Production of innovative radioisotopes for medical applications at the CERN-MEDICIS facility

Ana-Paula Bernardes, **Cyril Bernerd**[1,2], Alexandre Dorsival, Elodie Aubert, Philippe Bertreix, Richard Catherall, Eric Chevallay, Katerina Chrysalidis, Thomas Elias Cocolios, Bernard Crepieux, Matthieu Deschamps, Charlotte Duchemin, Valentin Fedosseev, Pascal Fernier, Reinhard Heinke, Umar Khalid, Qaiser Khan, Moazam Khan, Laura Lambert, Edgars Mamis, Bruce Marsh, Stefano Marzari, Nabil Menaa, Fabio Pozzi, Slavka Prvakova, Joao Pedro Ramos, Francesco Riccardi, Jean-Yves Rinchet, Ralf Rossel, Thierry Stora, Julien Thiboud, Joachim Vollaire.

[1]KU Leuven KU LEUVEN [2]CERN, SY, STI, LP

Plan

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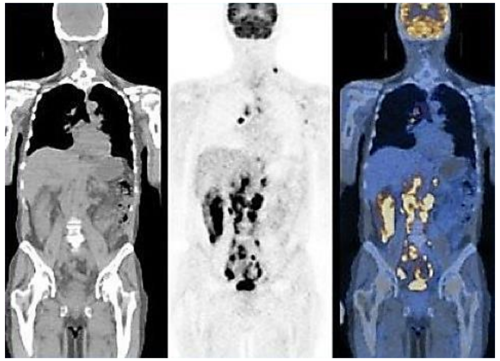
1. The CERN-MEDICIS project
2. The MEDICIS facility
3. Innovative radionuclide production since 2017
4. Highlights and Facility development
5. The PRISMAP consortium

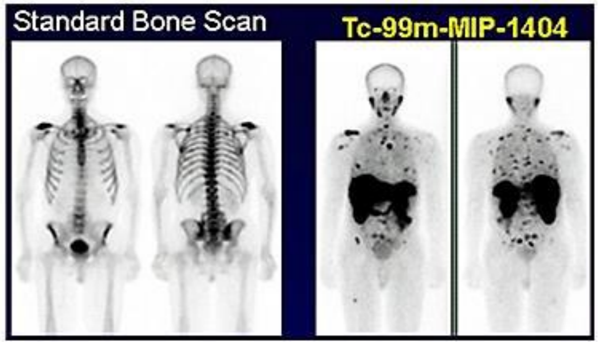
The CERN-MEDICIS project

MEDical Isotopes Collected from ISOLDE*

Functional Imaging

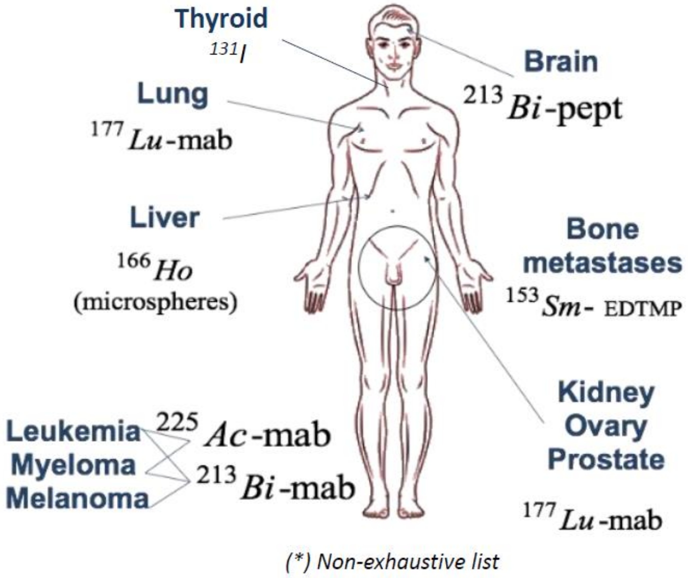
Position Emission Tomography (PET)





Single Photon Emission Computed Tomography (SPEC)

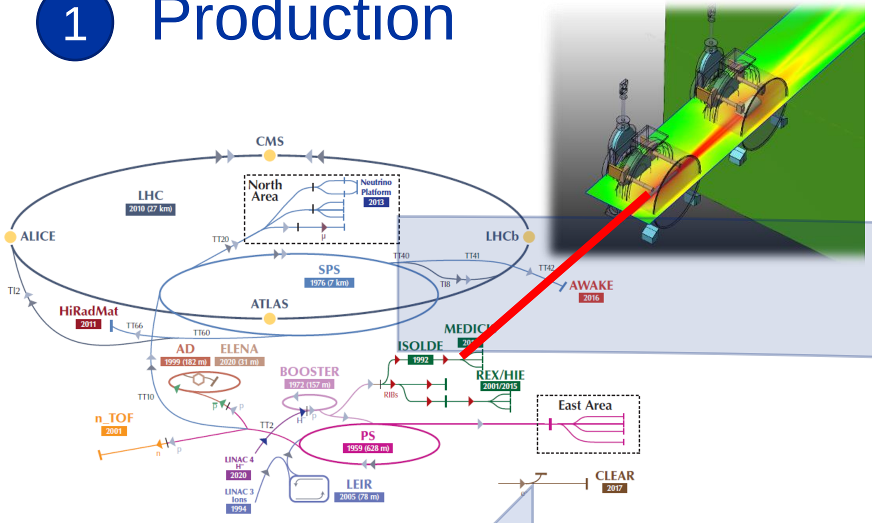
Internal Radiation Therapy



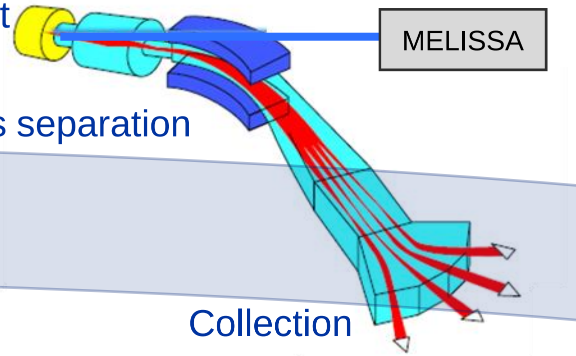
*R. M. dos Santos Augusto et al, *CERN-MEDICIS (Medical Isotopes Collected from ISOLDE): A New Facility,* Appl. Sci. **2014**, 4, 265-281

