CERN-MEDICIS

MEDical Isotopes Collected from ISolde

Facility Report

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MEDICIS experimental program coordinator & PRISMAP technical manager

On behalf of the MEDICIS local dream-team, collaboration and all contributors

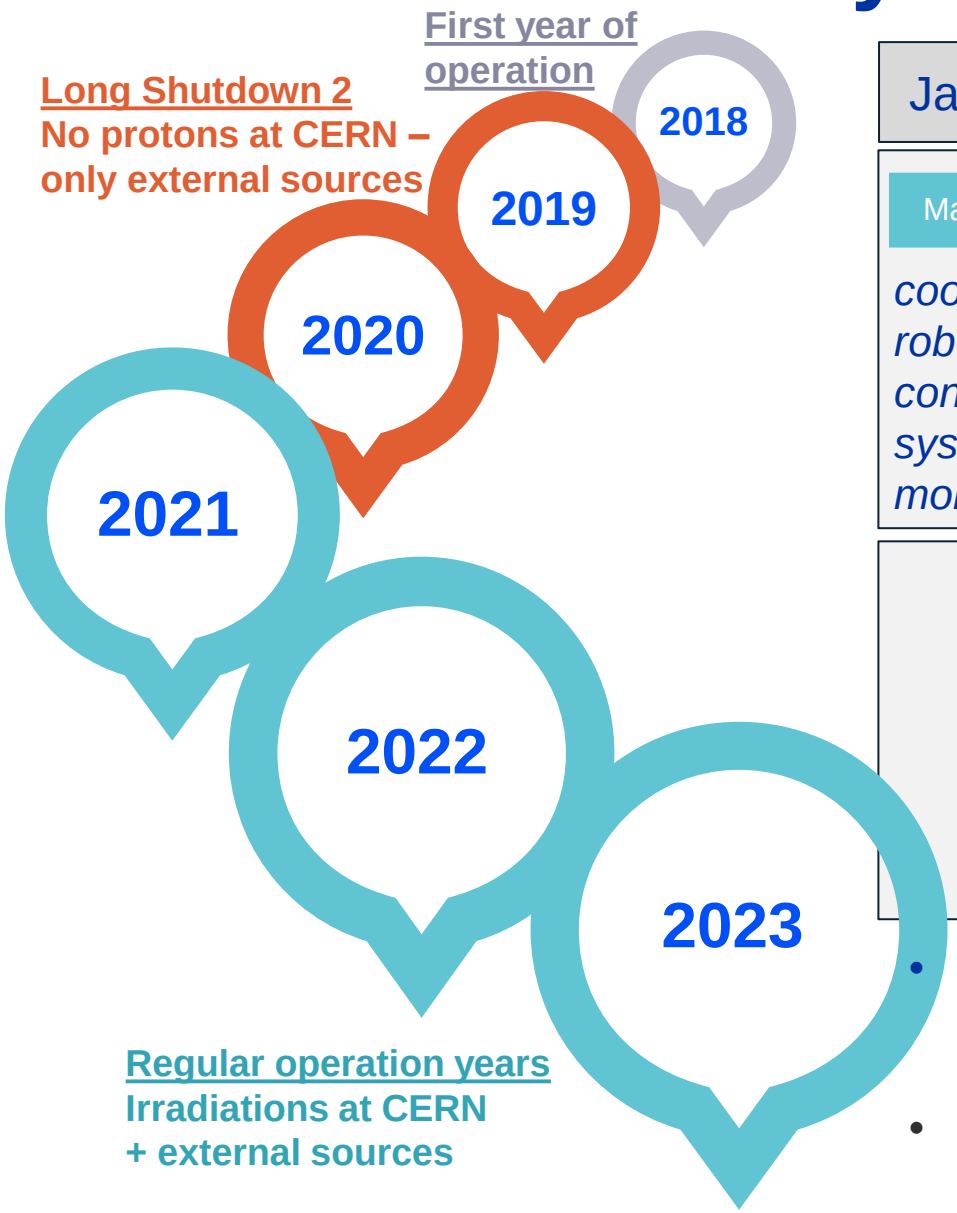
6 Dec 2023

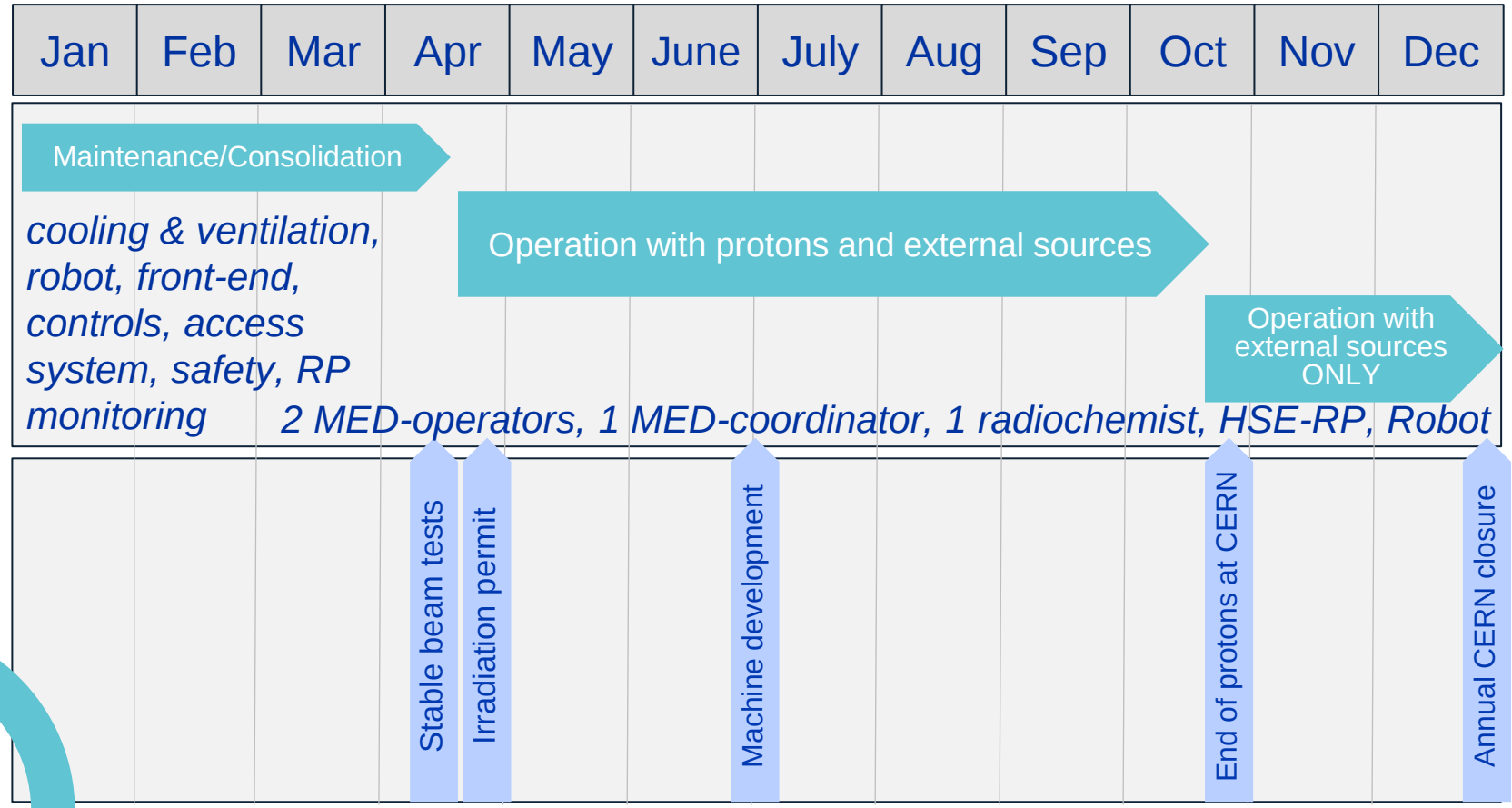
11th Collaboration Board

During the 10th Collaboration Board (22 Mar 2023)

- **We were at the end of the yearly technical stop**
  - Beam permit was obtained two days after (24 Mar 2023)
  - Planning was showing a running period from mid-April till mid-December
    - And that's what we did → we are still running today with Er-169 from ILL ☺
  - 3 new projects have been proposed and accepted by the board
    - MED-033, 034, 035
      - Targeted radiopeptide therapy with Tb-155 – IST Lisboa.
      - Ac-227 measurements and Ra/Ac-225 deliveries for incorporation measurement studies – CHUV/IRA, Lausanne.
      - First clinical translation of Sm-153 – University of Heildelberg (Ge) with sources produced at SCK CEN.

CERN-MEDICIS – yearly schedule (2023)





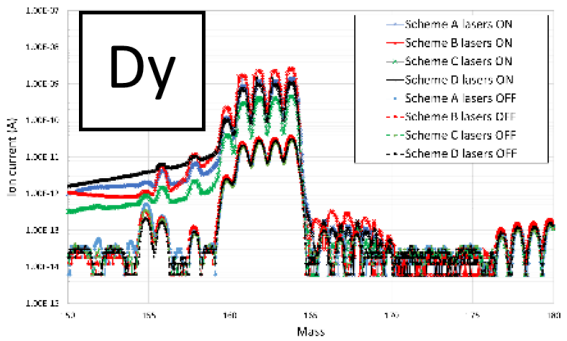
- **10 new targets operated this year – 6 reused**
  - **Target parameters fully traced (EAM light, JIRA, Wiki, yearly summary file …)**
