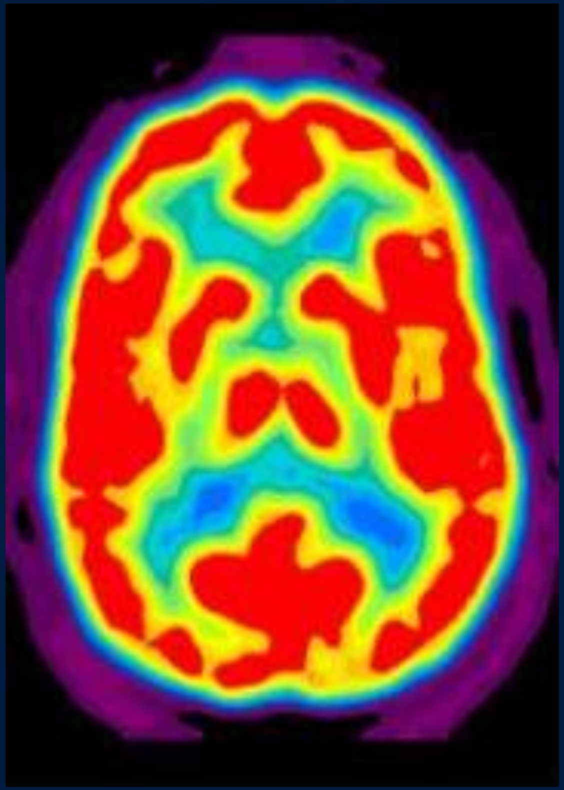


Nuclear medicine

Where nuclear science contributes to society

UK Nuclear Summer School – Monday 27 August 2026

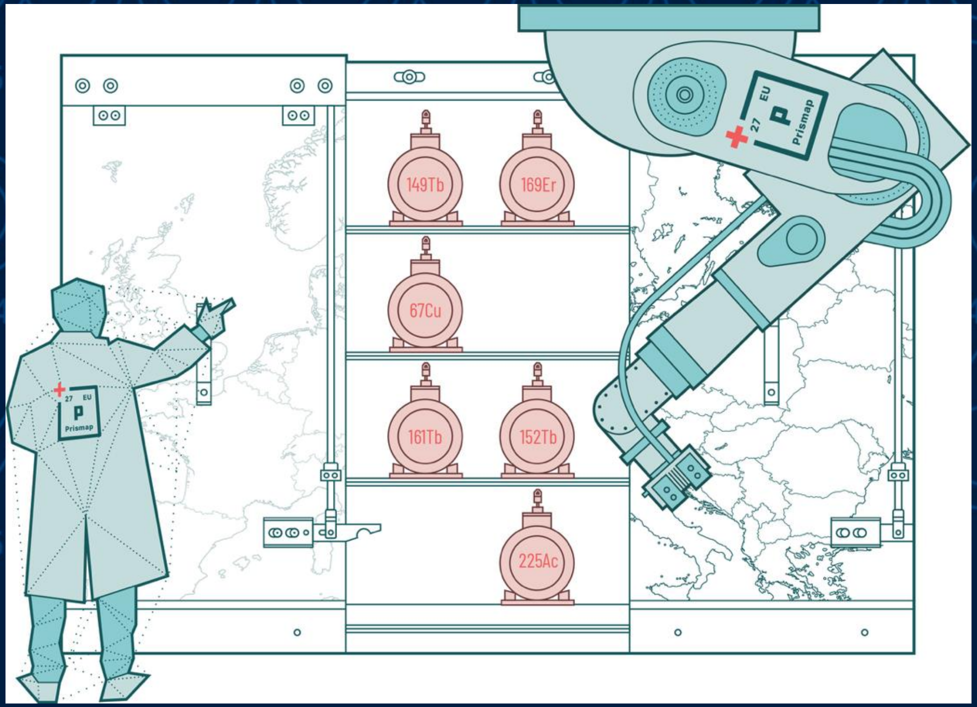
KU LEUVEN

- Nuclear medicine leverages the symbiosis of **controled delivery** of pharmaceutical products through specific body function with unique modalities offered by radioactive decays.
- This enables **functional imaging** of the human body – be it to monitor body function or product intake to be understand its working, or now often in the diagnosis of cancer.
- Thanks to charged-particle emission, **selective cell destruction** is also possible, supporting targeted radionuclide therapy, in particular against distributed cancers.
- The **theranostics** combination of patient selection and selective therapy opens the door for extremely potent cancer therapies.
- **The current radionuclide portfolio remains limited.**

Yesterday: Some basics of nuclear medicine

Today: Nuclear science for nuclear medicine

Radionuclide shopping:
How we choose the best radionuclide



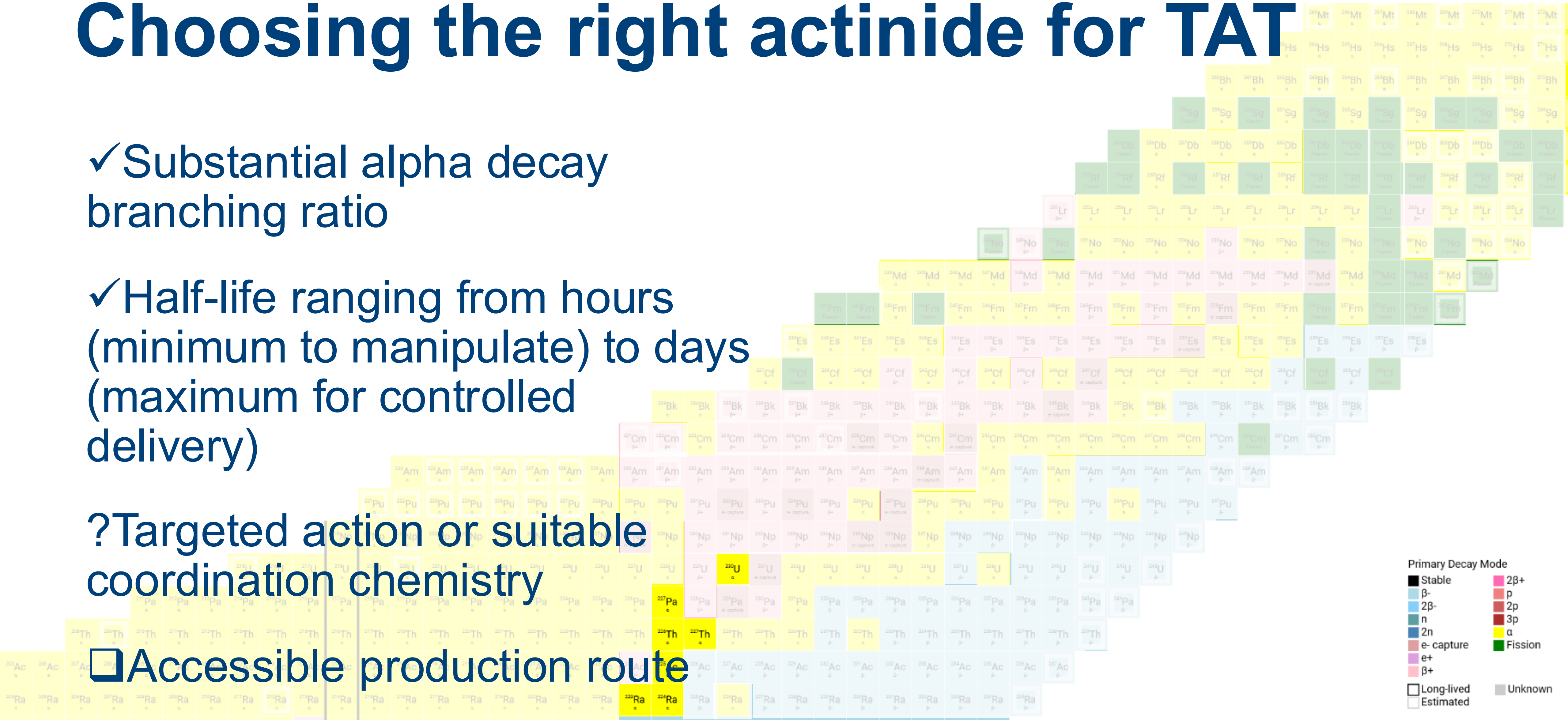
Choosing the right actinide for TAT

✓Substantial alpha decay branching ratio

✓Half-life ranging from hours (minimum to manipulate) to days (maximum for controlled delivery)

?Targeted action or suitable coordination chemistry

❑Accessible production route



The Colourful Nuclear Chart: https://people.physics.anu.edu.au/~ecs103/chart/

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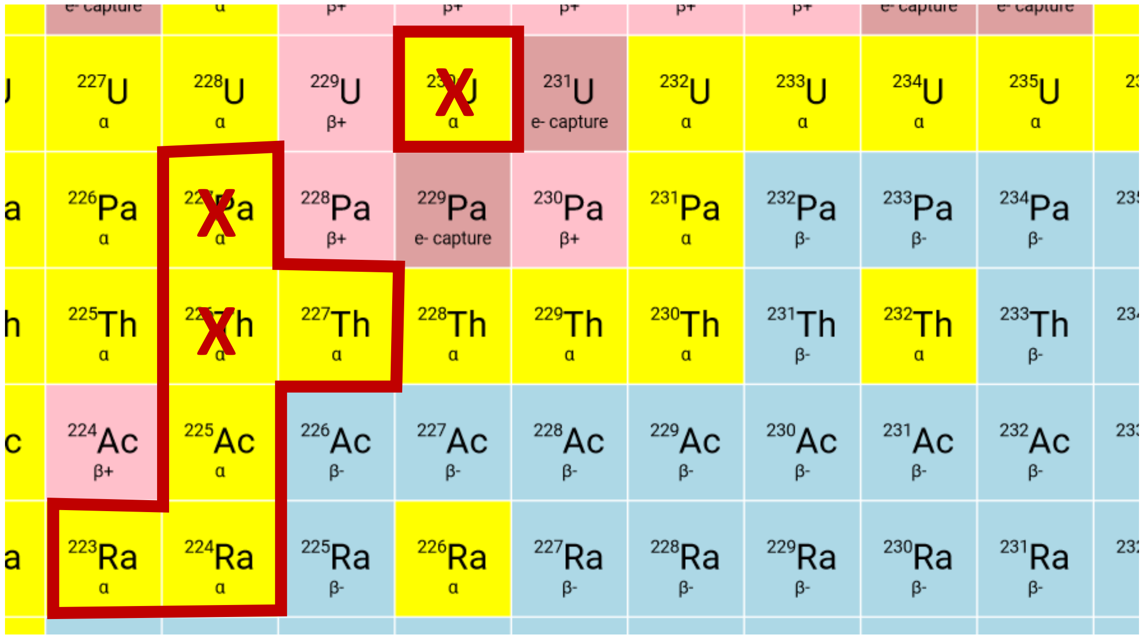
Isotopes effectively used

