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NUCLEAR AND RADIATION PHYSICS

Novel radioisotopes for medical applications: the CERN MEDICIS project and beyond

Prof Thomas Elias Cocolios

KU Leuven Institute for Nuclear & Radiation Physics

59th International Winter Meeting on Nuclear Physics – Bormio – 25 Jan 2023

Overview

- Nuclear medicine from a nuclear physicist’s perspective
- Why so few radionuclides?
- A new supply chain via mass separation: CERN MEDICIS
- PRISMAP – The European Medical Radionuclide Programme

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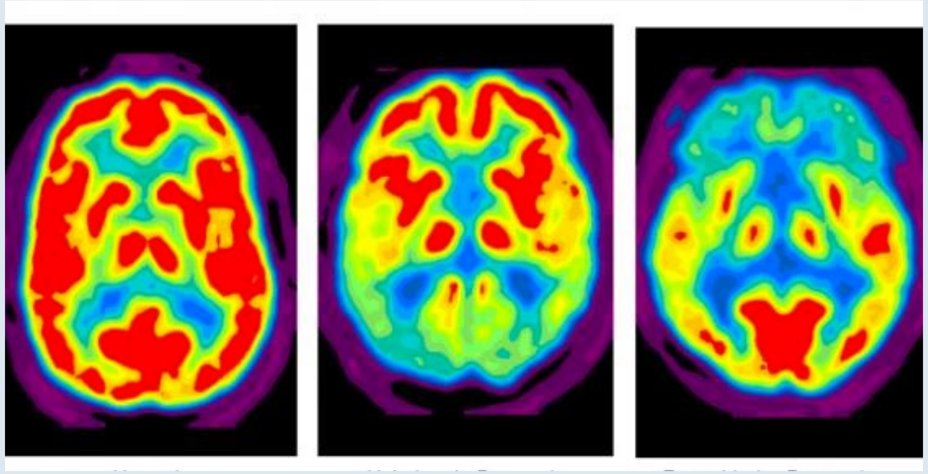
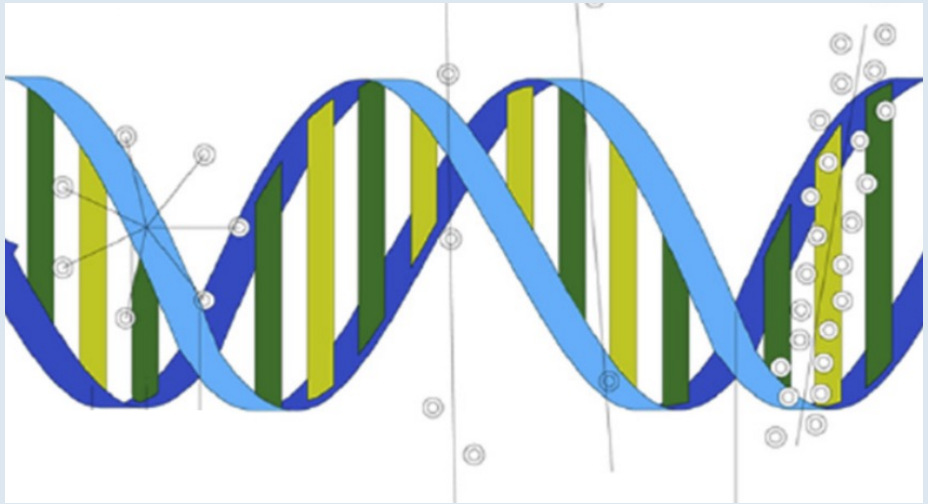
Nuclear medicine

Some very basic concepts





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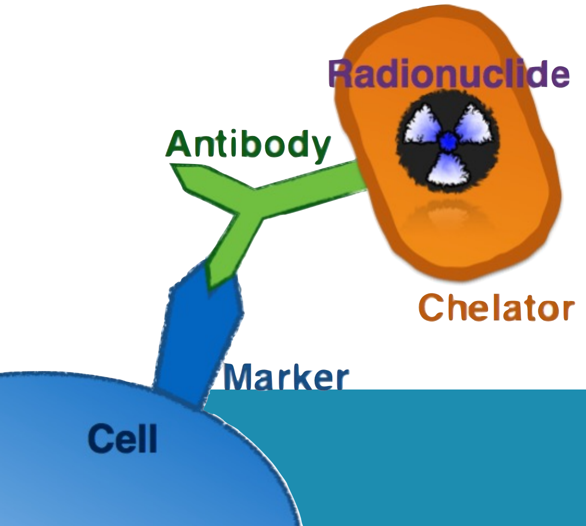
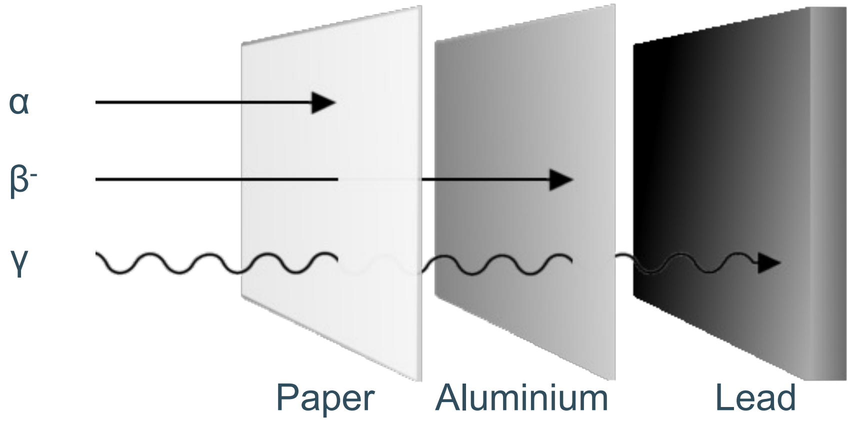
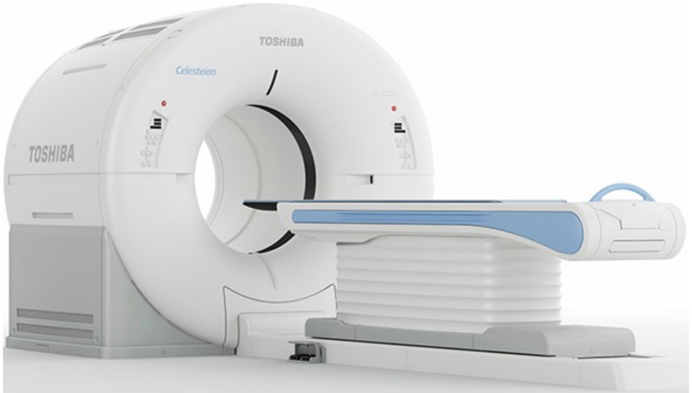
Molecular imaging

- A radionuclide is transported to a specific location in the body where it decays with the emission of a γ ray.
- The γ ray penetrates the tissues and exits the body so that it may be recorded externally to visualize where it decayed.
- Multiple orientations yield a 3D tomographic reconstruction of the image.



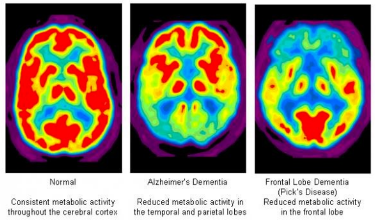




Targeted action

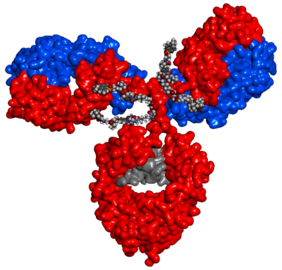
The body uses some trace elements for specific actions:

- iodine for thyroid functions
- calcium in the bones



A radioactive isotope can be included in a molecule involved in metabolic activities:

- sugar-equivalent FDG



Cells may display receptors that are specific and can be linked to by targ

- peptides
- hormones
- antibodies

Important to match biodistribution to half-life!

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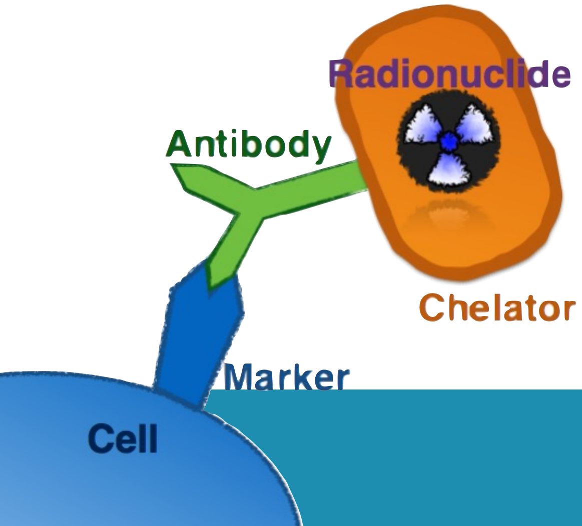
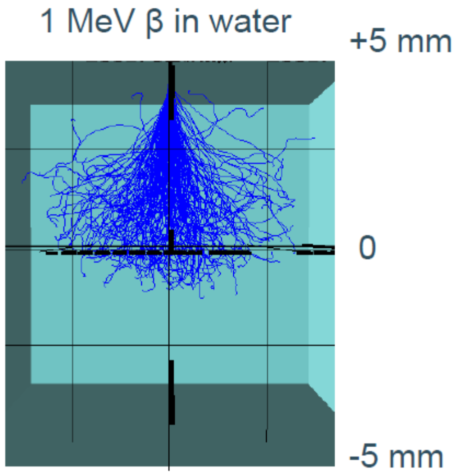
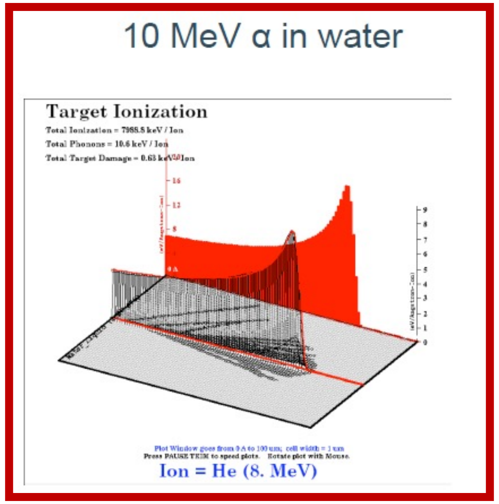
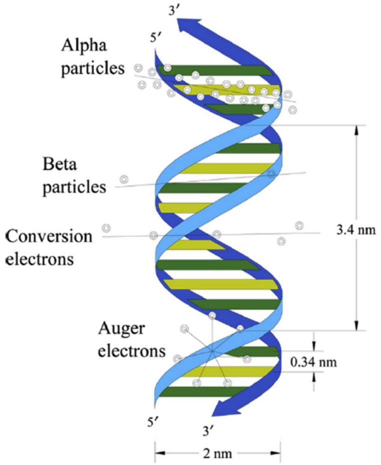
Switching to therapy

- Replacing the γ-ray emission with charged particle emission yields therapeutic effect.
- β^- particles may reach up to a few mm, α particles reach but a few cells, Auger electrons act within a cell.
- For an efficient treatment, the DNA of the targeted cell must be damaged beyond repair









Theranostics

- If a single vector molecule can be identified with interchangeable radioisotopes, then its efficacy and properties can be **tested with molecular imaging** and then **applied with therapy**.
- If a single radioisotope decays by both γ-ray or β^+ emission and α or β^- emission, then that single radioisotope can be used to **treat** and at the same time **monitor the patient dose** and the treatment's efficacy.

Important to match biodistribution to half-life!

Final aim: personalized medicine where the treatment is tailored to the needs of the patient

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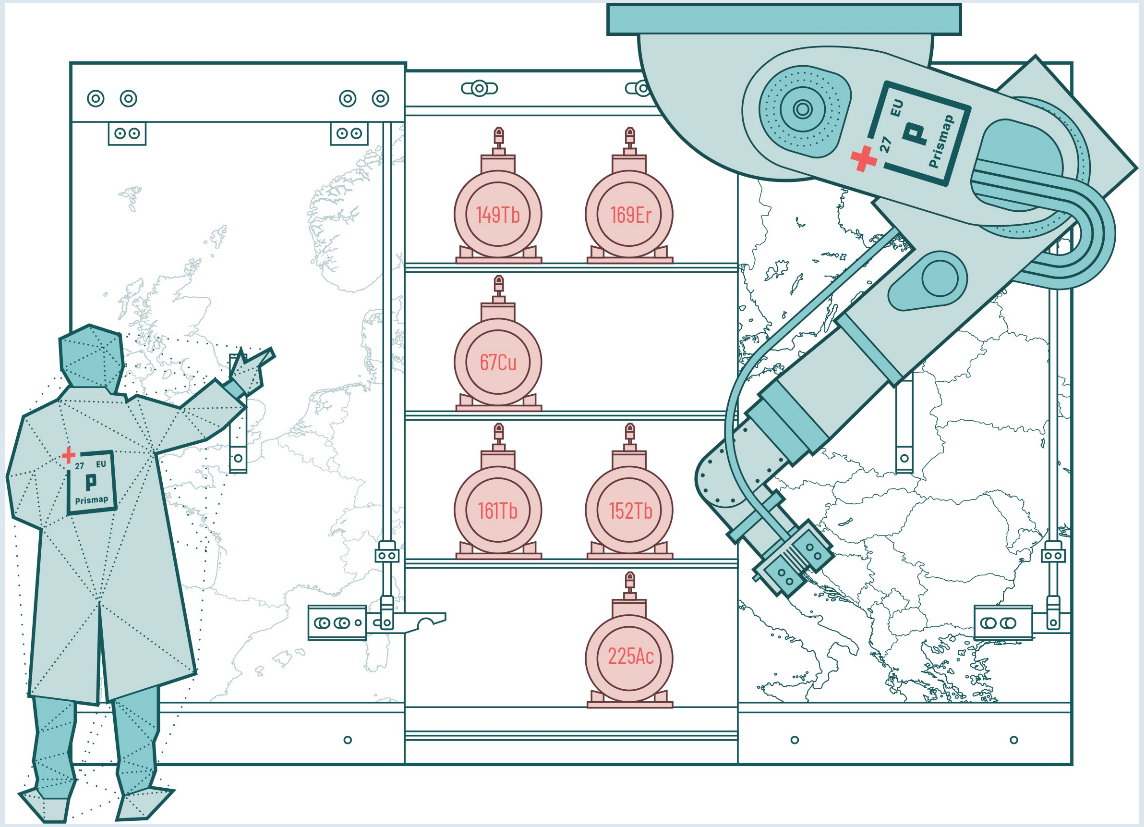
Key challenge: supply

What is used vs what could be used…



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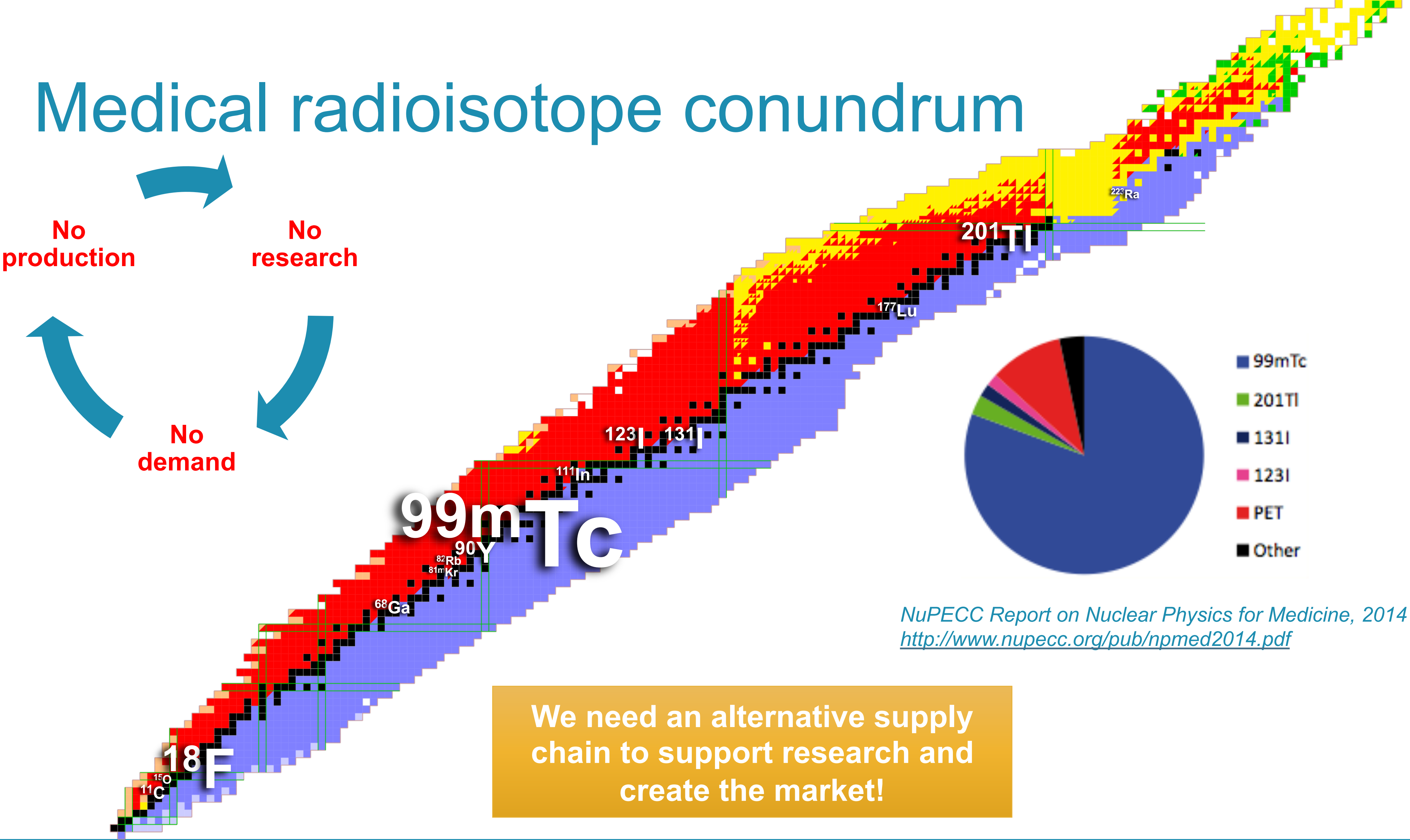
Medical radioisotope conundrum



NuPECC Report on Nuclear Physics for Medicine, 2014
http://www.nupecc.org/pub/npmed2014.pdf

We need an alternative supply chain to support research and create the market!

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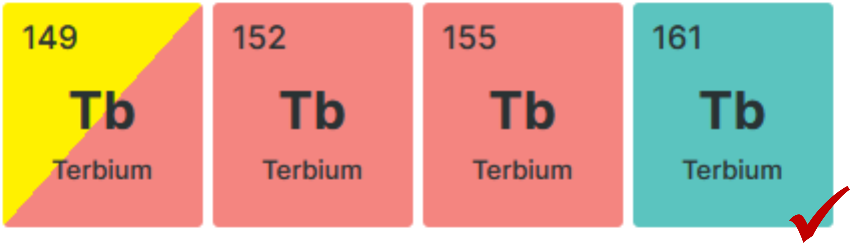
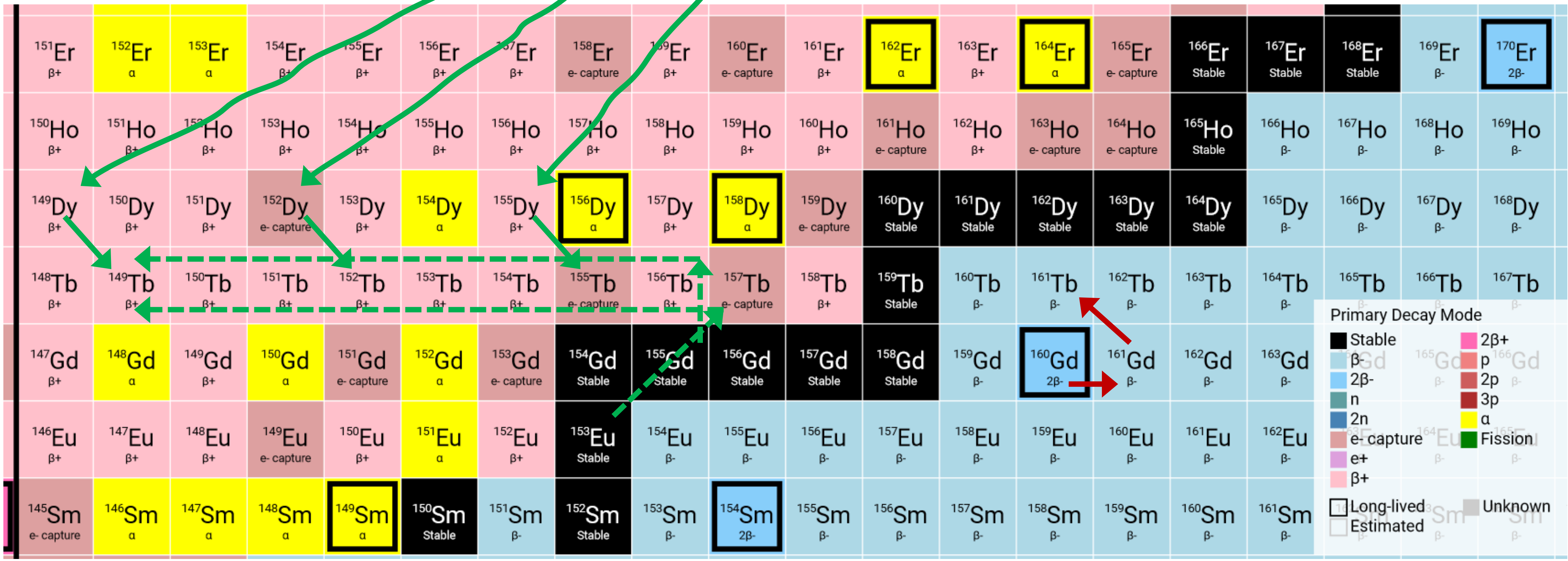
Producing the Tb isotopes