The CERN-MEDICIS route

1 Production



2 Offline separation batch

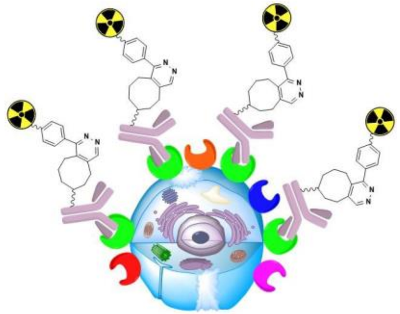


3 Radiochemistry

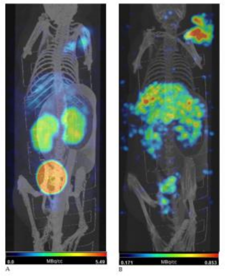
4 Packaging and shipment

5 Radiopharmaceutical synthesis

6 Radiolabelling

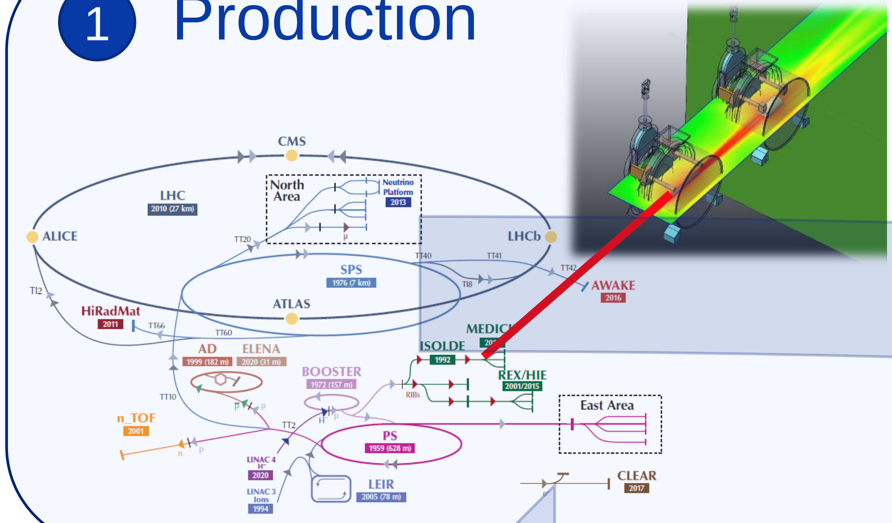


7 Pre-clinical tests

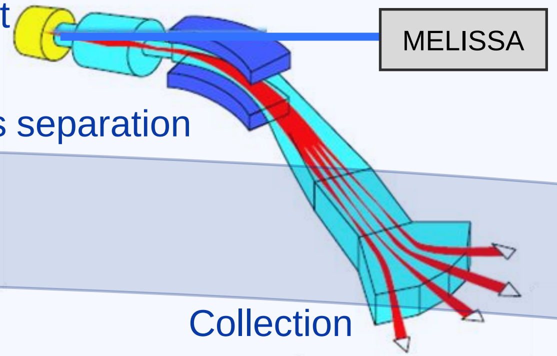


The CERN-MEDICIS route

1 Production



2 Offline separation batch



MEDICIS

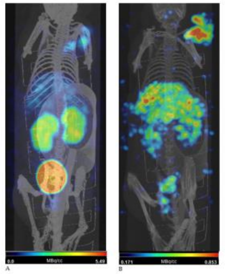
3 Radiochemistry

4 Packaging and shipment

5 Radiopharmaceutical synthesis

6 Radiolabelling

7 Pre-clinical tests



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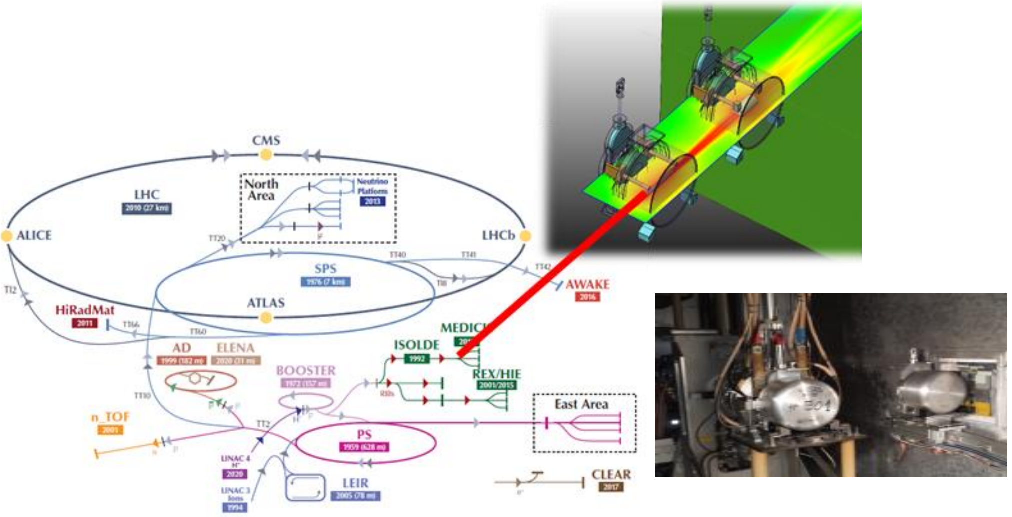
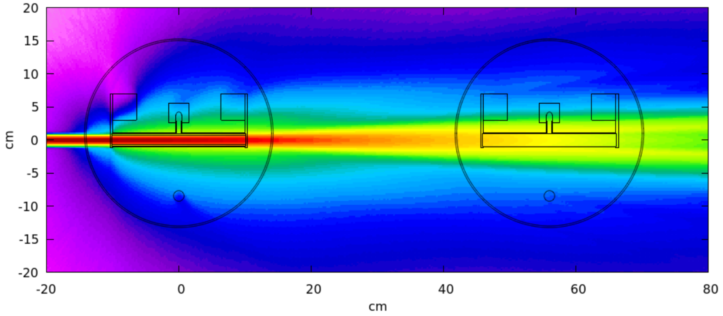
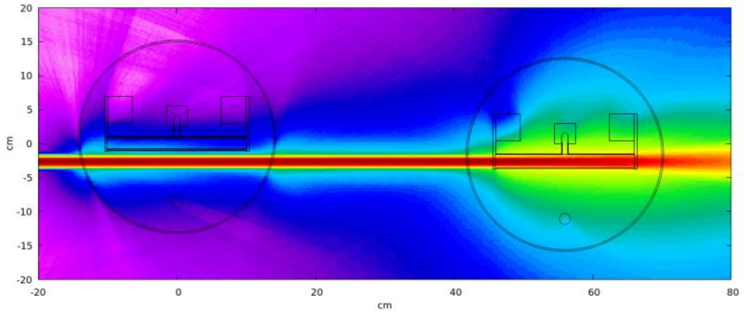
MEDICIS production



Indirect irradiation*