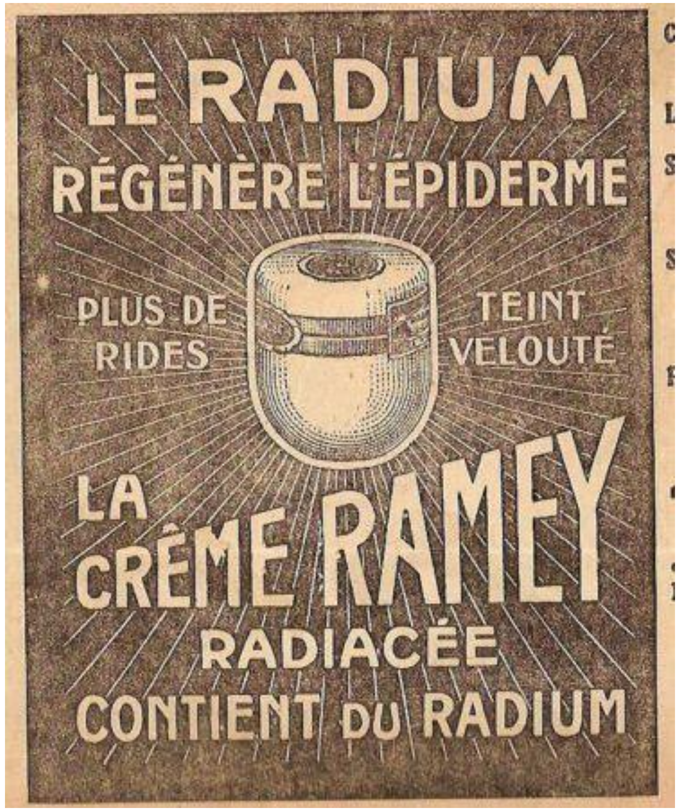
- ✓ ^{211}At
  - 6 clinical trials
- ✓ $^{223,224}Ra$
  - ✓ Xofigo® for the treatment of bone metastasis in castration resistant prostate cancer
  - ~200 clinical trials
- ✓ ^{225}Ac
  - 13 ongoing clinical trials
  - Mostly about prostate cancer
- ✓ ^{227}Th, ^{213}Bi, ^{212}Pb
  - <5 trials



 https://clinicaltrials.gov

Radium: a long tradition

Cutaneous application



Radium salts

Why Ra? - $RaCl_2$

p	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1	1 H																	2 He
2	3 Li	4 Be											5 B	6 C	7 N	8 O	9 F	10 Ne
3	11 Na	12 Mg											13 Al	14 Si	15 P	16 S	17 Cl	18 Ar
4	19 K	20 Ca	21 Sc	22 Ti	23 V	24 Cr	25 Mn	26 Fe	27 Co	28 Ni	29 Cu	30 Zn	31 Ga	32 Ge	33 As	34 Se	35 Br	36 Kr
5	37 Rb	38 Sr	39 Y	40 Zr	41 Nb	42 Mo	43 Tc	44 Ru	45 Rh	46 Pd	47 Ag	48 Cd	49 In	50 Sn	51 Sb	52 Te	53 I	54 Xe
6	55 Cs	56 Ba	57 La	72 Hf	73 Ta	74 W	75 Re	76 Os	77 Ir	78 Pt	79 Au	80 Hg	81 Tl	82 Pb	83 Bi	84 Po	85 At	86 Rn
7	87 Fr	88 Ra	89 Ac	104 Rf	105 Db	106 Sg	107 Bh	108 Hs	109 Mt	110 Ds	111 Rg	112 Cn	113 Nh	114 Fl	115 Mc	116 Lv	117 Ts	118 Og

lanthanoid series 6	58 Ce	59 Pr	60 Nd	61 Pm	62 Sm	63 Eu	64 Gd	65 Tb	66 Dy	67 Ho	68 Er	69 Tm	70 Yb	71 Lu
actinoid series 7	90 Th	91 Pa	92 U	93 Np	94 Pu	95 Am	96 Cm	97 Bk	98 Cf	99 Es	100 Fm	101 Md	102 No	103 Lr

Providing those novel radionuclides:

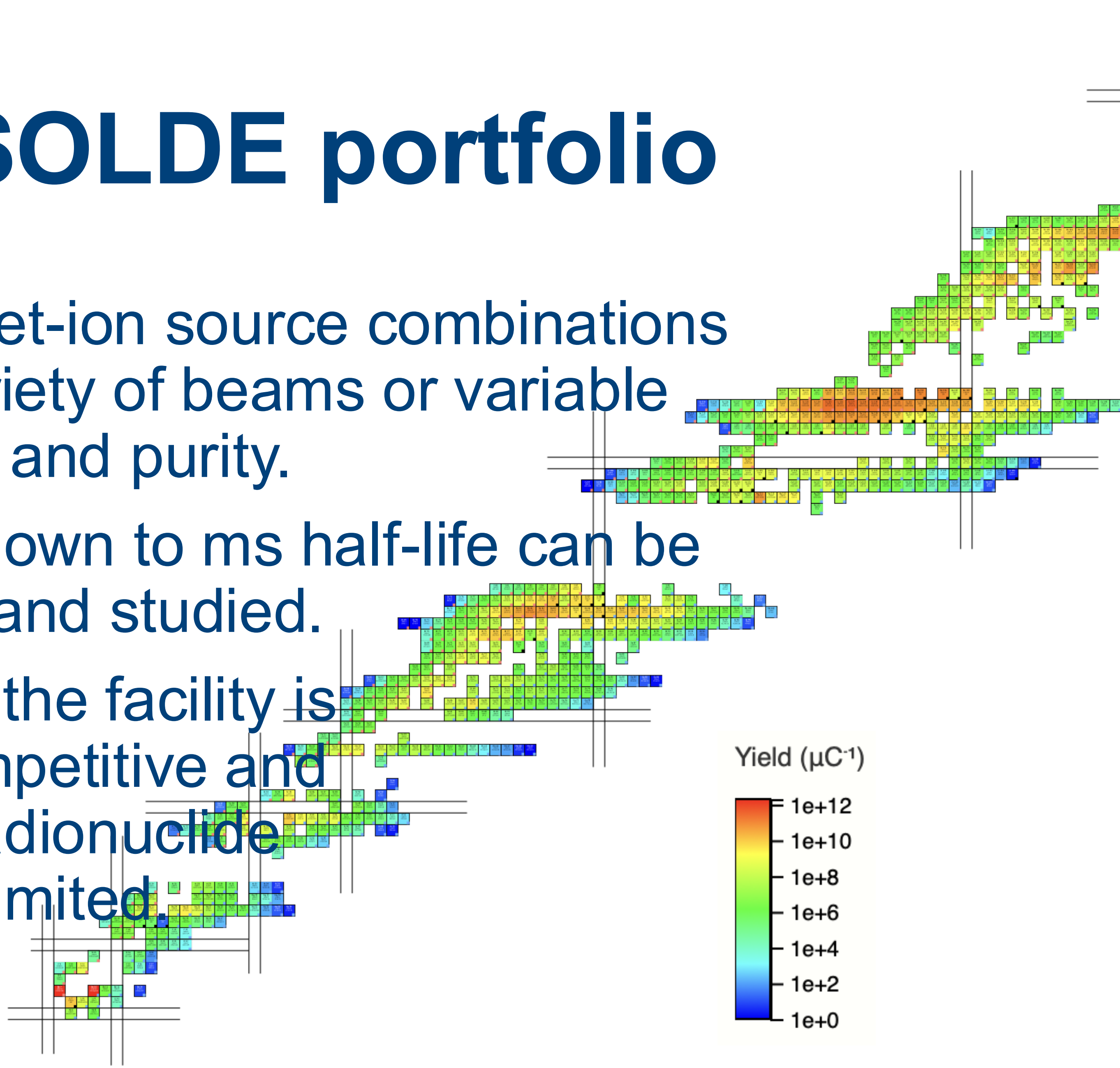
From CERN ISOLDE to CERN MEDICIS

The ISOLDE portfolio

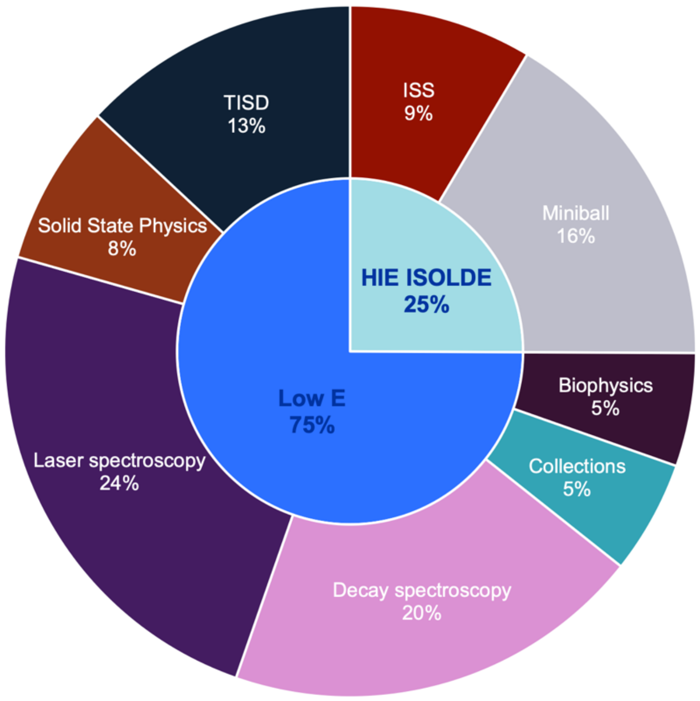
Many target-ion source combinations yield a variety of beams or variable intensities and purity.

Isotopes down to ms half-life can be extracted and studied.

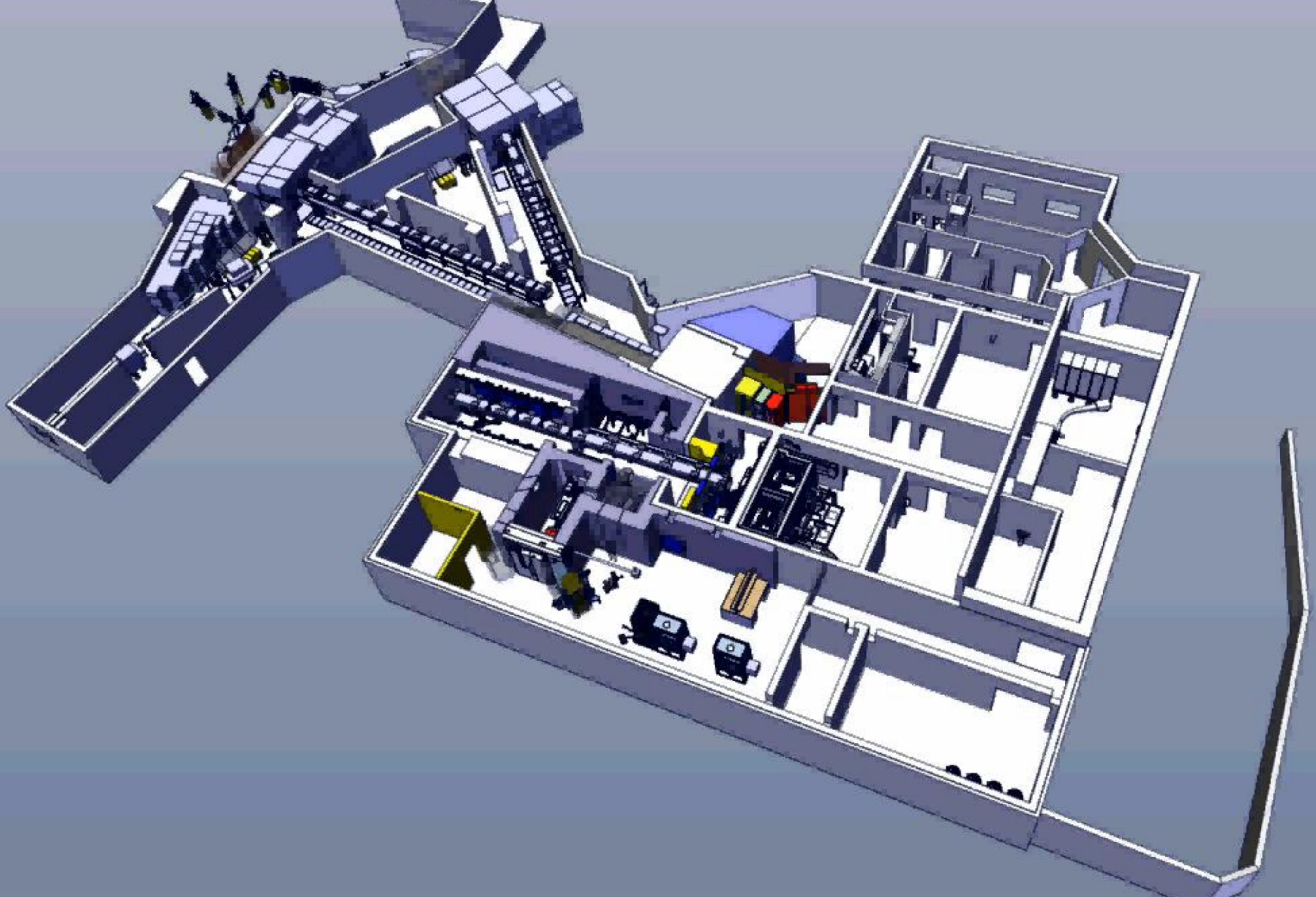
Access to the facility is highly competitive and medical radionuclide supply is limited.