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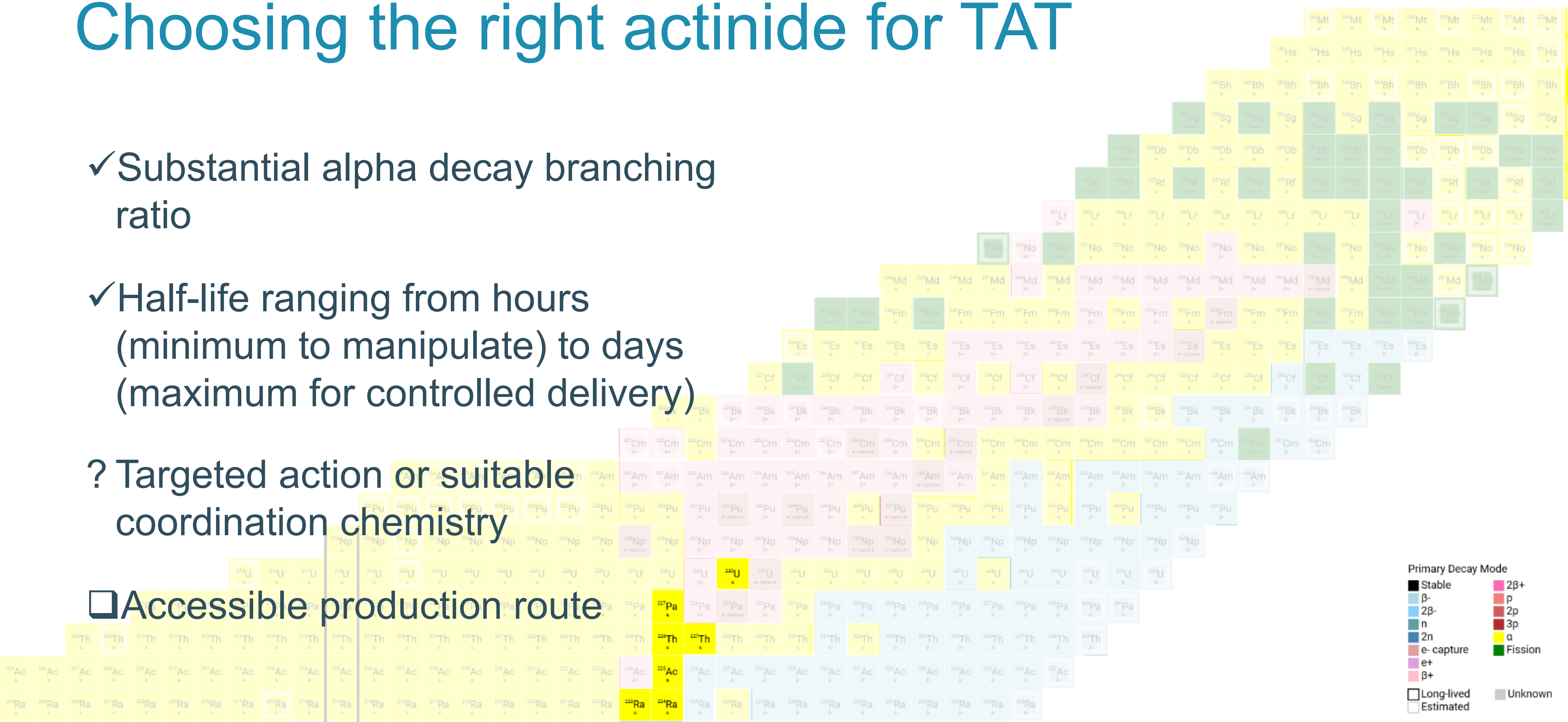
Choosing the right actinide for TAT

✓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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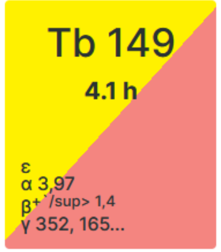
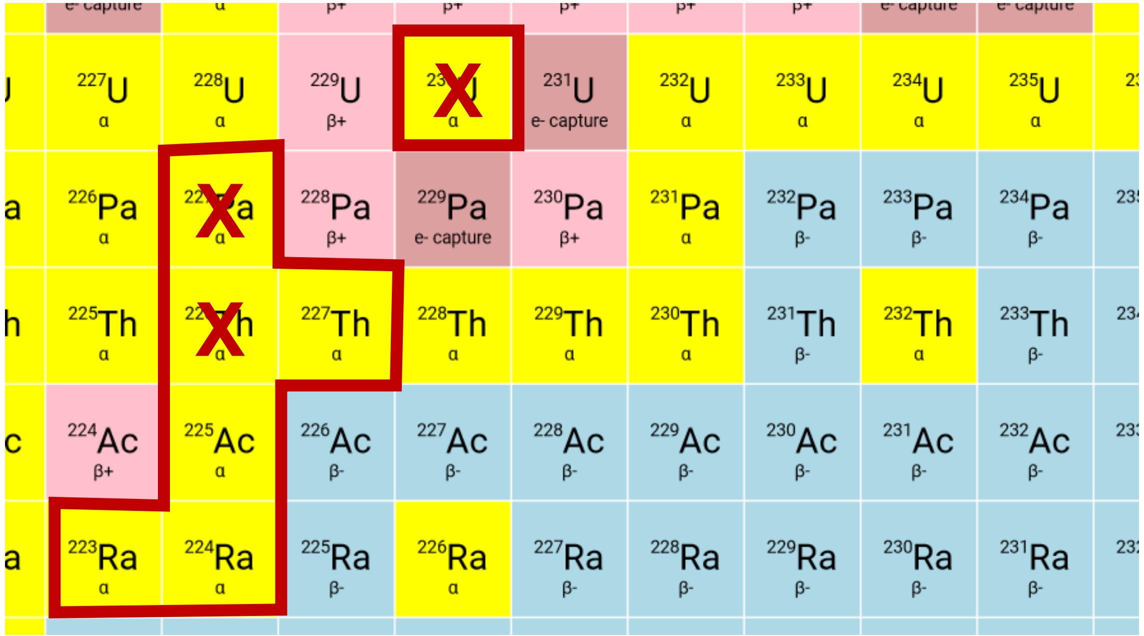
Isotopes effectively used



- ✓ ^{223,224}Ra
  - ✓ Xofigo® for the treatment of bone metastasis in castration resistant prostate cancer
  - 102+17 clinical trials
- ✓ ^{225}Ac
  - 14 clinical trials
  - Mostly about prostate cancer
- ✓ ^{227}Th
  - 4 clinical trials



https://clinicaltrials.gov

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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

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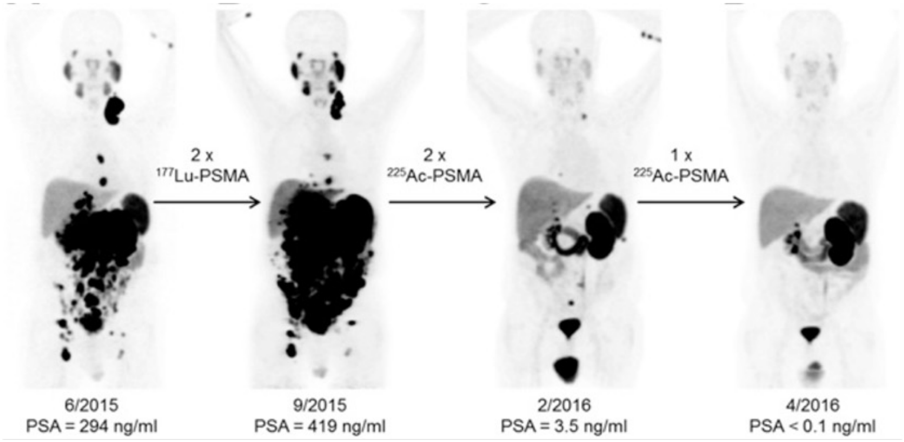
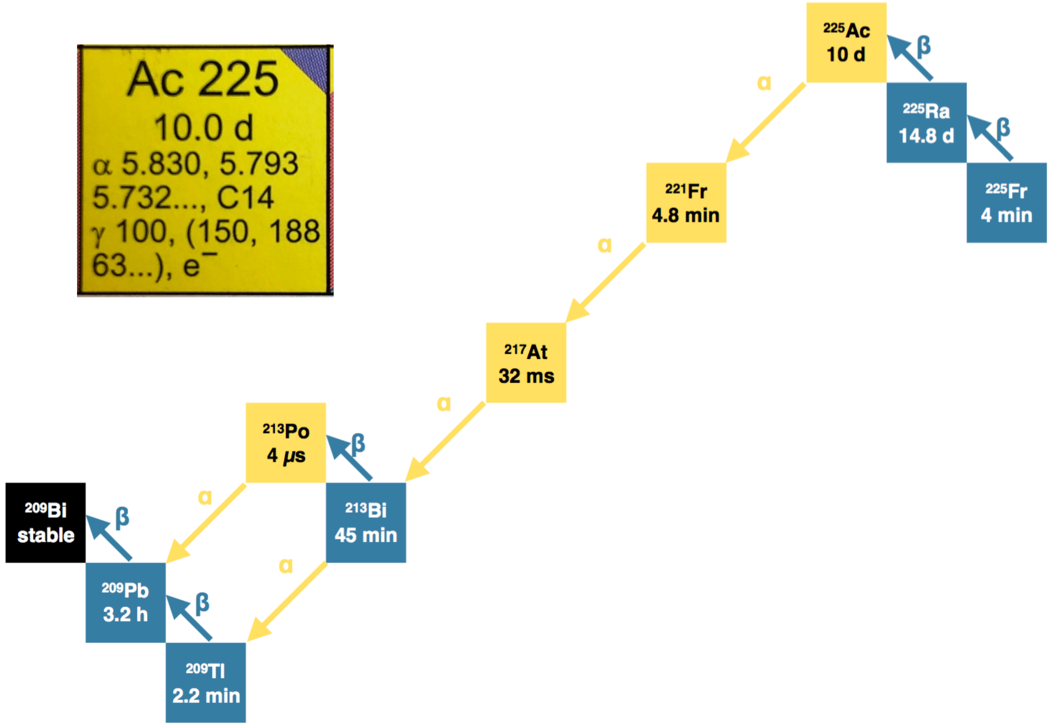
^{225}Ac in medicine





- From a single ^{225}Ac isotope, 4 α particles are emitted in a short time, resulting in the highest possible dose to short distance.
- ^{225}Ac may also be used as a long-lived generator for ^{213}Bi, which yields 1 α for each decay but with a half-life of 45 min only, perfectly fit to fast-acting medicine.
- Coordination chemistry appropriate for all sorts of vector molecules, and can be paired with PET-imaging using ^{68}Ga or ^{135}La.

*C. Kratochwil et al, The Journal of Nuclear Medicine **57** (2016) 1941-1944*

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Where does ^{225}Ac come from?

^{229}Th Generator
-70Gbq/a as of 2020

$^{233}U \xrightarrow{\alpha} {}^{229}Th \xrightarrow{\alpha} {}^{225}Ra \xrightarrow{\beta} {}^{225}Ac$

10 MBq per patient-dose
➔ 700 doses per year

! Potential demand for 100 000 patients...

Slide courtesy of Jake Johnson (KU Leuven),

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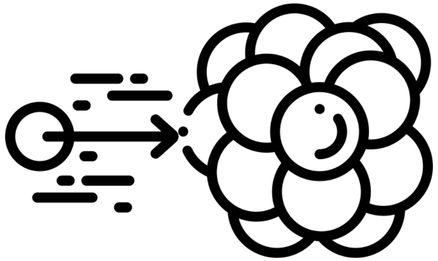
Alternative sustainable routes to produce ^{225}Ac

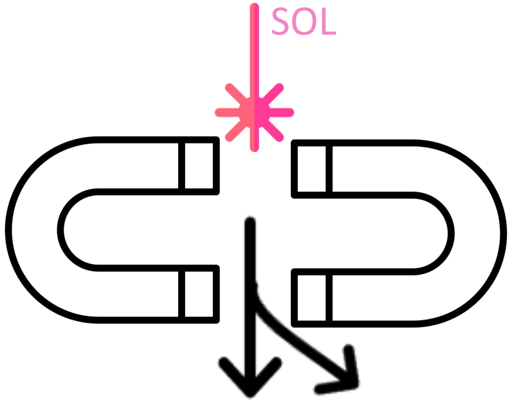
From ^{226}Ra

- $^{226}Ra(p,2n)^{225}Ac$
- $^{226}Ra(\gamma,n)^{225}Ra \rightarrow {}^{225}Ac$
- Challenge with radioactive target
- Waste management issues: ^{222}Rn



From ^{232}Th

- $^{232}Th(p,xpyn)^{225}Ra/Ac$
- Requires high-energy driver
- Co-production of many impurities and in particular ^{227}Ac



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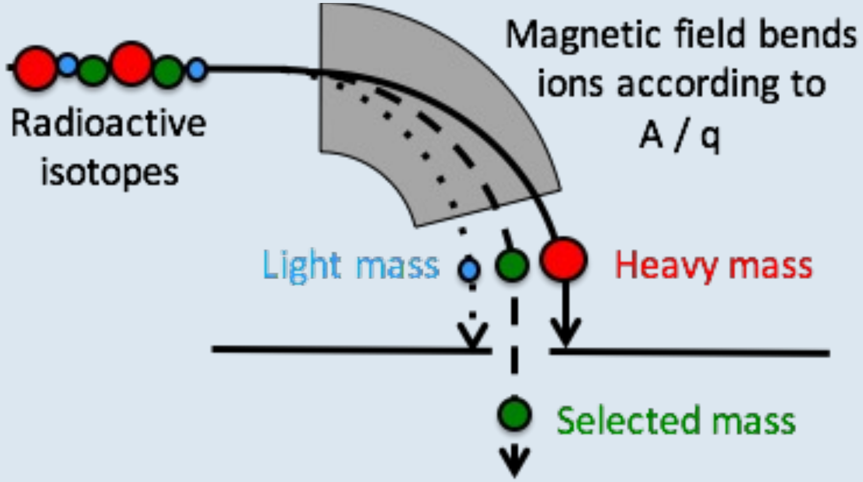
ISOL

The Isotope Separation On-Line technique



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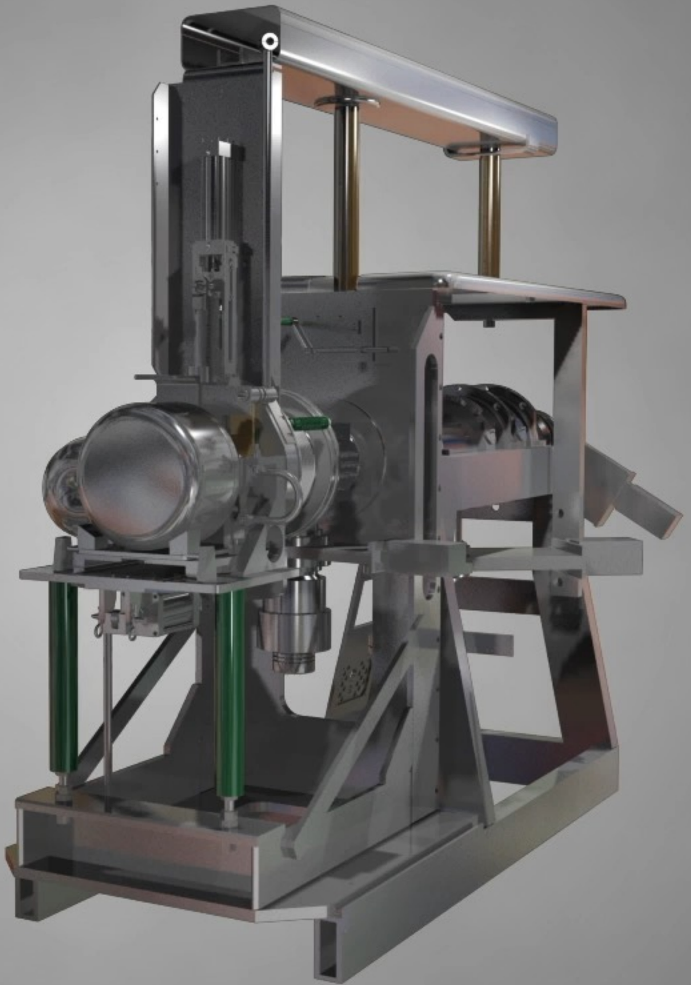
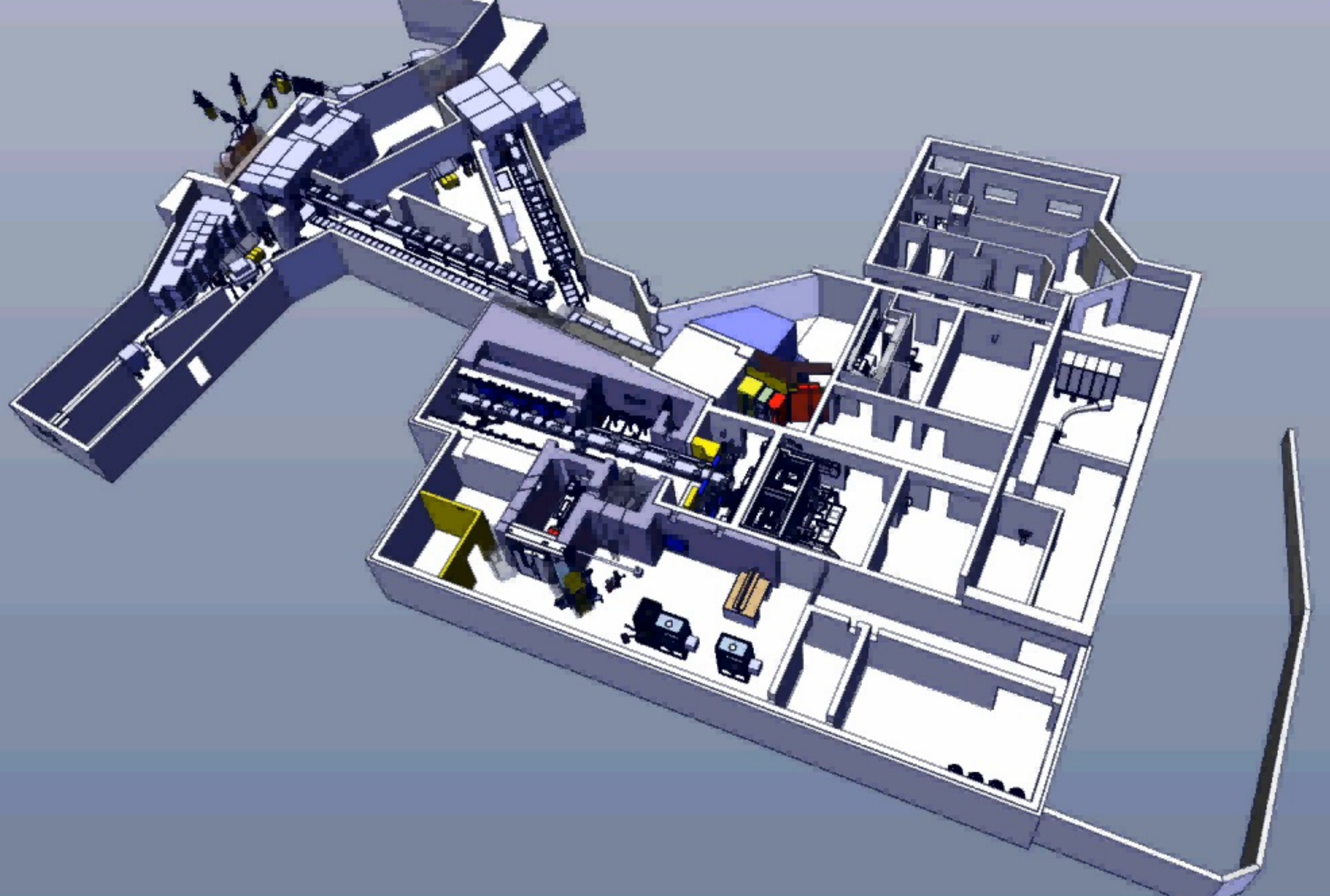
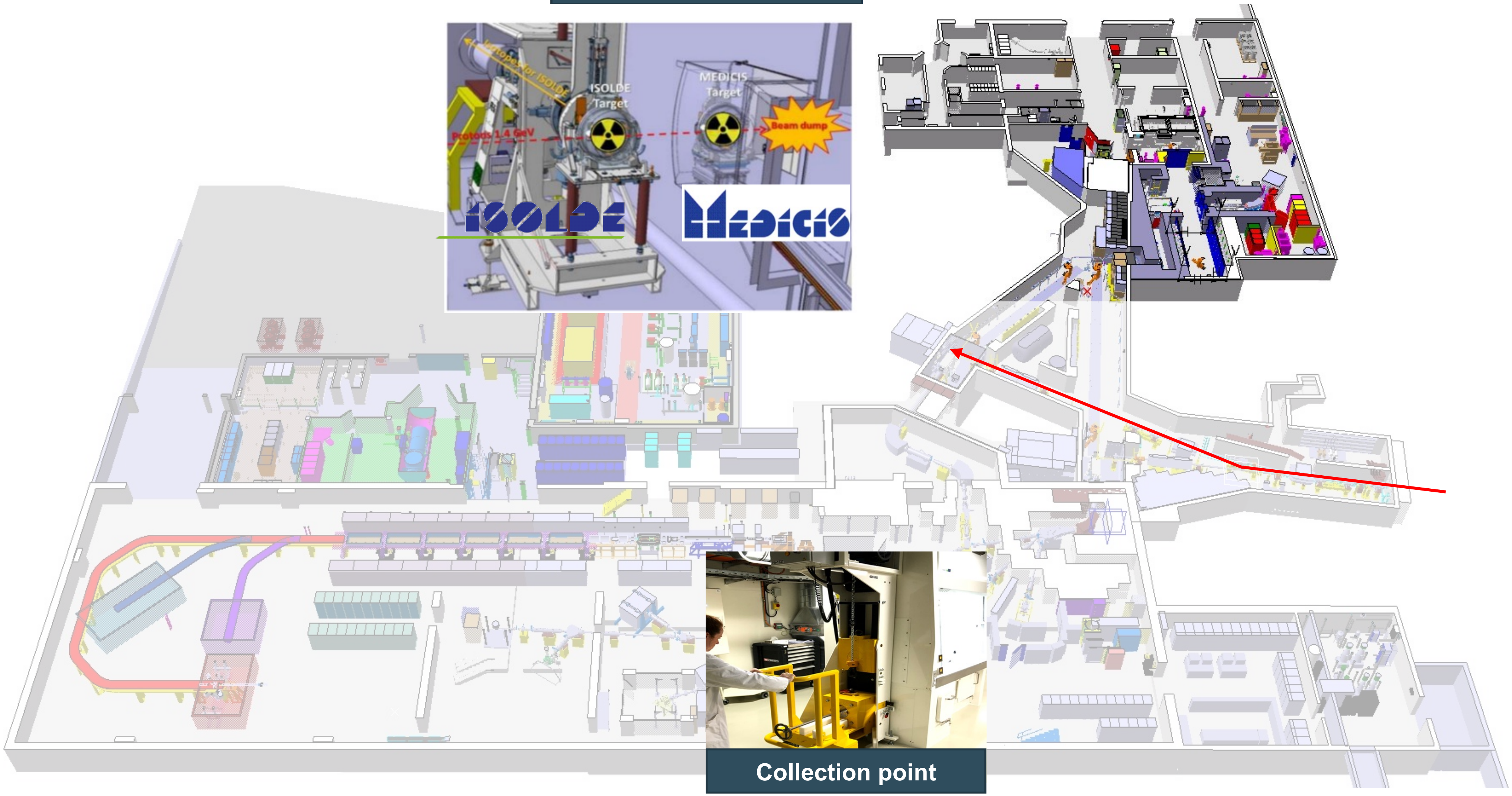




CERN MEDICIS

KUKA® handling arm



Collection point

the collection of
edical research
ns from CERN or
sources

Tb-IRMA-V: towards a sustainable supply

ISOL Production → Purification & Distribution → Radiopharma & pre-clinic → Clinical practice

