

Development of Terbium Fluoride Beams for Medical Applications

EMIS XX 2025, Whistler, Canada

23rd October 2025

Wiktoria Wojtaczka, KU Leuven

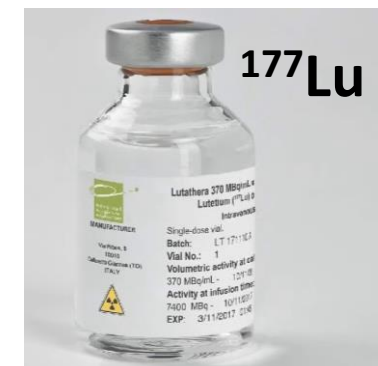
Why terbium?

Periodic Table: Medical radioactive isotopes

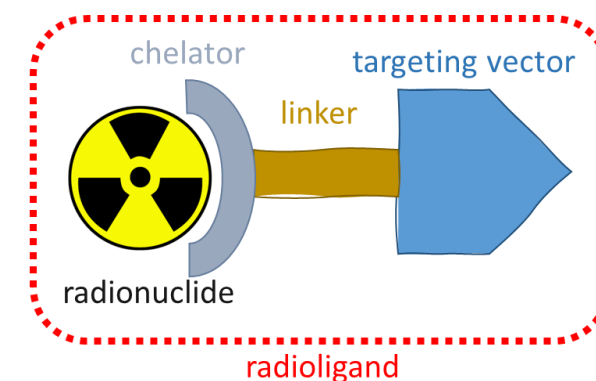
Periodic Table: Medical radioactive isotopes																		He						
H																								
Li		Be																B		C	N	O	F	Ne
																				11 14	13	15	18	19
Na		Mg																Al		Si	P	S	Cl	Ar
																					32 33	35	34m 36 38 39	
K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr							
38 42 43	45	43 44 46 47	44 46		48 51	52 52m 54	52 55 59	55 57 58 60	63	60 61 62 64 67	63 65 69m	66 67 68	68	72 73 74	75	75 76 77 82	85 77 79 79m 81m							
Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe							
81 82 84 86	85 87m 89 90	86 88 90	89	90 95	99	94m 95 99m	103	103m 105	103	109m 111		110m 111 113m 114m 115m	117m		123m	122 123 124 125 128 131 132	125 127 127m 133							
Cs	Ba	La	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn							
129 134 137	133m 137m	134 135		178		186 188		191m 192	191 193m 195 195m	195m 198 199	197 197m 203	199 201	203 212	204 205 206 207 212 213		211								
*Fr	*Ra	*Ac																						
	223 226	225																						
			Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu								
			139 141	140 143		149	153		153	149 152 155 161	157	166	165 169	167	169	172 177								
			*Th	*Pa	*U	*Np	*Pu	*A	*C	*BK	*Cf	*Es	*Fm	*Md	*No	*Lr								
			226 227																					

S. Zhang, Signal Transduction and Targeted Therapy **10**, 1 (2025)

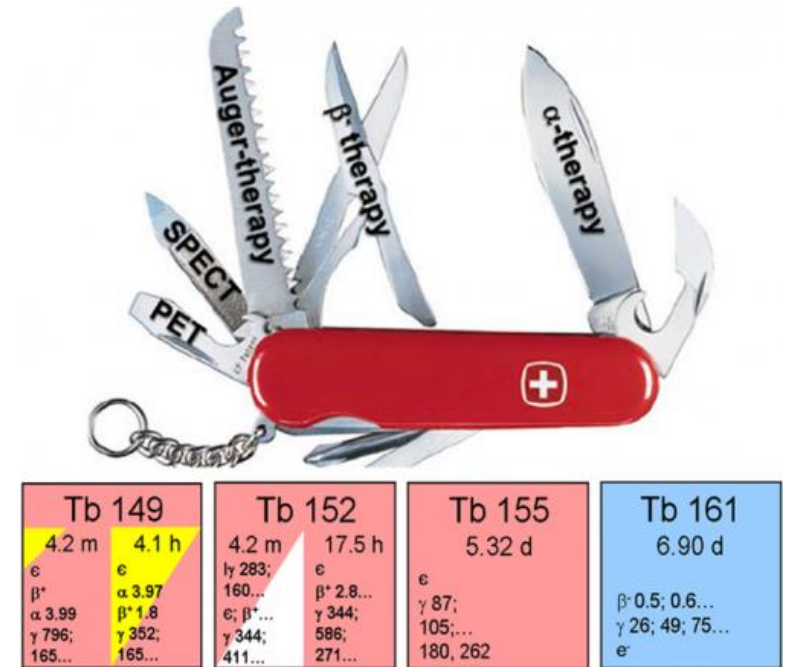
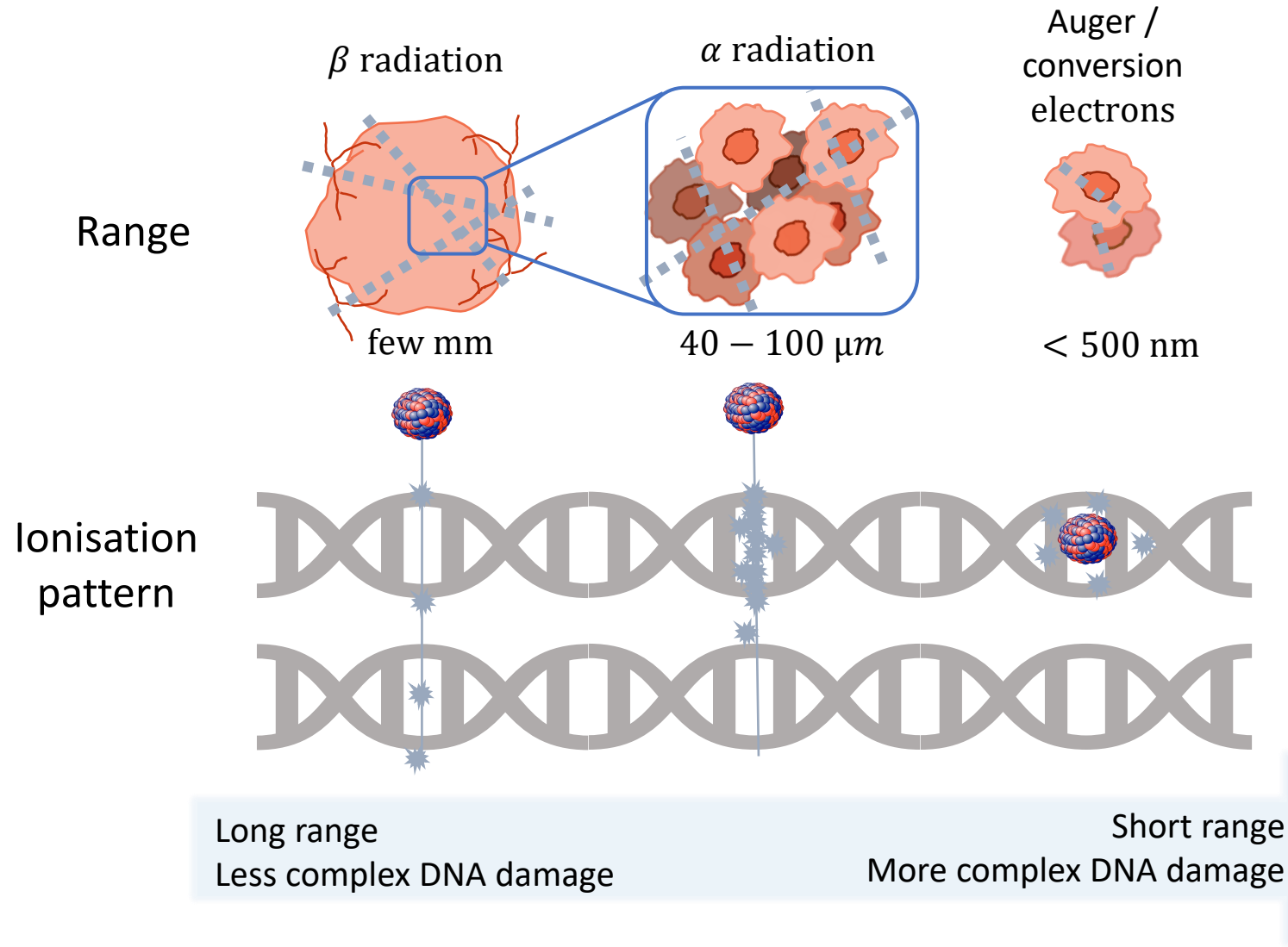
2 FDA-approved agents