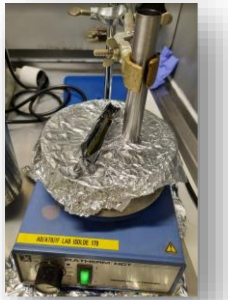
Direct irradiation*

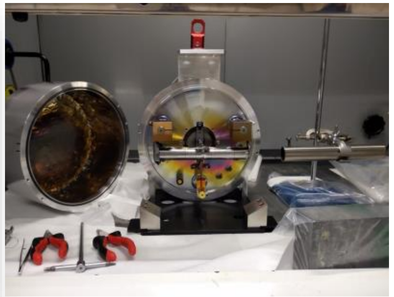


⇒ Strong collaboration with ISOLDE, benefiting from decades of experience on production and separation of exotic radionuclides

⇒ MEDICIS is one of the only facility at CERN that can operate during accelerator shutdown

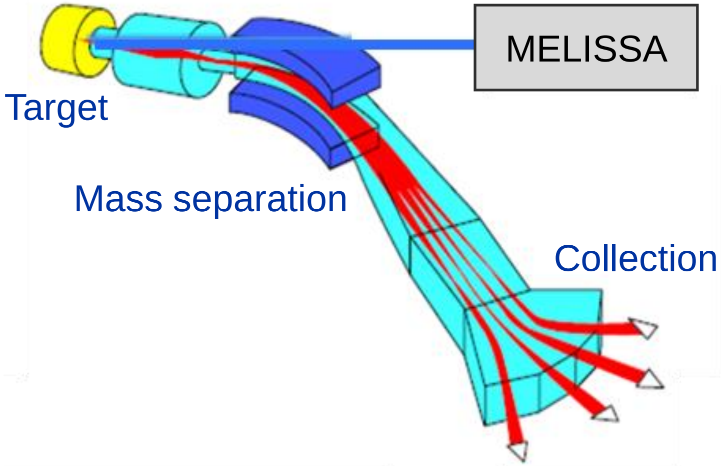
External Production



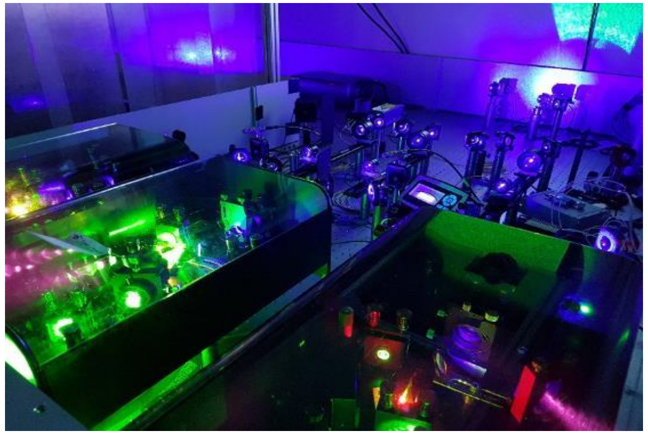


*C. Duchemin et al, *CERN-MEDICIS: a unique facility for the production of non-conventional radionuclides for the medical research*, IPAC’20 JaCoW Proceedings (2020)

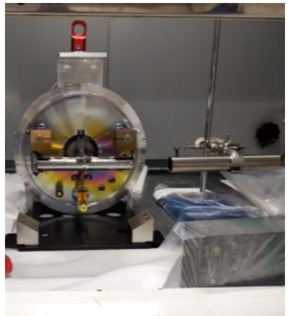
Separation in MEDICIS



MELISSA solid-state laser laboratory**

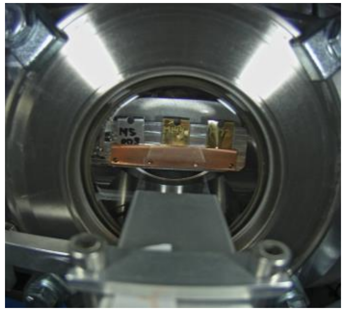


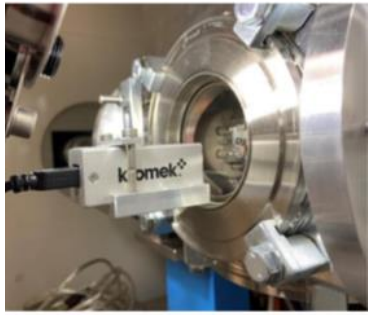
Target (ISOLDE/external)