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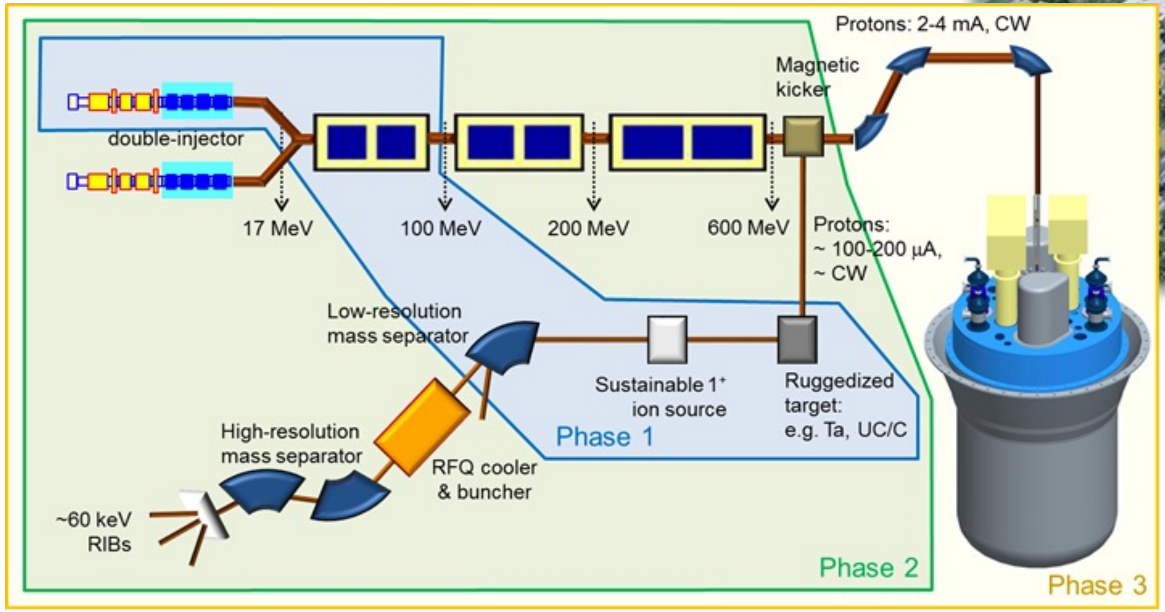
ISOL@MYRRHA: a new facility

Tb-IRMA-V

- Up to 600 MeV protons, 4 mA
- Phase 1 with 100 MeV, 0.5 mA
- Fundamental and applied programme

Phase 1 funded by the Belgium gvt in 2018!!
First beam planned for 2027
Synergy with reactor produced isotopes



Power(MEDICIS) = 2.8 kW
Power (MYRRHA) = 50 kW

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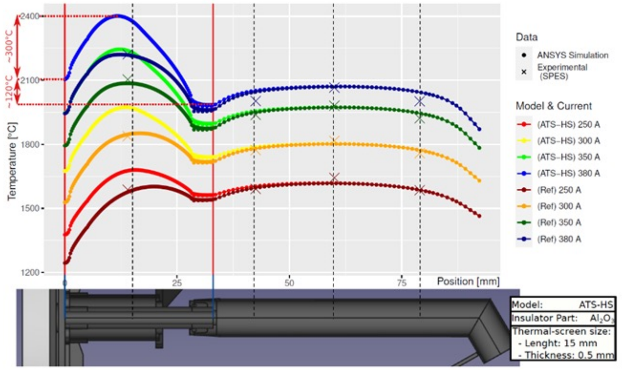
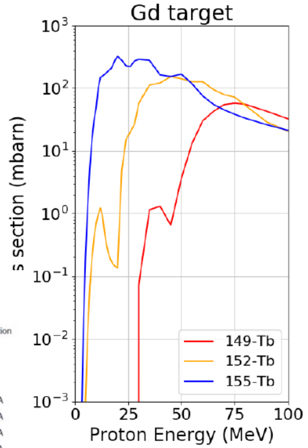
Tb-IRMA-V: ISOL Production

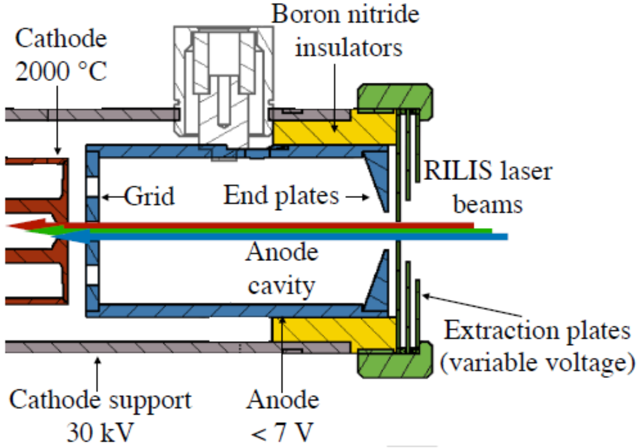
Power(MEDICIS) = 2.8 kW
Power (MYRRHA) = 50 kW

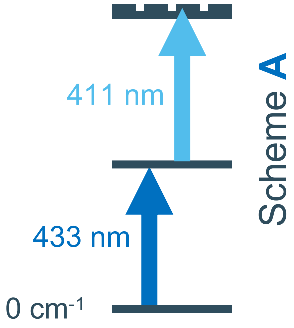
- Investigate the necessary developments towards the ISOL@MYRRHA facility
  - High-power target systems
  - Ion sources to handle high-intensity radioactive ion beam production
  - New laser ionization scheme for Tb

ISOL

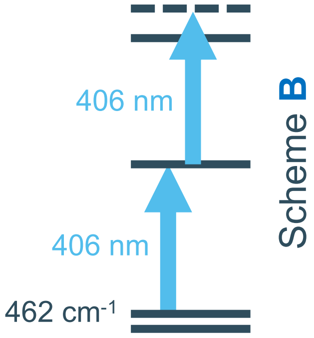








28% @ 2000°C



19% @ 2000°C

PhD work Benji Leenders, UGent & SCK CEN.
PhD work Sophie Hurier, KU Leuven & SCK CEN.
PhD work Kristof Dockx & Wiktoria Wojtaczka, KU Leuven.

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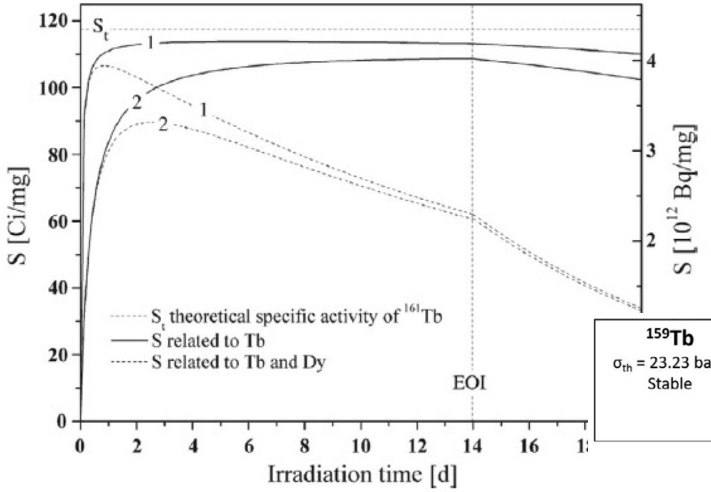
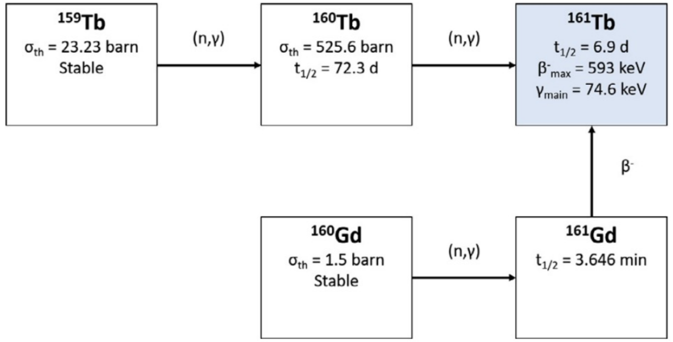
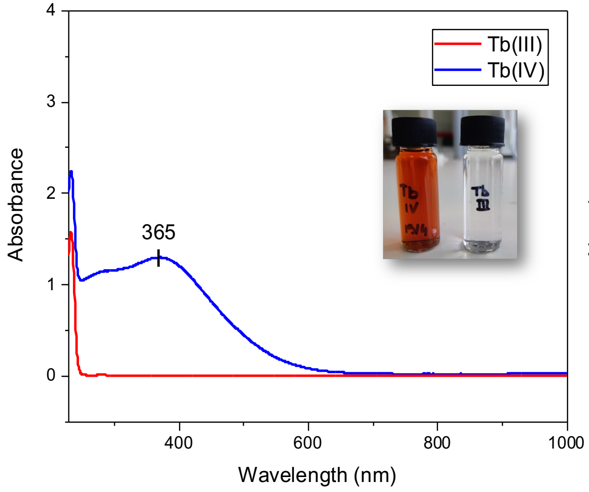
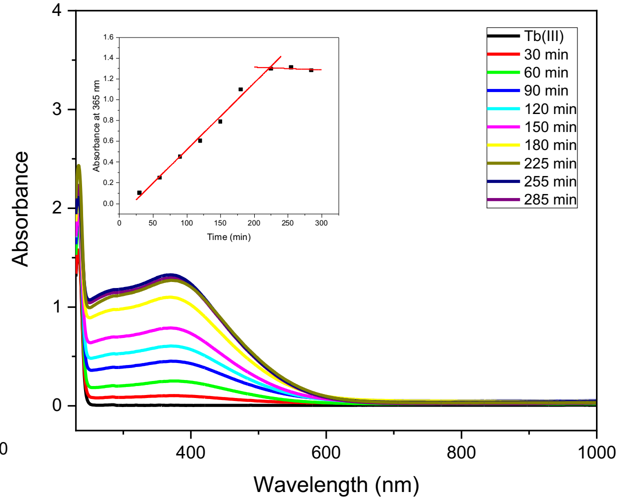
Tb-IRMA-V: Purification

- Concentrating on the Tb/Gd separation
  - ^{161}Tb production in the BR2 reactor at SCK, already delivering radioisotopes
  - Developed the oxidization of Tb(III) to Tb(IV) to go beyond the existing state-of-the-art with α-HIBA and establish a novel purification protocol.







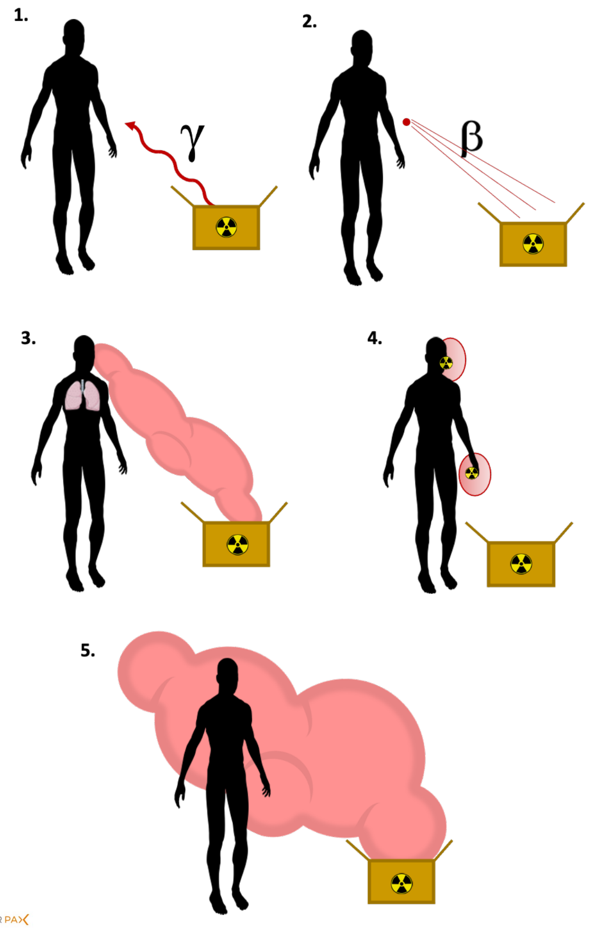


*M. Van de Voorde et al., Coordination Chemistry Review **382** (2019) 103-125.*
PhD work Meryem Arman, KU Leuven & SCK CEN.

Tb-IRMA-V: Distribution

- Limited international regulation on the transport of Tb radioisotopes
  - Basic regulations are very stringent and impractical for medical practice
  - New regulations from IAEA since 2019 on $^{149,161}Tb$
  - Calculations submitted to the Federal Agency for Nuclear Control for $^{152,155}Tb$
  - All values compatible for medical use

Isotope	IAEA	New A2
^{149}Tb	800 GBq	800 GBq
^{152}Tb	(20 GBq)	800 GBq
^{155}Tb	(20 GBq)	2 000 GBq
^{161}Tb	700 GBq	700 GBq



Distribution

 M.Sc. thesis V. Verelst, KU Leuven (2019).

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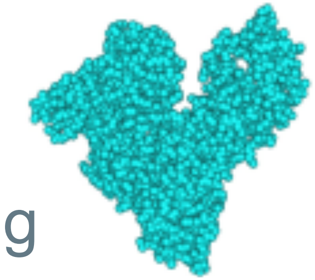
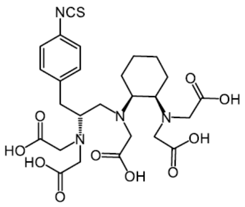
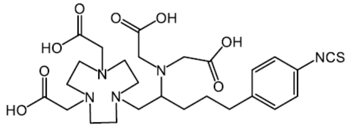
Tb-IRMA-V: Radiopharma

- Devising new radiopharmaceuticals
  - How to use the samples after the new radiochemistry
  - Producing peptides-based radiopharma that are heat sensitive (max 40°C), starting with Human Serum Albumin
  - Demonstrating the process with cold isotopes, then in-vitro, and finally in-vivo in mice models

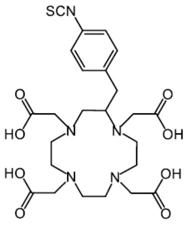




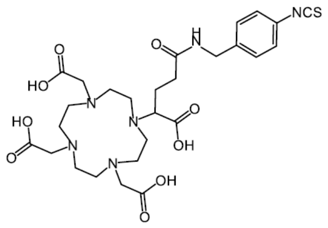
p-SCN-Bn-CHX-A"-DTPA



p-SCN-Bn-3p-c-NETA

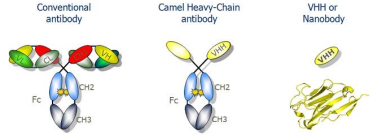


p-SCN-Bn-DOTA

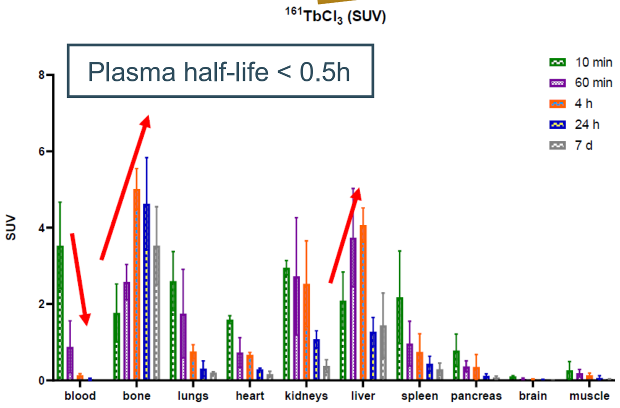


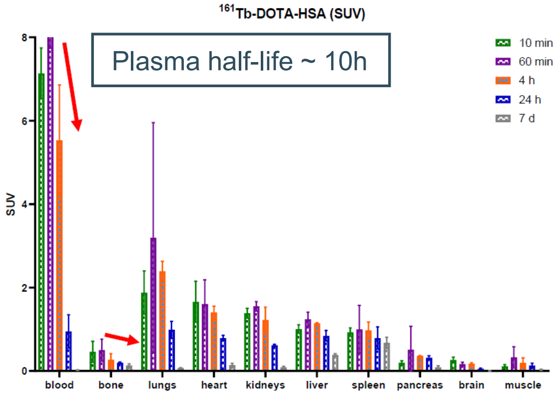
p-SCN-Bz-DOTA-GA

Ablynx A SANOFI COMPANY



^{161}Tb readily available!!



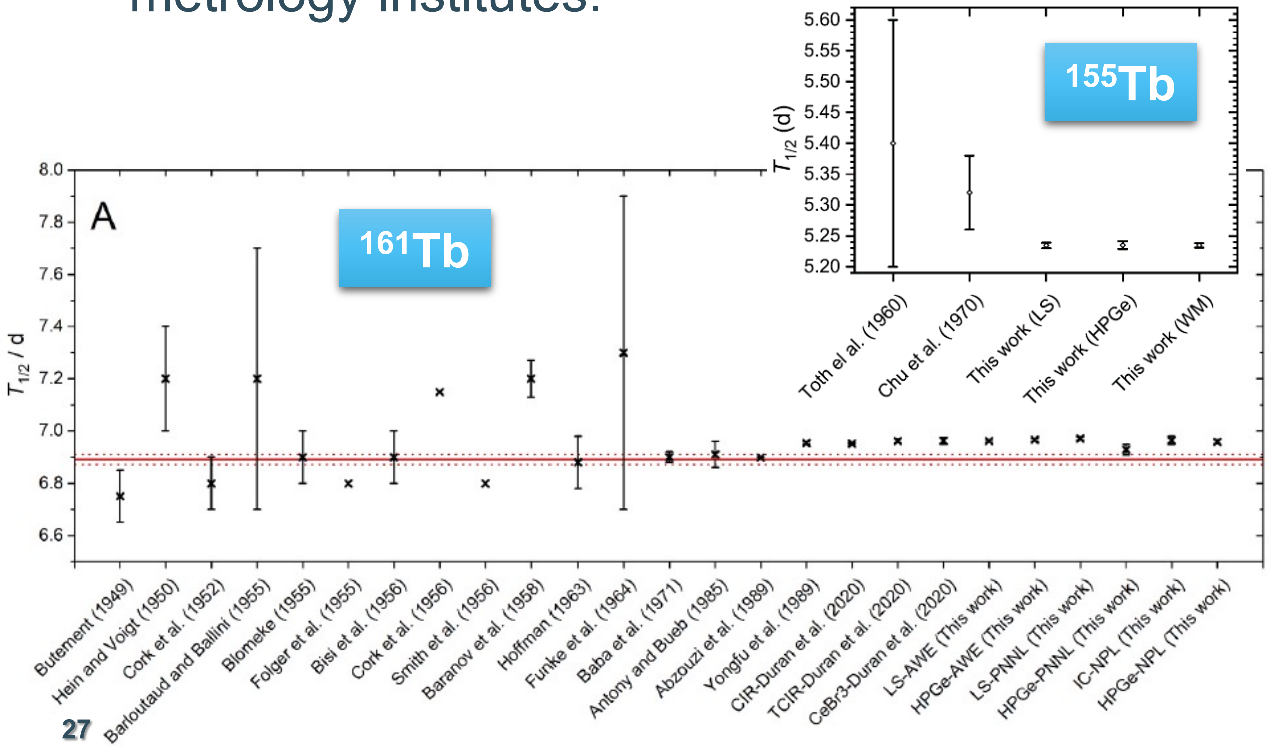


Radiopharma & pre-clinic

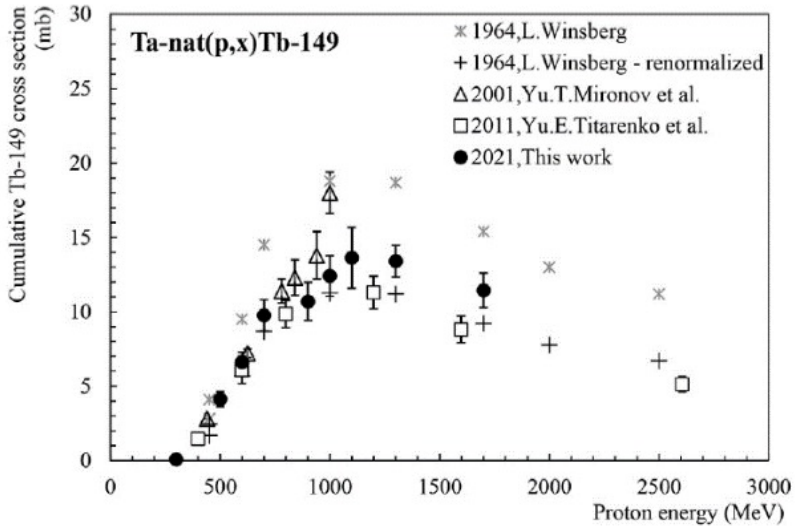
*I. Cassells et al., Frontiers in Medicine **8** (2021) 675122.*
PhD work Irwin Cassells, KU Leuven & SCK CEN.

Tb nuclear data

- Imprecise, inaccurate half-lives lead to ‘paper losses’ of radioactivity and poorly known injected radioactivity.
- Hospitals require secondary standards that they can readily used, determined by metrology institutes.



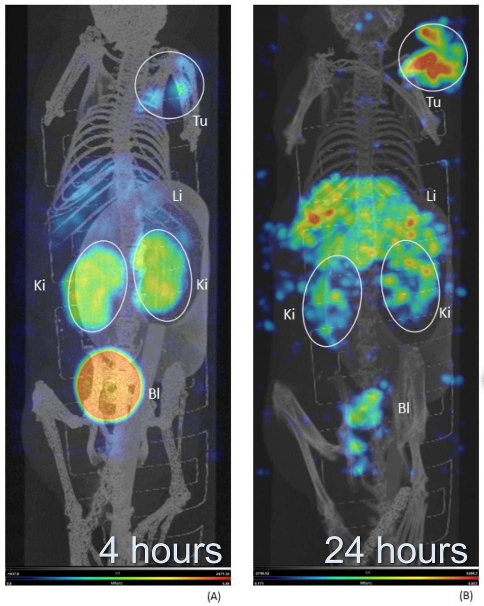
- Limited or contradictory knowledge of production cross sections lead to too high uncertainties in the production protocol and thus, too high uncertainty for the industry.
- A large effort is put into remeasuring the cross sections of isotopes of interest and possible contaminants.



