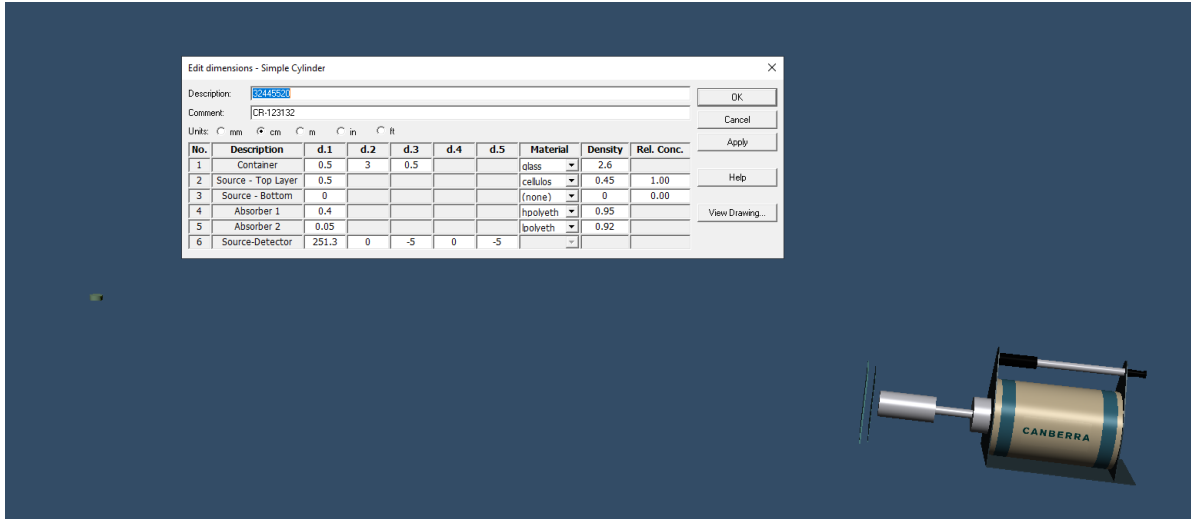
AlphaMET (Metrology for Emerging Targeted Alpha Therapies)

Ana Denis-Bacelar, National Physical Laboratory, United Kingdom

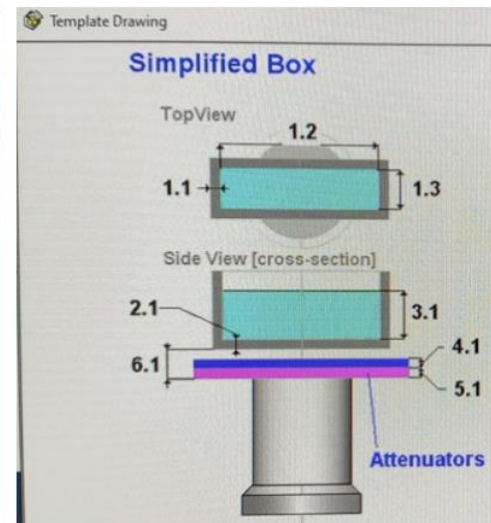
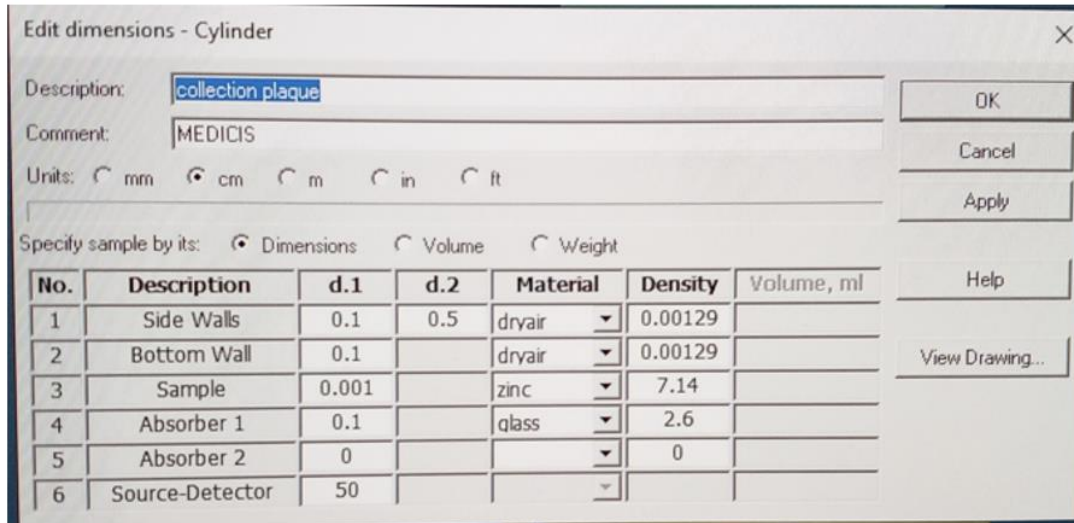
Also Ra-224 / Pb-212 request