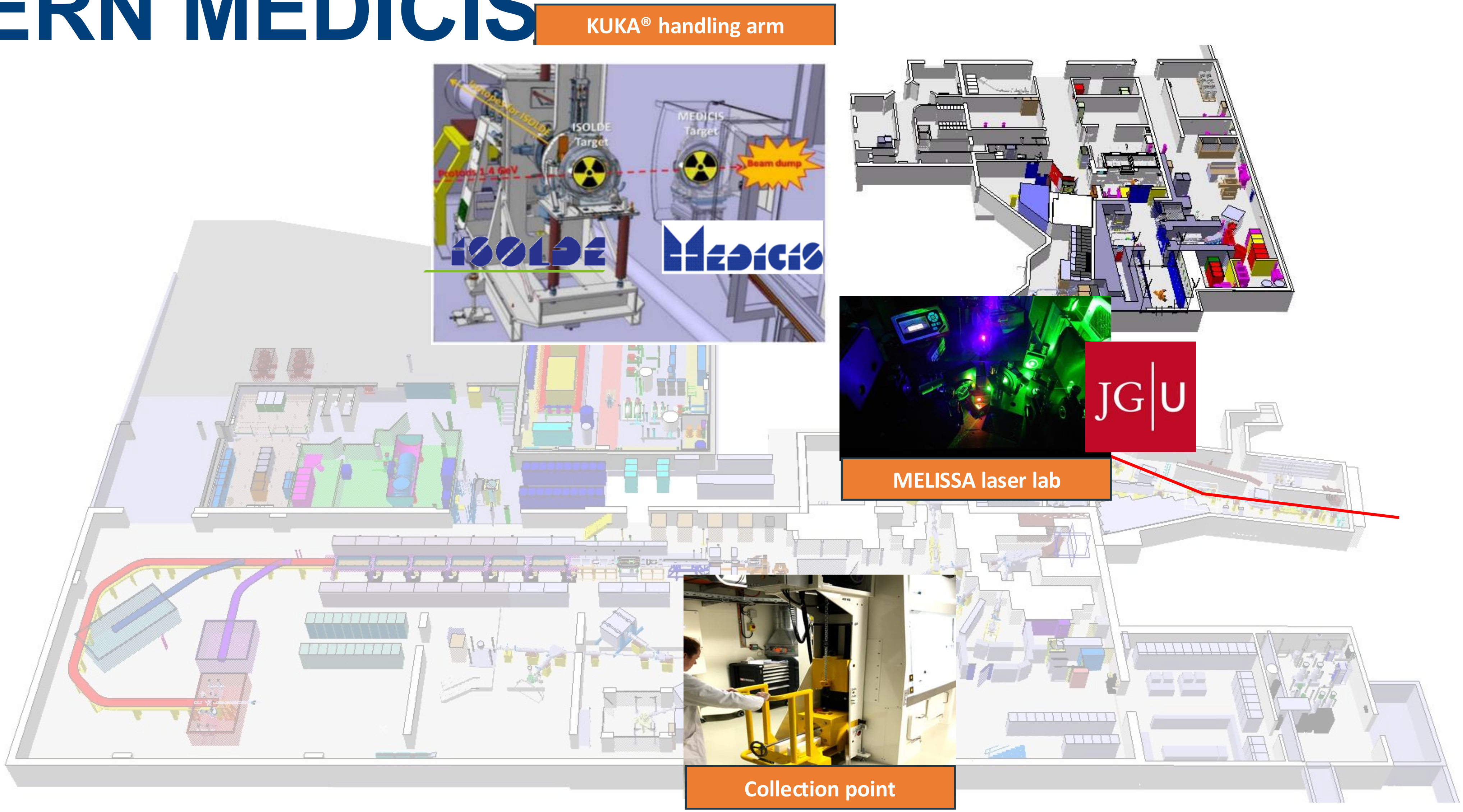
2023 ISOLDE beam allocation



https://isoyields2.web.cern.ch/IsoldeYieldChart.aspx



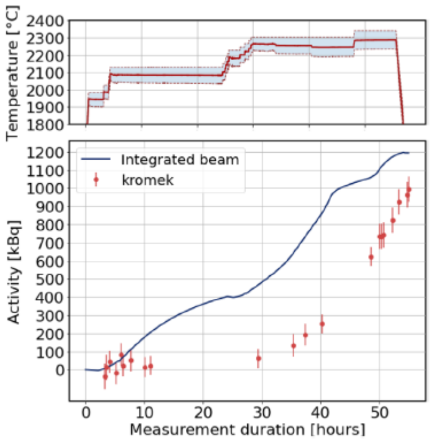
CERN MEDICIS

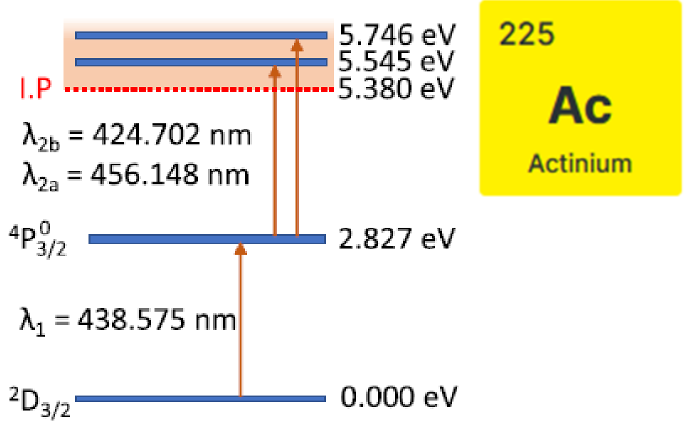


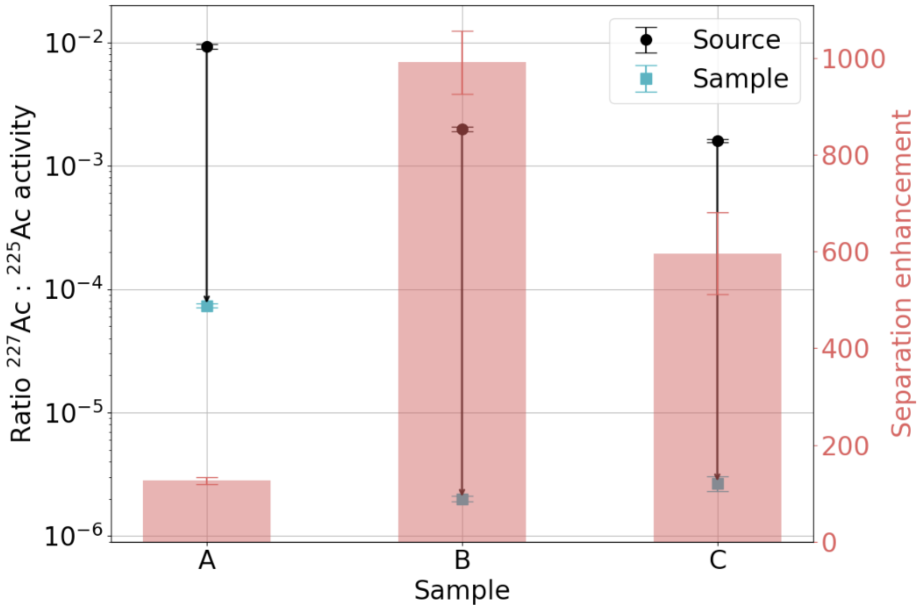
the collection of
edical research
s from CERN or
d sources

^{225}Ac production

- High-energy proton-induced spallation of ^{232}Th produces large amounts of ^{227}Ac.
- TRIUMF: ^{225}Ra generator by radiochemistry, limited production yields.
- MEDICIS: (laser +) mass separation.
- Highest achieved efficiencies are 75% on ^{225}Ra vs 1% on ^{225}Ac.
- Routine delivery of clinically relevant activities of ^{224,225}Ra (e.g., >100 MBq).

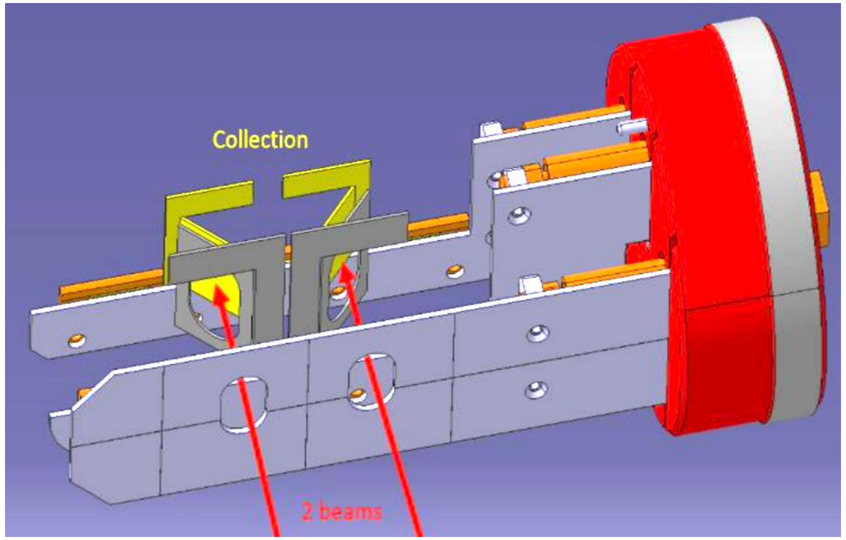




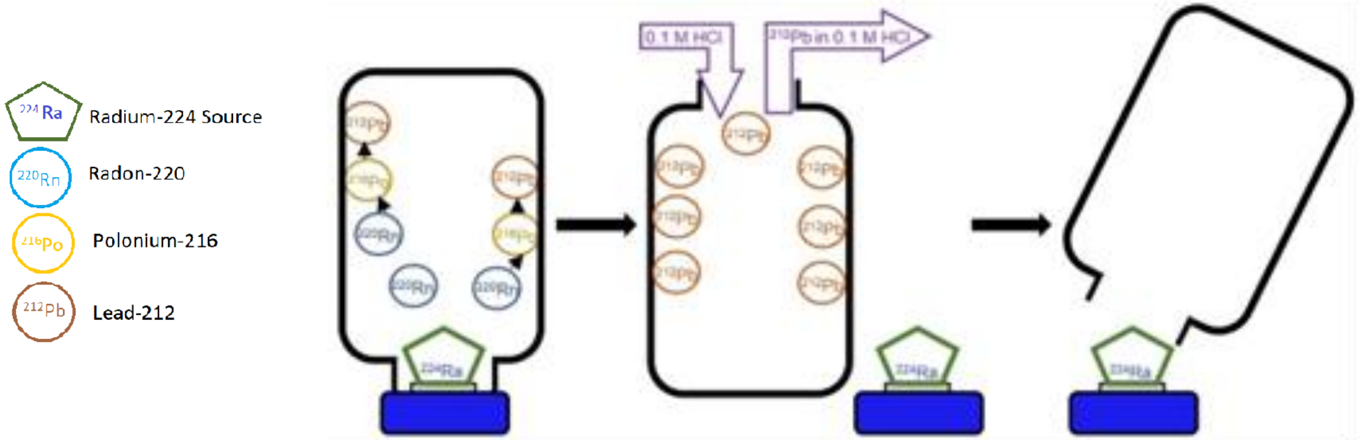


*J.D. Johnson et al, Resonant laser ionization and mass separation of ^{225}Ac, Scientific Reports **13** (2023) 1347.*
J.D. Johnson, PhD Thesis, KU Leuven (2024).