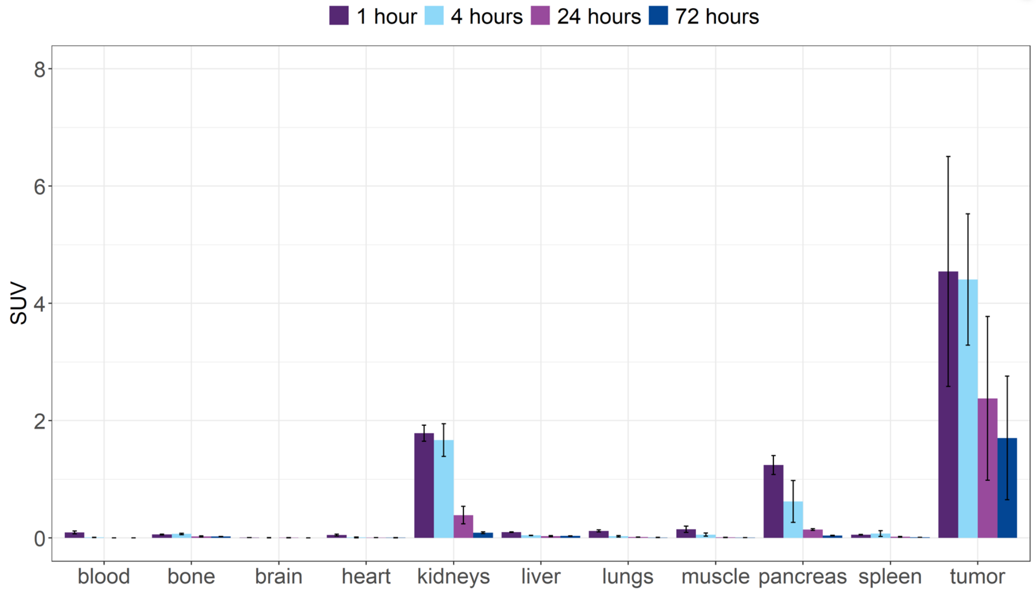
S. Collins et al., *Applied Radiation and Isotopes* **182** (2022) 110140.
S. Collins et al., *Applied Radiation and Isotopes* **190** (2022) 110480.
C. Duchemin et al., *Frontiers in Medicine* **8** (2021) 625561.

Building on our wins: ^{153}Sm

- Produced readily from ^{152}Sm(n,γ)^{153}Sm, however with too small specific activity (~2%) for nuclear medicine application.
- CERN MEDICIS offers the possibility to efficiently separate the ^{153}Sm to 99% enrichment. With a half-life below 2 days, the logistics is a challenge!
- Performed full development: production, radiochemistry, radiolabelling, in vitro AND in vivo studies within 18 months from proposal to publication.



[^{153}Sm]Sm-DOTA-TATE



*R. Heinke et al., Frontiers in Medicine **8** (2021) 712374.*
*K. Vermeulen et al., Pharmaceutics **14** (2022) 2566.*

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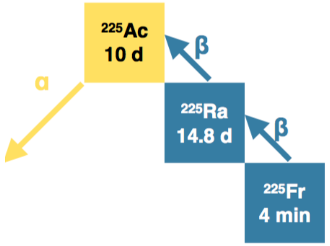
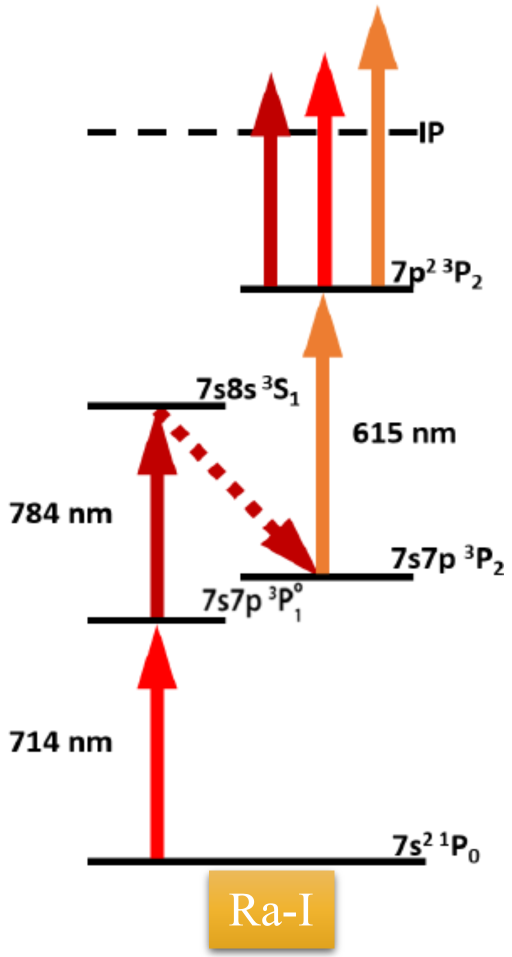
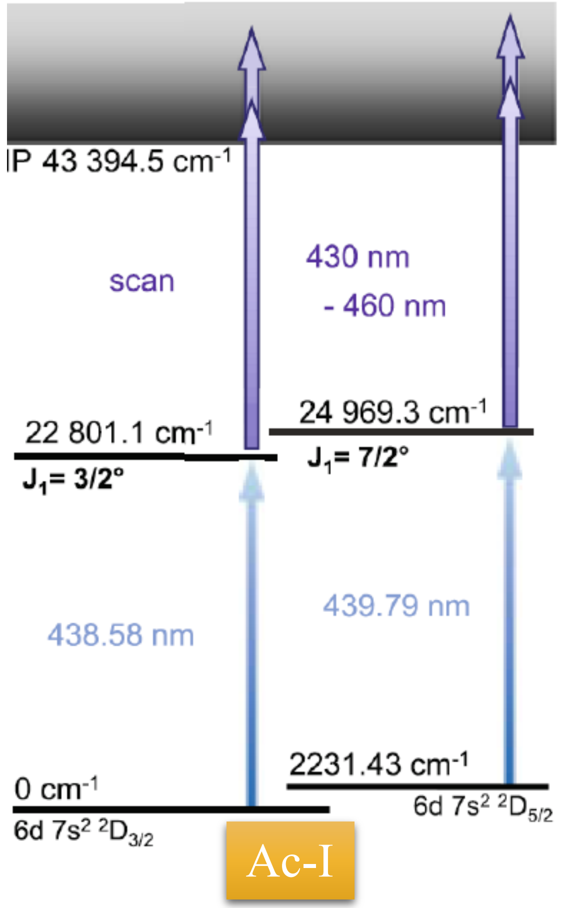
ISOLDE-produced ^{225}Ac



LASER IONISATION AND SPECTROSCOPY OF ACTINIDES

- At ISOLDE, the target materials are $^{238}UC_x$ and $^{232}ThO2$ with 1.4 GeV protons.
- ^{225}Fr (alkali metal) is very easily extracted online and ionized.
- ^{225}Ra (alkali earth) is also well extracted and its ionization can be enhanced with lasers (x4).
- ^{225}Ac (actinide) is harder to separate from the target matrix but has the highest production cross section.
- ISOLDE has reached 1% extraction from UCx and MEDICIS 10% from ThO_2.
- ^{227}Ac activity fraction of 6×10^{-7}.

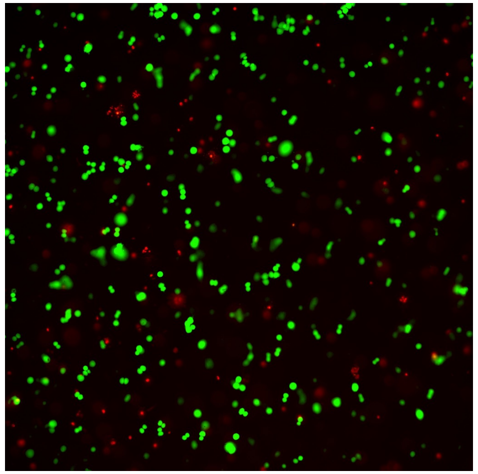


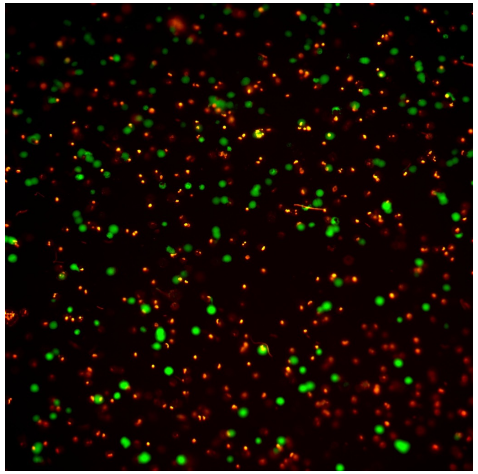


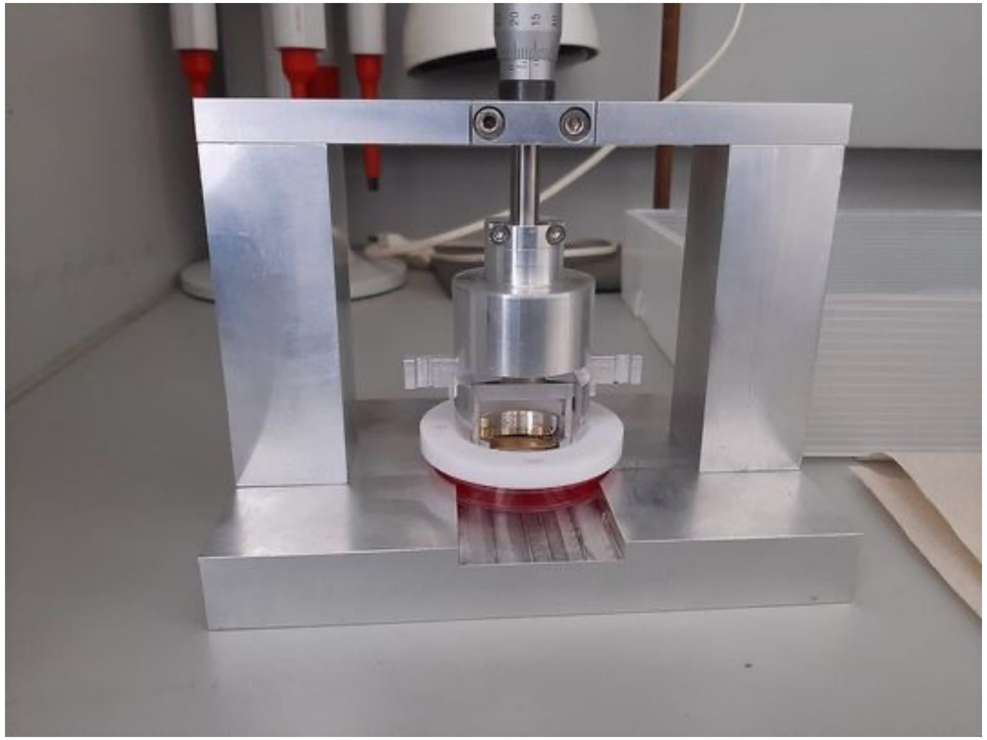
T. Day Goodacre et al., Radium ionization scheme development..., Spectrochimica Acta B ***150*** *(2018) 99-104*
S. Raeder et al., In-source laser spectroscopy developments at TRILIS..., Hyperfine Interactions ***216*** *(2013) 33-39*
PhD work Jake Johnson (KU Leuven)

Cell Irradiations

- A new setup has been designed for cell irradiation tests.
- Biophysics group has developed a protocol to suspend cells at the surface of a hydrogel.
- Staining with different fluorescent dyes allows to count surviving (green) from dead (red) cells.
- ^{225}**Ac collection sample from MEDICIS** was used to irradiate the cells [until it got damaged].
- Investigation of single or isolated cells and direct effects of the radiation.
- ^{241}Am sources with different activities to explore dose escalation and dose rate escalation.







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PRISMAP

The European Medical Radionuclide Programme…
…and what it means for Belgian Medical Physicists!

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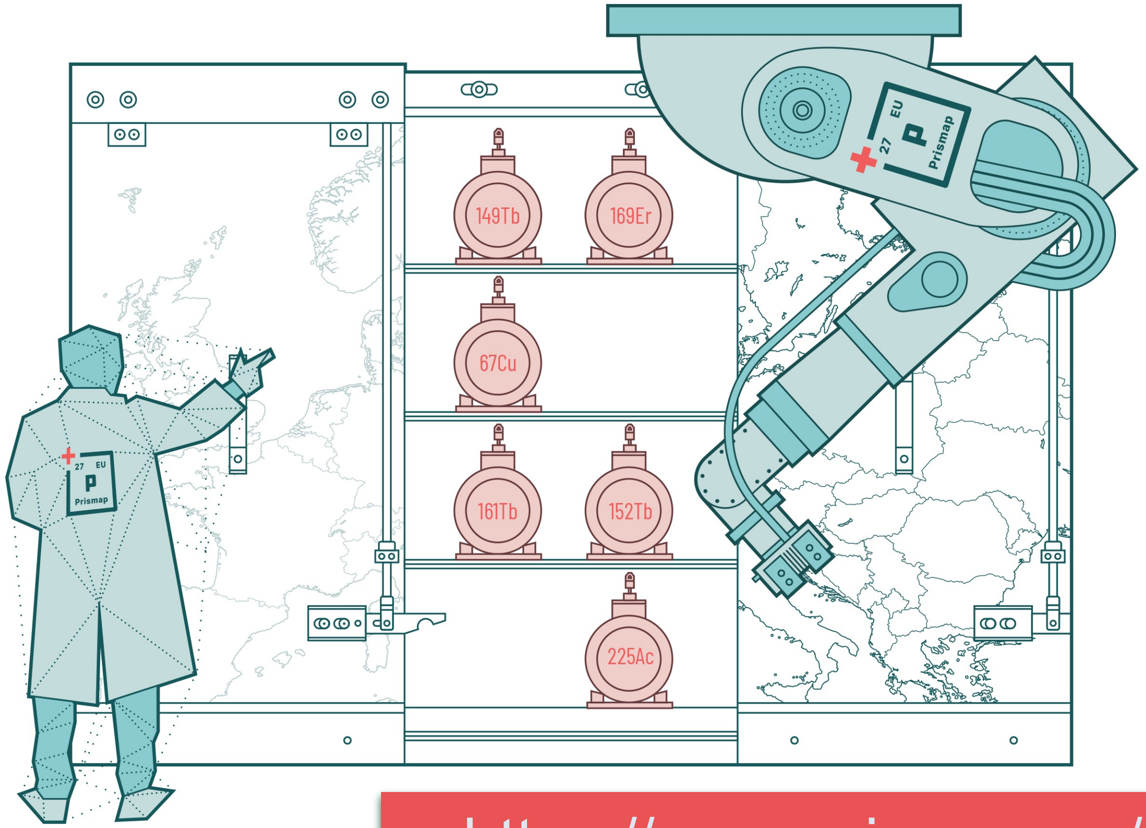
PRISMAP



- European infrastructure programme
- Provides transnational **access to novel radioisotopes** for medical research, as well as **access to facilities for biological research** with those isotopes.
- Excellence-based selection by a User Selection Panel. Two calls for project per year.
- **Open User Forum** to stay informed about our programme and to contribute to its future.

https://www.prismap.eu/radionuclides/user-forum/

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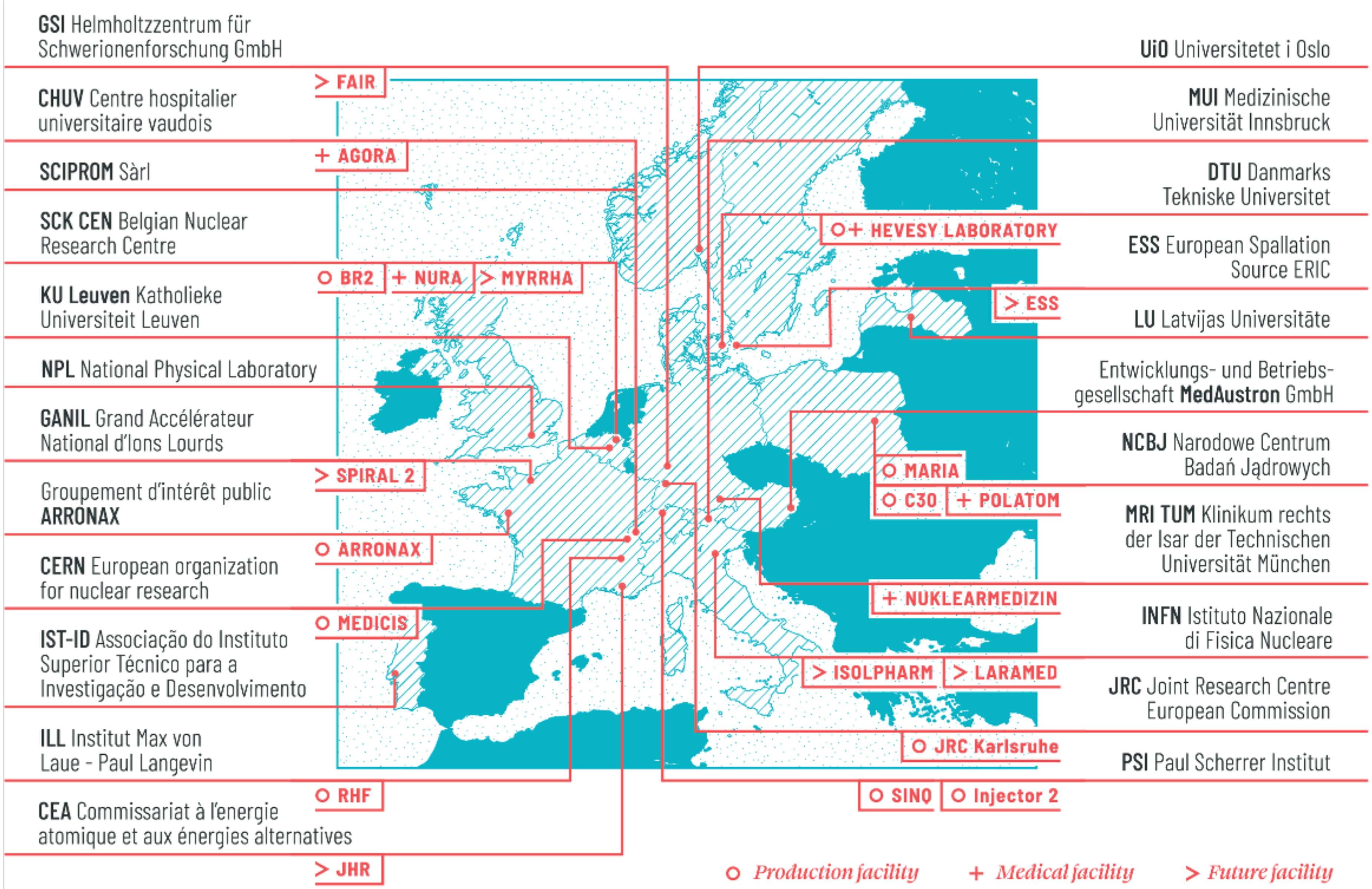
PRISMAP



27 EU PRISMAP Medical Radionuclides

https://www.prismap.eu/radionuclides/

PRISMAP portfolio

- PRISMAP third call under preparation
- Many isotopes require high-energy projectiles and/or mass separation to reach the necessary quality
  - ➢ Mass separation currently only available at CERN MEDICIS
- PRISMAP only offers transnational access for research purpose towards first-in-human trials

New facilities will be needed across Europe to supply medical institutions for patient care

https://www.prismap.eu/radionuclides/portfolio/

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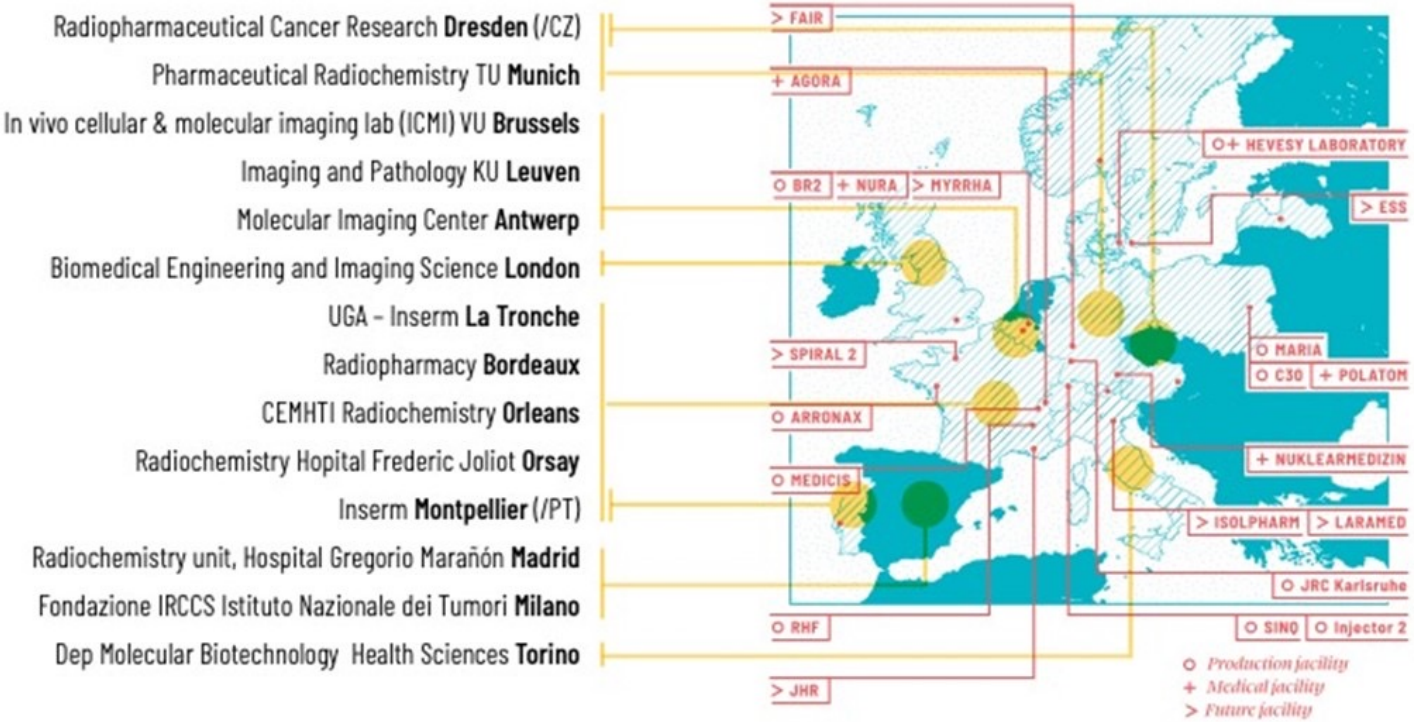
First two calls: overview

- 15 accepted projects so far
- Covers logistics, in vitro, and in vivo research
- Half of the proposals involve the Tb quadruplet
- Biomedical facilities are undersubscribed
- Deliveries have begun



Today's excitement is tomorrow's challenge!