Example : assessment of Ra-225/Ac-225



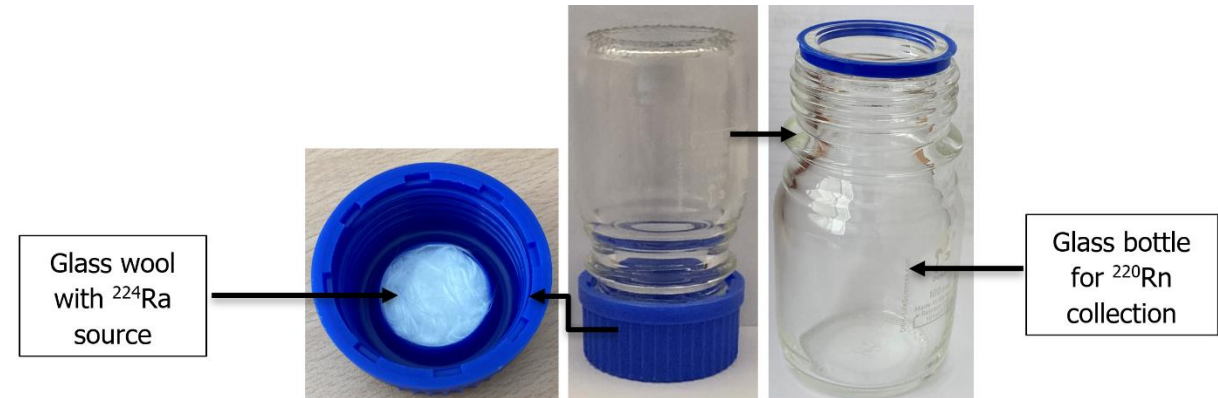
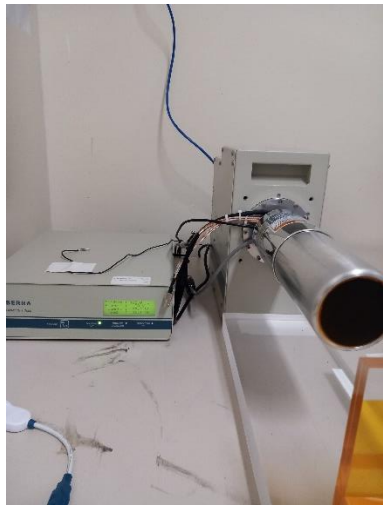
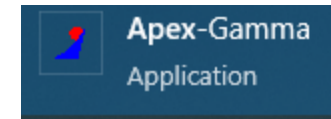
MS-029	Ra-225	14.80 d	18/09/2023 15:23	1.000	1.08E8 (94.00%)
	Ac-225	10.00 d		0.959	4.04E7 (28.97%)
	Ra-224	3.66 d		0.992	8.86E5 (73.45%)
	Fr-221	4.90 m		0.997	3.99E7 (48.45%)
	Bi-213	45.59 m		0.997	3.60E7 (24.41%)
	Pb-212	10.64 h		0.866	4.35E5 (52.09%)