- Target are re-used to **optimize the process, ressources and minimize waste production** : up to 12 times so far with external sources !

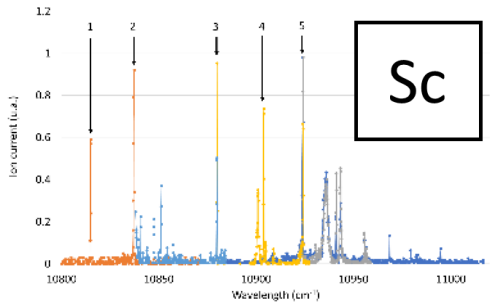
CERN-MEDICIS – MELISSA laser laboratory

- Used for more than 80% of the collected isotopes
- **In 2023 : operation supported by the ISOLDE-RILIS team**

+ strong support from KU Leuven (PJAS & PhD Students) and RILIS, since commissioning

Laser scheme development/comparison





Raman Z-fold laser using diamond for wavelength extension

=> First-ever use online for Radium ionization in MEDICIS last September

Developed by C. Bernerd

Operation in 2023

Month	Avril					May				June				July					August				September				October					November				D
Week nº	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49
Element	Er	Dy	DyTb					Ac	DyTb	Tm	Ac		Sc		Er	Sc		Ba	Sc	Ac				RaAc		Sc		Gd	Tm	Sm	Sc		Er	Sm		Er

Operation week Laser development week

Irradiation at CERN – some statistics

- **18 irradiation slots this year**
  - 3 dedicated to Ba-128 & Cs-129 (collected from the same irradiation)
  - 4 dedicated to Ra-224/Ra-225/Ac-225
  - 3 dedicated to Tb-155
  - 2 dedicated to Tm-165 & Tm-167 (double collection)
  - 6 dedicated to Sc-47 production (E. Mamis PhD thesis)