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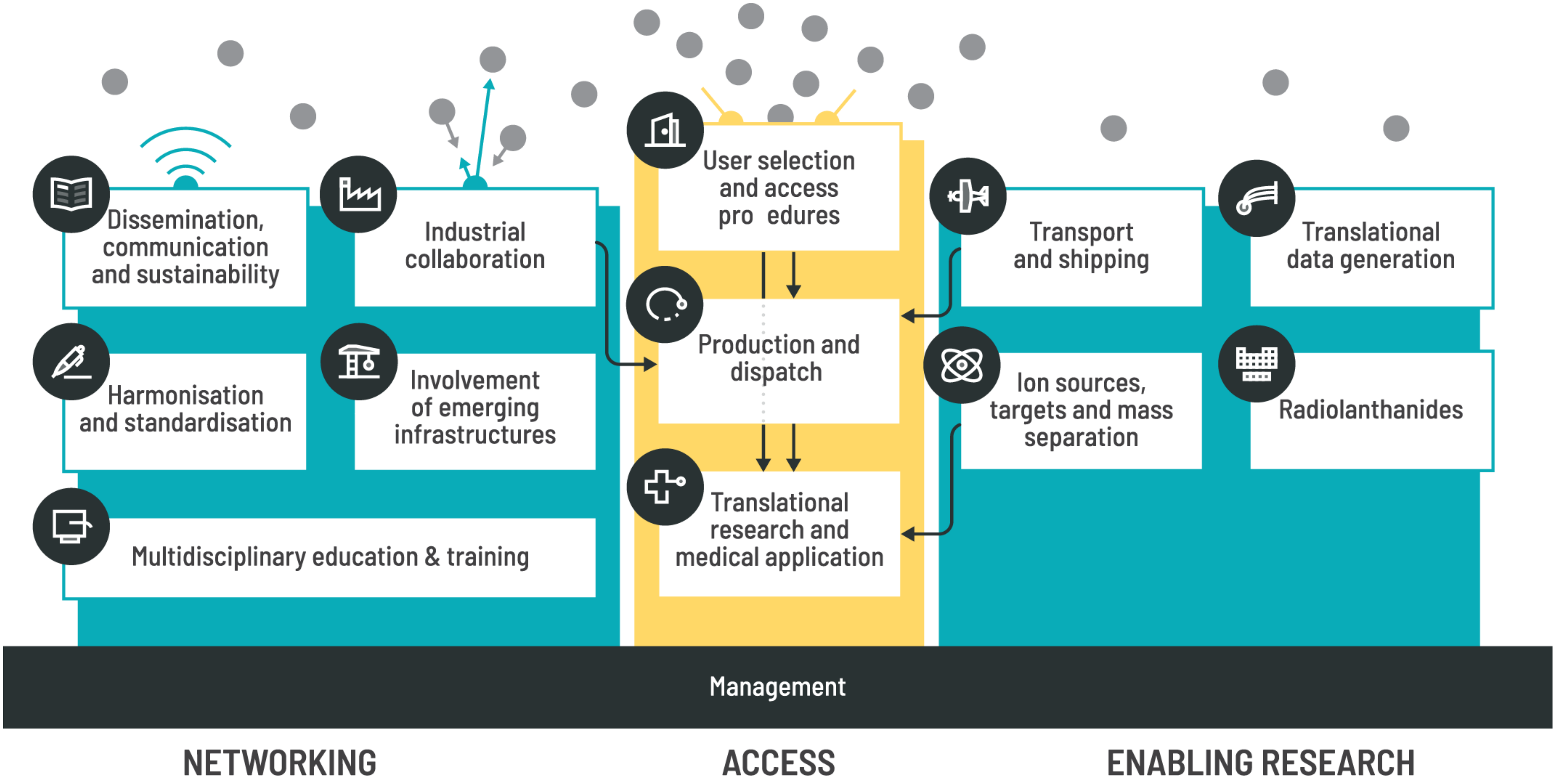

https://www.prismap.eu/

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- Nuclear medicine is undergoing an important transformation from routine operation with a handful of radioisotopes to new opportunities with innovative radioisotopes and theranostics applications.
- Europe is playing a major role in this transformation, driven by an active research community and guided by European interests (ERVI).
- CERN MEDICIS is the only mass separator for medical radioisotopes today and new facilities are needed: ISOLPHARM (IT), ISOL@MYRRHA (BE), SMILE (FR), TATTOOS (CH) are on the books for the next 5-10 years.
- Existing initiatives and strong pan-European partnerships such as PRISMAP and Tb-IRMA-V are paving the way towards realizing this objective.
- The community must be ready with the logistic and regulatory challenge!

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This work is supported by funding from the European Commission under Horizon 2020, Marie Sklodowska Curie Actions, ITN contract No. 861198 (LISA) and Horizon Europe research and innovation programme contract No. 101008571 (PRISMAP).

These activities are further supported by the Research Foundation – Flanders FWO contracts No. S005019N (Tb-IRMA-V) and No. I002619N (ISOLDE).

Extra slides ISOLDE

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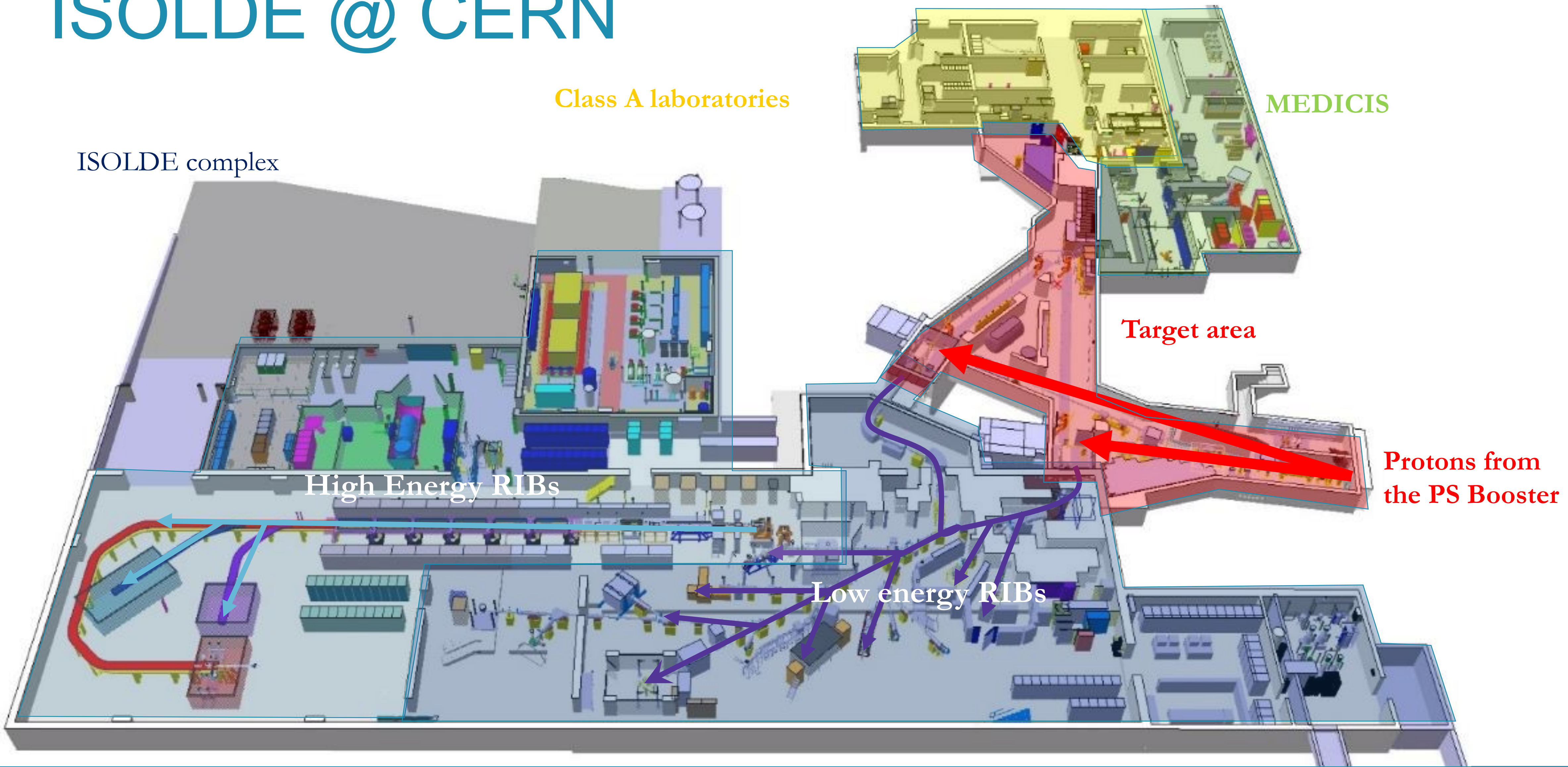
ISOLDE @ CERN



 Slide courtesy of R. Catherall

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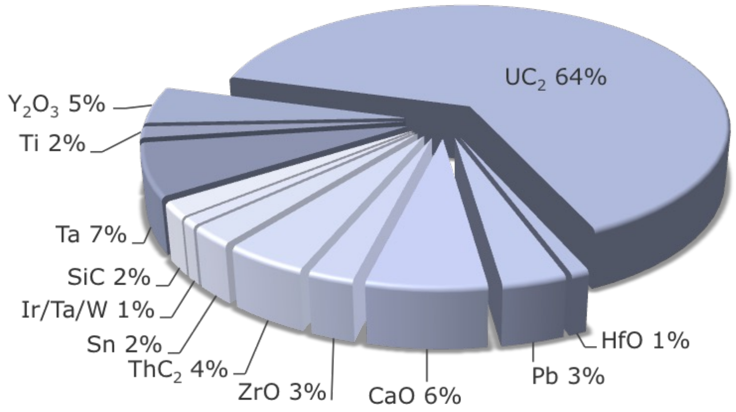
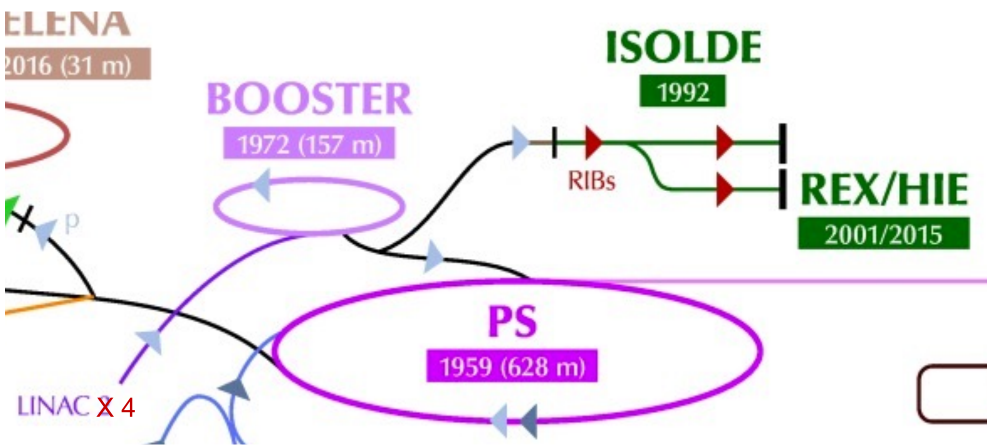
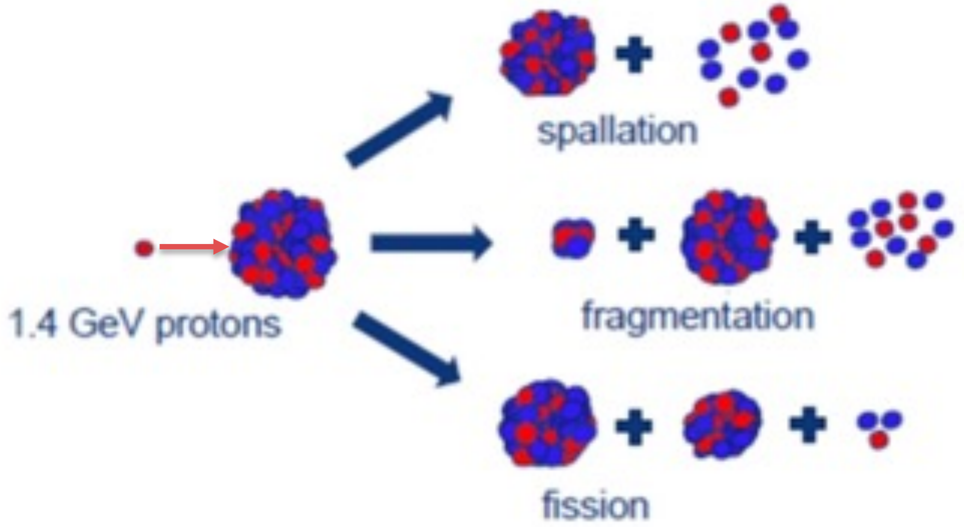
Step 1: Production

- 1.4 GeV protons from the PS Booster
- 2 μA on average
- Pulsed beam delivery
- Targets ranging from Li to U!







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Isotope release

Diffusion:

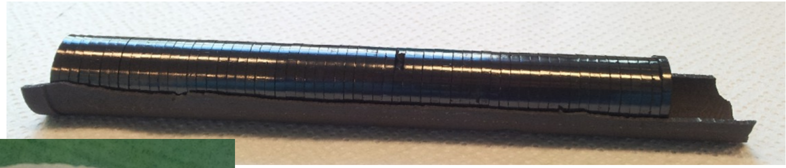
$$D = D_0 \cdot e^{-\frac{E}{RT}} \qquad \text{(Arrhenius eq.)}$$

$$\varepsilon_{diff} = \frac{3}{\pi}\sqrt{\frac{\mu}{\lambda}} \qquad \mu = \frac{\pi^2 \cdot D}{G^2}$$

$$\Rightarrow \varepsilon_{diff} \propto \frac{1}{G}$$

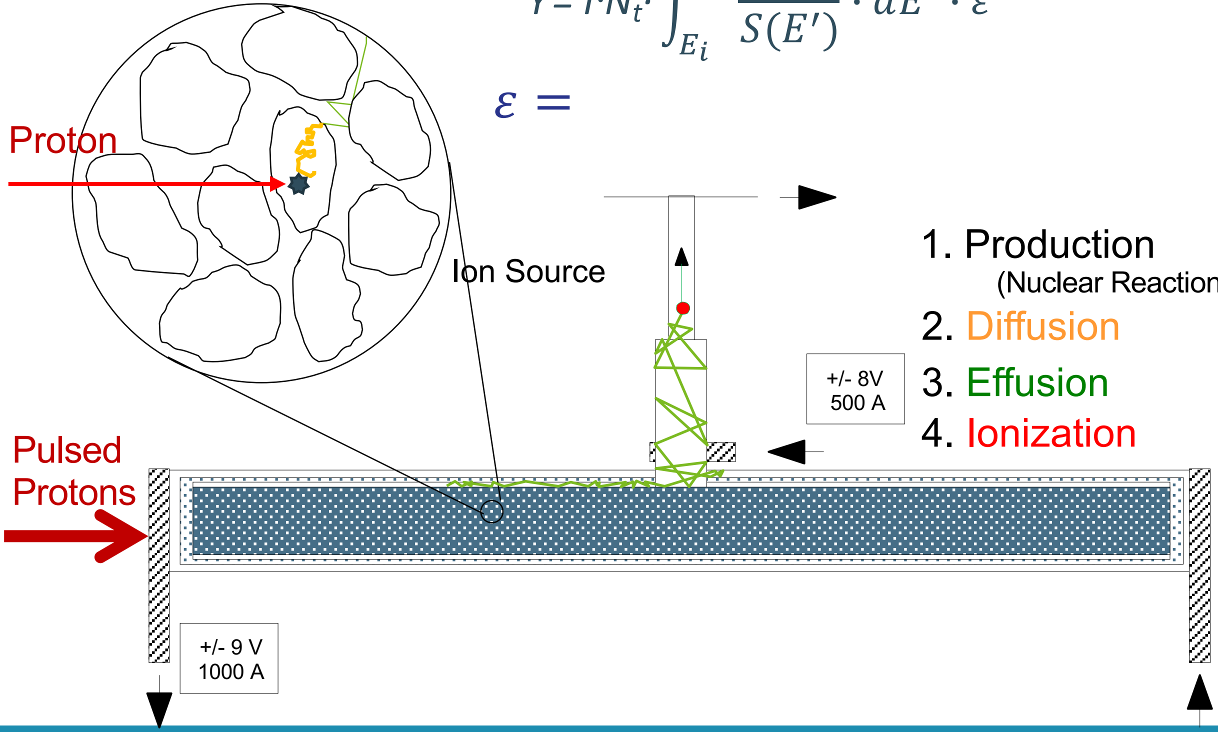
D: Diffusion coefficient
μ : Diffusion time
λ : Decay constant
G: Grain size

Control microstructure to enhance release properties



$$Y = I \cdot N_t \cdot \int_{E_i}^{E_f} \frac{\sigma(E')}{S(E')} \cdot dE' \cdot \varepsilon$$

$\varepsilon =$



1. Production (Nuclear Reactions)
2. Diffusion
3. Effusion
4. Ionization

Slide courtesy of J.P. Ramos, EMIS Conference Sept 2018
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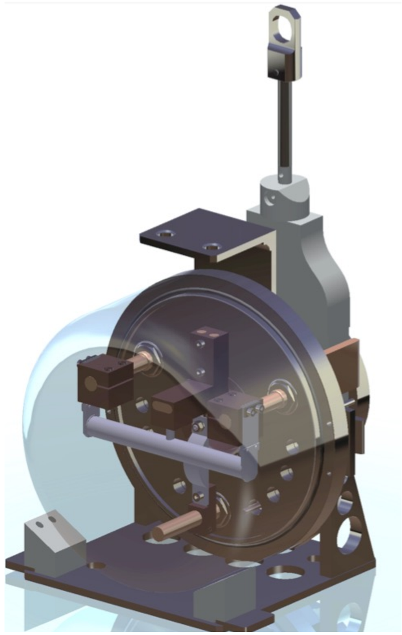
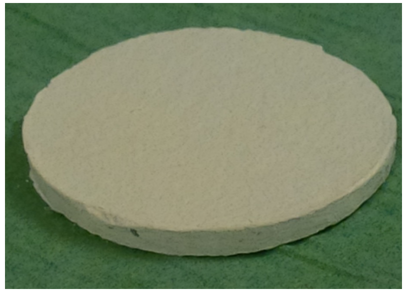
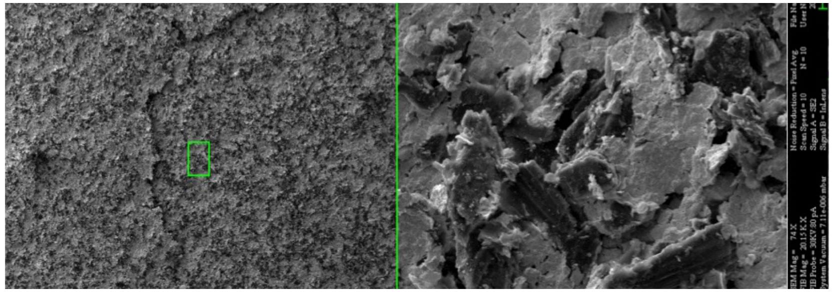
Step 2: Chemical selection





- Choice of target material:
  - Thick targets catch all isotopes; recoils diffuse under high temperature condition (2000°C)
  - Volatility dependence: refractory elements are trapped
  - Thin targets allow all recoils out and have a lesser chemical sensitivity but yields suffer linearly with number of target atoms.



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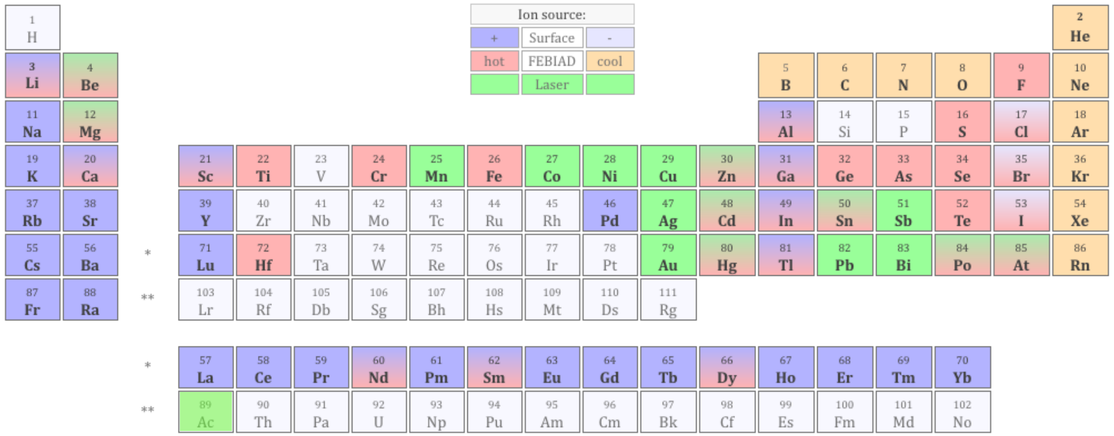
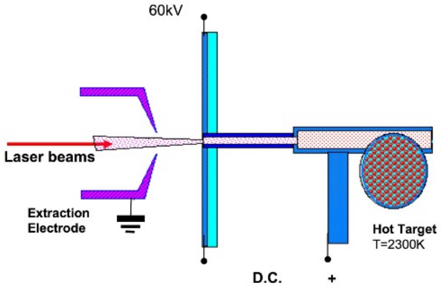
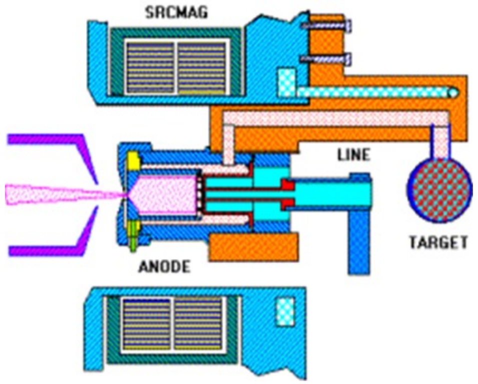
Step 2: Ion sourcery

- Choice of ion source :
  - Low-IP elements (alkali, alkali-earth, some rare-earth) ionize in contact with a hot surface;
  - High-IP elements (noble gases, halogens, light volatile elements) require highly energetic electron bombardment;
  - Transition metals are not appropriate with either and require a case-by-case laser ionization approach.