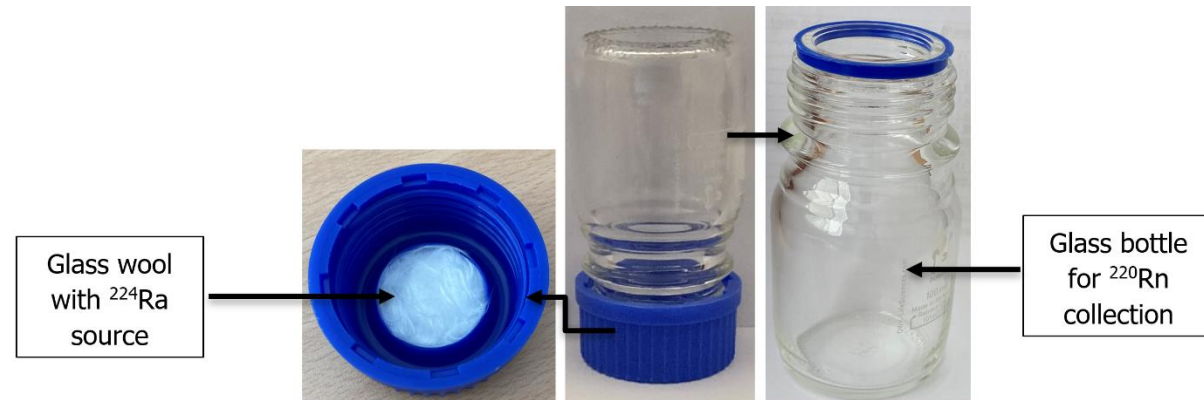
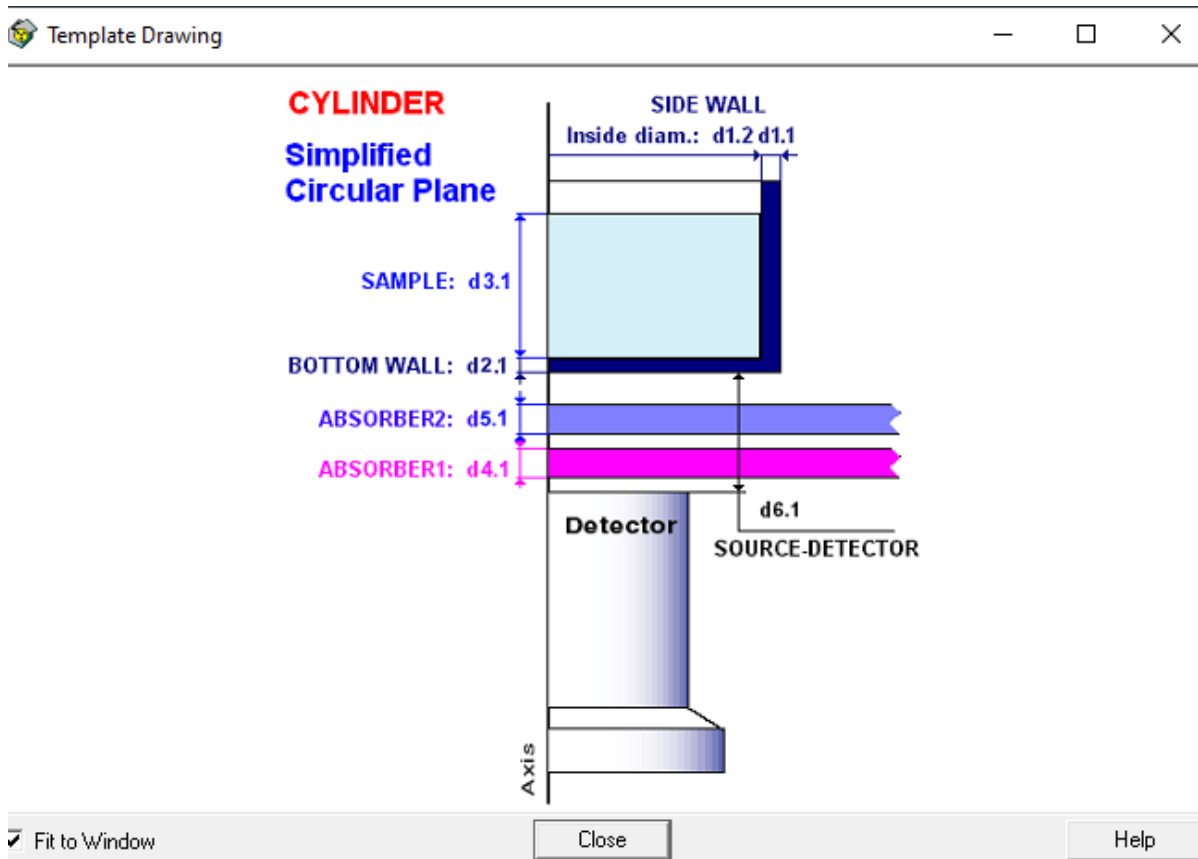
Databases used internally and for Shipment :
Nudat 3, JEFF, ENSDF