Mass separator*

Collection chamber





*Y. Martinez Palenzuela et al, *The CERN-MEDICIS Isotope Separator Beamline*, Front. Med. 8:689281 (2021)

** V. M. Gadelshin et al, *MELISSA: Laser ion source srtup at CERN-MEDICIS facility. Blueprint*, Nuclear Inst. And Methods in Physics Research B 463 (2020)

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Innovative radionuclide production :

MEDICIS portfolio

^{44}Sc	^{47}Sc		^{128}Ba
^{149}Tb	^{152}Tb	^{155}Tb	^{153}Sm
^{167}Tm		^{169}Er	^{175}Yb
^{191}Hg			^{225}Ac

Collaborators

NPL National Physical Laboratory

KU LEUVEN NUCLEAR AND RADIATION PHYSICS

CHUV

TÉCNICO LISBOA

ILL NEUTRONS FOR SOCIETY

HUG Hôpitaux Universitaires Genève L'ESSENTIEL, C'EST VOUS.

ARRONAX

fabis Fundación Andaluza Beturia para la Investigación en Salud

CERN

PAUL SCHERRER INSTITUT PSI

European Commission Joint Research Centre

JG|U JOHANNES GUTENBERG UNIVERSITÄT MAINZ

C. Duchemin et al, *CERN-MEDICIS: A Review Since Commissioning in 2017*, Front. Med. 8:693682 (2021)

Innovative radionuclide production :

MEDICIS operation since 2017

Year	Irradiation modes	Medical Isotopes	Collected activities (MBq)	Maximum collection efficiency (%)	Number of batches delivered
2018	- CERN PSB - External irradiation	C-11, Tb-149, Tb-152, Tb-155, Tm/Er-165	235	1.6	4
2019	- External irradiation	Tb-155, Er-169, Yb-175, Pt-195m	870	6.0	15
2020	- External irradiation	Sm-153, Tb-155, Tm-167, Ac-225	540	22.5 (40% separation efficiency)	**16**
2021	- CERN PSB - External irradiation	Sc-44, Sc-47, Ba/Cs-128, Sm-153, Tb-155, Tm-167, Hg-191, Yb-175, Ac-225	1300	**46%**	10
2022*	- CERN PSB - External irradiation	**Sc-44, Sc-47, Ba/Cs-128, Sm-153, Tb-155, Tm/Er-165, Tm-167**	Ongoing	Ongoing	Ongoing

2022: Implementation of Key Performance Parameters (KPI) for MEDICIS performances monitoring

C. Duchemin et al, *CERN-MEDICIS: A Review Since Commissioning in 2017*, Front. Med. 8:693682 (2021)

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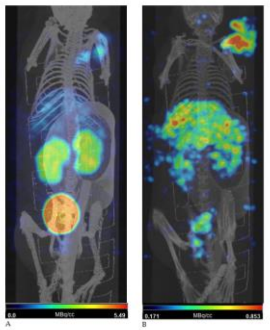
Highlights:

^{153}Sm



Article

Exploring the potential of high-molar activity Samarium-153 for targeted radionuclide therapy with [^{153}Sm]Sm-DOTA-TATE

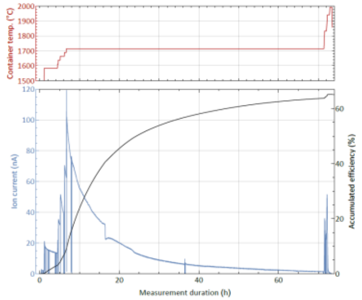
Koen Vermeulen [1], Michiel Van de Voorde [1], Charlotte Segers [1], Amelie Coolkens [1], Sunay Perez Rodriguez [1], Noami Daems [1], Charlotte Duchemin [2,3], Melissa Crabbé [1], Tomas Opsomer[1], Clarita Saldarriaga Vargas [4], Reinhard Heinke [2,3], Julie Nonnekens [5], Laura Lambert [3], Cyril Bernerd [3], Andrew R. Burgoyne[1], Thomas E. Cocolios[2], Thierry Stora[3], Maarten Ooms[1,*]

1 NURA research group, Belgian Nuclear Res
2 Institute for Nuclear and Radiatio
3 MEDICIS, CERN, Geneva, Switze
4 Research in Dosimetric Applicatio
Belgium
5 Department of Radiology & Nuclea
the Netherlands
* Correspondence: maarten.ooms@sck

To be submitted

^{167}Tm

>40% separation efficiency



Efficient production of high specific activity thulium-167 at Paul Scherrer Institute and CERN-MEDICIS

R. Heinke [1,2,*], E. Chevallay [2], K. Chrysalidis [2], T. E. Cocolios [1], C. Duchemin [1,2], V. N. Fedosseev [2], S. Hurier [3,1], L. Lambert [2], B. Leenders [3,4,1], B. A. Marsh [2], N. P. van der Meulen [5,6], P. Sprung [7], T. Stora [2], M. Tosato [6], S. G. Wilkins [2], H. Zhang [8], Z. Talip [6,*]

[1] Institute for Nuclear and Radiation Physics, KU Leuven, Belgium
[2] European Organization for Nuclear Research CERN, Geneva, Switzerland
[3] Belgian Nuclear Research Centre SCK CEN, Mol, Belgium
[4] Department of Electromechanical, Systems and Metal Engineerin
University, Belgium
[5] Laboratory of Radiochemistry, P
[6] Center for Radiopharmaceutic
Villigen-PSI, Switzerland
[7] Analytic Radioactive Materials,
[8] Division Large Research Faciliti ... illigen-PSI, Switzerland