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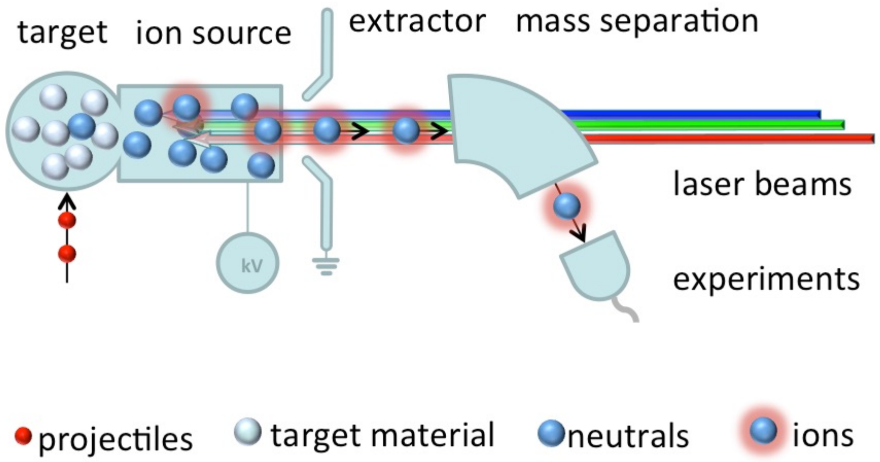
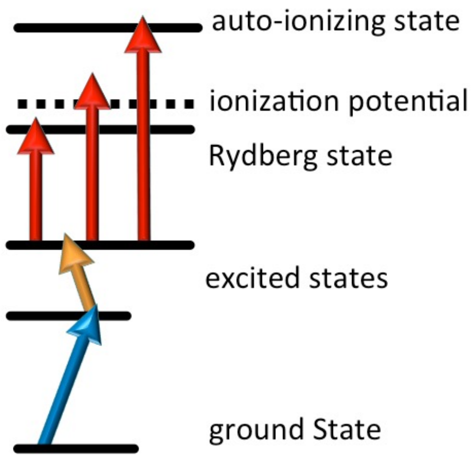
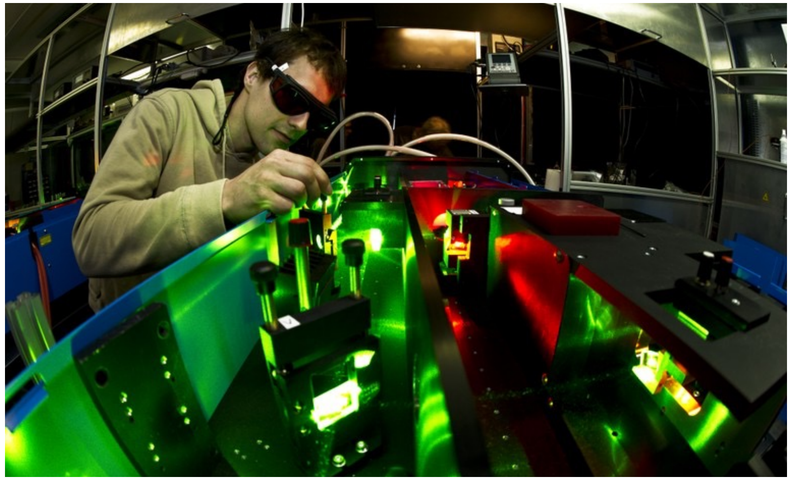
Step 2: shining light on the elements

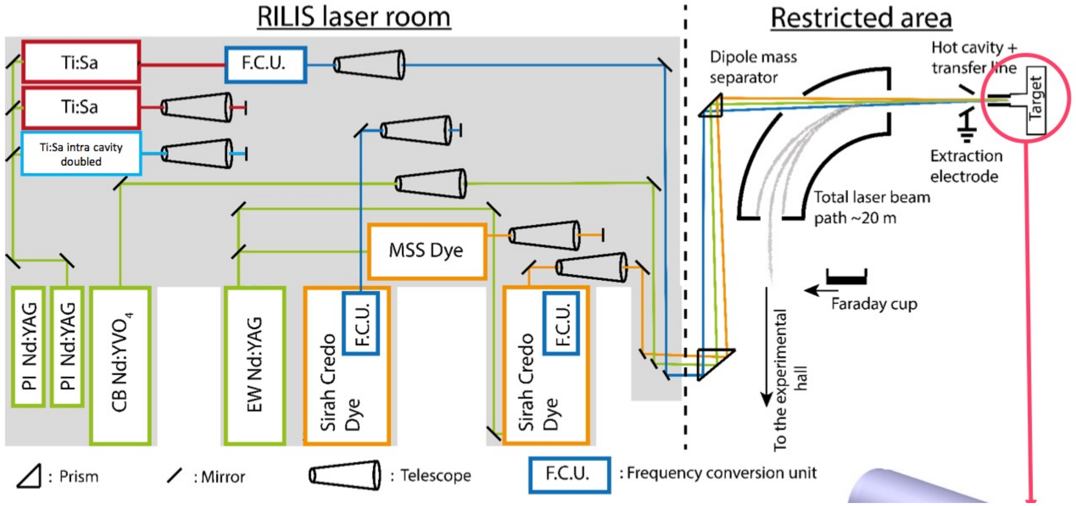
Resonance
Ionisation
Laser
Ion
Source





- > 50% of beams produced
- > 2 500 hours of operation per year





 https://rilis-web.web.cern.ch/node/182

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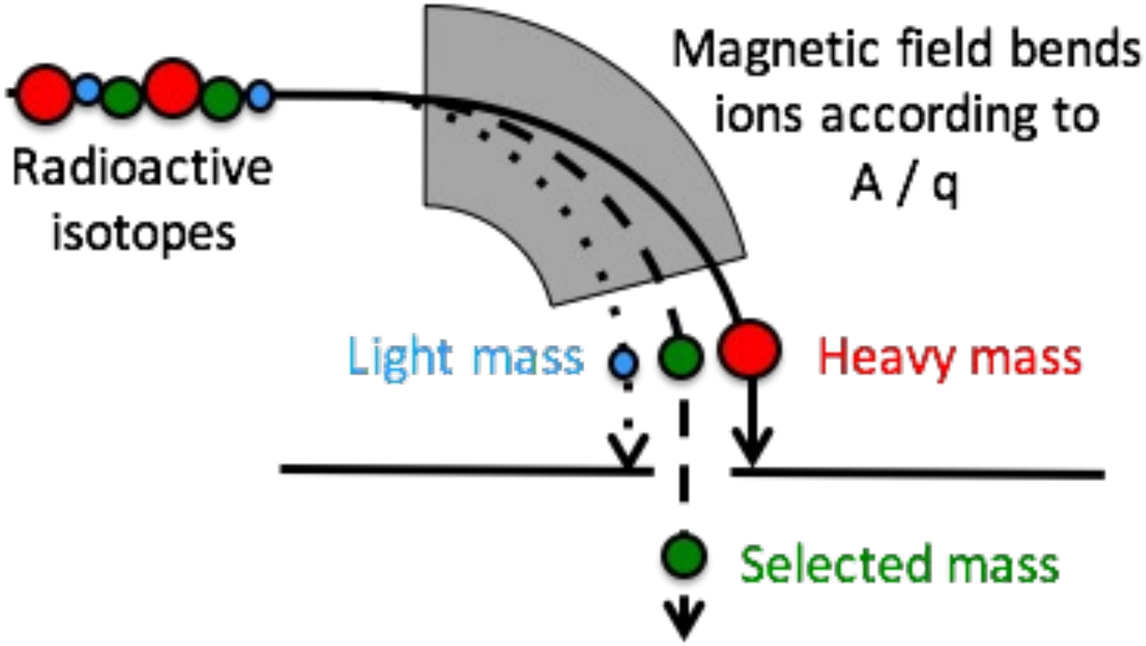
Step 3: mass separation

- A mono-energetic beam at energy 30-60 keV is extracted, shaped, and transported to a dipole magnet.
- The magnetic rigidity (bending radius) of each element is dependent upon the magnetic field and the mass-to-charge ratio ${}^{m}/_{q}$.
- Tuning the magnetic field allows to select a given ${}^{m}/_{q}$, though beams typically have $q = 1$, resulting in mass separation.
- Resolution varies from $R = {}^{m}/_{\Delta m}$ 500 to 20,000 for the most ambitious. 500 corresponds to single mass separation, while 20,000 is enough to separate molecules from single-element ions.

$$E = \frac{1}{2}mv^2 \Rightarrow v = \sqrt{\frac{2E}{m}}$$

$$F = qv \times B = ma$$



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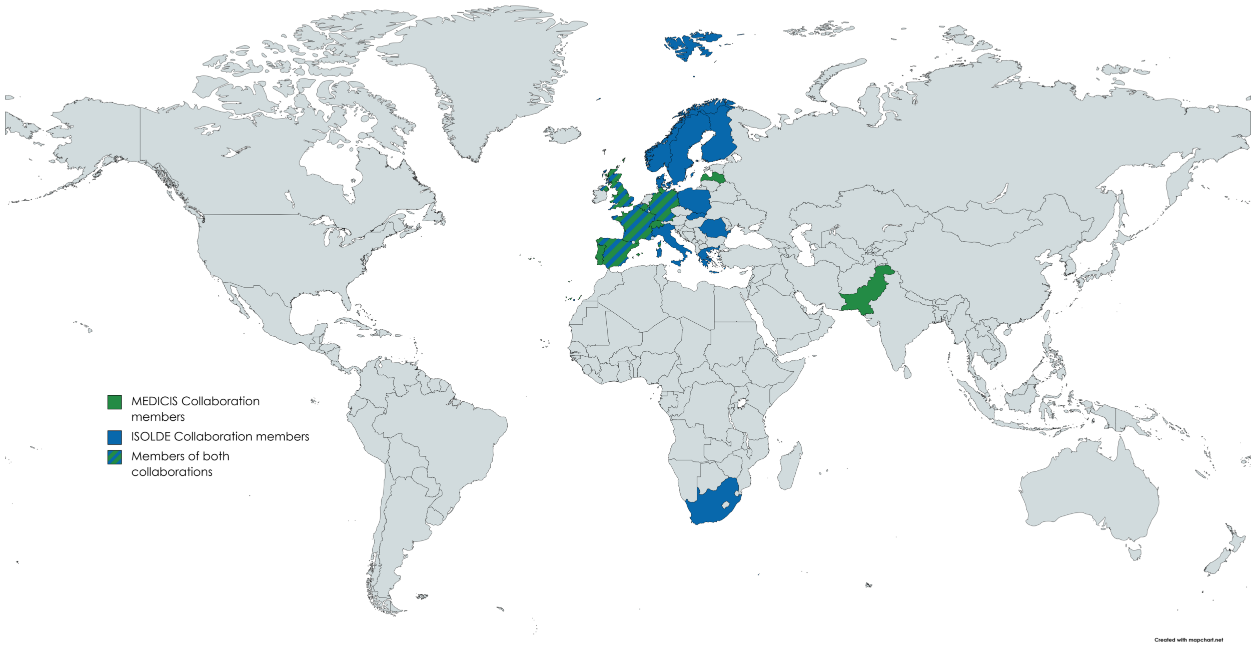
The Isotope Separator OnLine DEvice

- Approved by the CERN Council in **1964**; received its first beam in **1967**
  - Initially using 600 MeV protons from the SC
  - Moved to the PS Booster in **1992** where it received 1.0 GeV protons – now 1.4 GeV
- ~0.1% of the CERN budget
  ~7% of the CERN scientists
  >60% of the CERN protons
- ~50 staff/students/fellows
  ~500 active users



- The ISOLDE Collaboration includes CERN and 15 countries: BE, DE, DK, FI, FR, GR, IT, NO, PL, RO, SK, ZA, ES, SE, UK
- Other international collaborators participate in experiments (e.g. MIT, ORNL)

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Extra slides MEDICIS

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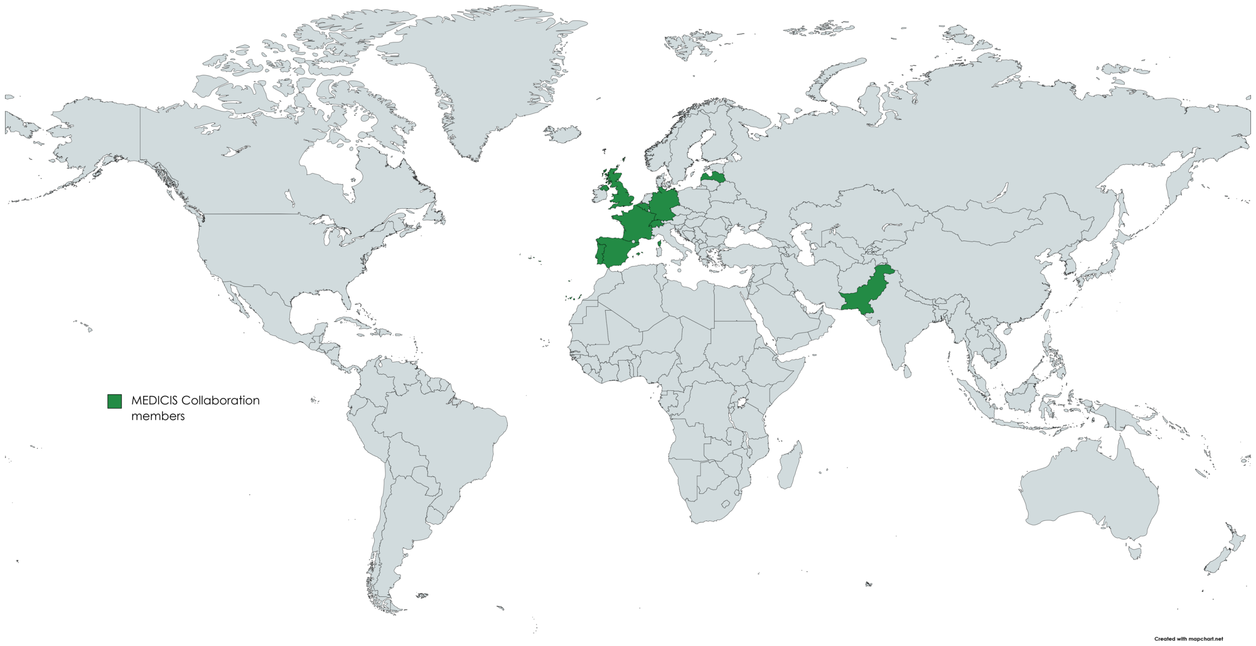
The MEDICIS Collaboration

- Born from ISOLDE but separate entity.
  - Approved in 2013
  - Commissioned in 2017
  - Operated in 2019-2020 in spite of LS2
- 2 annual Collaboration Boards to report on progress and discuss scientific proposals.
- 31 approved projects (4 completed)



- The MEDICIS Collaboration includes CERN and 12 institutes from BE, DE, FR, LV, PK, PR, ES, CH, UK
- The European Association of Nuclear Medicine acts as an advisory member

Map generated on mapchart.net

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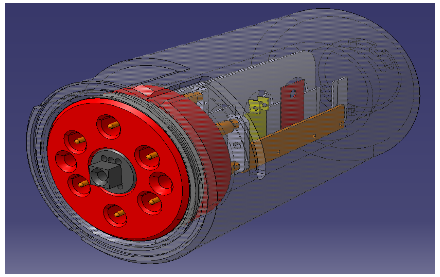
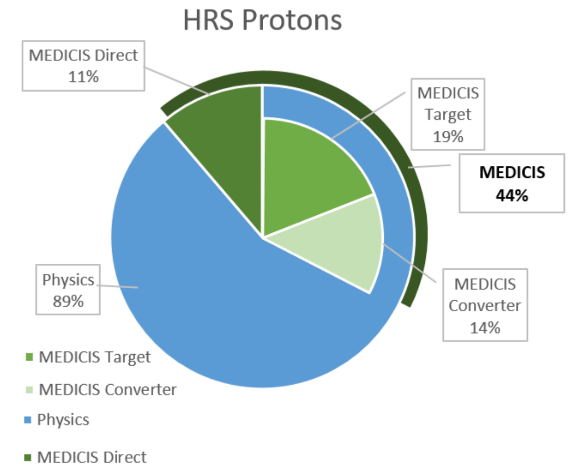
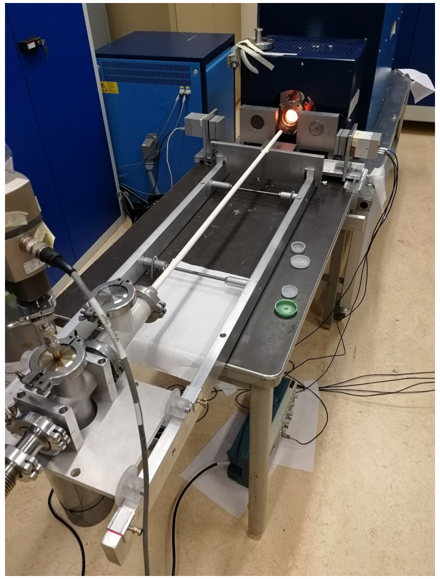
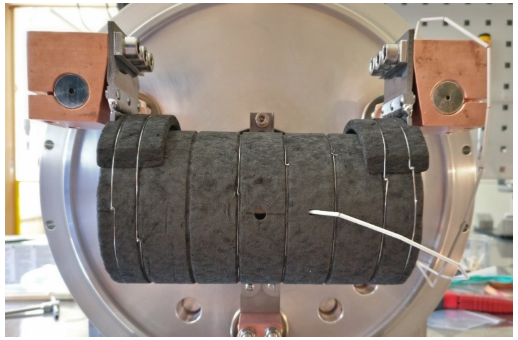
2018 achievements

- 26 target irradiations over the 2018 campaign.
- Separation of radioisotopes produced with the nuclear reactor from Institut Laue-Langevin (Grenoble, France).
- Activities up to 75 MBq for ^{155}Tb and 100 MBq for ^{149}TbO & 120 MBq for ^{165}Tm.
  1 GBq extracted in total.
- 5% surface ionization reached
- Radiochemistry performed at NPL
- Samples distributed to HUG, CHUV, IST, …









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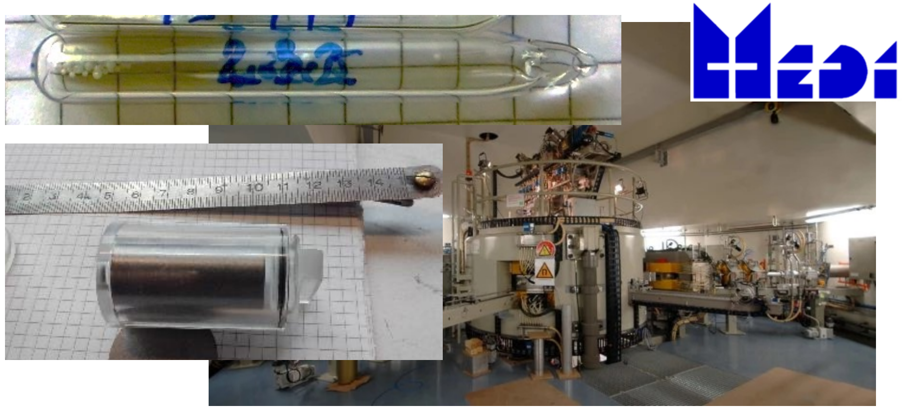
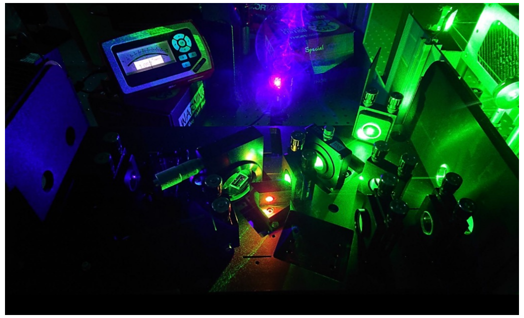
2019 achievements



- 100% operation with imported sources from ILL and from the ARRONAX cyclotron (Nantes, France) [30-70 MeV, ^{1}H, ^{2}H, ^{4}He]
- Installation of the MELISSA laser laboratory for laser ionization and of a dedicated fume hood for samples
- Tb/Gd radiochemistry pre-separation and new laser ionization scheme
- 15 collections of ^{155}Tb, ^{169}Er, ^{175}Yb over 15 weeks for a total of 870 MBq delivered to KUL, HUG, NPL, PSI



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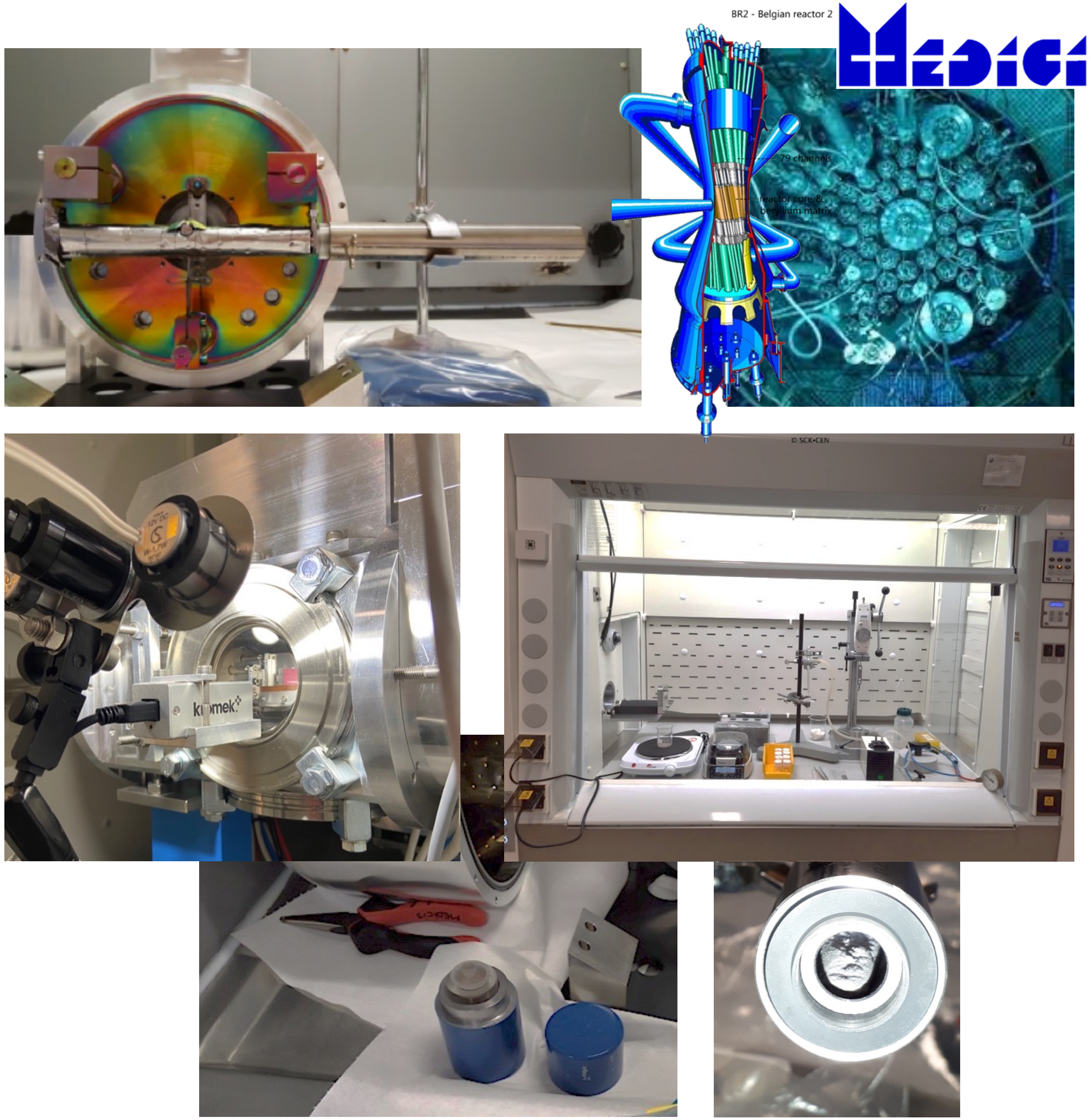
2020 achievements