Clinical trials for many indications

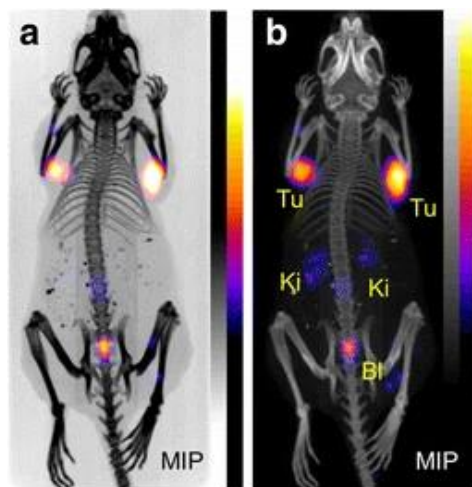


By studying Tb molecules, we also learn about other lanthanides



All modalities in nuclear medicine
Chemically identical
Elegant theragnostics

**α -Therapy
PET (β^+)**



EUROPEAN ORGANIZATION FOR NUCLEAR RESEARCH

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

Terbium-149 for targeted alpha therapy

11 January 2023

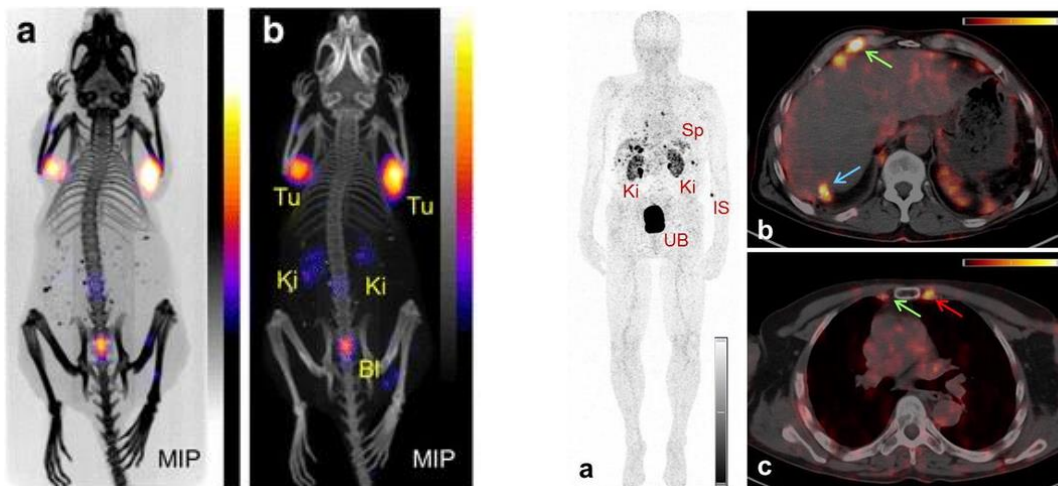
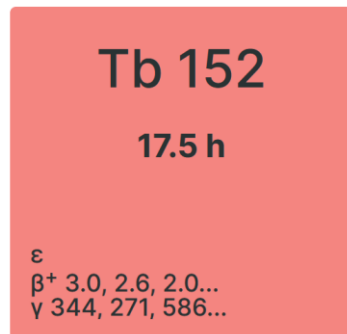
Nick van der Meulen¹, Cristina Müller¹, Anzhelika Moiseeva¹, Colin Hillhouse¹, Pascal Grundler¹, Stuart Warren¹, Maryam Mostamand¹, Ana Katrina Mapanao¹, Avni Mehta¹, Karl Johnston², Ulli Köster³

C. Müller et al. 2017 EJNMMI radiopharm. chem. 1, 5

**α -Therapy
PET (β^+)**



PET (β^+)

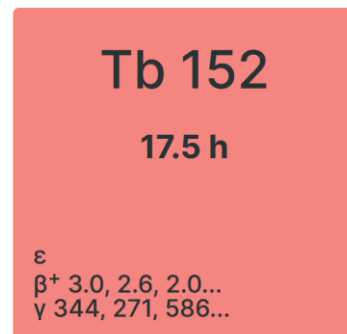


C. Müller et al. **2017** EJNMMI radiopharm. chem. **1**, 5 R. Baum et al. Dalton Trans **2017**;46:14638–46

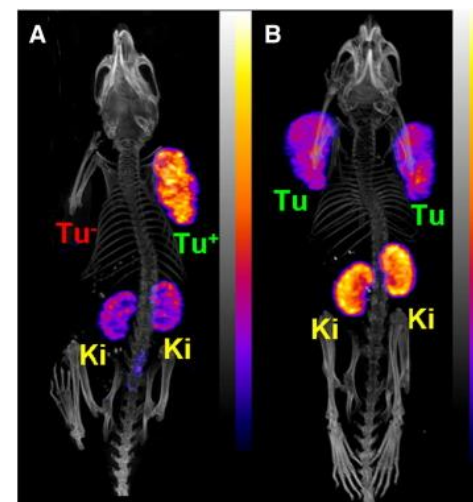
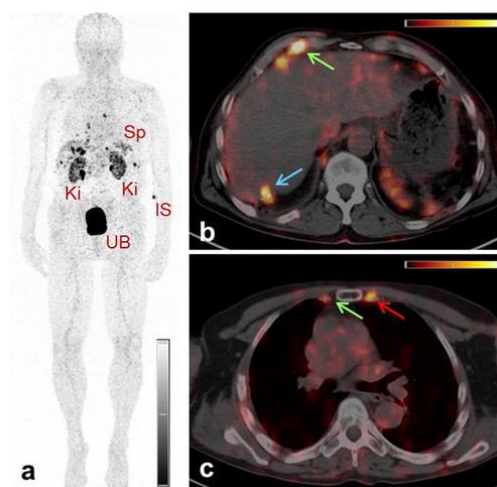
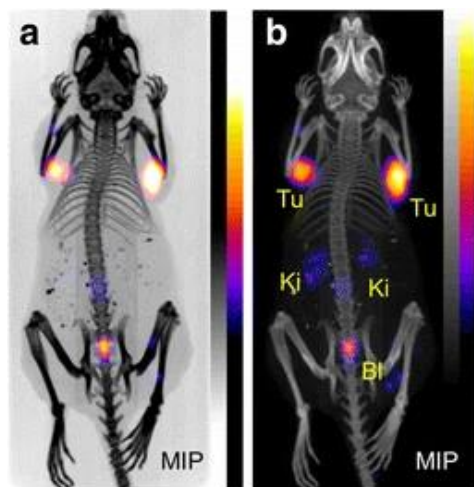
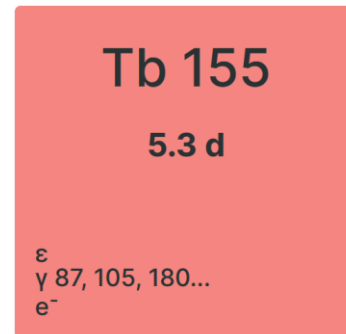
**α -Therapy
PET (β^+)**



PET (β^+)



SPECT (γ)



C. Müller et al. **2017** EJNMMI radiopharm. chem. **1**, 5

R. Baum et al. Dalton Trans **2017**;46:14638–46

C. Müller et al **2014** Nuc Med Biol 41:e58-e65

α -Therapy PET (β^+)

Tb 149
4.1 h

PET (β^+)

Tb 152
17.5 h

SPECT (γ)

Tb 155
5.3 d

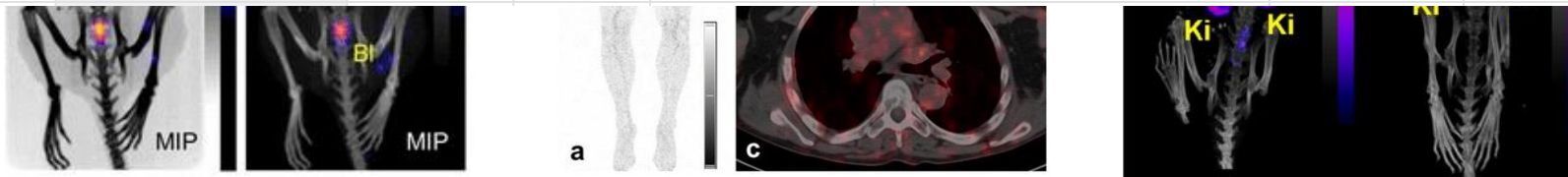
SPECT (γ) β^- -Therapy Auger- e^- Therapy