^{224}Ra: ^{212}Pb generator



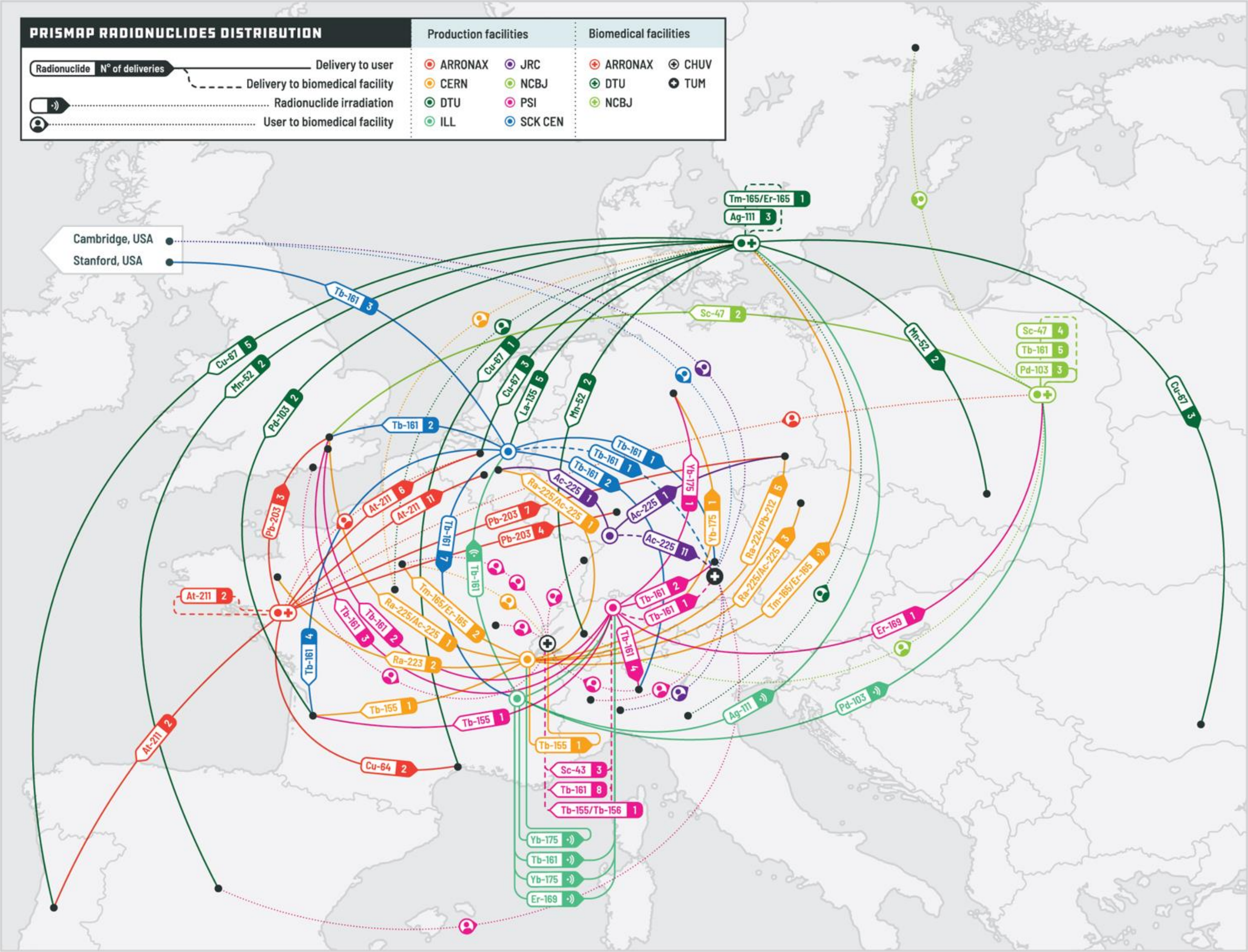
- Collections of ^{224}Ra next to ^{225}Ra with high purity.
- 100s MBq can be collected, making these relevant clinical quantities.
- ^{224}Ra is a generator for ^{212}Pb



Next step: clinical trial?

PRISMAP
The European Medical Radionuclide Programme

A European success story



 https://www.prismap.eu/

The PRISMAP infrastructure

MEDICIS
European organization for nuclear research - CERN

PSI
Paul Scherrer Institut – PSI

Hevesy Laboratory
Danmarks Tekniske Universitet – DTU

BR2
Belgian Nuclear Research Centre — SCK CEN

ARRONAX
Groupement interet public ARRONAX — ARRONAX

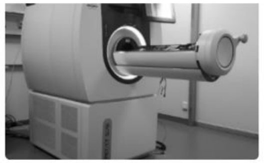
RHF
Institut Max von Laue - Paul Langevin – ILL

JRC Karlsruhe
Joint Research Centre - European Commission – JRC

NCBJ
Narodowe Centrum Badań Jądrowych — NCBJ

Hevesy Laboratory
Danmarks Tekniske Universitet – DTU

AGORA
Centre hospitalier universitaire vaudois — CHUV



NURA
Studiecentrum voor Kernenergie / Centre d'étude de l'énergie nucleaire — SCK CEN

Nuklearmedizin
Klinikum rechts der Isar der Technischen Universität München — TUM

POLATOM
Narodowe Centrum Badań Jądrowych – NCBJ

- 4 **neutron irradiation facilities**, including 3 research reactors and a spallation source.
- 5 **accelerators** delivering protons with energy ranging from 18 MeV to 1.4 GeV.
- 2 accelerators delivering other particles (**deuteron**, **alpha**) at medium energy (K30 & K70).
- **1 mass separator.**
- Access to the ^{229}**Th generator** for $^{225}Ac/^{213}Bi$ supply from JRC Karlsruhe.
- 5 **biomedical research facilities** bound to production centers (x3) or embedded within university hospitals (x2).
- **Regional clusters** for access to short-lived radionuclides.

https://www.prismap.eu/radionuclides/production-facilities/
https://www.prismap.eu/radionuclides/medical-facilities/

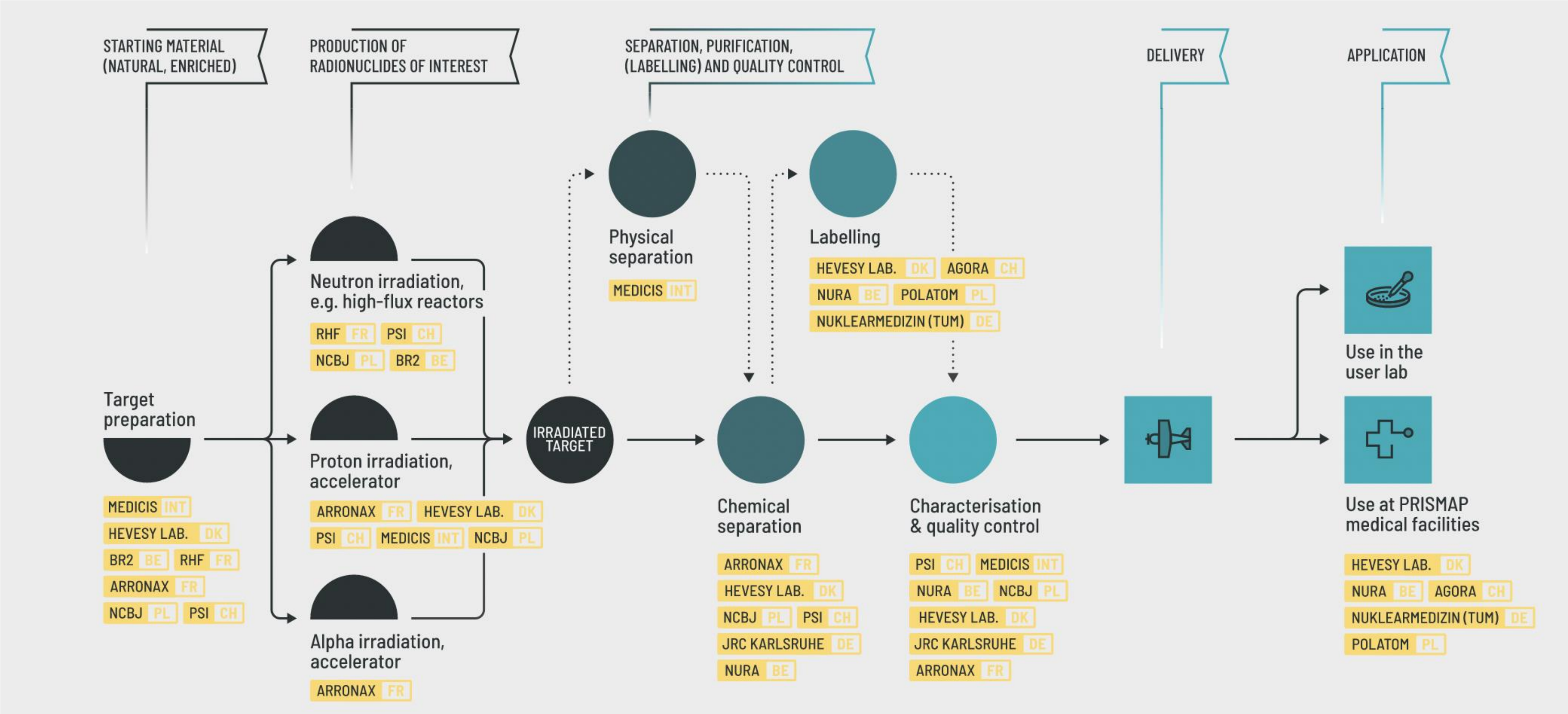
The PRISMAP portfolio

Suggest!