- 100% operation with imported sources again, from ARRONAX, from the Proton Injector 2 cyclotron at PSI (Villigen, Switzerland), from the Belgian Reactor 2 (Mol, Belgium), and the European Commission's Joint Research Centre (Karlsruhe, Germany)
- Adding a CZT gamma-ray detector at the collection point to monitor the growth of activity; developing on-site radiochemistry for radiolanthanides
- 17 collections of ^{153}Sm, ^{155}Tb, ^{167}Tm, and ^{225}Ac, for 540 MBq for KUL, NPL, PSI



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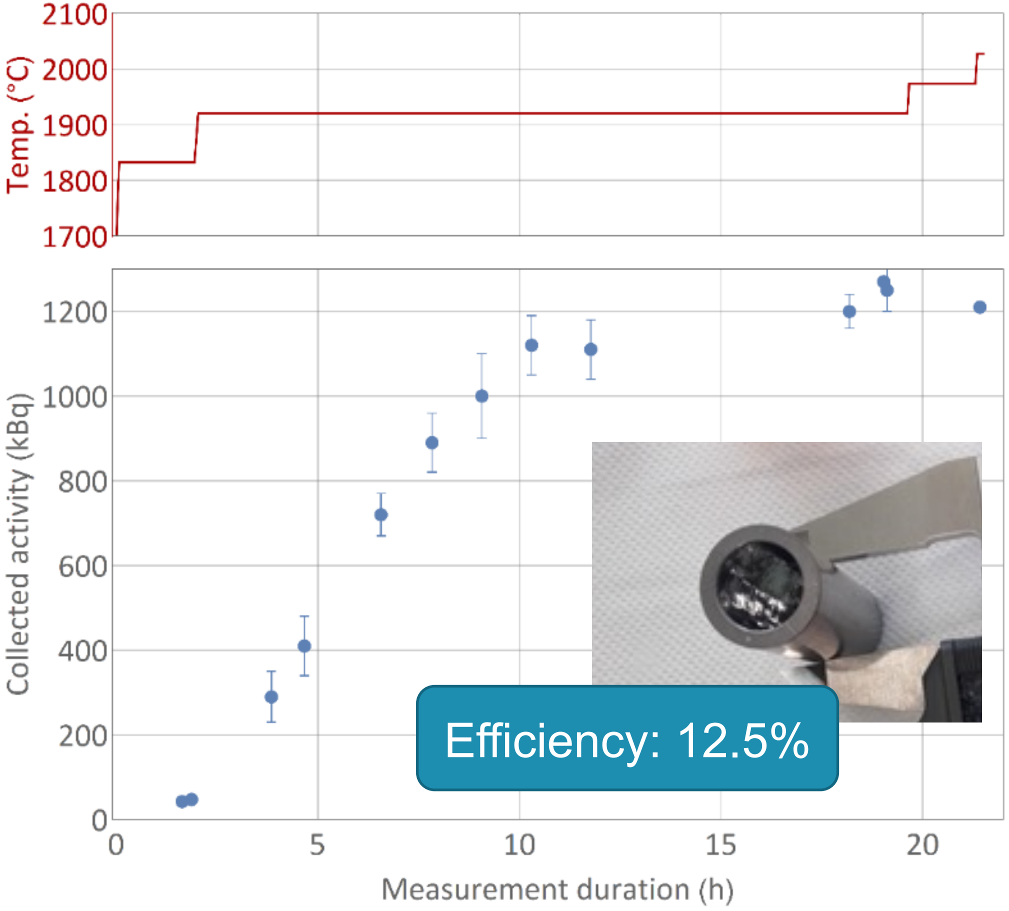
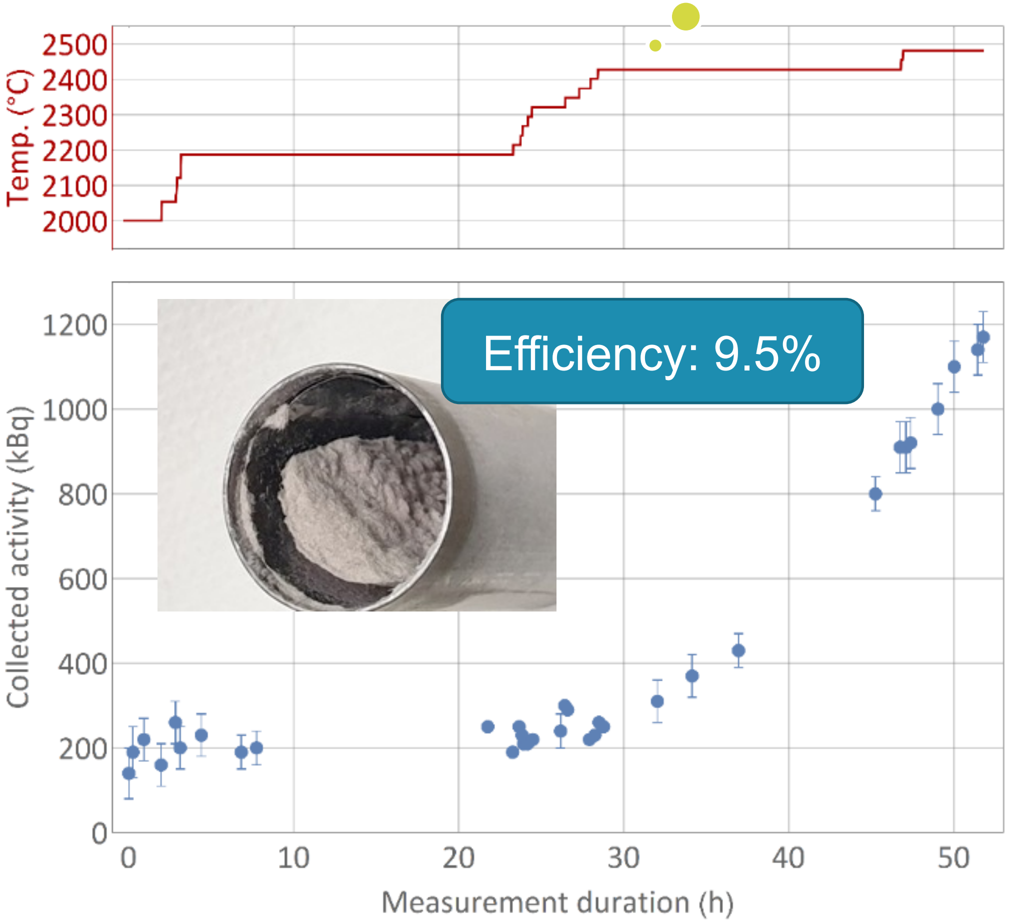
Status update MED024

MED024: ^{225}Ac extraction at MEDICIS

Required 500° more from ThO_2 than it did from Re!

$$\varepsilon = \varepsilon_{diff}\varepsilon_{eff}\varepsilon_{ion}\varepsilon_{sep}\varepsilon_{trans}$$





PhD work Jake Johnson, KU Leuven.

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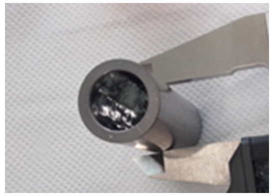
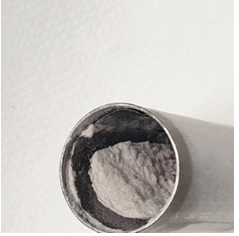
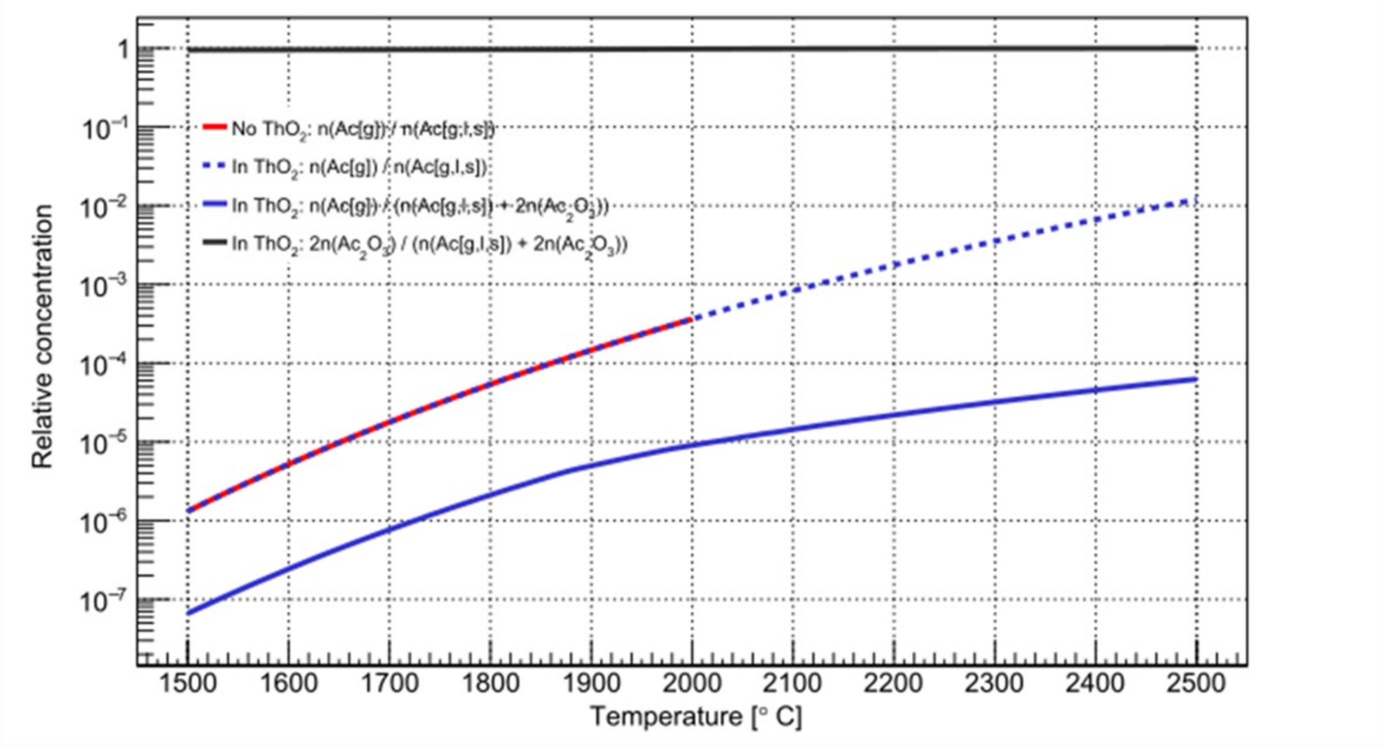
Status of data from MED024

$\varepsilon = \varepsilon_{ion}\varepsilon_{sep}\varepsilon_{trans}$ 10.0(2)% $\varepsilon_{ion} = 12.8(2)\%$ $T_{rel} = 1890°C$



$\varepsilon = \varepsilon_{eff}\varepsilon_{ion}\varepsilon_{sep}\varepsilon_{trans}$ 9.8(1)% $T_{rel} = 2260°C$

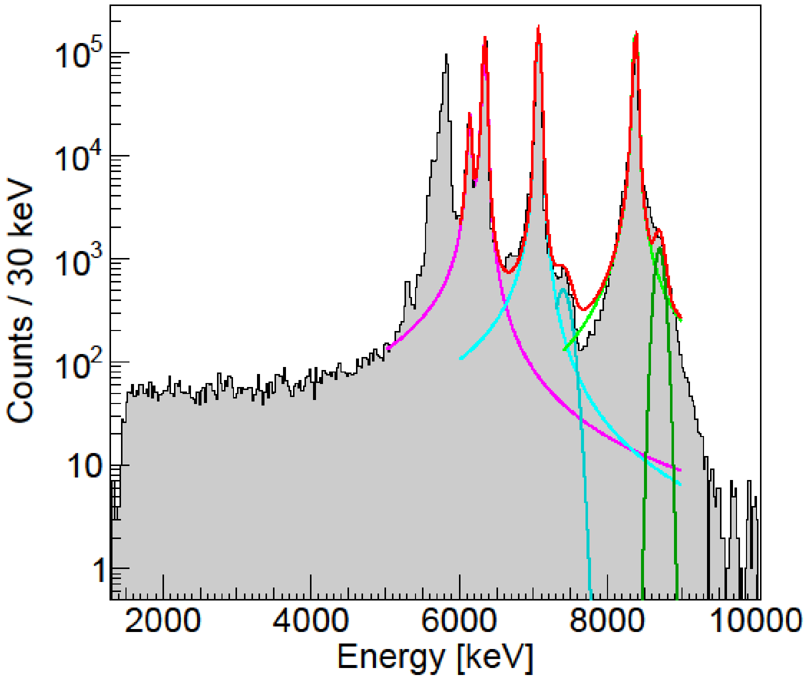


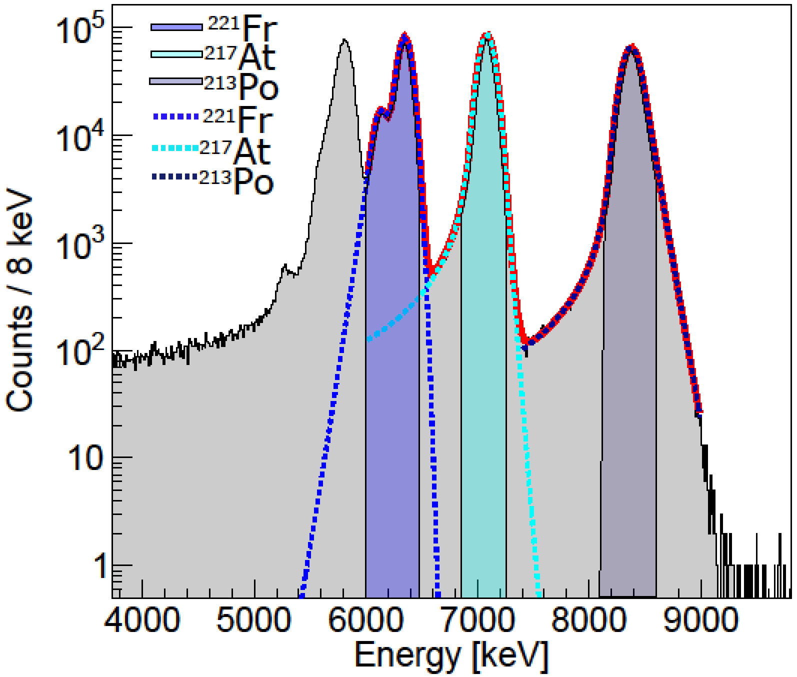


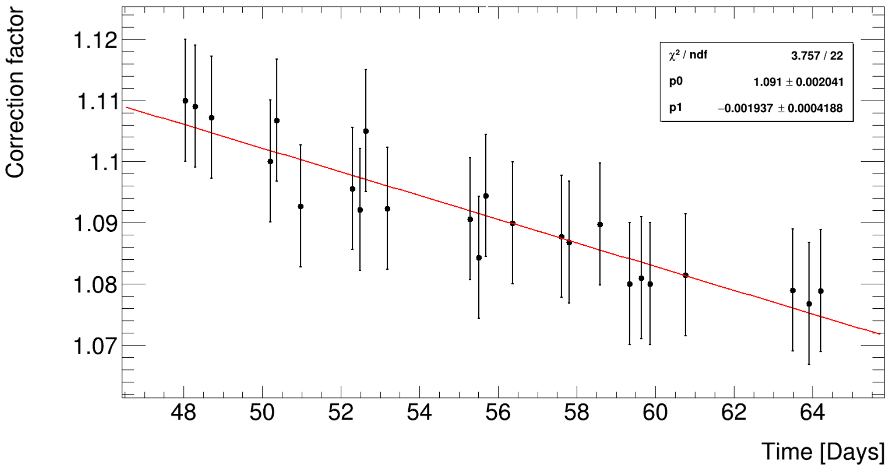
Conclusions:

- 225Ac extraction is not effusion limited.
- A high target temperature (~2260 is required, probably due to formation of Ac2O3 in target.
- The ionization efficiency was the main limiting factor in collection efficiency. Expected to worsen for irradiated target conditions

Decay spectroscopy of 2020 ^{225}Ac collections







KU LEUVEN
NUCLEAR AND RADIATION PHYSICS

Suitability of resonance ionization and mass separation of heavy elements for medicine

- High ionization efficiency of other Actinides
- High ionization efficiencies achieved at CERN MEDICIS
- Laser ionization and mass separation is a viable method to collect heavy elements from irradiation targets for medical purposes.
- But are other unwanted species collected too?

Element	Ion current (nA)	Ionization efficiency	Facility
^{232}Th	50	38.6%	ORNL[1]
^{242}Pu	10	51.1%	ORNL[2]
^{167}Tm	50	55%	MEDICIS[3]
^{153}Sm		12.7%	MEDICIS[4]
^{177}Lu	40	52%	RISIKO[5] (Mainz)
^{225}Ac	0.01	12.8%	MEDICIS[*]

[4]Van de Voorde, M.et al.Production of sm-153 with very high specific activity for targeted radionuclide therapy.Front.Medicine8, 1153(2021).
[3]Talip, Z.et al.Efficient production of high specific activity 167tm at psi and cern-medicis.Lab. Radiochem.52 (2020).
[2]Galindo-Uribarri, A., Liu, Y., Romero Romero, E. & Stracener, D. W. High efficiency laser resonance ionization ofplutonium.Sci. Reports11, 1–11 (2021).
[1].Liu, Y. & Stracener, D. High efficiency resonance ionization of thorium. Nucl. Instruments Methods Phys. Res. Sect. B, 95–101(2020)
[5] Gadelshin, V. M.et al.Measurement of the laser resonance ionization efficiency for lutetium.Radiochimica Acta107,653–661 (2019)
[*] Publication in preparation

MED030: Characterising ^{225}Ac collected from irradiated target

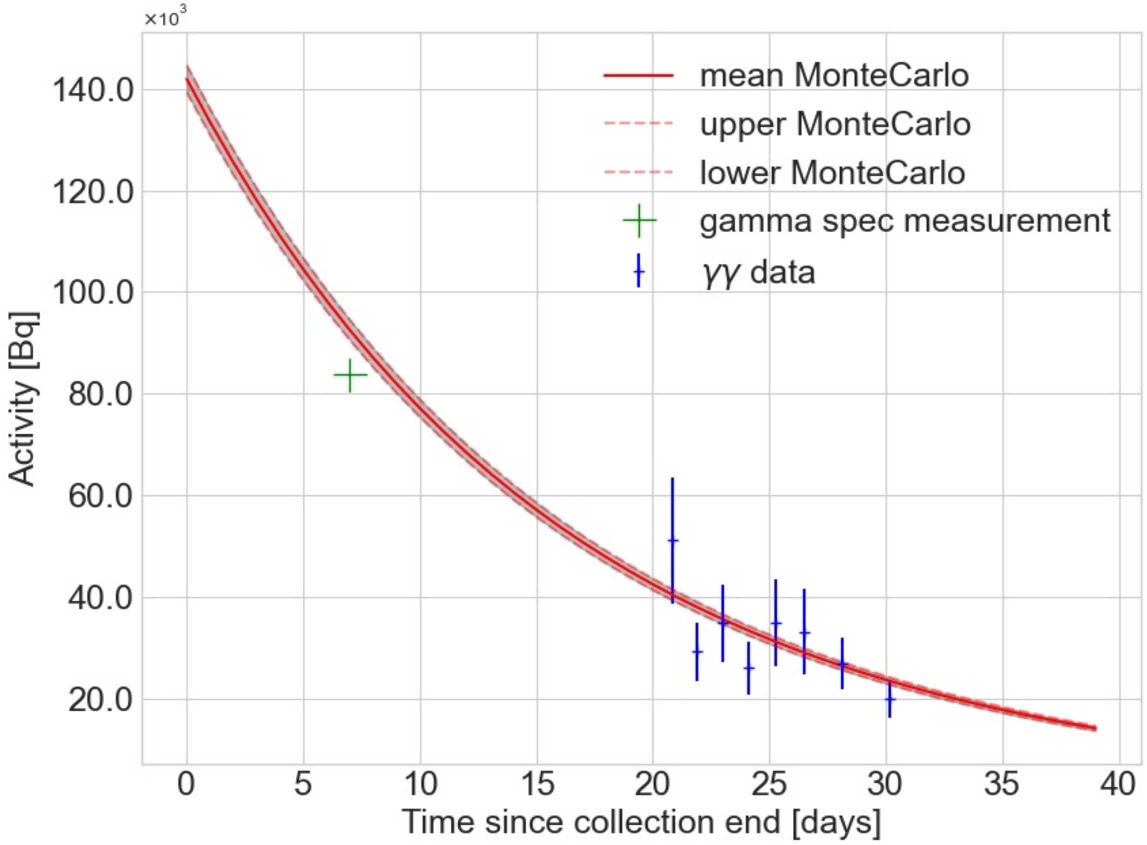
End of Collection Activity

- Gamma gamma coincidence spectroscopy
- Alpha spectroscopy

227Ac contamination

residual recoil method

MED030: End of collection activity



Preliminary 225Ac activity:140 kBq
Preliminary 225Ra activity: 17kBq

Alpha spectroscopy analysis ongoing to supplement this information.