Published

^{225}Ac

10% separation efficiency
4.3(3)x10^{-7} ratio of
^{227}Ac/^{227}Ac purification reached*

^{155}Tb

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

Dr Sean Collins; Andrew P Robinson; Peter Ivanov; Ulli Köster; Thomas E Cocolios; Ben Russell; Ben Webster; Andrew J Fenwick; Charlotte Duchemin; Joao P Ramos; Ulrika E Jakobsson; Simon T Stegemann; Patrick H Regan; Thierry Stora; Eric Chevallay

Accepted for publication

^{175}Yb

0.6 GBq collected

^{44}Sc **^{47}Sc**

Molecular ScF_2 beam collection from new target**

^{128}Ba

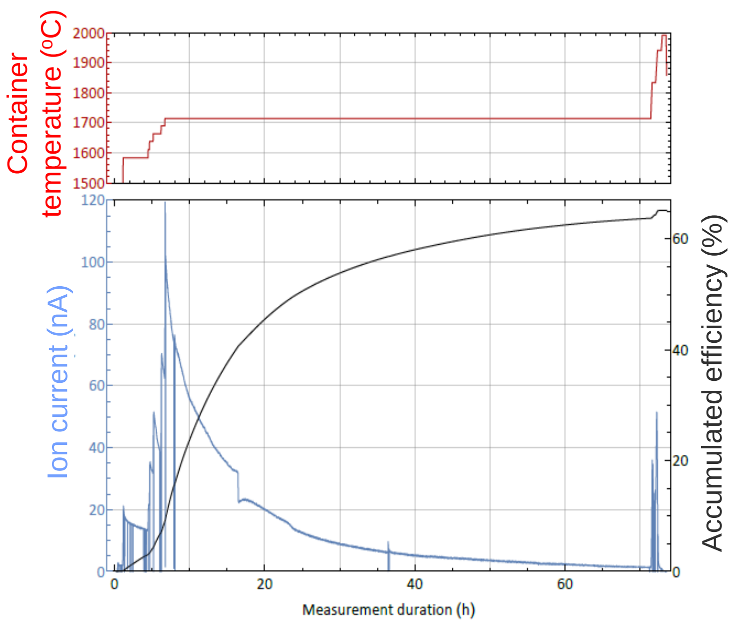
Release modelling of Ba from Ta foils

*PhD of J. Johnson (KU Leuven)
**PhD of E. Mamis (University of Latvia)

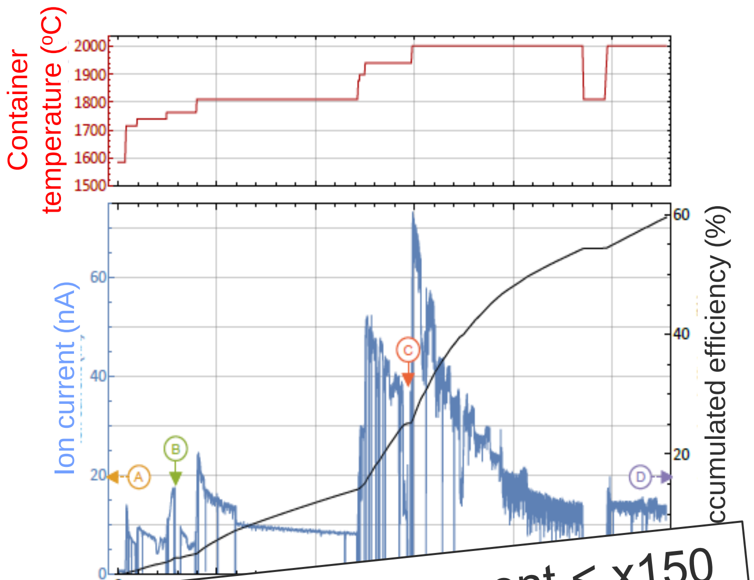
Highlights and Facility development :

^{167}Tm

Stable ^{169}Tm on Ta cylinder

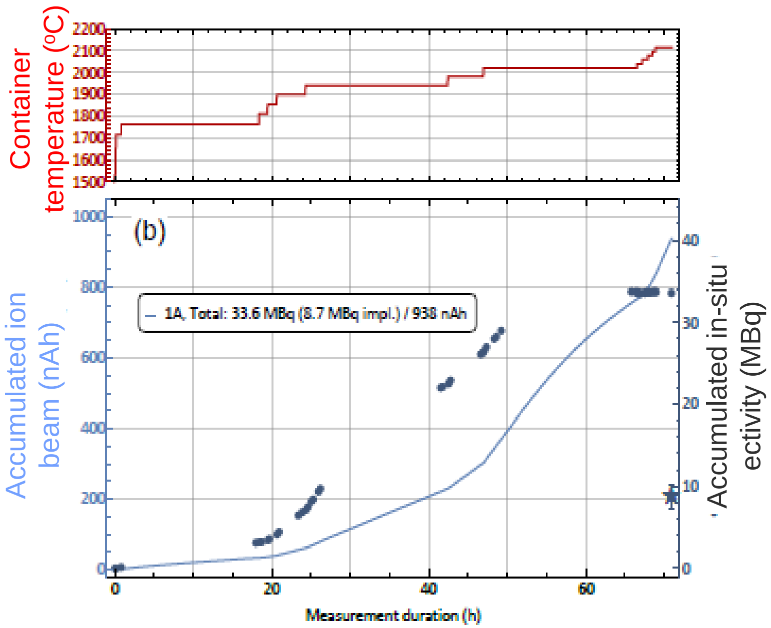


Stable ^{169}Tm on erbium oxide



x30 < Laser enhancement < x150

^{167}Tm from proton-irradiated erbium oxide (PSI)



Machine development for ^{167}Tm from proton-irradiated Ta target (ISOLDE)