Measurement of a Ra-224/Pb-212 in a generator by emanation

- HP Ge coaxial hyperpur (>40%) from Mirion technologies (Canberra)
- Use of APEX-Gamma for spectrum acquisition
- Use of ISOCS/LABSOCS for geometry and efficiency modelisation

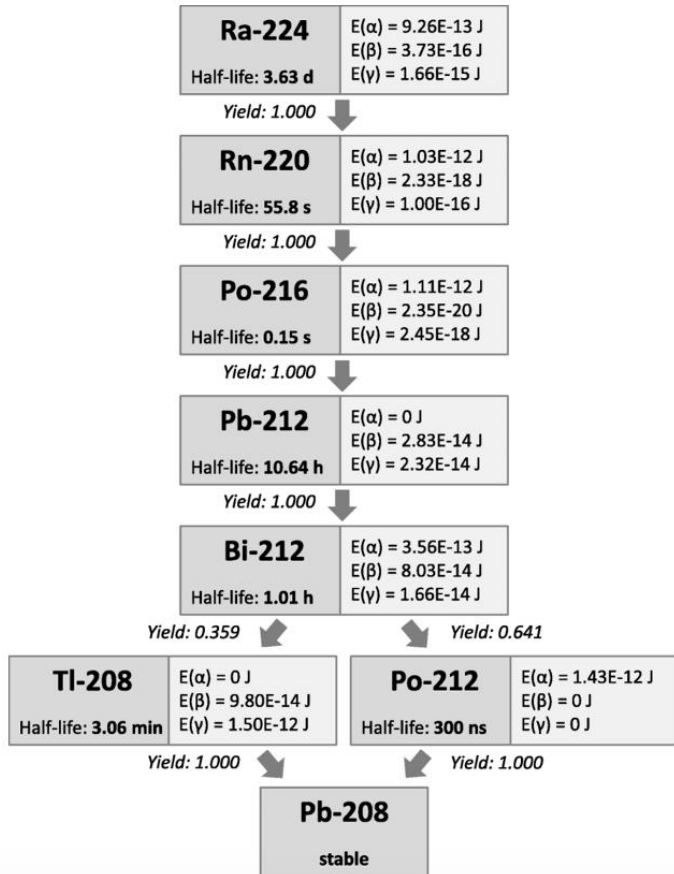


Measurement of a Ra-224/Pb-212 in a generator by emanation



- Activity to be measured is deposited on the glass wool
- modelisation of the glass wool as the **sample/source** taking into account the thickness of the **blue bouchon**
- taking into account the thickness of the **glass going into the blue bouchon**
- distance between detector and source (d.6.1) also taken into consideration in the modelisation

Measurement of a Ra-224/Pb-212 in a generator by emanation



Collection foil	Radionuclide	Half-life	Ref.	Conf.	Weighted Mean Activity (Bq/unit)
MS-031 dissolved and deposited on glass wool	Ra-225	14.80 d	21/08/2023 13:05	0.993	2.21E6 (94.58%)
	Ra-224	3.64 d		1.000	7.99E7 (60.68%)
	Rn-220	55.80 s		1.000	8.61E7 (77.94%)
	Pb-212	10.64 h		0.993	3.53E7 (43.78%)
	Bi-212	1.01 h		0.998	3.18E7 (20.93%)
	Tl-208	3.05 m		0.998	1.12E7 (21.06%)

Also ongoing in PRISMAP – the Terbium quadruplet

Tb-149

- Precision measurements of the half-lives of Tb-149 and its decay progenies (Eu-145 and Gd-149) are needed.
- New studies are required to improve the precision of the alpha decay branching ratio.
- There is a requirement for new studies of the gamma-ray emission intensities to confirm the accuracy of the single study and to improve the precision.
- There is also a requirement to improve the gamma-ray emission intensities of the decay progenies.