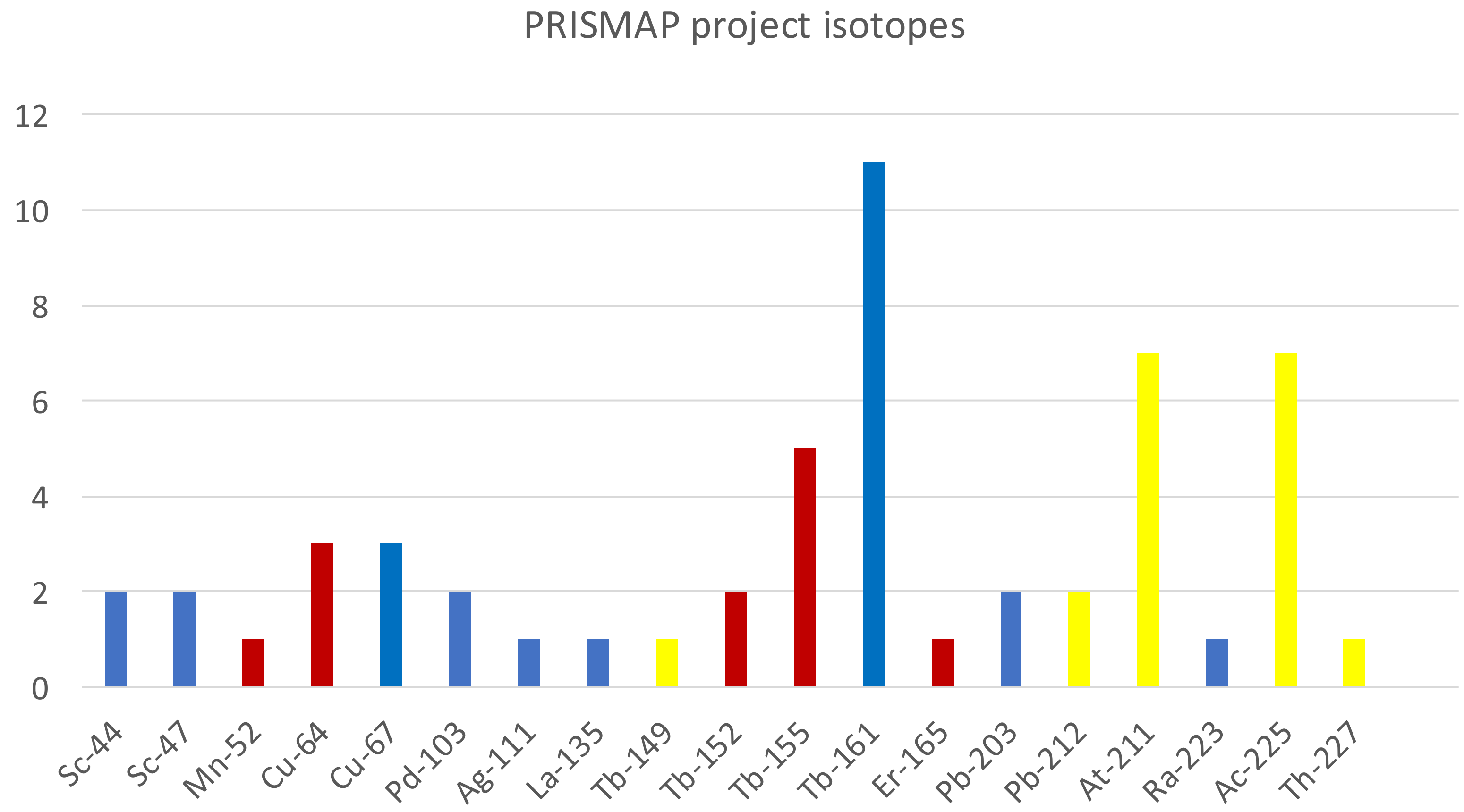
43 Sc Scandium	44 Sc Scandium	47 Sc Scandium	52 Mn Manganese	64 Cu Copper	67 Cu Copper	103 Pd Palladium
111 Ag Silver	128 Ba Barium	128 Cs Caesium	135 La Lanthanum	153 Sm Samarium	149 Tb Terbium	152 Tb Terbium
155 Tb Terbium	161 Tb Terbium	165 Tm Thulium	165 Er Erbium	169 Er Erbium	175 Yb Ytterbium	199 Au Gold
203 Pb Lead	211 At Astatine	213 Bi Bismuth	223 Ra Radium	224 Ra Radium	225 Ac Actinium	

- 28 radionuclides offered on our portfolio.
- Covering SPECT and PET imaging, and beta, alpha, and Auger therapy radionuclides.
  - Many offer theranostic sets while others may be combined for novel theranostics approach (e.g., ^{135}La/^{225}Ac).
  - Some are uniquely available through our infrastructure, in particular those requiring mass separation of the radionuclides (^{128}Ba, ^{149,152,155}Tb, ^{165}Tm, ^{169}Er, ^{175}Yb).
  - We are open to your suggestion. Let us know!

PRISMAP: the supply chain



Est. 2021



- 5 calls
- 45 projects approved
  5 projects completed
- > 60 deliveries
- 21 radionuclides from our portfolio
- Covering all stages of development:
  - new generator concepts
  - radiochemical investigations
  - radiopharmaceutical synthesis
  - radiobiology
  - in vitro & in vivo pre-clinical
- 2 projects already published and 10 having reported at international conferences.
- 2 returning users.
- 2 projects moving for clinical proof of concept.

Transport highlight: door to door in 4.25 h

Transporting ^{165}Tm from CERN to DTU
$T_{1/2}$=1.25 day

Expected departure: Friday morning

Classic transport: held at CDG until next flight Monday morning.
Projected delivery time: 3.2 days ➔ 83% loss

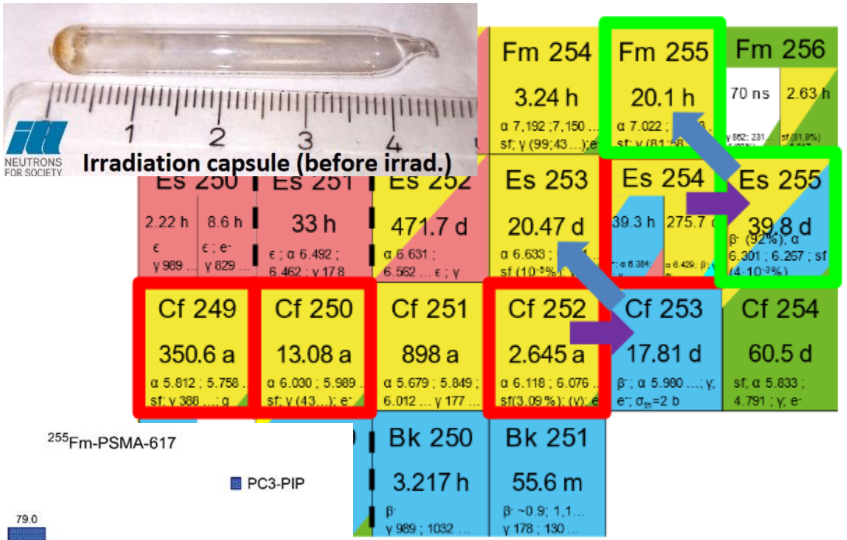
Charter flight: car-flight-car, delivered on Friday before end of day, in 4.25 hours.

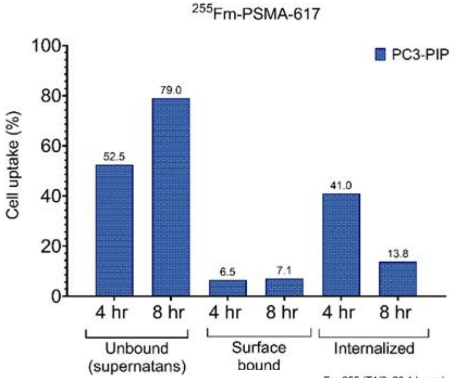
Price x5, for time /17.

WORLD INFINITY SERVICES

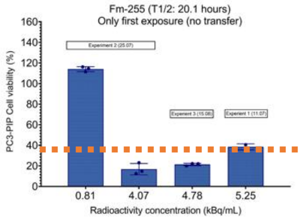
Beyond supply: proof of principle

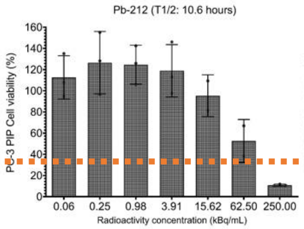
Fm 255
20.1 h
α 7.022; 6.963...
sf
γ (81, 58...), e⁻

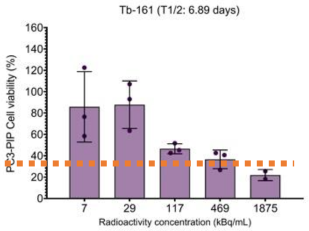




- Single alpha decay allows to compare with ^{225}Ac in terms of both efficacy and citotoxicity.
- Produced ^{255}Es at ILL from pre-irradiated sample from ORNL, in similar way as other medical radionuclides generators.
- Radiochemistry processing at JGU Mainz.
- First proof of principle in vitro at GSI with PSMA-617.
  - ➢ Uptake comparable to ^{161}Tb and ^{177}Lu
  - ➢ Cell viability compared against ^{212}Pb and ^{177}Lu







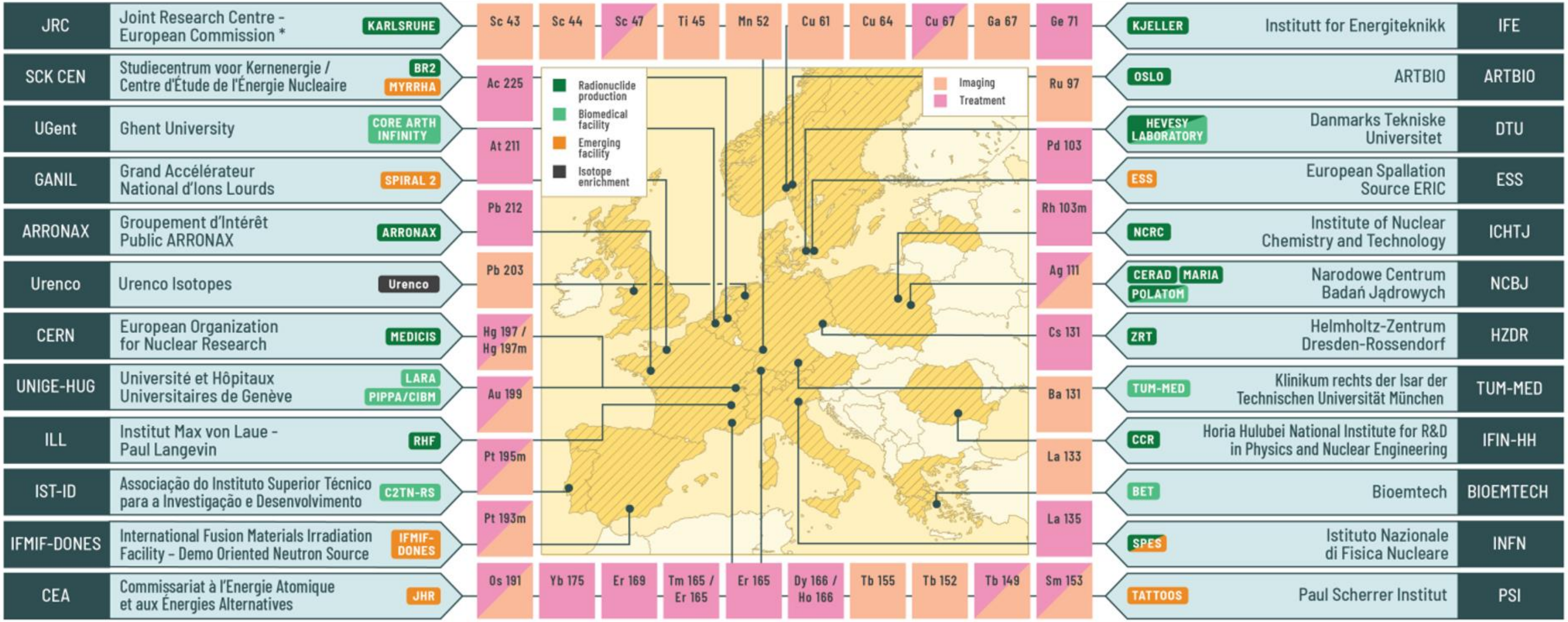
Production illustrations courtesy Ulli Köster (ILL).
Pre-clinical work by C. Vandevoorde & P. Riß (GSI).

PRISMAP+
Furthering the European Medical Radionuclide Programme

PRISMAP+
Medical-Radionuclides.eu

KU LEUVEN

PRISMAP+



https://www.medical-radionuclides.eu/

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Noticed what is missing?

On 14 June 2023, the Dutch company TERTHERA signed an agreement with the Belgian Nuclear Research Center SCK CEN operating the BR2 reactor, about the industrial supply of ^{161}Tb.