Tb 161
6.95 d

β^- 0.5, 0.6...
 γ 26, 49, 75...
 e^-

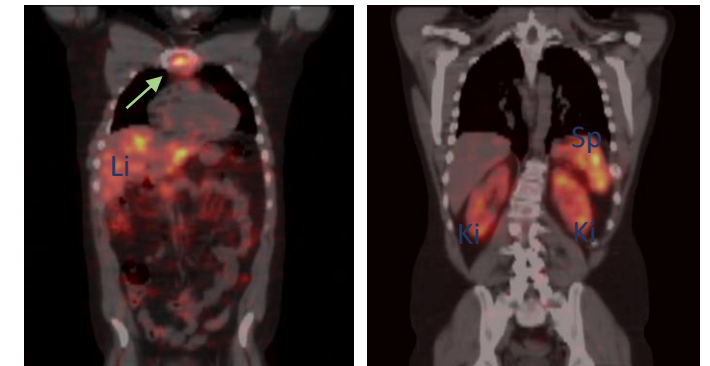
☐	1	Combined Beta- Plus Auger Electron Therapy Using a Novel Somatostatin Receptor Subtype 2 Antagonist Labelled With Terbium-161 (¹⁶¹Tb-DOTA-LM3)	NCT05359146	Recruiting	- Neuroendocrine Neoplasia's (NENs) - Gastroenteropancreatic Neuroendocrine Tumour (GEP-NET)	- Drug: ¹⁶¹Tb-DOTA-LM3 - Drug: 177Lu-DOTATOC	University Hospital, Basel, Switzerland	Interventional
☐	2	Evaluation of radioligand treatment in mEn With Metastatic Castration-resistant Prostate Cancer With [¹⁶¹Tb]Tb-PSMA-I&T	NCT05521412	Recruiting	- Prostate Cancer - Metastatic Castration-resistant Prostate Cancer	Drug: [¹⁶¹Tb]Tb PSMA I&T	Peter MacCallum Cancer Centre, Australia	Interventional
☐	3	Targeted Radionuclide Therapy in Metastatic Prostate Cancer Using a New PSMA Ligand Radiolabelled With Terbium-161 (¹⁶¹Tb-SibuDAB) - Dose Identification/Escalation Phase Ia/b Study	NCT06343038	Recruiting	Castration-resistant Prostate Cancer	- Drug: Injection, ¹⁶¹Tb-SibuDAB, 1GBq - Drug: Injection, 177Lu-PSMA-I&T, 1GBq - Drug: Injection, ¹⁶¹Tb-SibuDAB, Dose Escalation	University Hospital, Basel, Switzerland	Interventional

clinicaltrials.gov



C. Müller et al. 2017 EJNMMI radiopharm. chem. 1, 5 R. Baum et al. Dalton Trans 2017;46:14638–46 C. Müller et al 2014 Nuc Med Biol 41:e58-e65

Patient with NEN (600 MBq ¹⁶¹Tb-DOTATOC)



R. Baum & A. Singh et al. 2021, J Nucl Med 62:1391.

3 clinical trials ongoing
many cases of compassionate use

**Why are the other isotopes not in
the clinics?**



Possible production routes of Tb



Tb 149

4.1 h

ϵ
 α 3, 97
 β^+ 1, 4...
 γ 352, 165...

Tb 152

17.5 h

ϵ
 β^+ 3.0, 2.6, 2.0...
 γ 344, 271, 586...

Tb 155

5.3 d

ϵ
 γ 87, 105, 180...
 e^-

Tb 161

6.95 d

β^- 0.5, 0.6...
 γ 26, 49, 75...
 e^-

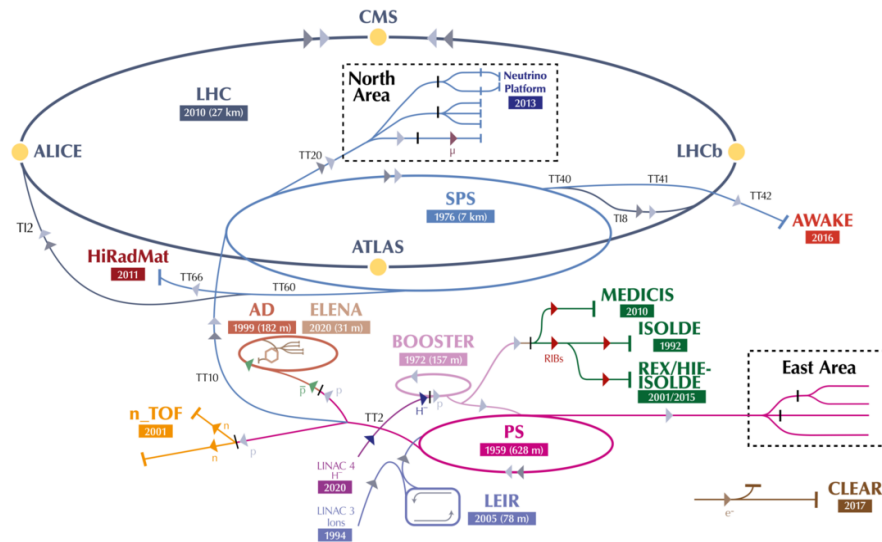


NEA (2020), BR2-reactor of SCK-CEN, OECD Publishing, Paris



in most cases mass
separation required

Producing Tb at CERN



Overview of ISOL facilities and production techniques

João Pedro Ramos

MacDonald AB, Fairmont Chateau Whistler

10:30 - 11:00

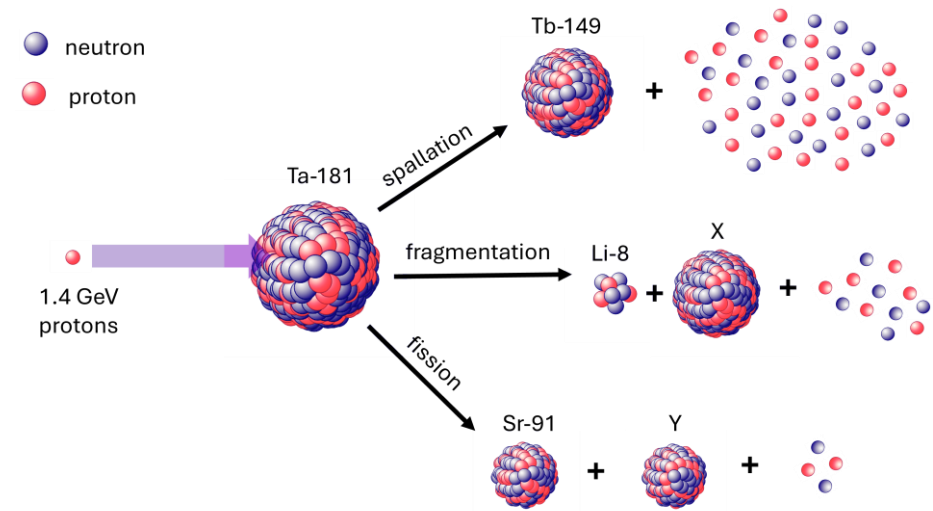
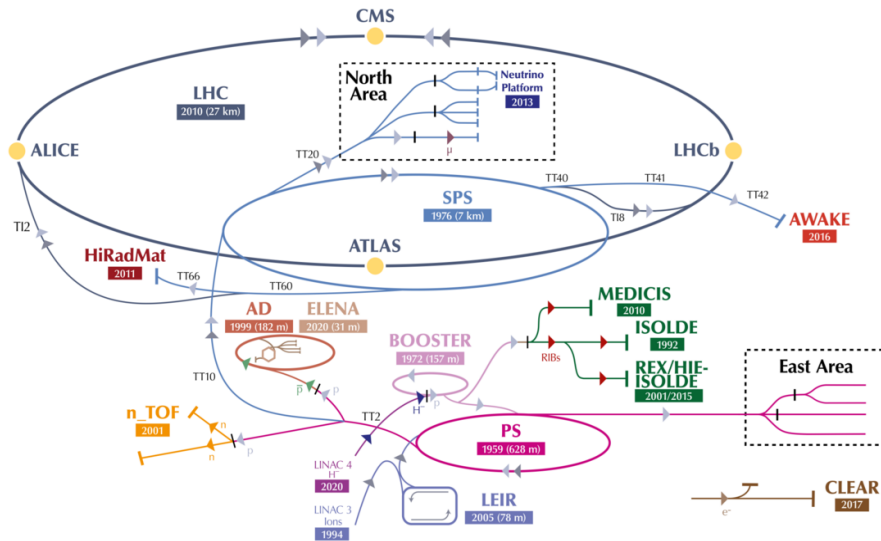
Development of molecular beams at ISOLDE