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Article | [Open access](#) | Published: 26 July 2019

Chemical Purification of Terbium-155 from Pseudo-Isobaric Impurities in a Mass Separated Source Produced at CERN

[Ben Webster](#), [Peter Ivanov](#), [Ben Russell](#), [Sean Collins](#), [Thierry Stora](#), [Joao Pedro Ramos](#), [Ulli Köster](#), [Andrew Paul Robinson](#) & [David Read](#)

Scientific Reports 9, Article number: 10884 (2019) | [Cite this article](#)



Applied Radiation and Isotopes

Volume 190, December 2022, 110480



Half-life determination of ^{155}Tb from mass-separated samples produced at CERN-MEDICIS

[S.M. Collins](#)^{a, b}, [A.P. Robinson](#)^{a, c, d}, [P. Ivanov](#)^a, [U. Köster](#)^e, [T.E. Cocolios](#)^f, [B. Russell](#)^g, [B. Webster](#)^{a, b}, [A.J. Fenwick](#)^g, [C. Duchemin](#)^{f, g, h}, [J.P. Ramos](#)^{f, g, h}, [E. Chevallay](#)^g, [U. Jakobsson](#)ⁱ, [S. Stegemann](#)^f, [P.H. Regan](#)^{a, b}, [T. Stora](#)^g



Applied Radiation and Isotopes

Volume 202, December 2023, 111044

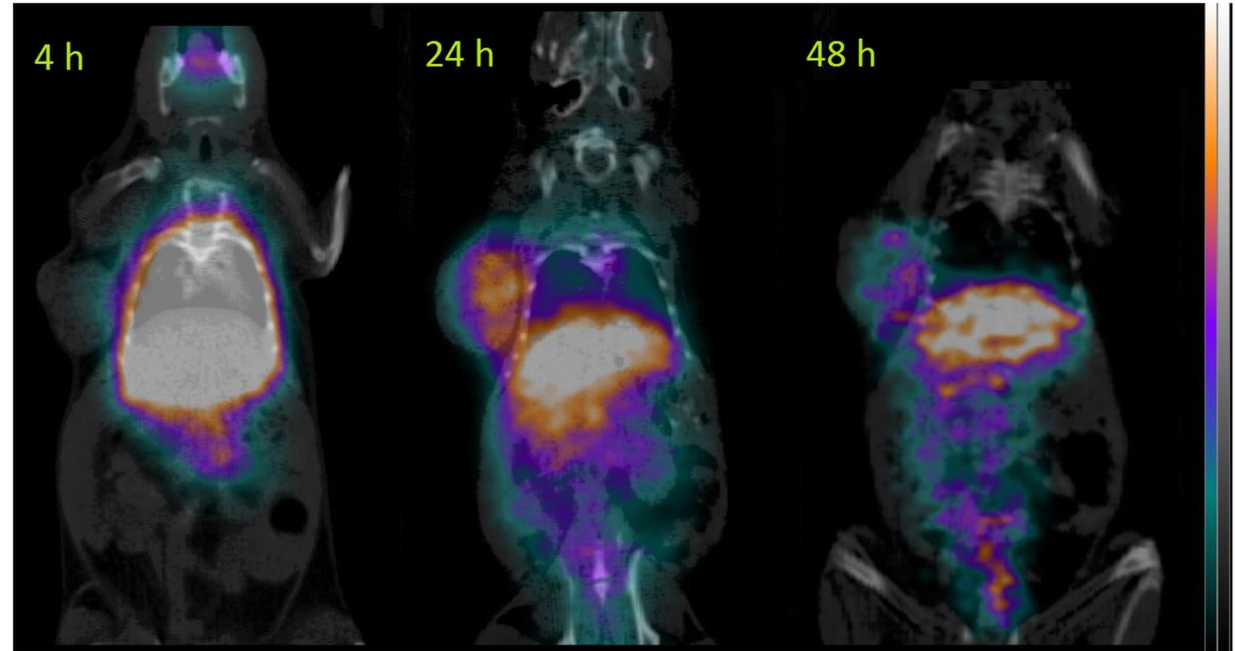
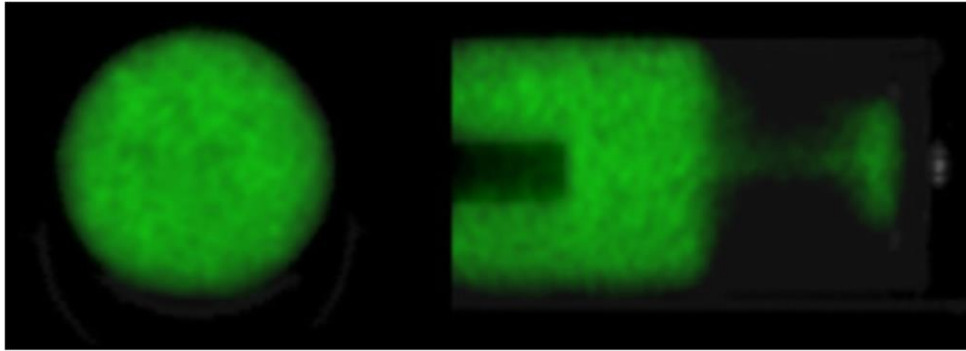
Determination of the Terbium-152 half-life from mass-separated samples from CERN-ISOLDE and assessment of the radionuclide purity