FLUKA simulation to verify in-target production

Information on amount shipped to colleagues in Pakistan and for radiochemistry tests needed

MED030: Characterising ^{225}Ac collected from irradiated target

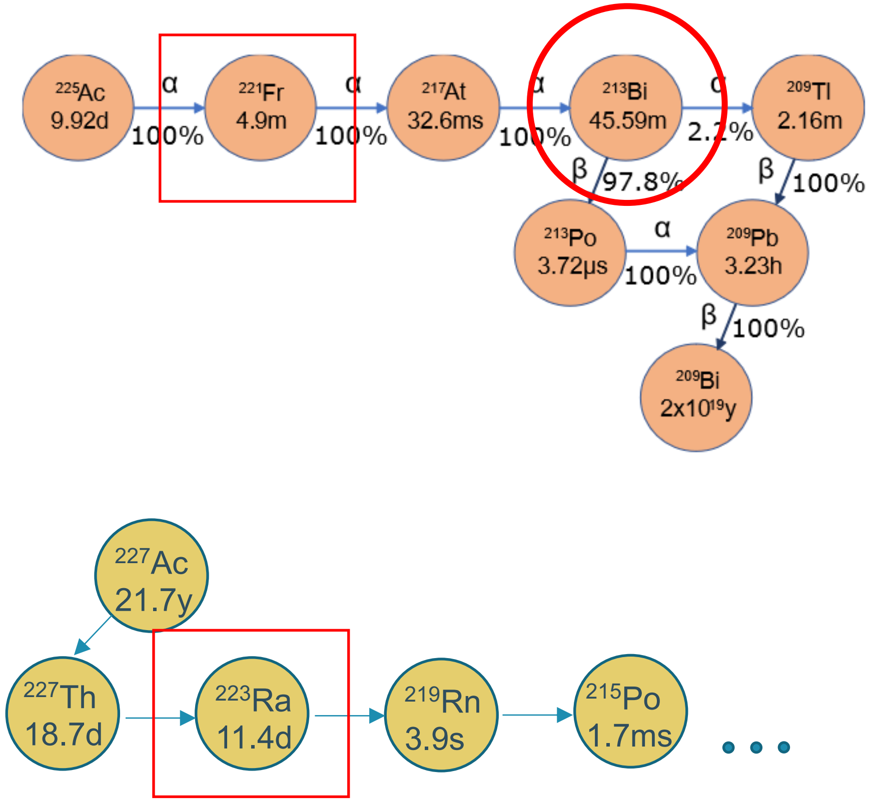
End of Collection Activity

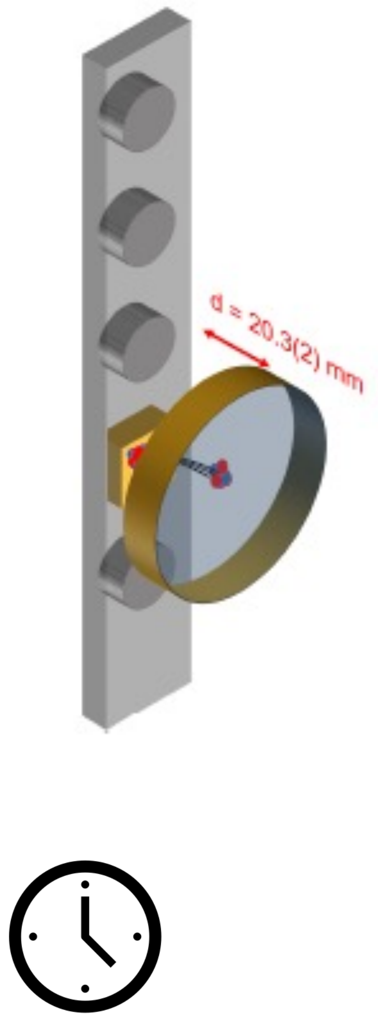
- Gamma gamma coincidence spectroscopy
- Alpha spectroscopy

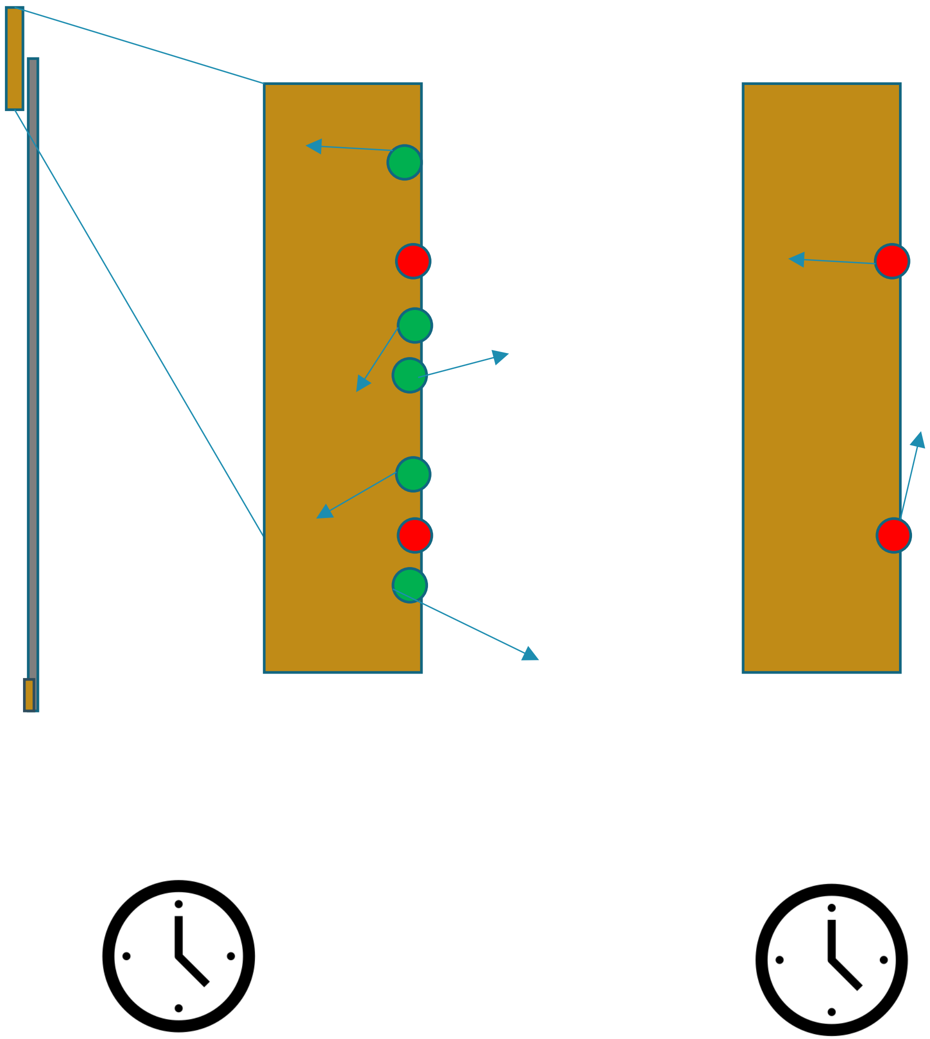
227Ac contamination

residual recoil method

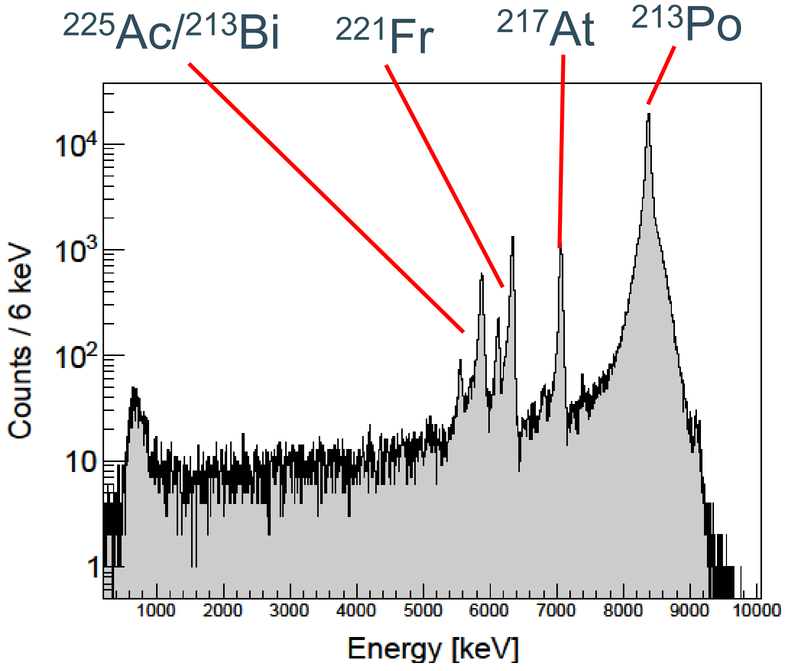
^{225}Ac purity determination by residual recoil method



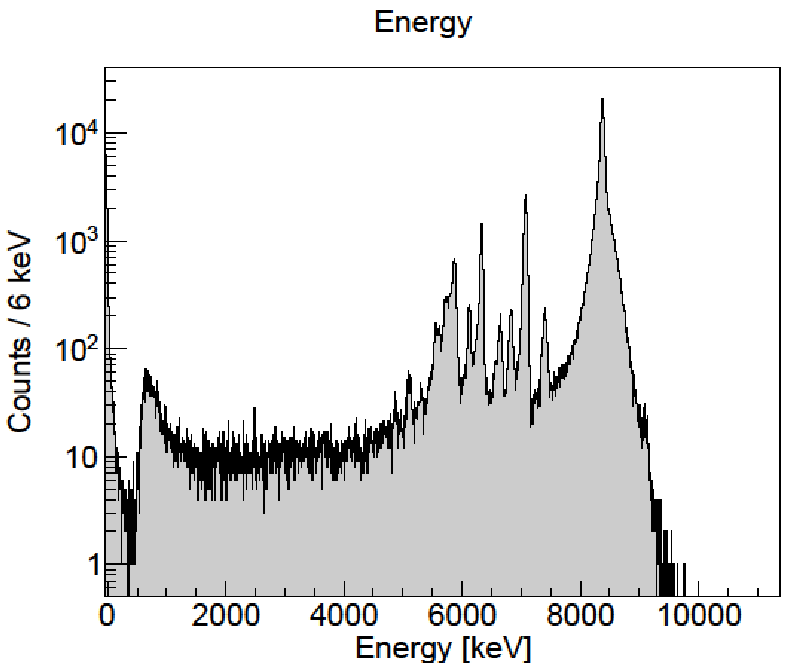




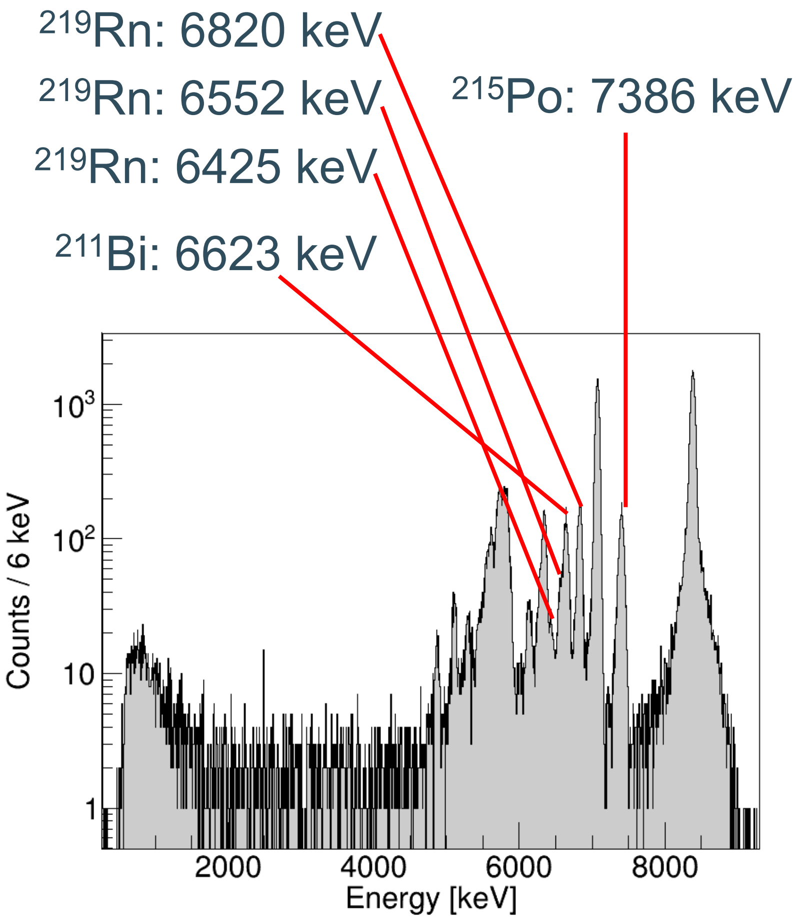
Preliminary Results



1st day of measuring: Nothing impressive

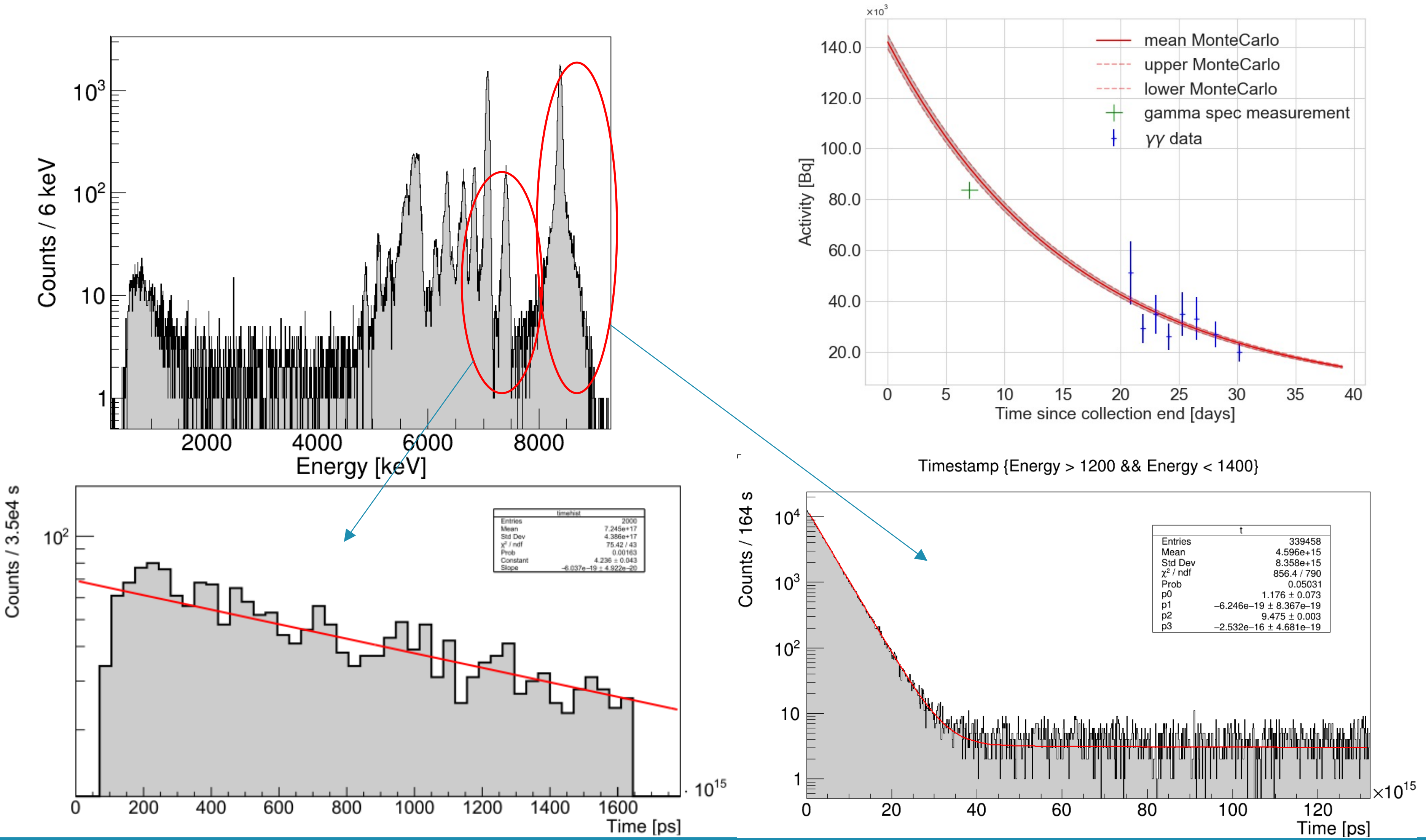


19 days of measuring: Ac-227 daughters appear!



18 days of measuring with day 1 removed

Preliminary purity results



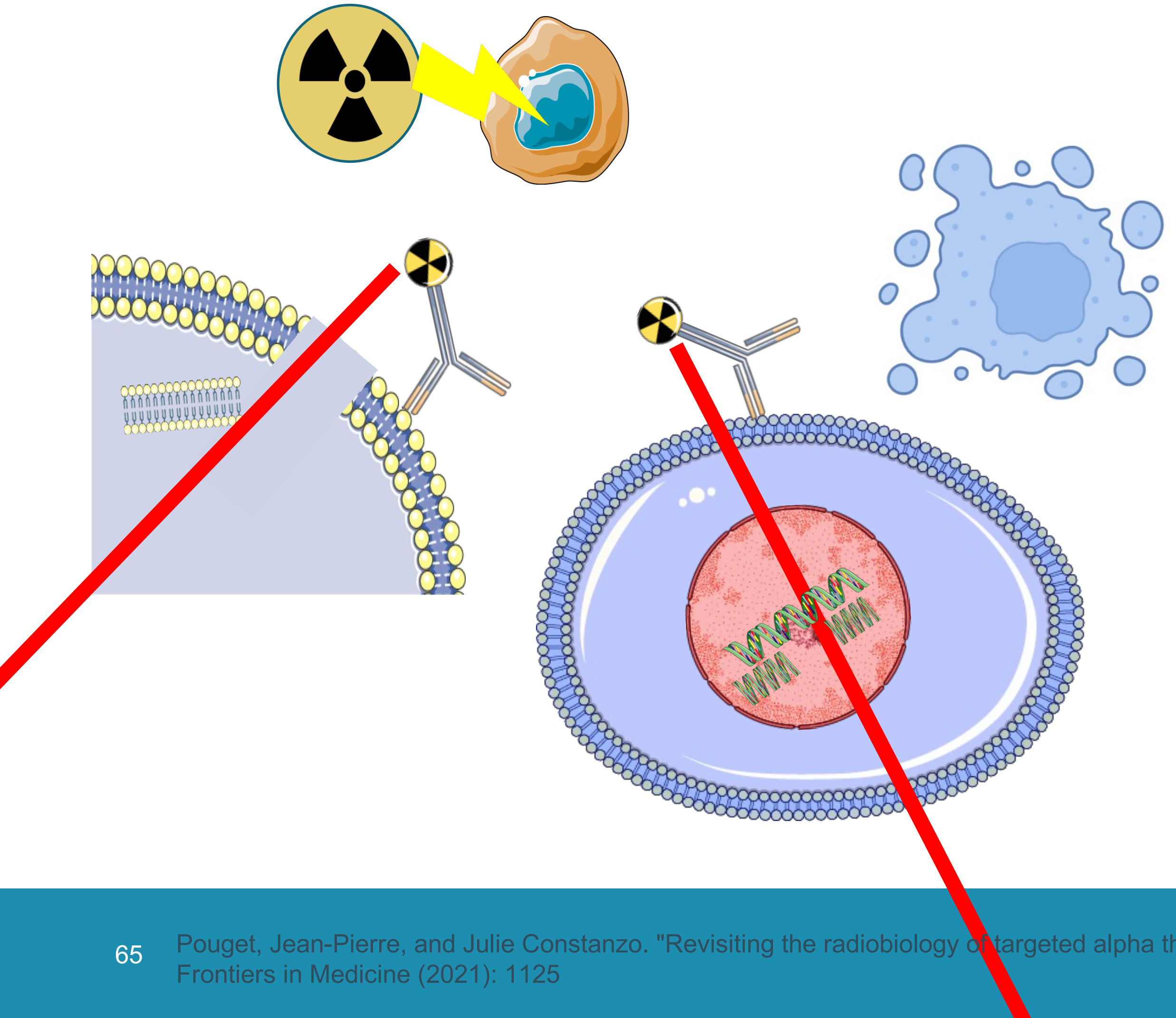
- Using ^{215}Po peak: 2 x 10^{-3} counts per second at $t=t_r$
- Using ^{213}Po peak: 79 counts per second at $t=t_r$.
- $r(t_r)/A(t_r) = \varepsilon_{geo}$ = 3.1%.
- $\varepsilon_{sat} \approx 80\%$
- Estimate of A(^{227}Ac): 0.002/0.031/0.8/0.986 Bq = 0.083 Bq
- ^{225}Ac activity at end of collection = 140kBq
- A(^{227}Ac)/ A(^{225}Ac) = 5.9 x 10^{-7}

Developing Project: CELLRAD

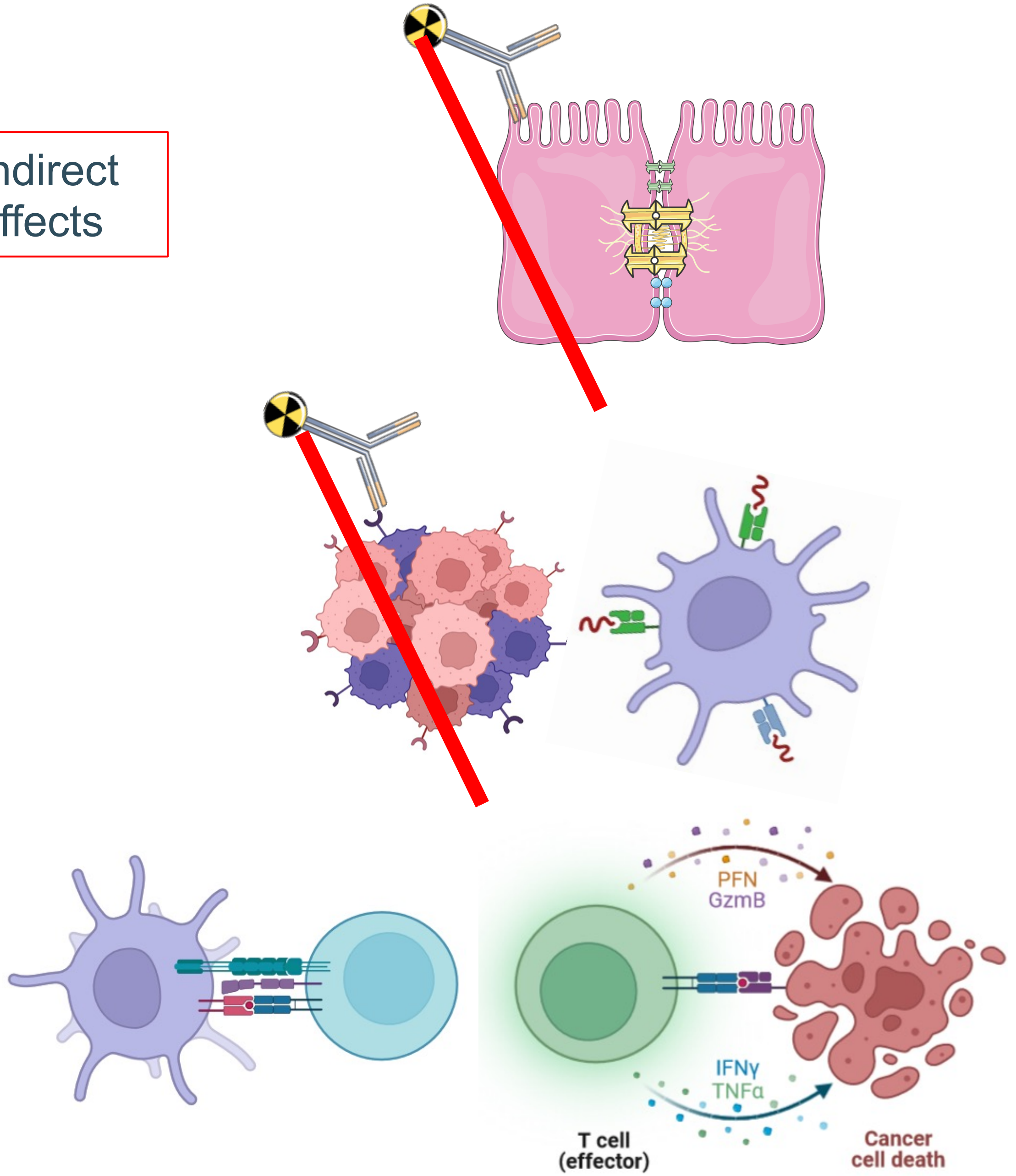
Alpha radiation and Cells

How does α radiation damage cells?

Direct effects



Indirect effects



Pouget, Jean-Pierre, and Julie Constanzo. "Revisiting the radiobiology of targeted alpha therapy." Frontiers in Medicine (2021): 1125