Mia Au

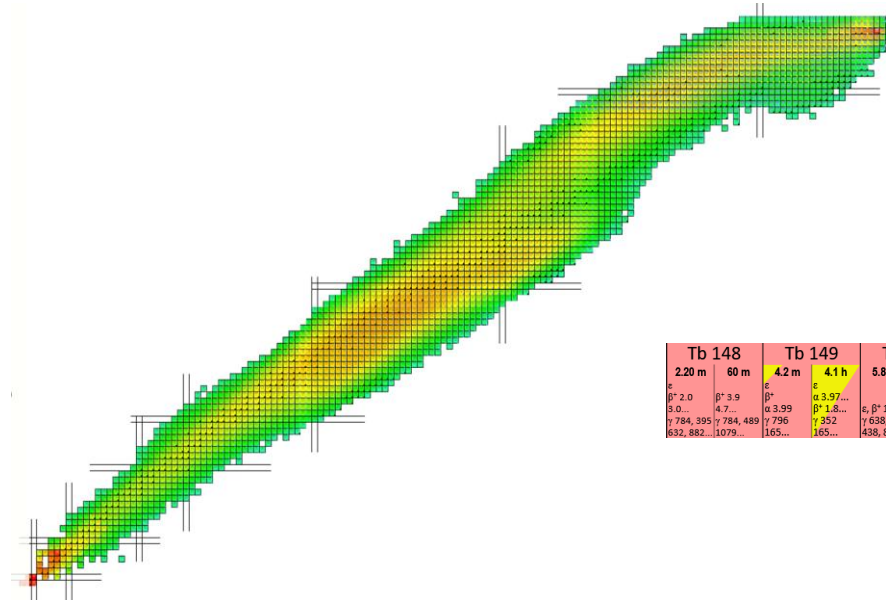
MacDonald AB, Fairmont Chateau Whistler

08:30 - 09:00

Producing Tb at CERN



1.4 GeV protons, spallation on Ta



Tb 148		Tb 149		Tb 150		Tb 151		Tb 152		Tb 153		Tb 154		Tb 155		Tb 156		Tb 157		Tb 158		Tb 159		Tb 160		Tb 161																					
2.20 m		60 m		4.2 m		4.1 h		5.8 m		3.48 h		25 s		17.609 h		4.2 m		17.5 h		2.34 d		22.7 h		9.994 h		21.5 h		5.32 d		5.3 h		24.4 h		5.35 d		71 a		10.70 s		180 a		100		72.3 d		6.89 d	
β^- 2.0		β^- 3.9		β^- 3.9		β^- 3.9		β^- 3.0		β^- 3.0		β^- 3.0		β^- 3.0		β^- 3.0		β^- 3.0		β^- 3.0		β^- 3.0		β^- 3.0		β^- 3.0		β^- 3.0		β^- 3.0		β^- 3.0		β^- 3.0		β^- 3.0		β^- 3.0		β^- 3.0		β^- 3.0					
3.0...		4.7...		3.0...		3.0...		3.0...		3.0...		3.0...		3.0...		3.0...		3.0...		3.0...		3.0...		3.0...		3.0...		3.0...		3.0...		3.0...		3.0...		3.0...		3.0...		3.0...		3.0...		3.0...			
784, 395		784, 489		796		7352		7538, 650, 406...		7980		7252, 287		7344		386...		7212, 110, 102		170, 83...		7248		347		1223		787, 105, 180		7123		750		3222		7534		7199		7944		962		966...		726, 49, 75...	
632, 882, 1079...		165...		165...		438, 827...		3.49		831...		108...		411...		87?		170, 83...		170, 83...		170, 83...		170, 83...		170, 83...		170, 83...		170, 83...		170, 83...		170, 83...		170, 83...		170, 83...		170, 83...		170, 83...		170, 83...			