- **793 hours of irradiation**
- 2.7E19 PoT received (25% of ISOLDE p)
  - 1.1E19 direct beam
  - 1.1E19 indirect beam on GPS ISIS
  - 2.5E18 indirect beam on HRS

Beam position checks

External samples – SCK CEN, PSI & ILL

- **6 operation weeks with external samples**
  - 1 dedicated to Sc-43/44 provided by PSI for E. Mamis PhD thesis on Sc mass separation
  - 2 dedicated to Sm-153 from SCK CEN for Heidelberg Hospital (MED-035)
  - 3 dedicated to Er-169 for PSI produced at ILL

CERN-MEDICIS – view of 2023 productions so far

Cs-129
1x 91 MBq
1x 140 MBq
1x 1 GBq

Ba-128
1x 60 MBq
1x 340 MBq

CHUV, Lausanne, CH

Ra-224/Pb-212*
1x 50 MBq
1x 80 MBq
*M.Inzamam project

DTU, Denmark

Ra-225/Ac-225*
1x 60 MBq Ra-225
+
1x 11 MBq Ac-225

PAEC, Pakistan
KUL, Belgium
IRA, Lausanne, CH

1x 35 MBq Ra-225
+
1x 4 MBq Ac-225

KUL, Belgium

1x 15 MBq Ra-225

NPL,UK

1x 140 MBq Ra-225

*J.Johnson PhD thesis

PAEC, Pakistan

40% efficiency repeated twice for elemental Ra !

Tm-167
1x 20 MBq
1x 92 MBq

NPL,UK
PSI, CH

Tm-165
1x 12 MBq
1x 180 MBq

NPL,UK
DTU, Denmark

Er-169
1x 150 MBq
1 x 30 MBq
1x last separation ongoing this week

PSI, CH

Sm-153
1x 130 MBq
1x 1.2 GBq

Heidelberg Hospital, GE

In development:

Univ. Bordeaux, FR
NPL, UK

Tb-155
1x 4 MBq
1x 2 MBq*
W. Wojtaczka PhD thesis

Sc-47 (+Sc-44m)
1x 4 MBq
1x 3 MBq

Sc-46
1 x 2.5 MBq
(>2% eff. ! *)
E.Mamis PhD thesis

All values presented are at the time of the End Of Collection (EOC)

Status on 06/12/2023

CERN-MEDICIS within PRISMAP

Activity delivered for **3 User Projects** in 2023:

- Tb-155 to Univ. of Bordeaux (C. Morgat)
- Tm-165 to DTU (for I. Da Silva)
- Ac-225 to KU Leuven (Michel Koole) – project completed

+ Ra-224/Pb-212 generator for development at DTU

(see M. Inzamam presentation)

Several samples sent to NPL,UK for characterisation

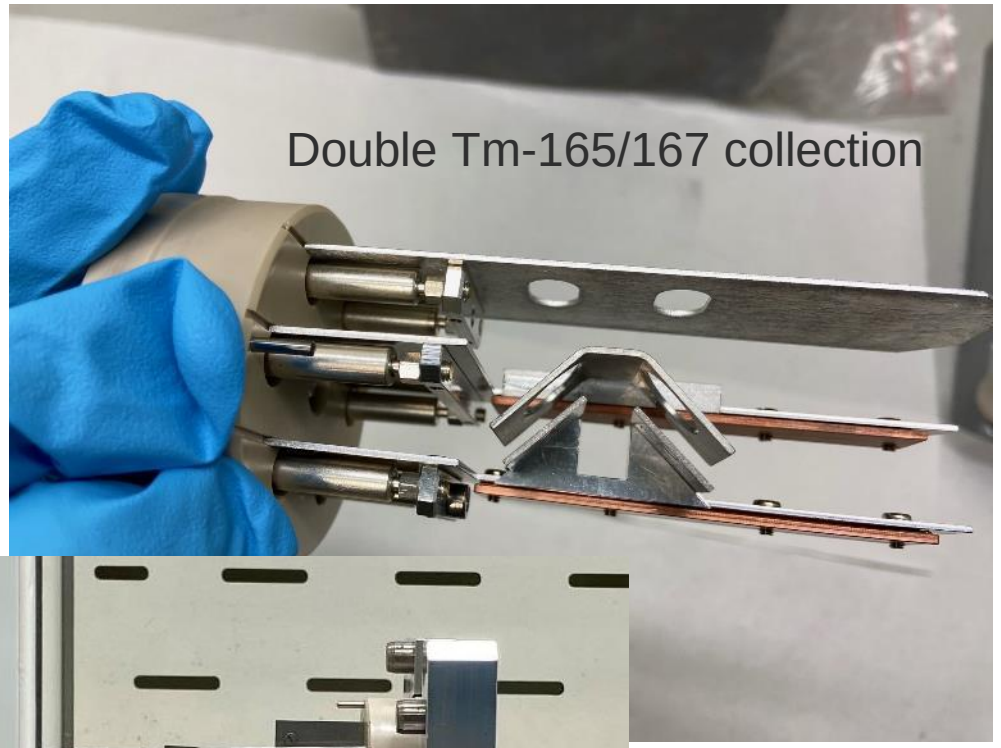
Dedicated flight (WP9):
Tm-165 (30 h half-life) delivered from
MEDICIS to DTU, DK in 4 hours door-to-door