[S.M. Collins](#)^{a, b}, [U. Köster](#)^e, [A.P. Robinson](#)^{a, d, e}, [P. Ivanov](#)^a, [T.E. Cocolios](#)^f, [B. Russell](#)^g, [A.J. Fenwick](#)^g, [C. Bernerd](#)^{f, g}, [S. Stegemann](#)^f, [K. Johnston](#)^g, [A.M. Gerami](#)^g, [K. Chrysalidis](#)^g, [H. Mohamad](#)^g, [N. Ramirez](#)^g, [A. Bhaikare](#)^g, [J. Mewburn-Crook](#)^g, [D.M. Cullen](#)^g, [B. Pietras](#)^g, [S. Pells](#)^g, [K. Dockx](#)^f, [P.H. Regan](#)^{a, b}



Cicone, F et al. "Internal radiation dosimetry of a ^{152}Tb -labeled antibody in tumor-bearing mice." *EJNMMI research* 9.1 (2019): 1-10.

Going beyond imaging – exploitation of matched diagnostics pairs

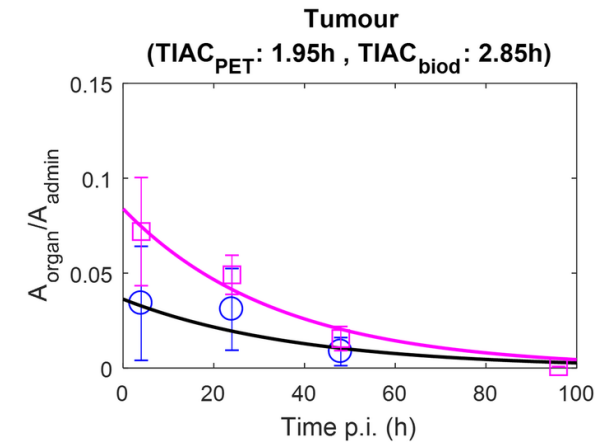
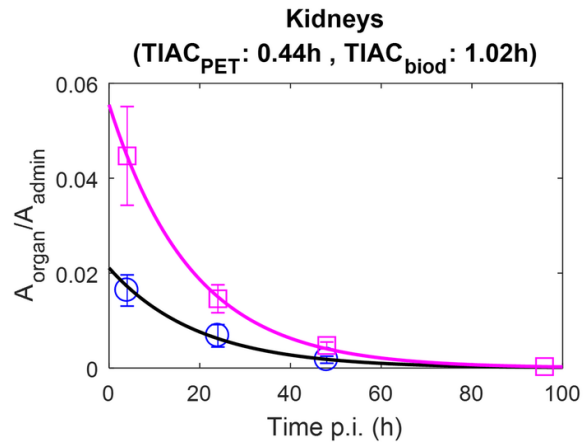
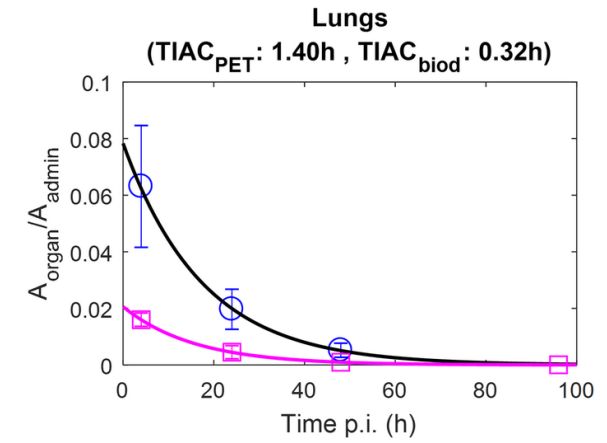