many Tb isotopes produced

Medical grade $^{149,152,155}\text{Tb}$ product

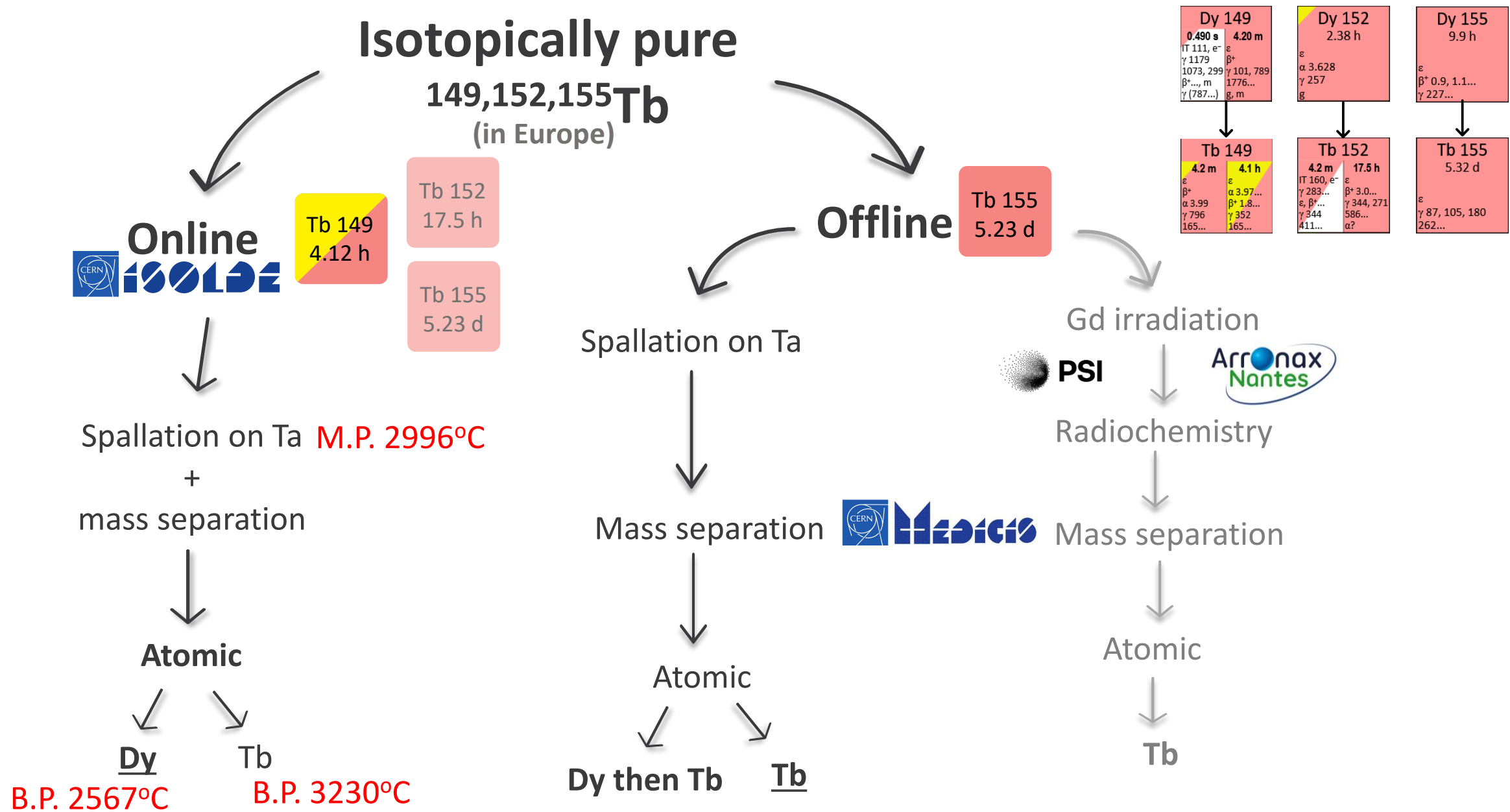
Mass separation for
isobaric selection

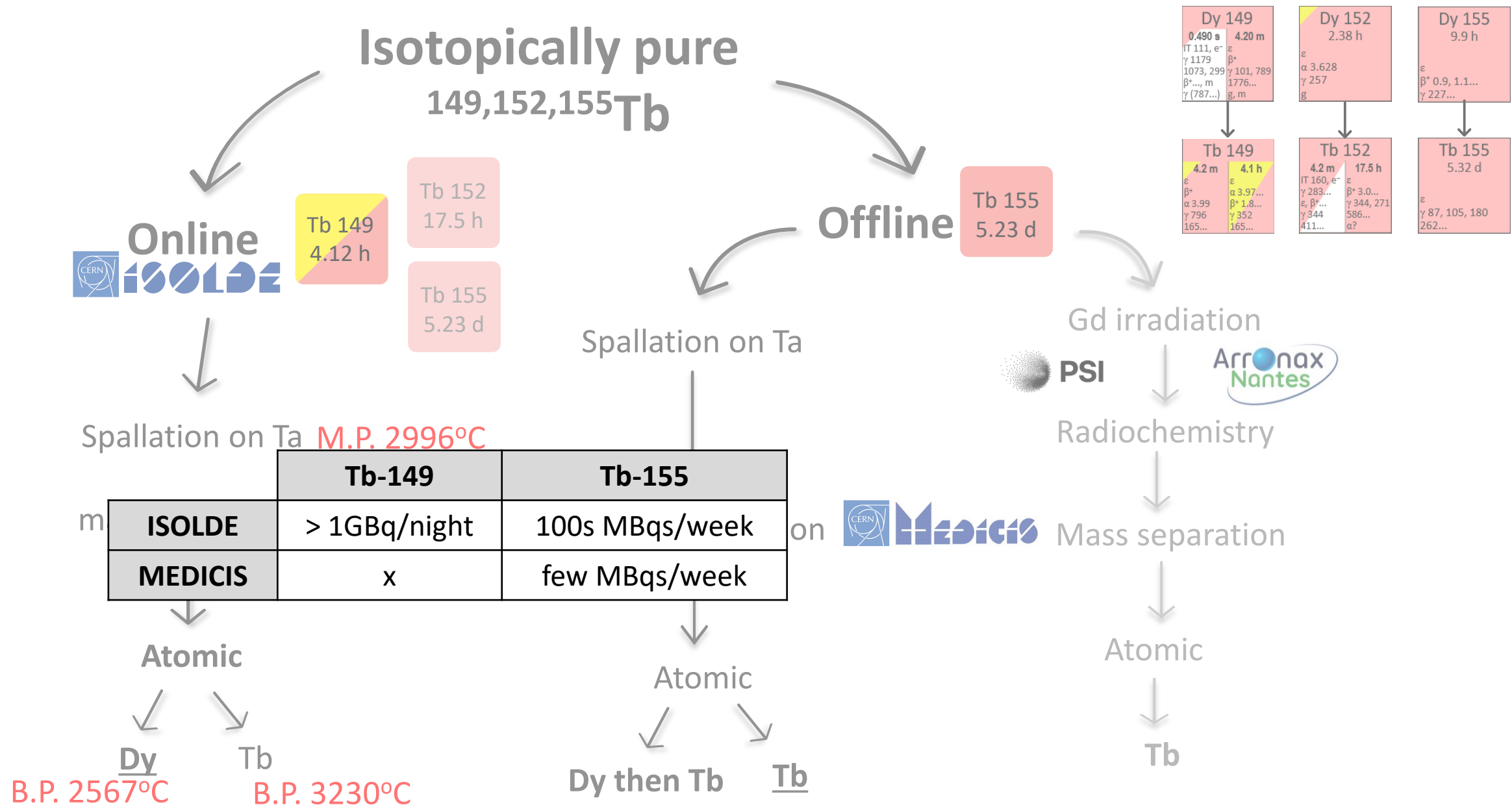
+

Chemical separation for
elemental selection

Yb 149 0.7 s	Yb 150 0.000000 s	Yb 151 1.8 s	Yb 152 3.09 s	Yb 153 4.2 s	Yb 154 0.409 s	Yb 155 1.793 s	Yb 156 26.1 s	Yb 157 38.6 s	Yb 158 1.49 m	Yb 159 1.87 m	Yb 160 4.8 m
Tm 148 8.7 s	Tm 149 0.9 s	Tm 150 2.3 s	Tm 151 52 s	Tm 152 52 s	Tm 153 26 s	Tm 154 33 s	Tm 155 46 s	Tm 156 83.8 s	Tm 157 3.63 m	Tm 158 ~20 ns?	Tm 159 9.13 m
Er 147 1.8 s	Er 148 2.6 s	Er 149 4.6 s	Er 150 8.9 s	Er 151 4.38 s	Er 152 10.3 s	Er 153 37.1 s	Er 154 3.73 m	Er 155 5.3 m	Er 156 19.5 m	Er 157 18.65 m	Er 158 2.29 h
Ho 146 3.32 s	Ho 147 5.8 s	Ho 148 1.1 s	Ho 149 56 s	Ho 150 23 s	Ho 151 47.2 s	Ho 152 35.2 s	Ho 153 83 m	Ho 154 34 m	Ho 155 48 m	Ho 156 7.8 m	Ho 157 12.6 m
Dy 145 14.5 s	Dy 146 33.2 s	Dy 147 56.2 s	Dy 148 1.3 m	Dy 149 8.49 s	Dy 150 4.29 m	Dy 151 17 m	Dy 152 2.38 h	Dy 153 6.4 h	Dy 154 3.0-10 ⁷ s	Dy 155 9.9 h	Dy 156 0.056
Tb 144 4.25 s	Tb 145 38.9 s	Tb 146 26.1 s	Tb 147 1.82 m	Tb 148 1.85 h	Tb 149 4.1 h	Tb 150 5.3 s	Tb 151 25 s	Tb 152 42 m	Tb 153 2.34 d	Tb 154 20.7 h	Tb 155 5.32 d
Gd 143 119 s	Gd 144 4.5 m	Gd 145 88 s	Gd 146 48.27 d	Gd 147 38.1 h	Gd 148 9.28 d	Gd 149 1.15 s	Gd 150 120 d	Gd 151 1.08-10 ¹⁰ s	Gd 152 240.4 d	Gd 153 2.18	Gd 154 2.18
Eu 142 1.223 m	Eu 143 2.34 s	Eu 144 2.59 m	Eu 145 10.2 s	Eu 146 5.93 d	Eu 147 4.61 d	Eu 148 24.1 d	Eu 149 93.1 d	Eu 150 12.3 h	Eu 151 47.81	Eu 152 13.81 d	Eu 153 52.19
Sm 141 22.8 m	Sm 142 72.49 m	Sm 143 46 s	Sm 144 3.08	Sm 145 340 d	Sm 146 6.8-10 ¹¹ s	Sm 147 1.5-10 ¹¹ s	Sm 148 1.1-10 ¹¹ s	Sm 149 13.82	Sm 150 1.08-10 ¹⁰ s	Sm 151 94.7 s	Sm 152 26.74
Pm 140 5.95 m	Pm 141 20.90 m	Pm 142 40.5 s	Pm 143 265 d	Pm 144 1.0 s	Pm 145 17.7 s	Pm 146 5.39 s	Pm 147 2.62 s	Pm 148 5.38 d	Pm 149 53.1 h	Pm 150 2.1 s	Pm 151 28.4 h
Nd 139 8.91 h	Nd 140 3.37 d	Nd 141 42.8 s	Nd 142 27.132	Nd 143 12.174	Nd 144 23.728	Nd 145 8.293	Nd 146 17.188	Nd 147 10.96 d	Nd 148 7.26	Nd 149 1.75 h	Nd 150 9.1-10 ¹¹ s

Tb 149 4.1 h ϵ α 3,97 β^+ 1,4... γ 352, 165...	Tb 152 17.5 h ϵ β^+ 3.0, 2.6, 2.0... γ 344, 271, 586...	Tb 155 5.3 d ϵ γ 87, 105, 180... e^-
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Isotope Separation OnLine