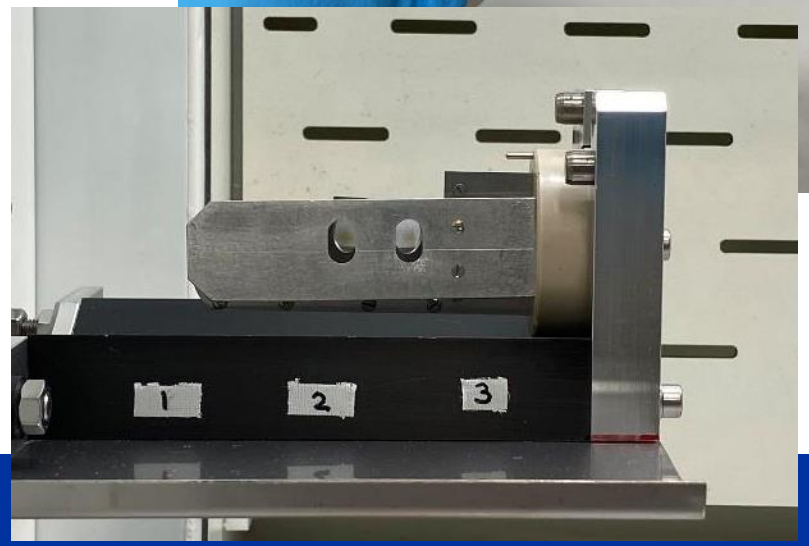
CERN-MEDICIS – double collections for Ra and Tm

Alpha emitters systematically handled inside the glovebox

Ra-224/Ra-225 collected at the same time !!

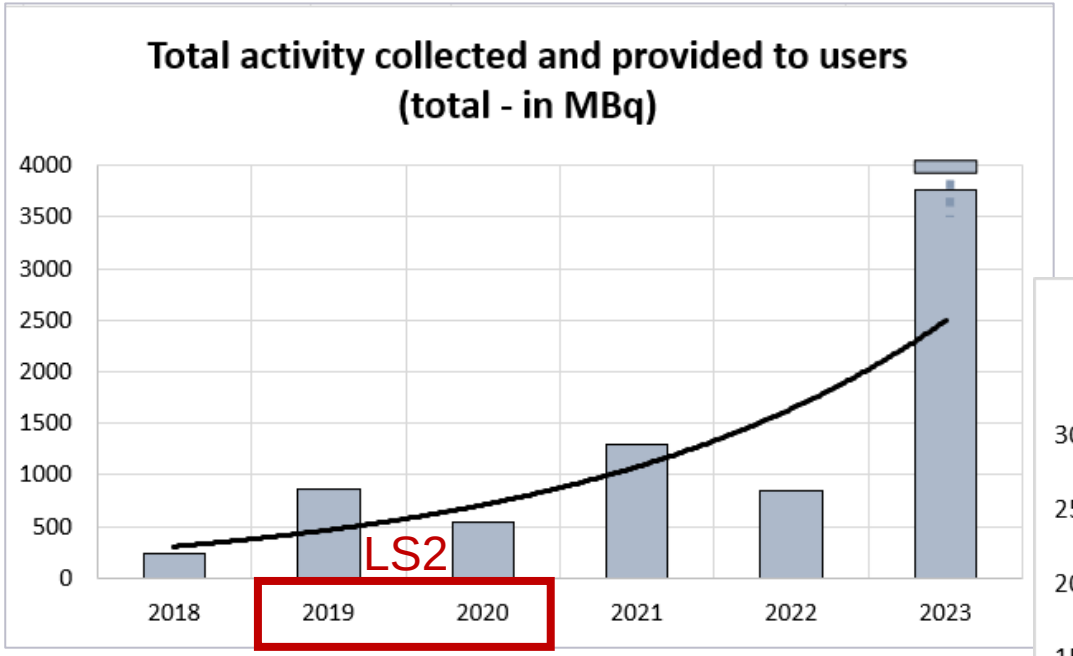
Consolidated with a week of stable beam tests with gaf-chromic films to validate the exact distances between two masses at different masses of interest

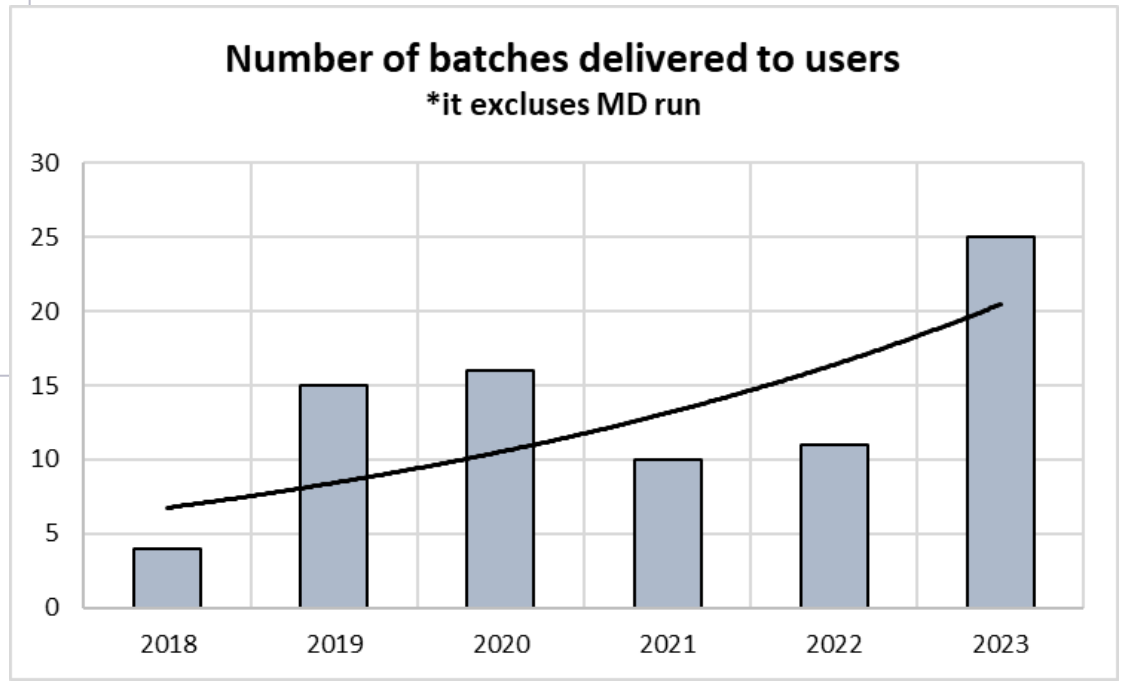




CERN-MEDICIS – an overview since commissioning

Year	Mode of operation
2018	CERN PSB External sources
2019	External sources (Long shutdown)
2020	External sources (long shutdown)
2021	CERN PSB External sources
2022	CERN PSB External sources
2023	CERN PSB External sources