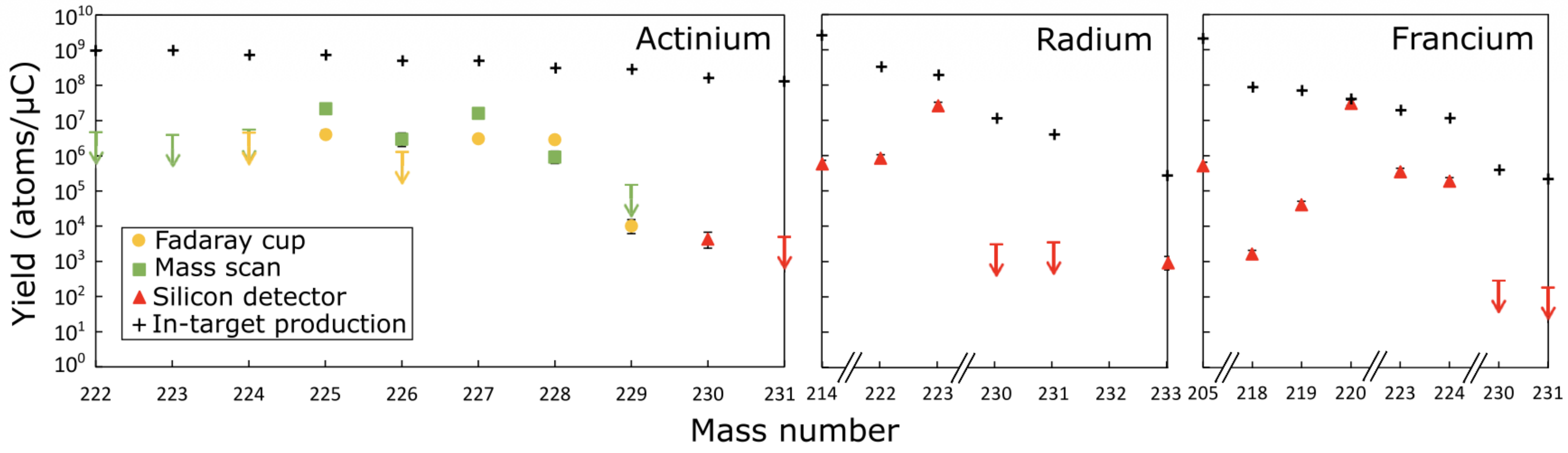
Having made it from 'emerging radionuclide' to industrially supplied, it is no longer part of the PRISMAP+ portfolio and can be purchased just like any other radionuclide for medical application.

Many clinical trials are currently starting with that isotope, with evidence in many cases of its superiority to ^{177}Lu.

Note in passing: enriched ^{161}Gd and ^{176}Yb are key to producing 161Tb and 177Lu, and Russia is the only supplier…

Nuclear data

Cross sections: for spallation of U



A systematic study of the yields of Fr, Ra and Ac was performed at ISOLDE, highlighting the difficulty in extracting Ac (eff~1.5%) compared to radium (eff~50%) or francium (eff~100%).

 E. Jajčišinová et al., Scientific Reports ***14*** *(2024) 11033.*

Cross sections: for spallation of Ta

A systematic study of the cross section of the spallation of Ta was performed at COSY in Jülich to determine the best condition for the production of the Tb radionuclides.

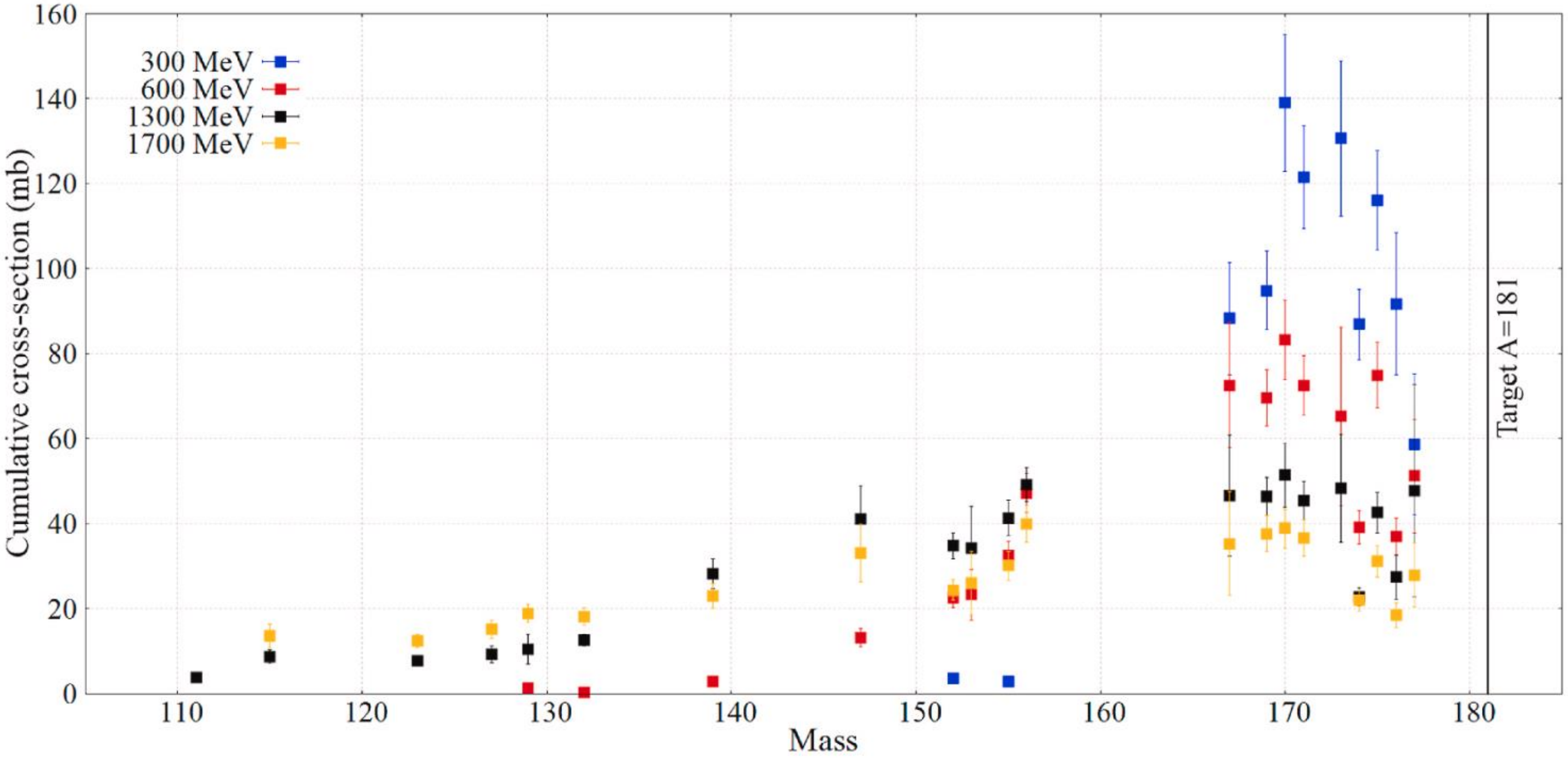


Fig. 7. Cumulative cross-sections for the last radionuclide of the decay chain as a function of mass and beam energy.

 C. Duchemin et al., *Applied Radiation and Isotopes* ***178*** *(2021) 109983.*

Cross sections: for spallation of Ta

This revealed the excitation function for all 3 radionuclides of interest as well as for the possible contaminants, suggesting that the optimal operation energy is at ~600-800 MeV → Perfect for the new ISOL@MYRRHA facility!

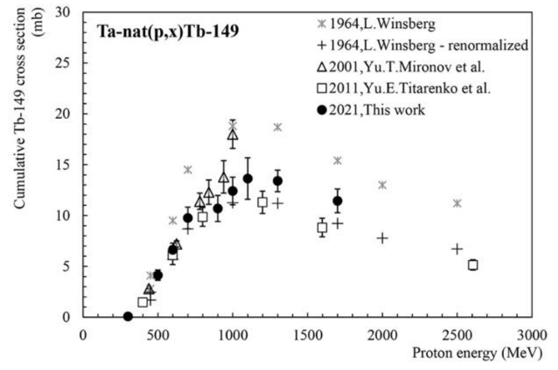


FIGURE 3 | Cumulative cross-section for Tb-149 production as a function of the proton beam energy.

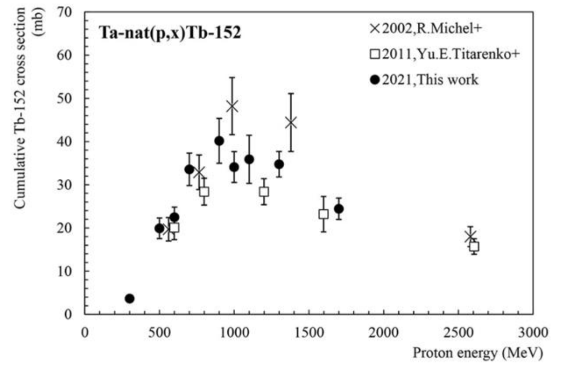


FIGURE 4 | Cumulative cross-section for Tb-152 production as a function of the proton beam energy.

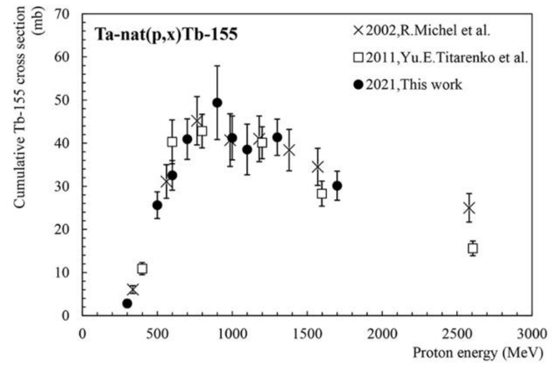


FIGURE 5 | Cumulative cross-section for Tb-155 production as a function of the proton beam energy.

C. Duchemin et al., Frontiers in Medicine ***8*** *(2021) 625561.*

Cross sections: for spallation of Ta

It also indicated that most of the Tb is produced as decay product of other radionuclides and is not direct.

Moreover, Tb is known to be difficult to extract from Ta and this is why Dy beams are a much better approach in the online extraction of ^{149}Tb.

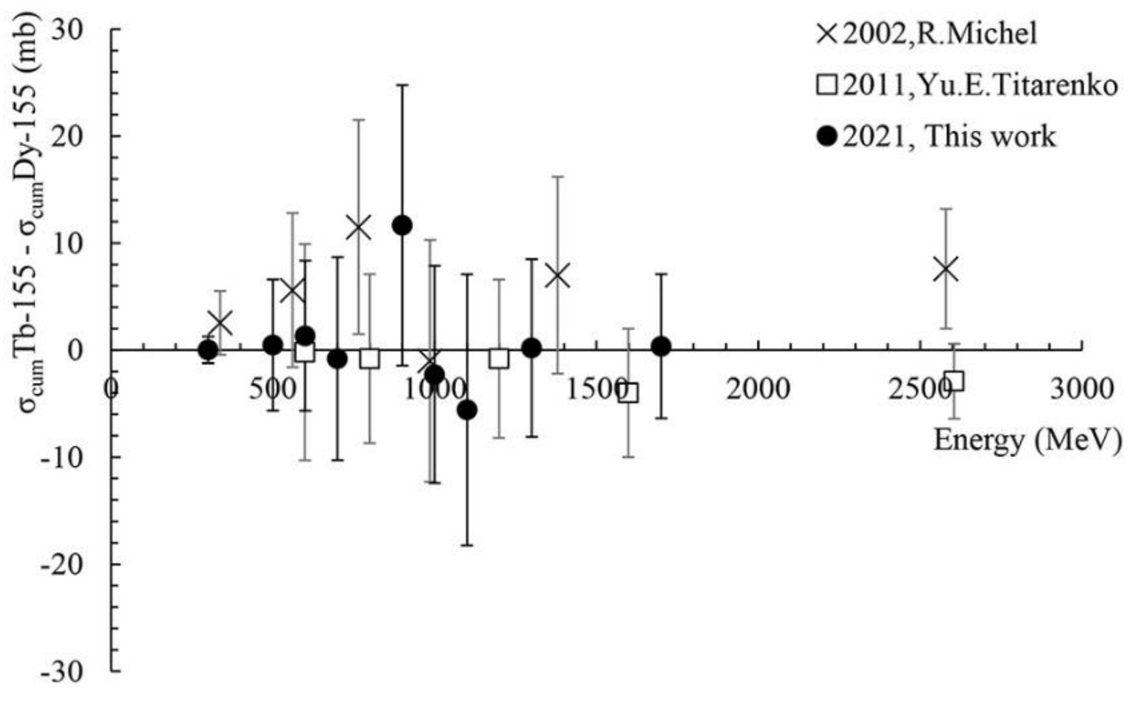


FIGURE 7 | Difference [$\sigma_{Cum.}$Tb-155–$\sigma_{Cum.}$Dy-155] based on the cross-section data measured in "This work (2021)" and the ones available in the literature.