Overview of ISOL facilities and production techniques

João Pedro Ramos

MacDonald AB, Fairmont Chateau Whistler

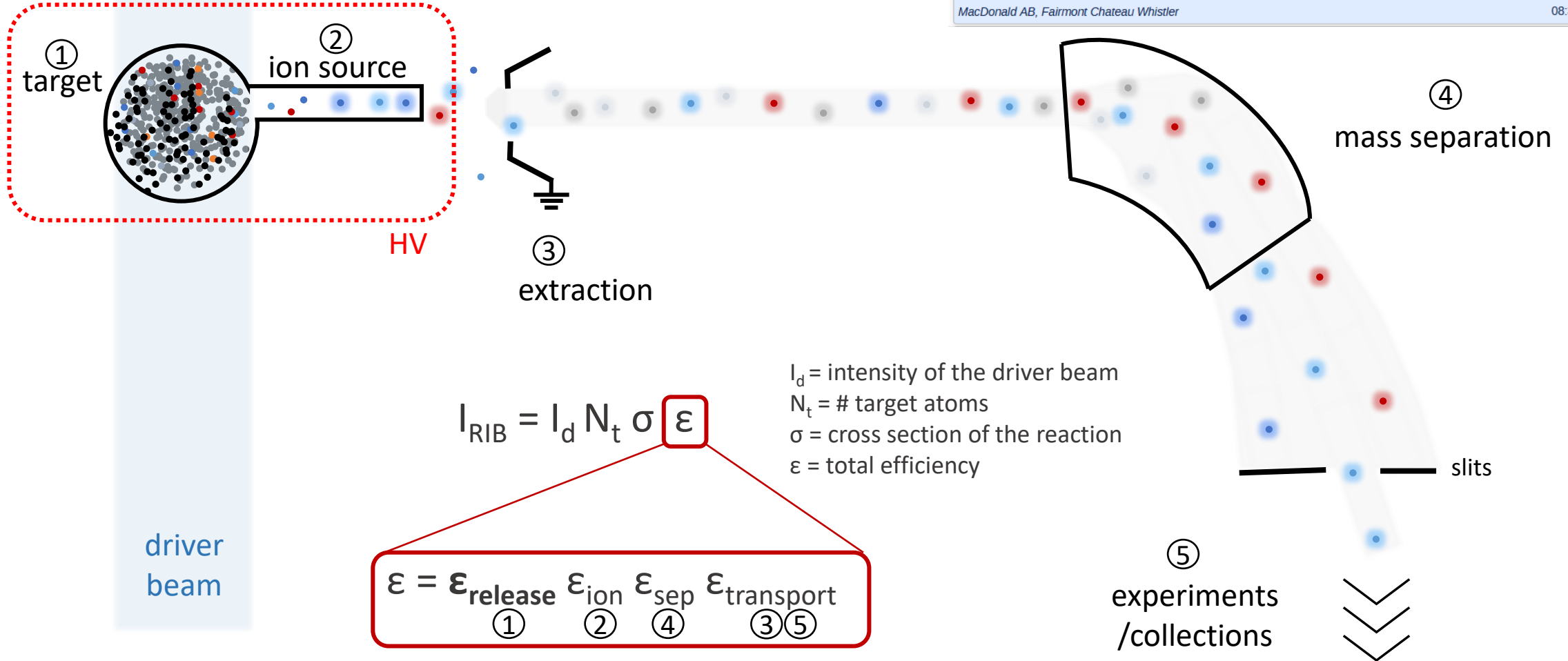
10:30 - 11:00

Development of molecular beams at ISOLDE

Mia Au

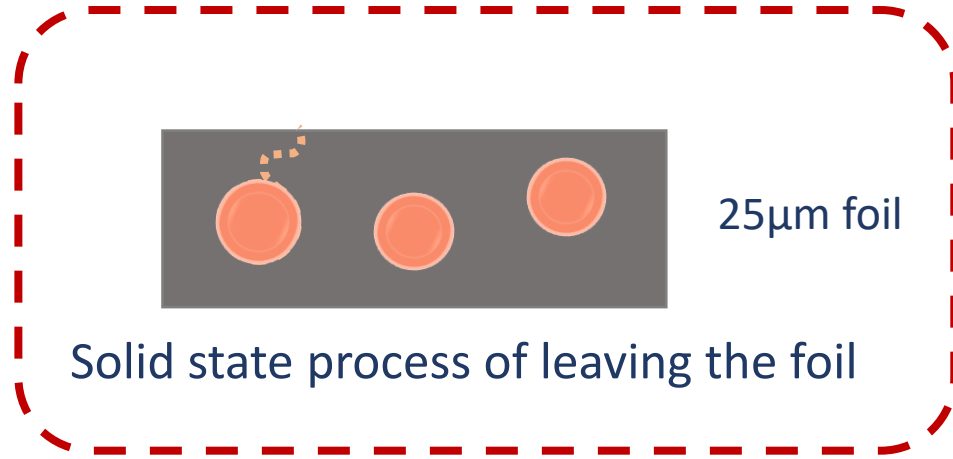
MacDonald AB, Fairmont Chateau Whistler

08:30 - 09:00

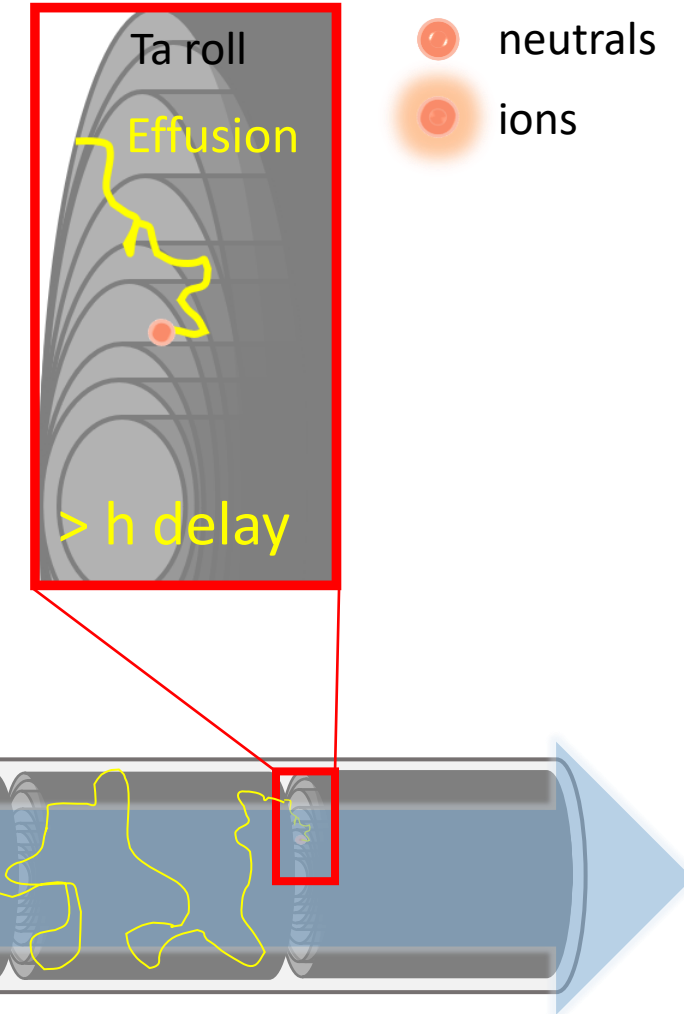


Release

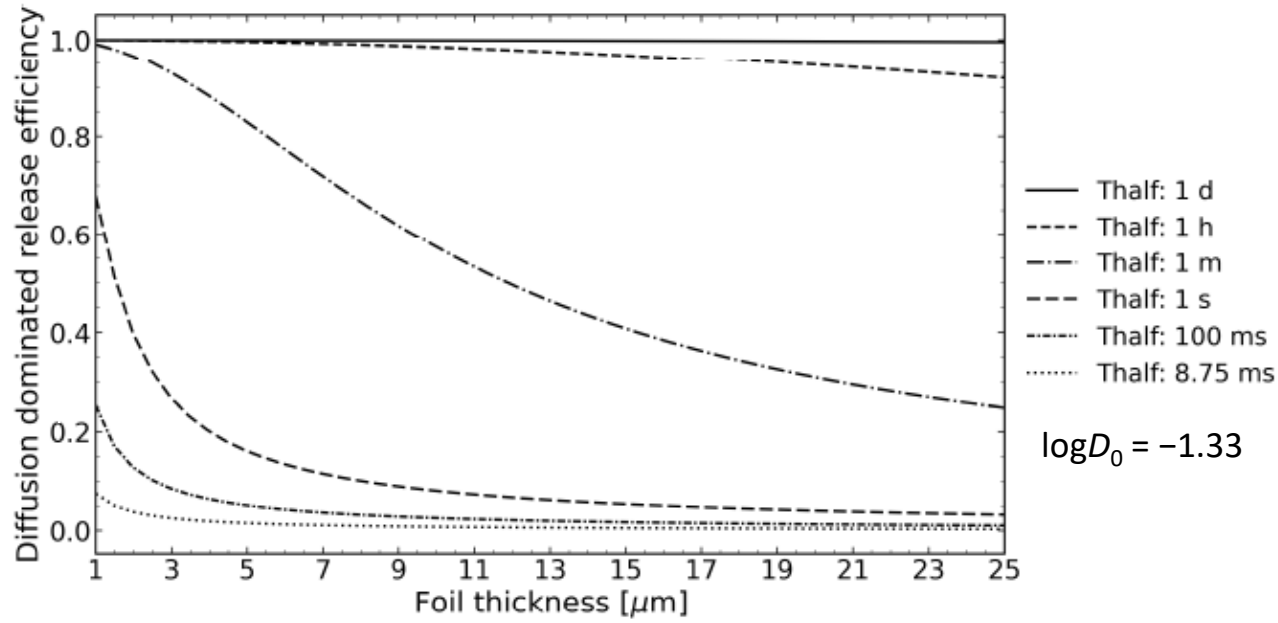
① Diffusion



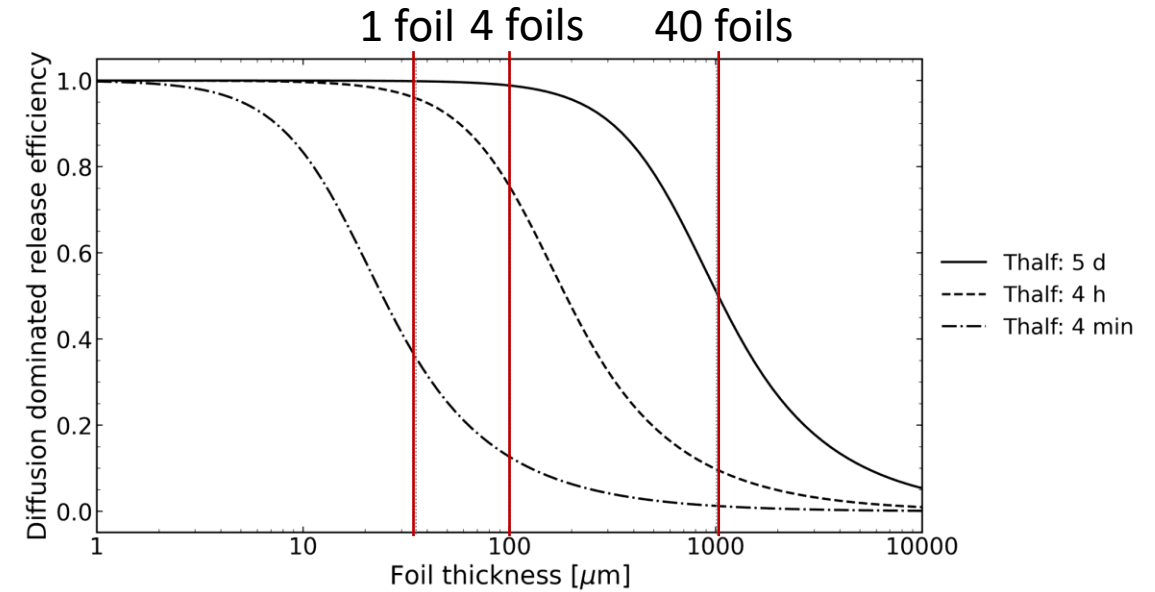
② Effusion



1. Diffusion