3.8 GBq collected until now in 2023
… and we are still in operation !

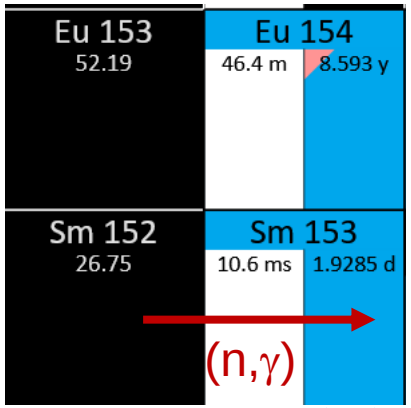
Intervention doses remain low despite significant increase of activity collected (ALARA)

CERN-MEDICIS – an overview since commissioning

Year	Mode of operation	Radionuclides	Activity collected (total – in MBq)	Max. coll. efficiency (%)	#batch delivered
2018	CERN PSB External sources	C-11, Tb-149, Tb-152, Tb-155, **Tm-165**, Er-169	235	1.6	4
2019	External sources (Long shutdown)	Tb-155, Er-169, **Yb-175**, Pt-195m	870	6.0	15
2020	External sources (long shutdown)	Sm-153, Tb-155, **Tm-167**, Ac-225	540	22.5	16
2021	CERN PSB External sources	Ac-225, Pt-191, Yb-175, **Tm-167**, Tb-155, Sm-153, Tb-149, Ba/Cs-128, Sc-47, Sc-46, Sc-44	1300	34.8	10
2022	CERN PSB External sources	Ra-225/Ac-225, Hg-195/Hg-197, Tm-165/Tm-167, Tb-155, Sm-153, **Ba/Cs-128**, Sc-47, Sc-44	840	5.9	11
2023	CERN PSB External sources	**Ra-225**/Ac-225, Ra-224, Er-169, Tm-165/Tm-167, Tb-155, Sm-153, Cs-129, Ba/Cs-128, Sc-47, Sc-44	3800 (and still ongoing …)	40.0	25 (including last foresseen one)

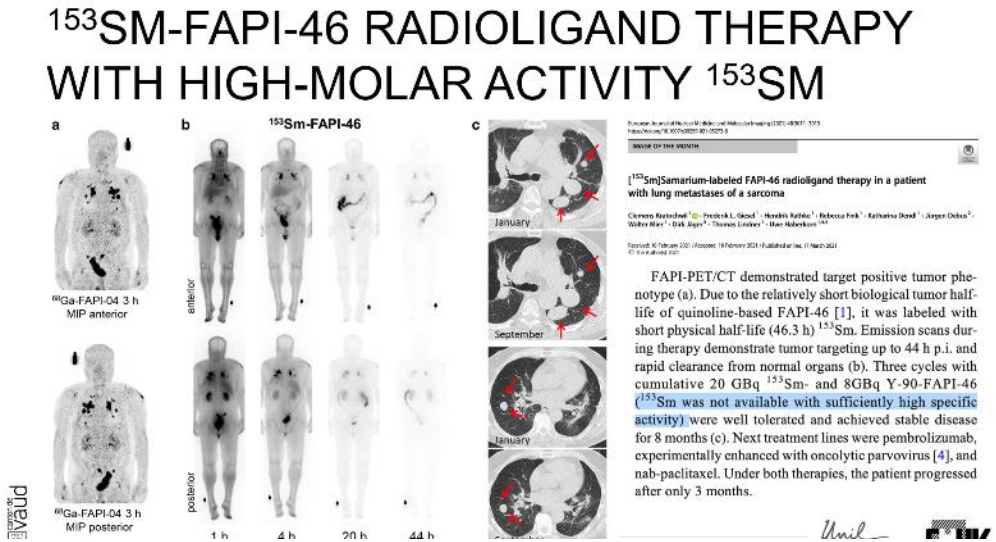
CERN-MEDICIS: radionuclides and research projects

Sm-153



MED-035

153SM-FAPI-46 RADIOLIGAND THERAPY WITH HIGH-MOLAR ACTIVITY 153SM



Courtesy of Prof. MD John Prior (CHUV)

Clinical trial will start in 2024 !

To prepare for it:

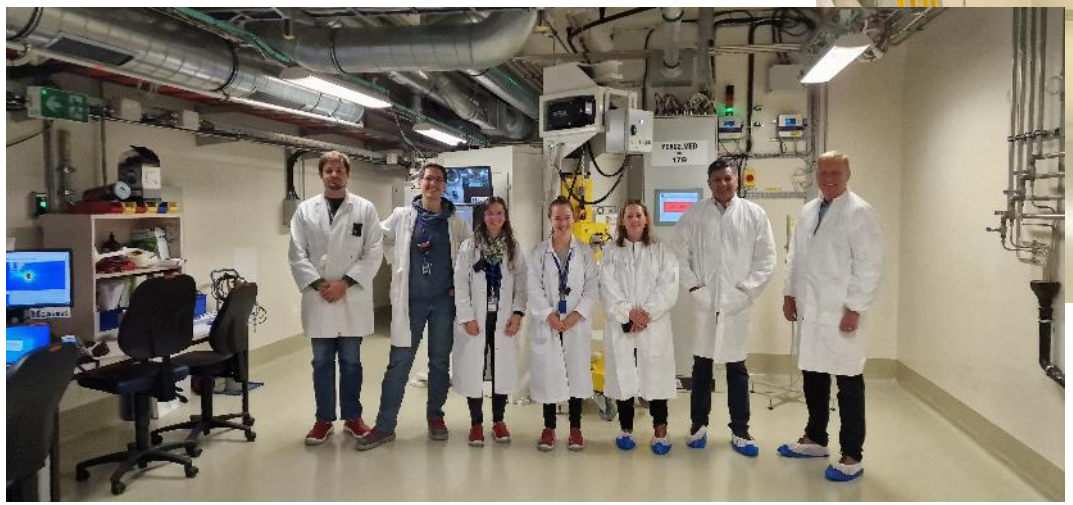
- We prepared a procedure based on the dose rate measured for faster shipping process – shipped within one hour after retrieval
- We received two sources of Sm-153 in 2023 to test the pipeline and produced a **batch of 1.2 GBq** !
- **More than 99% radiolabelling yield** achieved by Heidelberg at the end of 2023.

CERN-MEDICIS - Visits

- Many “VIP” visit during the year : DEBIOPHARM, the BBC, NPL CEO, European Comission Officers, ORNL Research Acc. Director …
- MEDICIS is included in the Protocol Office schedule for visits at CERN

Visit of the BBC for BBC click report

Visit of the NPL CEO



Fulvia Pilat - Research Accelerator Director @ Oak Ridge National Laboratory

CERN-MEDICIS – over the year, milestones & outlooks

One of the few facilities at CERN to run during Long Shutdowns

already proven in 2019 and 2020 with great achievements !

2017

Facility commissioning
1st Radioactive Ion Beam produced !

2018

First board meeting and projects approved

First year of operation
- First direct irradiation at ISOLDE

Start of radiochemistry

2019

Commissioning of MELISSA laser laboratory
First laser ionized beam

First full year of operation with external sources only

1 GBq total collected and shipped

2020

2nd year successful year of operation with external sources only
Despite Covid Crisis

Record efficiency of 53% !

Online g-spec monitoring
Enabled the detection of sputtering effect/issue
Evolution of implantation layers

2021

Restart with proton at CERN-ISOLDE

Glovebox purchase

Introduction of KPIs

First irradiation on new irradiation station (GPS ISIS)

Start of the PRISMAP European Project

2022

Double collection system in place

Successful first double collection !

Use of glovebox for Ac-227 manipulation

On-site HP Ge detector for shipping optimization

2023

34 projects approved so far

Optimization of beam position for direct irradiation

First double Ra-224/225 collection

- First proof of concept of Ra-224/Pb-212 generator
- First Raman laser ionization study for radium

1 GBq collected in a single batch from irradiated target
1 GBq collected in a single batch from external target

2024

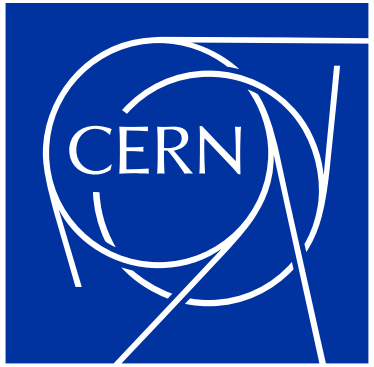
First clinal translation of mass separated Sm-153 !

New collimator system to avoid early saturation of online-γ-spectrometer

A BIG THANKS TO ALL THE PEOPLE, GROUPS, SERVICES, INSTITUTES, COLLABORATION … INVOLVED IN MEDICIS!

THANK YOU FOR YOUR ATTENTION !

Charlotte.Duchemin@cern.ch



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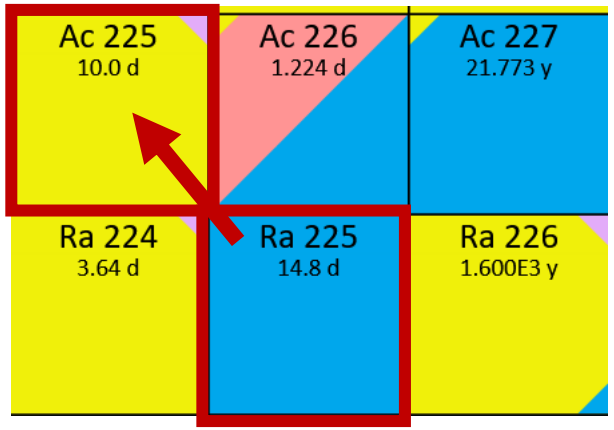
CERN-MEDICIS: radionuclides and research projects

Ra-225/Ac-225



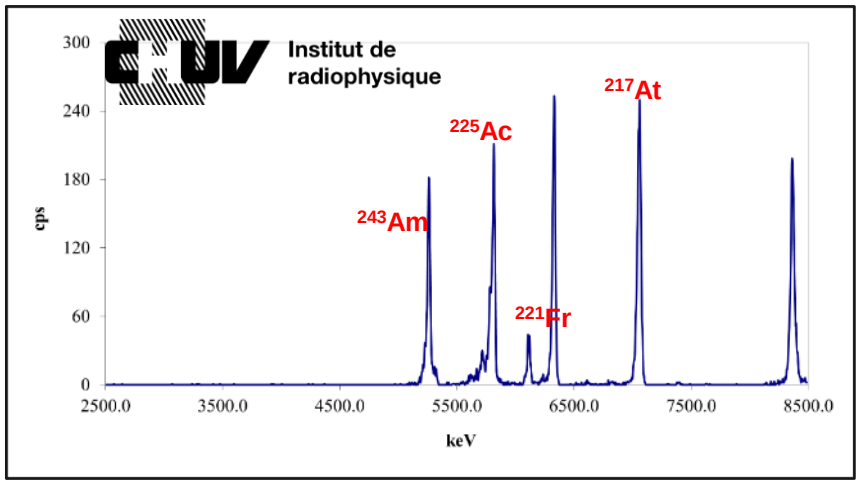
Collaboration CERN-MEDICIS, JRC Karlsruhe, KU Leuven → reach the highest Ac-225 efficiency