C. Duchemin et al., Frontiers in Medicine ***8*** *(2021) 625561.*

Cross sections: Tb from fusion evap.

For scaling up, producing Tb directly from nearby targets with fusion evaporation is much more appealing than spallation of Ta.

Multiple approaches have been considered based on Gd targets, whether natural or enriched, and excitation function measurements are still ongoing to determine the achievable yields and best conditions.

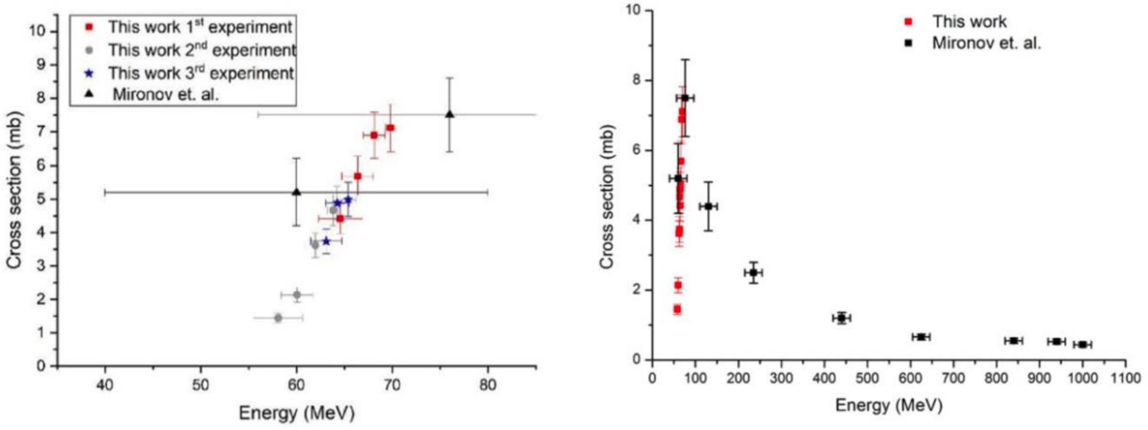
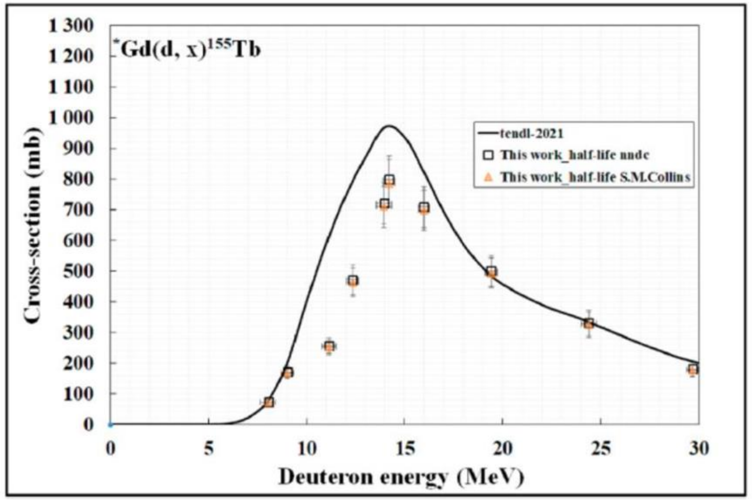
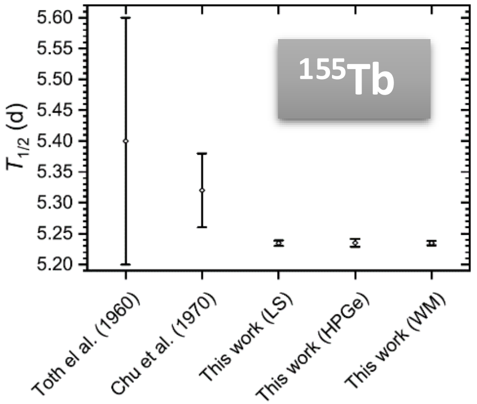


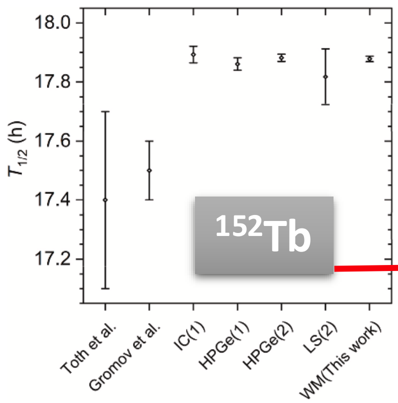
Figure 3. Gd-154(p,6n) Tb-149 cross section values measured by ARRONAX group compared to existing data

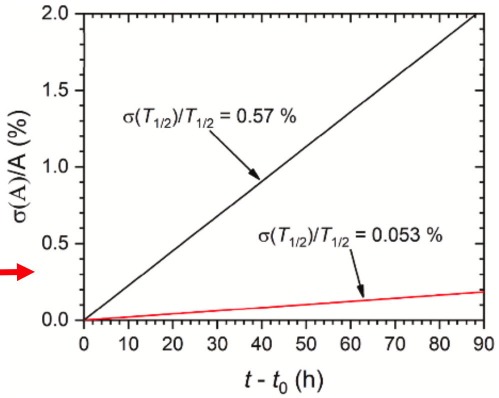


F. Haddad et al., PRISMAP deliverable D12.1.
https://www.prismap.eu/about/outcomes/

Tb standardisation

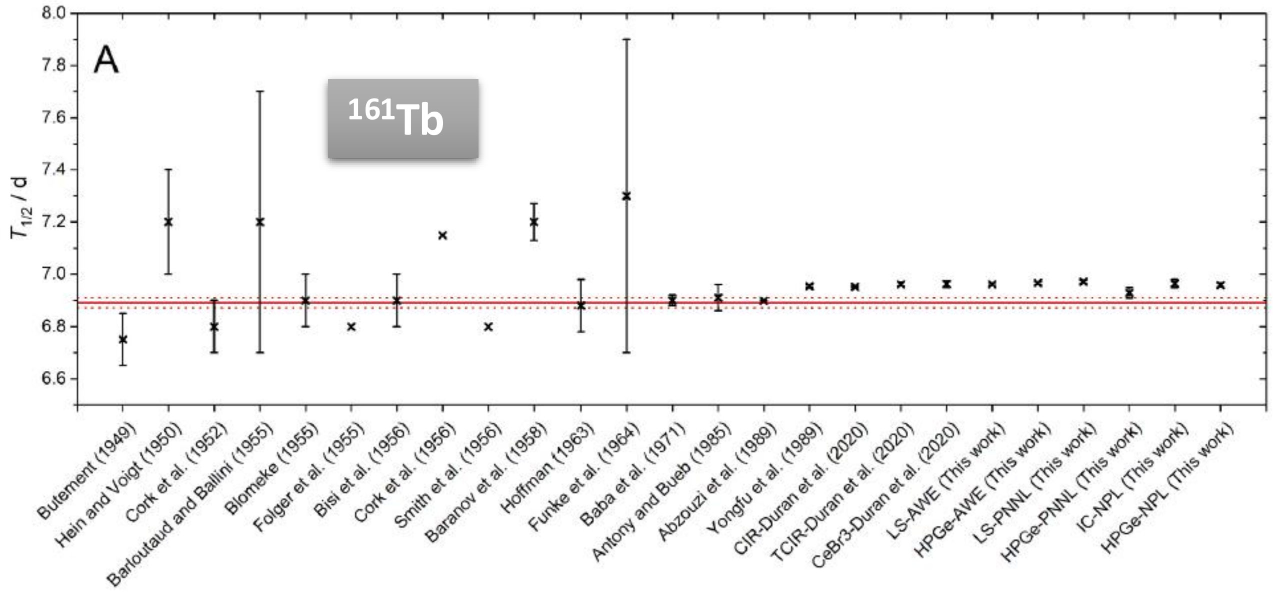






149Tb

Radionuclide	Recommended T1/2 (days)	PRISMAP T1/2 (days)
Tb-149	4.12(3)	4.1618(52)
Gd-149	9.28(10)	9.273(10)
Eu-145	5.93(4)	5.9193(43)



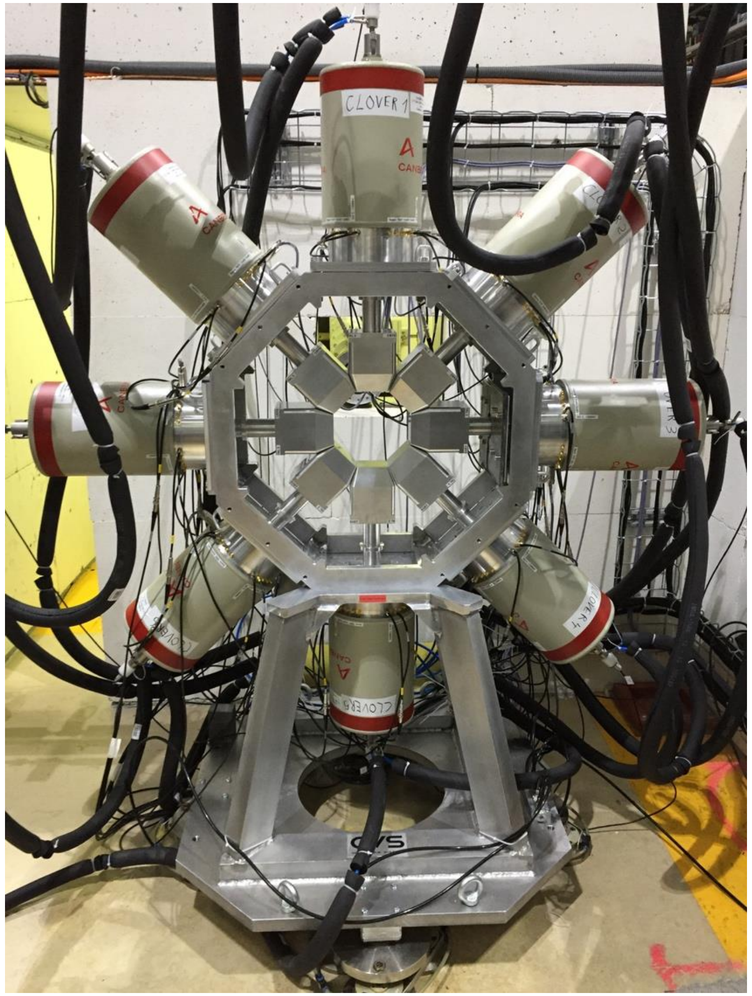
- Many of those isotopes were studied in the early days of radioisotopes synthesis (1950-1970) and the accuracy on their nuclear data is questionable.