for 25 μm foil >95% of Tb with half-life 1h should leave the foil



In the case of foil welding, the release efficiency decreases

2. Effusion

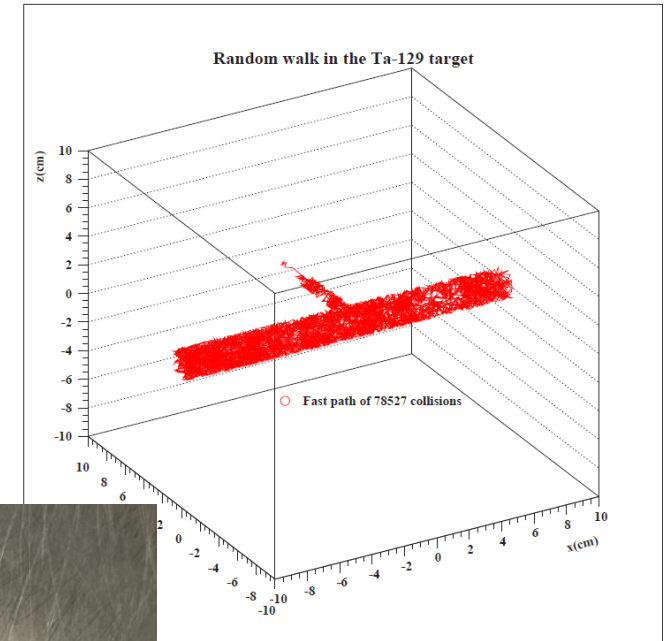
>> 60 000 collisions in a Ta target

Tb 0.03s sticking time at 2400°C for Ta*

→ average delay on the order of **hours**

(Dy ~0.0003s sticking time – 100x faster)

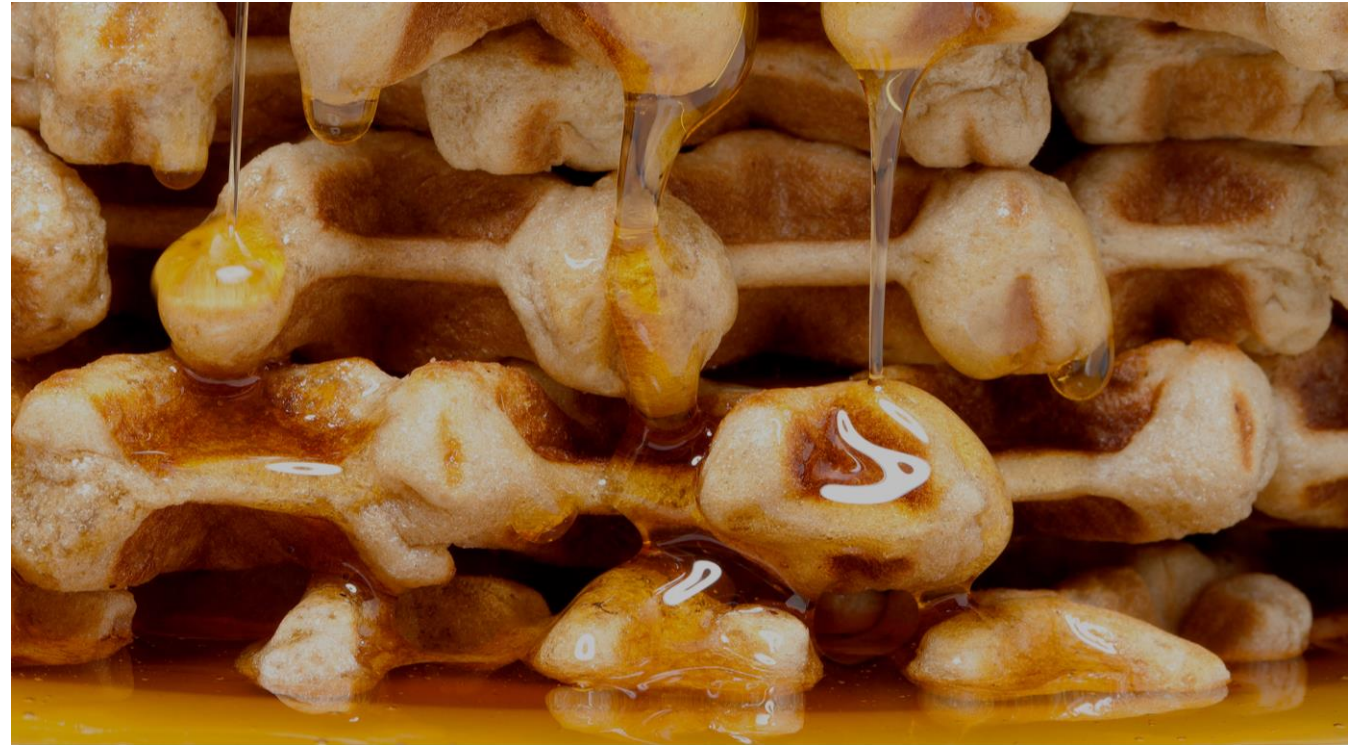
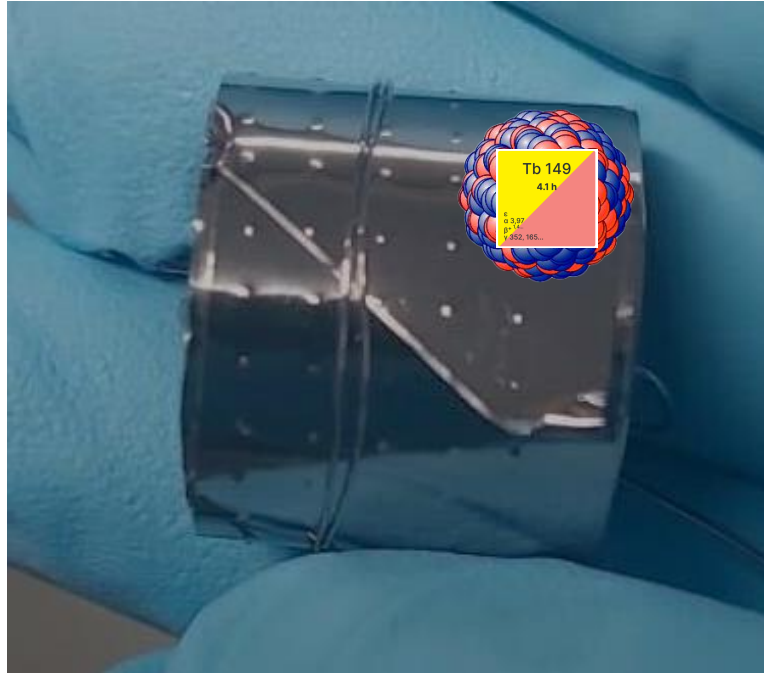
$$\tau_a = \tau_0 e^{\frac{-\Delta H_{ads}}{RT}}$$