- Ac-225 collected from an **external** sample: **10%** reached* (measured)
- Ra-225/Ac-225 collected from **Th target** irradiated at ISOLDE: up to **40%** reached via Ra-225** (in-target production yield simulated with FLUKA)
  - Ac-225 labelled with PSMA-617 with efficiency of >97% (INMOL Cancer Hospital, Lahore)

- **Intercomparison KU Leuven (BE) / CHUV-IRA (CH) / NPL (UK)**
  "to determine the amount (if any) of Ac-227 impurities in Ac-225 produced at MEDICIS"

  Recent results: two ^{225}Ac productions (May 2023 / June 2023) were characterized at CHUV/IRA
  Outcome:
  no ^{227}Ac impurity (< mBq) was identified in both ^{225}Ac samples

- **Dosimetric and radiochemistry study by CERN & CHUV-IRA (CH)**

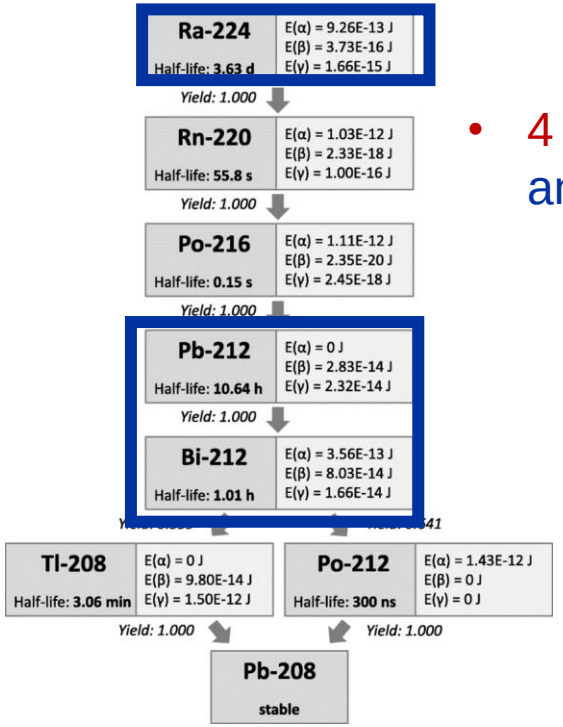


Alpha spectrum of a ^{225}Ac aliquot from a June 2023 production showing no trace of Ac-227. Measured after > 100 days (courtesy of R. Cusnir)

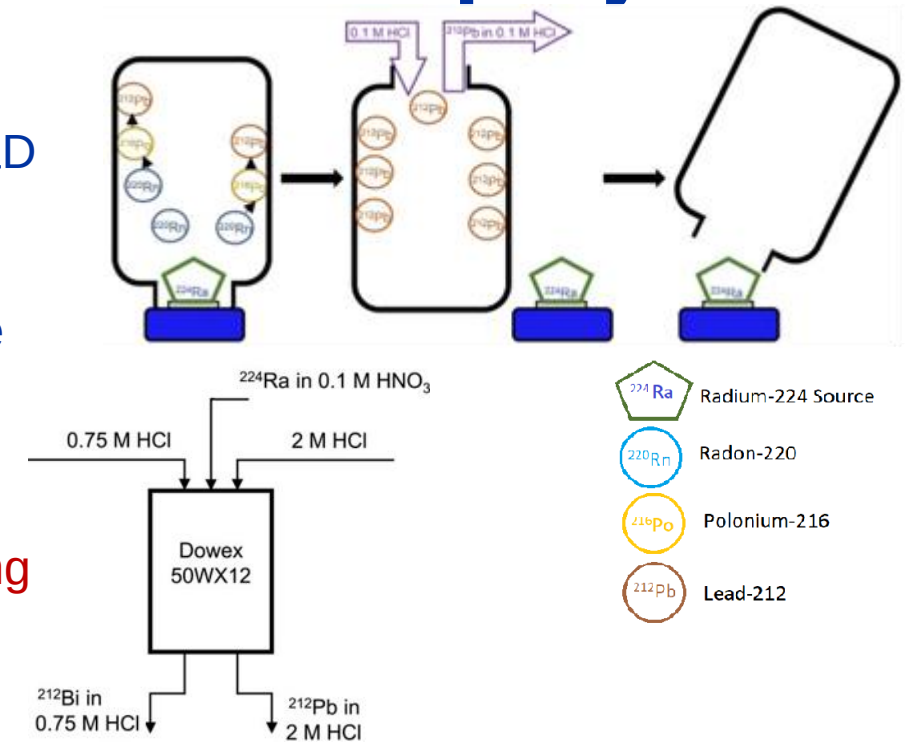
*Johnson, *et al. Sci Rep* **13**, 1347 (2023)
**Radchenko et al. Journal of nuclear medicine, 62, 11 (2021)*

CERN-MEDICIS: radionuclides and research projects

Ra-224



- 4 collections performed in 2023 up to 80 MBq for R&D and feasibility tests
  - 3 collections and generators produced using the "gas collection method": collection of emanated Rn-220
  - 1 collection used to produce a generator by using the chromatographic separation of the radionuclides.