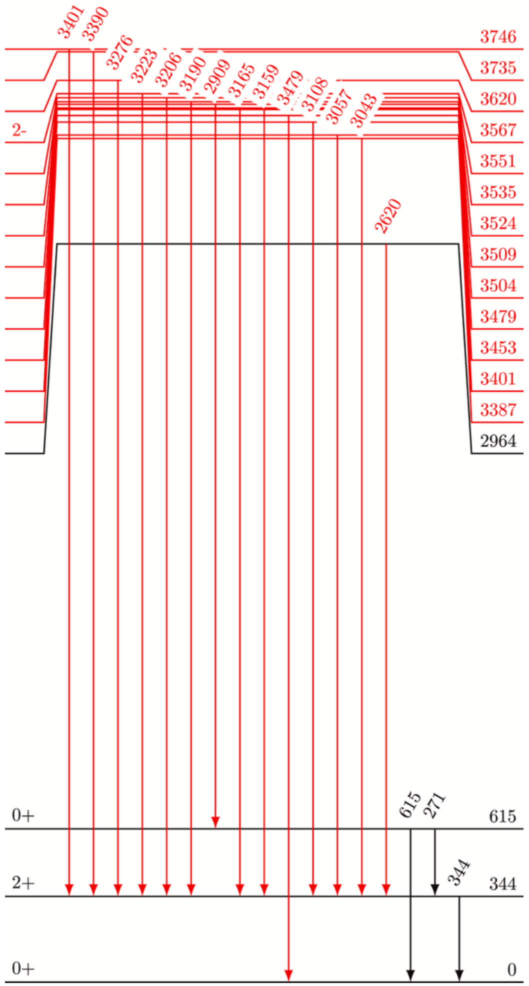
S.M. Collins et al., *Applied Radiation and Isotopes* **182** (2022) 110140.
S.M. Collins et al., *Applied Radiation and Isotopes* **190** (2022) 110480.
S.M. Collins et al., *Applied Radiation and Isotopes* **202** (2023) 111044.

^{152}Tb decay at FIPPS

A sample of ^{152}Tb was produced at CERN and brough to ILL where it was investigated by FIPPS.

Many previously unknown high-energy transitions were identified.





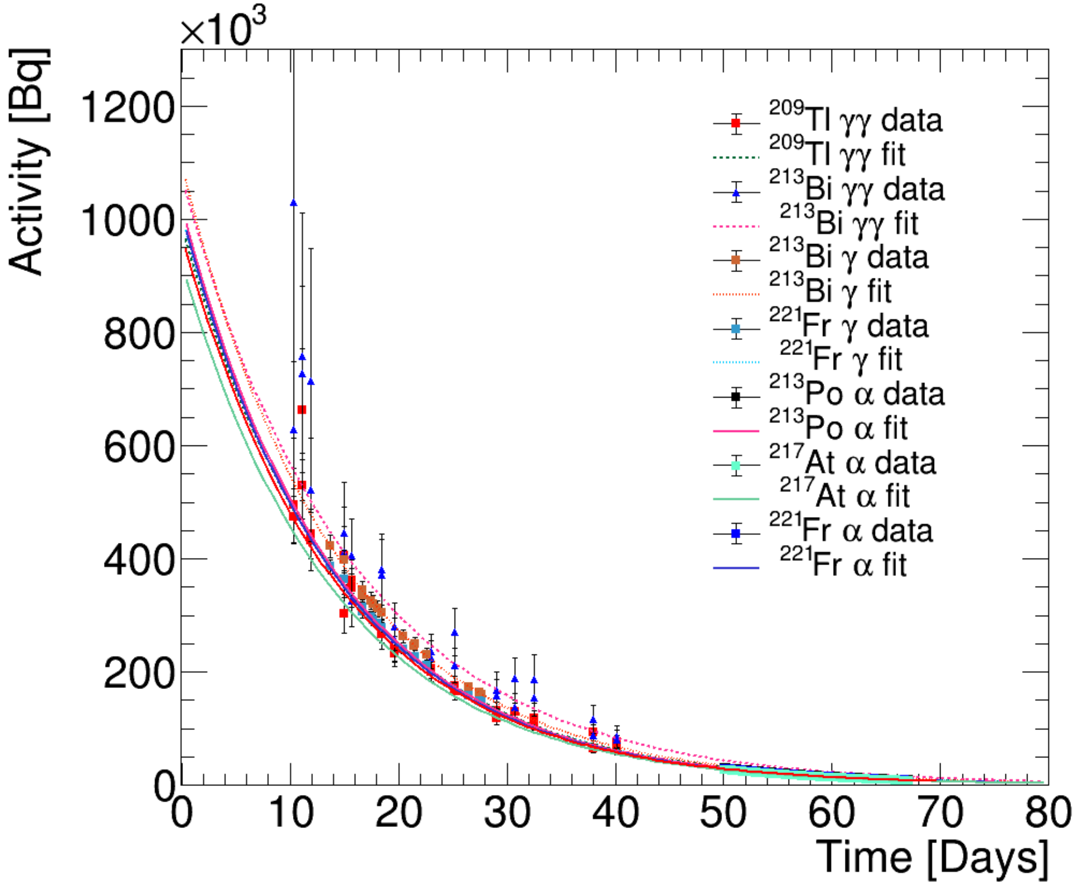
E.B. O'Sullivan et al., Radiation Physics and Chemistry ***232*** *(2025) 112641.*

Ac-225 decay cunundrum

A sample produced at CERN MEDICIS was analysed through multiple ways:

- Single γ-ray spectroscopy of ^{221}Fr at CERN
- Single γ-ray spectroscopy of ^{221}Fr and ^{213}Bi at KU Leuven
- Coincidence γγ spectroscopy fo ^{213}Bi and ^{209}Tl at KU Leuven
- Alpha-decay spectroscopy all along the chain at KU Leuven

No two results agreed!



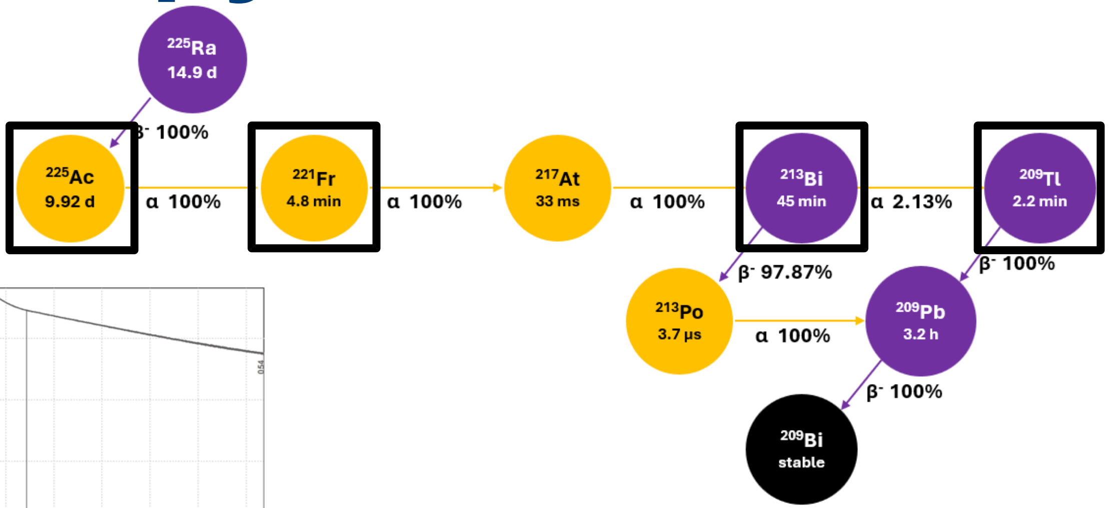
J.D. Johnson et al., Scientific Reports ***13*** *(2023) 1347*

IS741: decay spectroscopy of ^{225}Ac

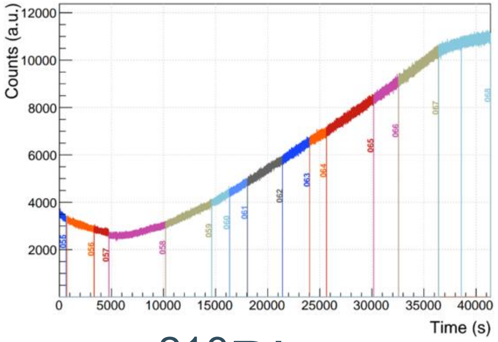
Main issue with historical studies of those isotopes: they were always investigated in equilibrium across the whole chain, most of the time also including ^{229}Th and ^{225}Ra.

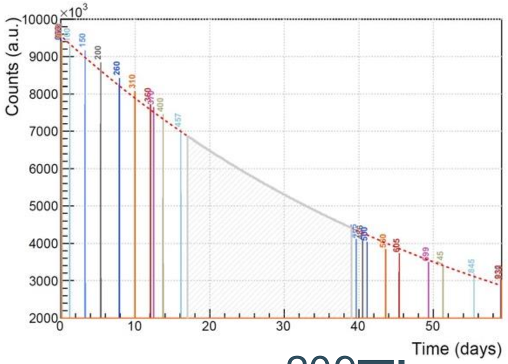
At CERN ISOLDE, it is possible to produce and study clean beams of ^{225}Ra, ^{221}Fr, ^{213}Bi and ^{209}Tl with the ISOLDE Decay Station.

IS741: decay spectroscopy of ^{225}Ac

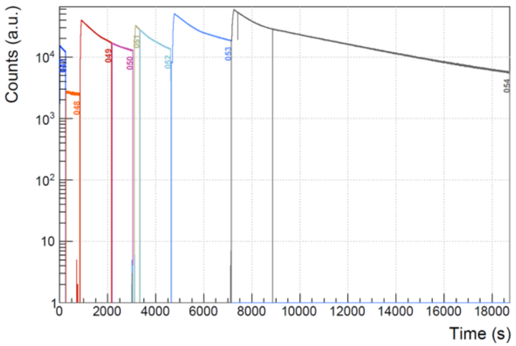


^{225}Ac

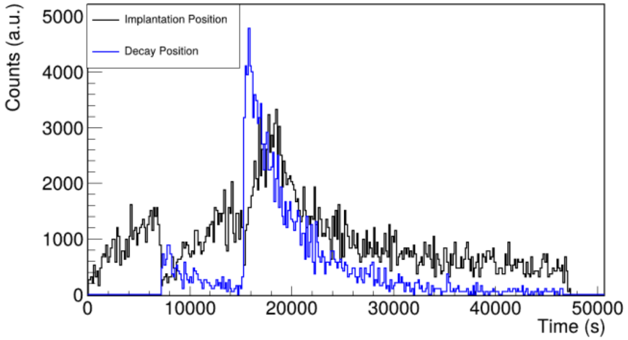




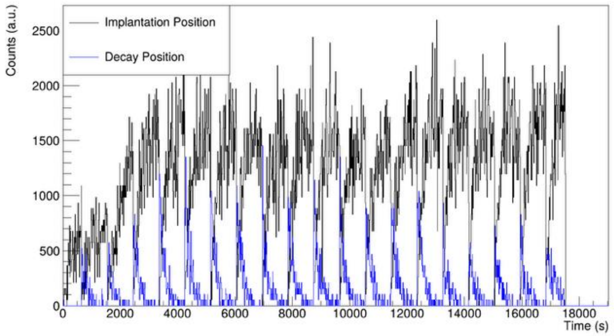
^{221}Fr



^{213}Bi



^{209}Tl



Many huge data sets have been collected over two campaigns, including 2 months of data on ^{225}Ac.

- **The Nuclear Science community has a lot to offer in support of the development of nuclear medicine.**
- We need to **leverage our facilities** to support medical research into innovative medical radionuclides by providing them regularly and reliably until it is picked up by industry.
- Our knowledge of **nuclear data** is still insufficient for medical applications.
- Many **cross sections** remain of interest to identify the best production pathways for scaled-up production of promising radionuclides.
- **Decay data** of many radionuclides of interest are insufficient precise and often inaccurate, requiring a thorough, metrology-level analysis.

Thinking points for the tutorials

- How are ^{177}Lu and ^{161}Gd produced and what are the key questions to ensure the quality of the product.

- How much can we trust the historical data from the 1960s-1970s? What should be done about that?

Kennis kent geen einde

KU LEUVEN

Knowledge knows no end