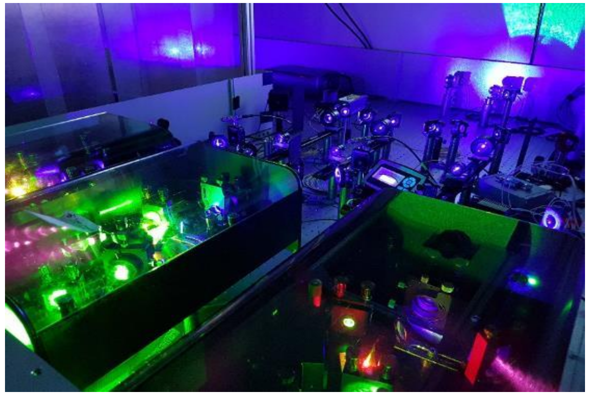
⇒ x20 Laser enhancement < x1000

⇒ Tm-167 and Tm-165 parallel collection last week (29/09-30/09 2022)

⇒ **350 MBq Tm-165 and 100 MBq Tm-167**

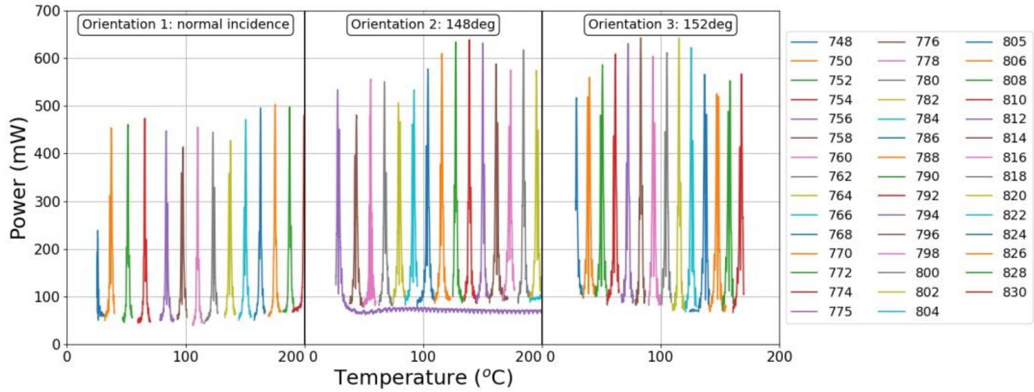
R. Heinke et al, *Efficient production of high specific activity thulium-167 at Paul Scherrer Institute and CERN-MEDICIS*, Front. Med., 12 October 2021

Highlights and Facility development :



Importance of the MELISSA laser lab, used for ionization of 80% of the MEDICIS portfolio

^{128}Ba	^{153}Sm	^{155}Tb	^{167}Tm	^{169}Er	^{169}Yb	^{225}Ac

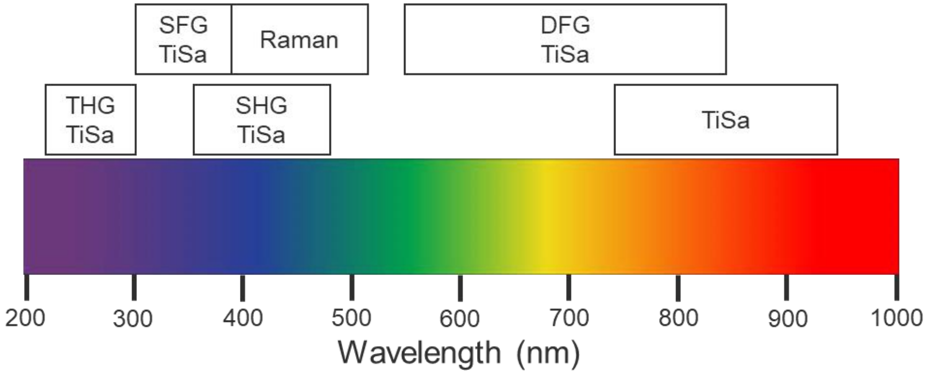


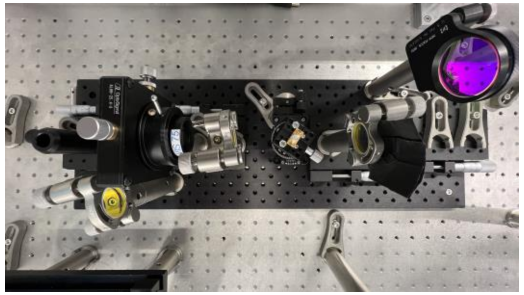
Stability :

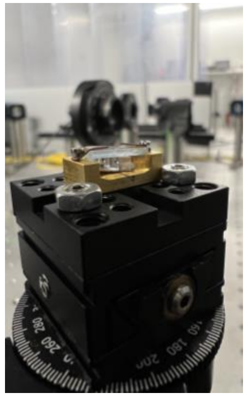
- Temperature controled Phase-Matching with BiBO in an oven

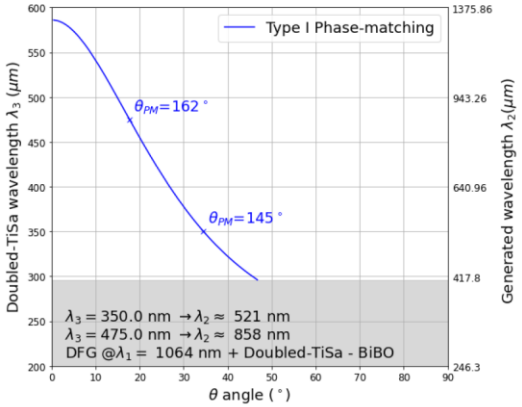
Versatility :