- 80 MBq generator dispatched to DTU, Hevesy Lab, DK (PRISMAP partner institute)
  - Very successful first elution and labelling with DOTATATE combined with stability study in mouse serum
- Chromatographic generator at CERN: the **efficiency is up to 60%**
  - Working on further optimization

Li, R.G., Stenberg, V.Y. and Larsen, R.H. (2022) 'An experimental generator for production of high-purity212pb for use in radiopharmaceuticals', *Journal of Nuclear Medicine*, 64(1), pp. 173–176. doi:10.2967/jnumed.122.264009.
M. Pruszyński *et al*. (2021) 'Radiochemical separation of ^{224}Ra from ^{232}U and ^{228}Th sources for ^{224}Ra/^{212}Pb/^{212}Bi Generator', Applied Radiation and Isotopes, 172, pp. 109655. doi:10.1016/j.apradiso.2021.109655

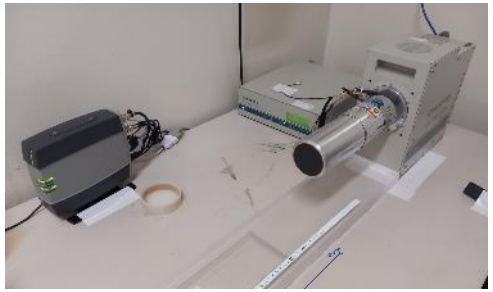
Ongoing project
Scandium thermal release studies from irradiated nat-Ti and nat-V foils

Goal is to understand the thermal release of Sc from nat-Ti and nat-V for subsequent efficient mass separation at CERN-MEDICIS to produce high specific activity Sc-44m/g and Sc-47 for medical applications.

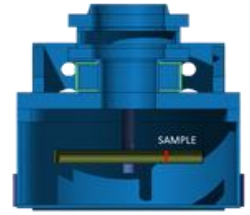
1 g of nat-Ti or 3.4 g of nat-V*

*the mass difference is to compensate from the lower production yield in V in comparison with Ti

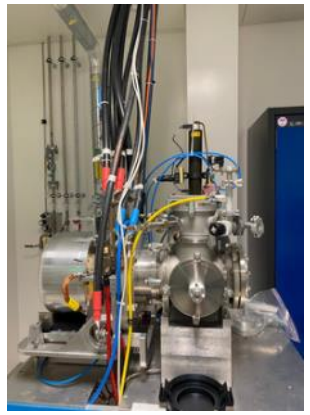
Irradiation at CHARM facility by the secondary neutrons produced from the impact of 24 GeV protons impinging on a metallic target with an average intensity of 5E10 protons/second over 5 days



Gamma spectrometry to determine sample activity before and after heating



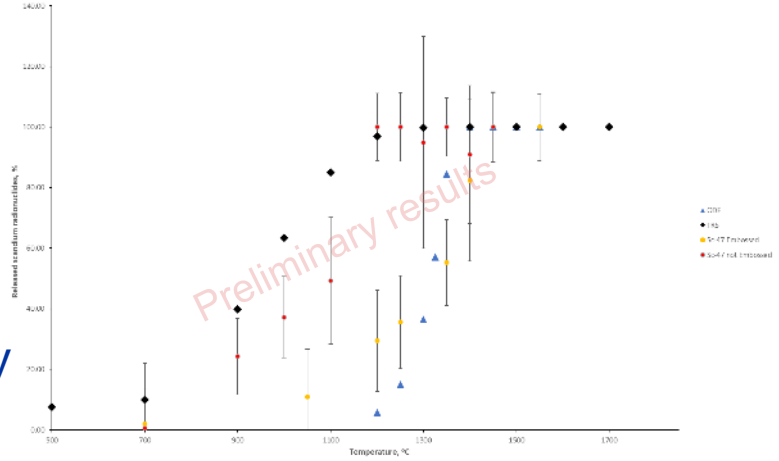
View of a sample placed inside the target container of a typical ISOL target unit. The vacuum and heating is controlled. Temperature up to 2000 degrees Celsius can be reached with a vacuum around 1E-6 mbar

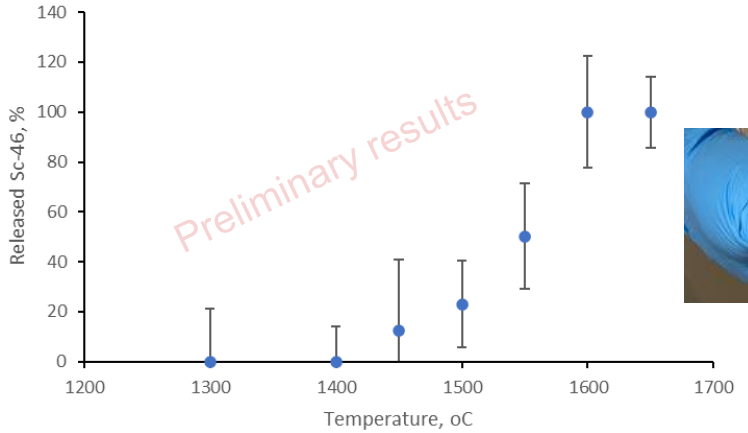


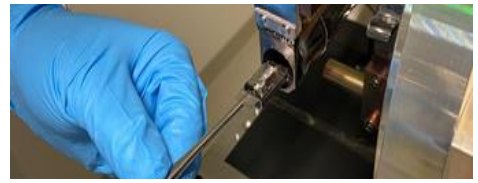
Experimental setup for scandium thermal release studies

Led to a positive impact on the Sc mass separation efficiency increase !

Systematically do this study for non-easy-to-release radionuclides !!!







Sample retrieval after heating

Courtesy of P. Kalnina, E. Mamis.
Strong support from HSE-RP for irradiation opportunities at CHARM and experiments