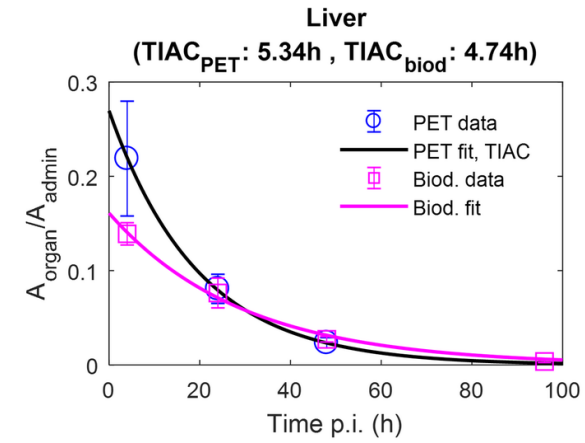


Phantom, calibration and dosimetry

Cicone, F et al. "Internal radiation dosimetry of a ^{152}Tb -labeled antibody in tumor-bearing mice." EJNMMI research 9.1 (2019): 1-10.

First PET imaging of $^{152}\text{Tb-CHX-A''-DTPA-ScFv78Fc}$

Ewing Sarcoma cell line A673

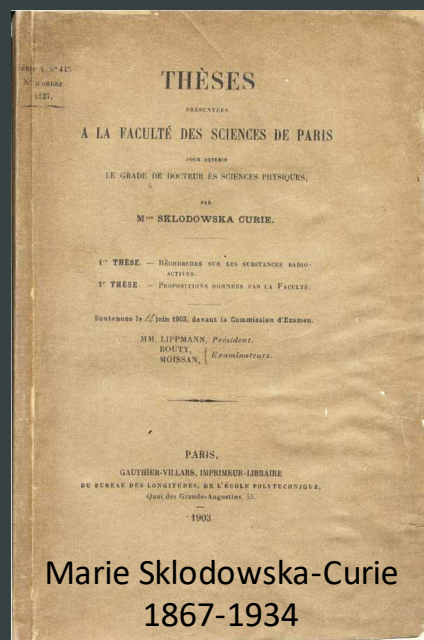


Cicone, F et al. "Internal radiation dosimetry of a ^{152}Tb -labeled antibody in tumor-bearing mice." EJNMMI research9.1 (2019): 1-10.

What's next in PRISMAP

- (Likely) targeted calls : eg whole body PET
- Working on shaping PRISMAP+
- Structuring the PRISMAP community

WWW.PRISMAP.EU/RADIONUCLIDES/USER-FORUM/



WWW.PRISMAP.EU



@MEDRADIONUCLIDE



PRISMAP PROJECT



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