- Nonlinear optics processes (SHG-THG-SFG-DFG)
- Raman laser









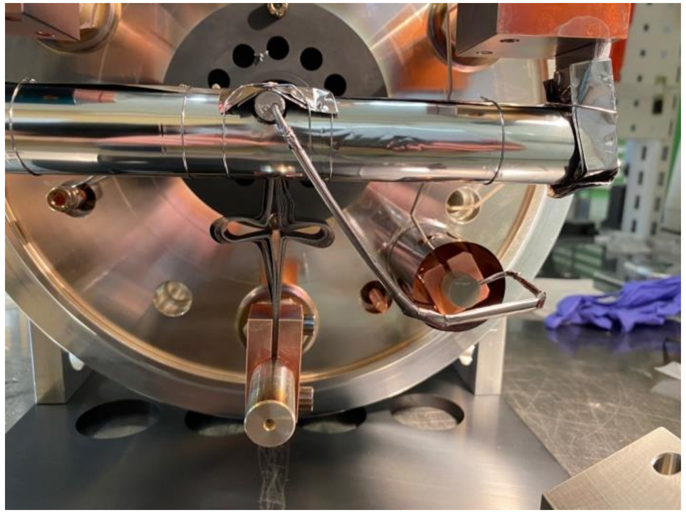
Highlights and Facility development :

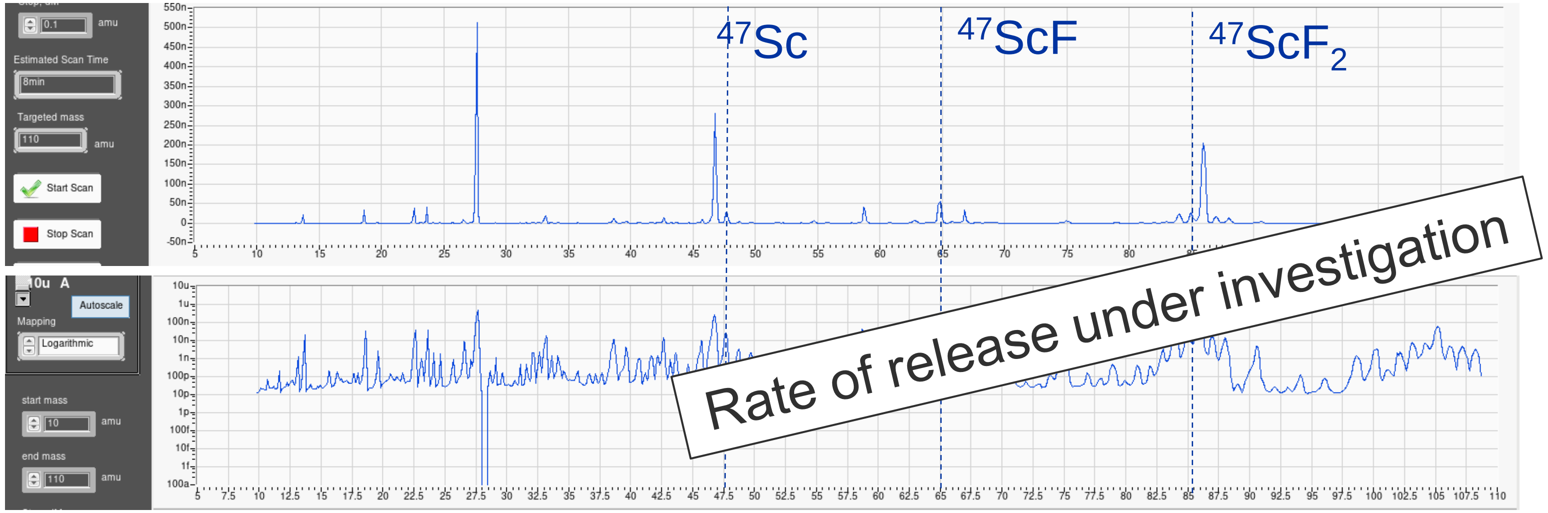
^{44}Sc

^{47}Sc

Strong interest for theranostic (imagery and therapy)
Limitation of collection due to low release of Sc from target material
⇒ Need for a new technique of production and separation

New target material investigation for production improvement
Implementation of a gas-injection system for molecular formation with CF_4
VADIS source





PhD of E. Mamis (University of Latvia)

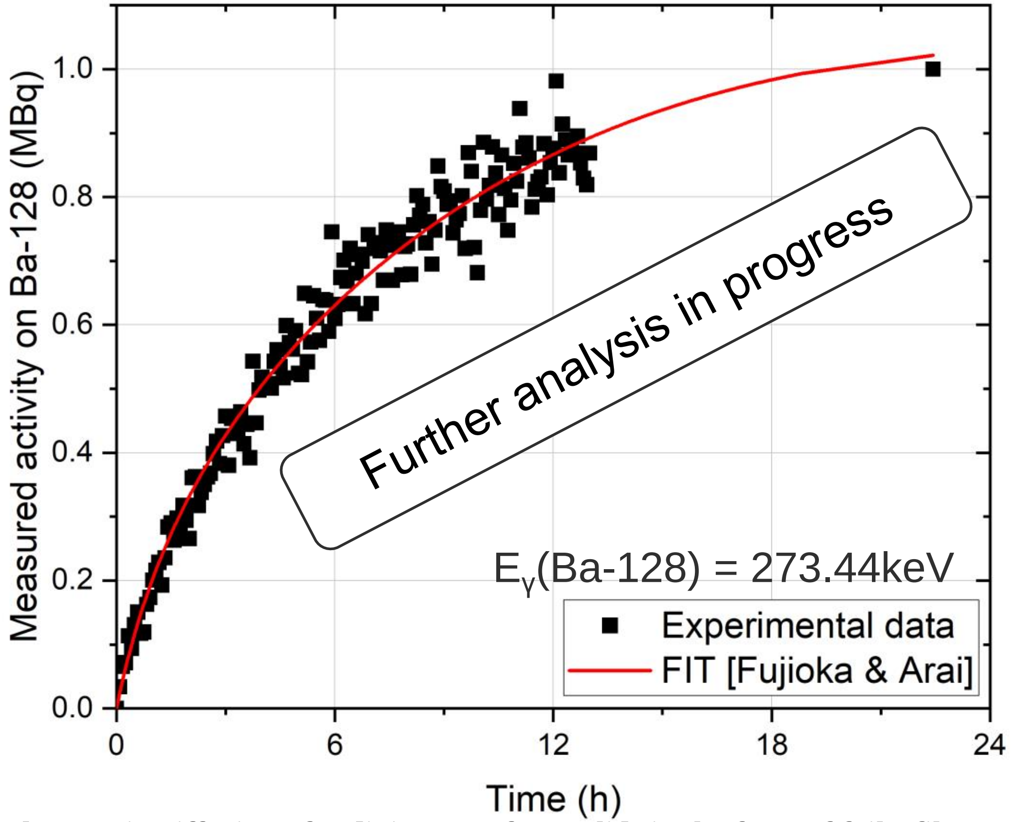
Highlights and Facility development :

^{128}Ba

MEDICIS collection 21/09/2022 – 22/09/2022

Irradiation conditions : 750µm-thick Ta foils, $8e^{17}$ protons received

Collection overview :



⇒ Temperature fixed at 2200ºC during the whole collection

⇒ Diffusion-dominated release from a foil of thickness $2a$ can be fitted with diffusion equation from [1]

$$f(\hat{t}) = \frac{2n}{\pi} \sum_{m=1}^{\infty} c_m^{-1} e^{-c_m \hat{t}},$$

$$with \quad c_m = (m - \frac{1}{2})^2 \; and \; \hat{t} = {t(\pi^2 D)}/{a^2}$$

⇒ Possibility to extract the diffusion coefficient of Ba on Ta.

[1] **M.Fujioka and Y. Arai,** ***Diffusion of radioisotopes fron solids in the form of foils, fibers and particules*****, Nuclear Instruments and Methods, 186 (1981)**

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https://medicis.cern

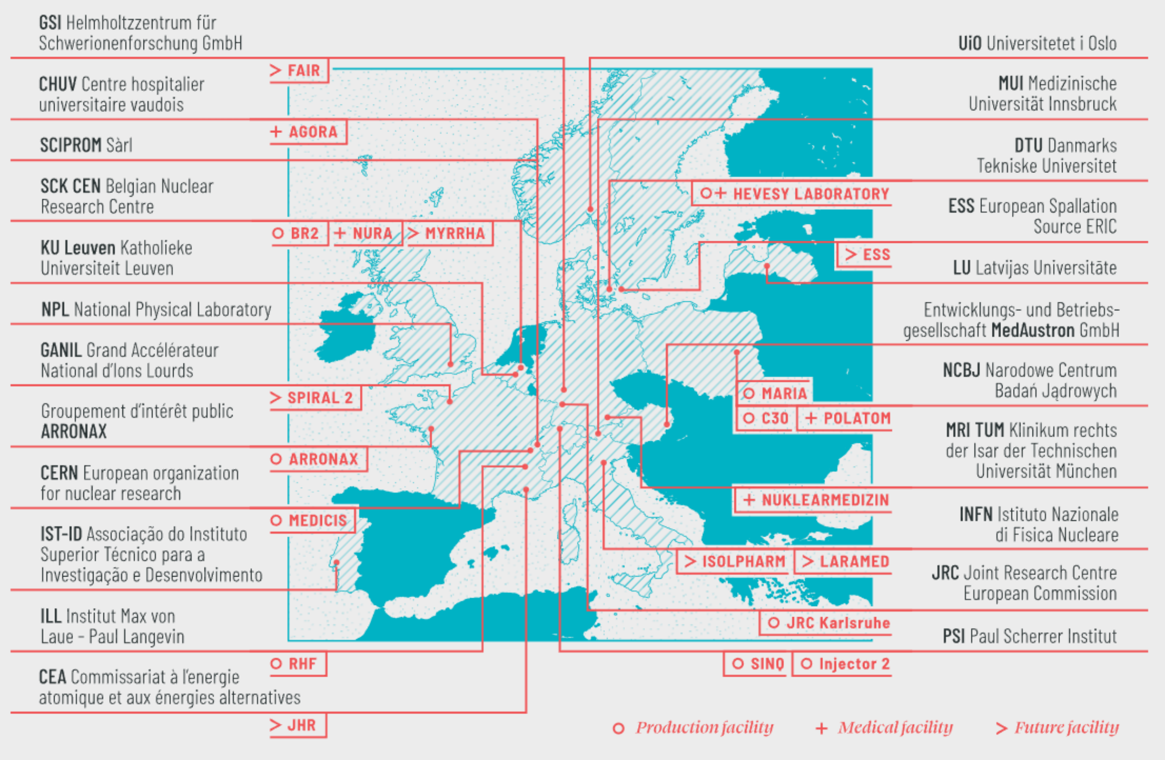
The PRISMAP consortium

https://www.prismap.eu

⇒ European consortium for medical radionuclide application

⇒ Common objectives of providing a large panel of high-purity exotic radionuclides available for medical research

⇒ Second call for project closed on the 30th of September 2022



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No.101008571 (PRISMAP)

Conclusion

⇒The CERN-MEDICIS facility has been operating every years since its commissioning (end of 2017)

⇒Production of 12 different exotic radio-nuclides for medical applications and shipped around Europe

⇒Several milestones have been reached, in terms of facility research outcome, production performances and medical applications with high specific activity already

⇒Possible thanks to the constant development of the facility

⇒Triggered the creation of a European consortium aiming at breaking the difficult access of exotic radionuclide for medical application

Thank you for your attention

정말 감사합니다

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