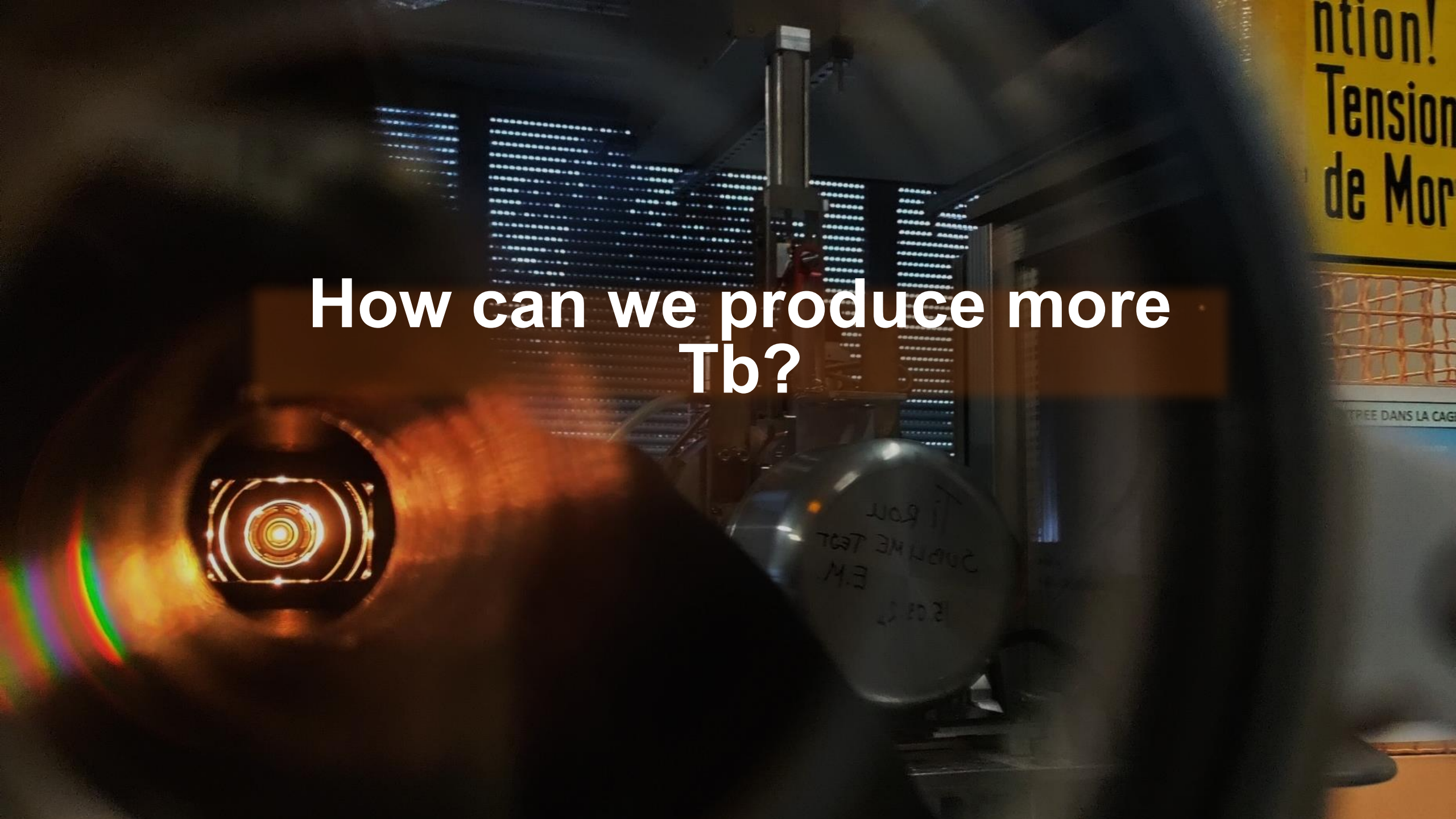


Leitner PhD thesis 2005

*lower limit! Estimated through Eichler systematics. U. Koster PhD thesis 2000

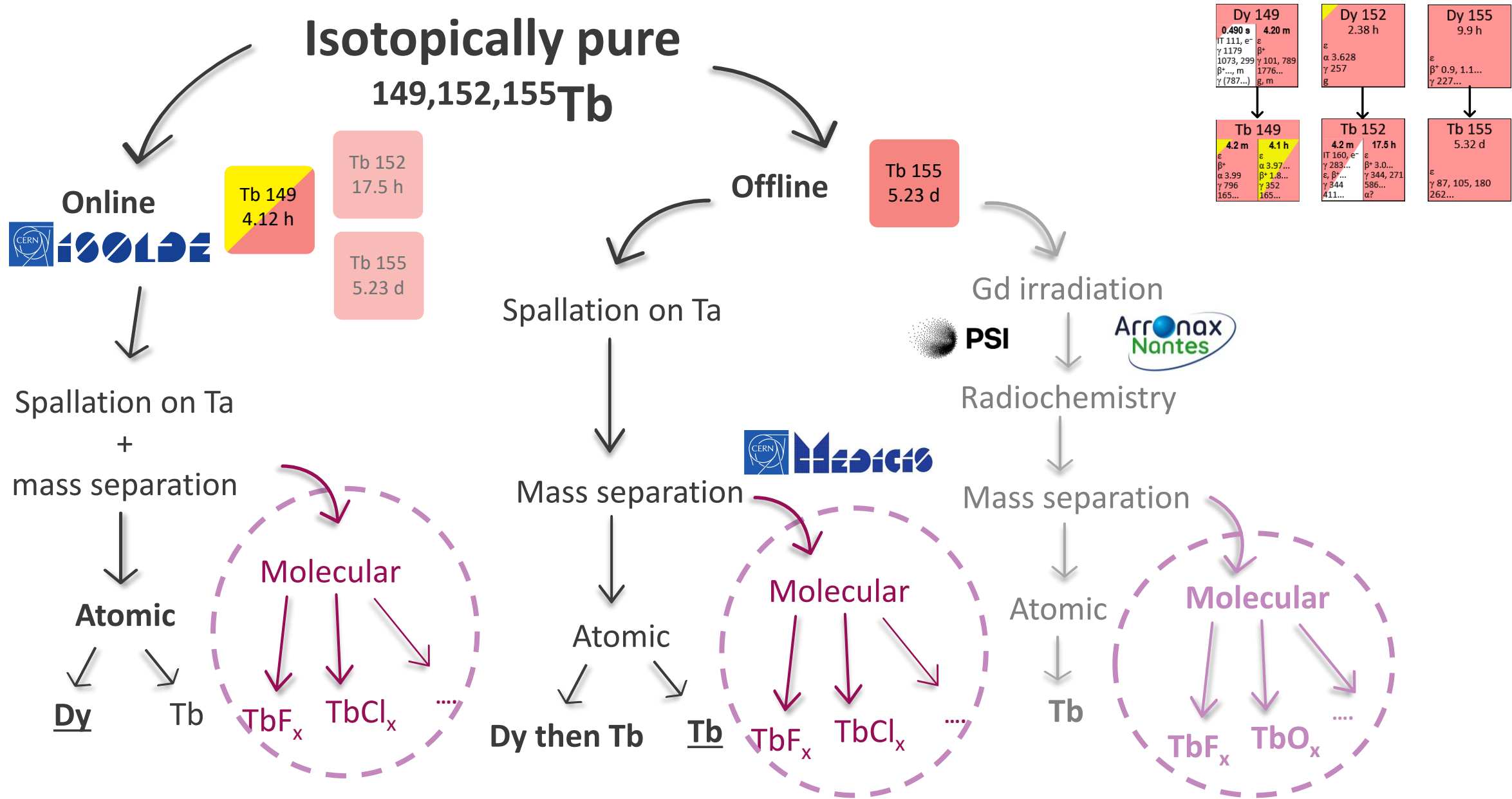
Tb is “sticky”

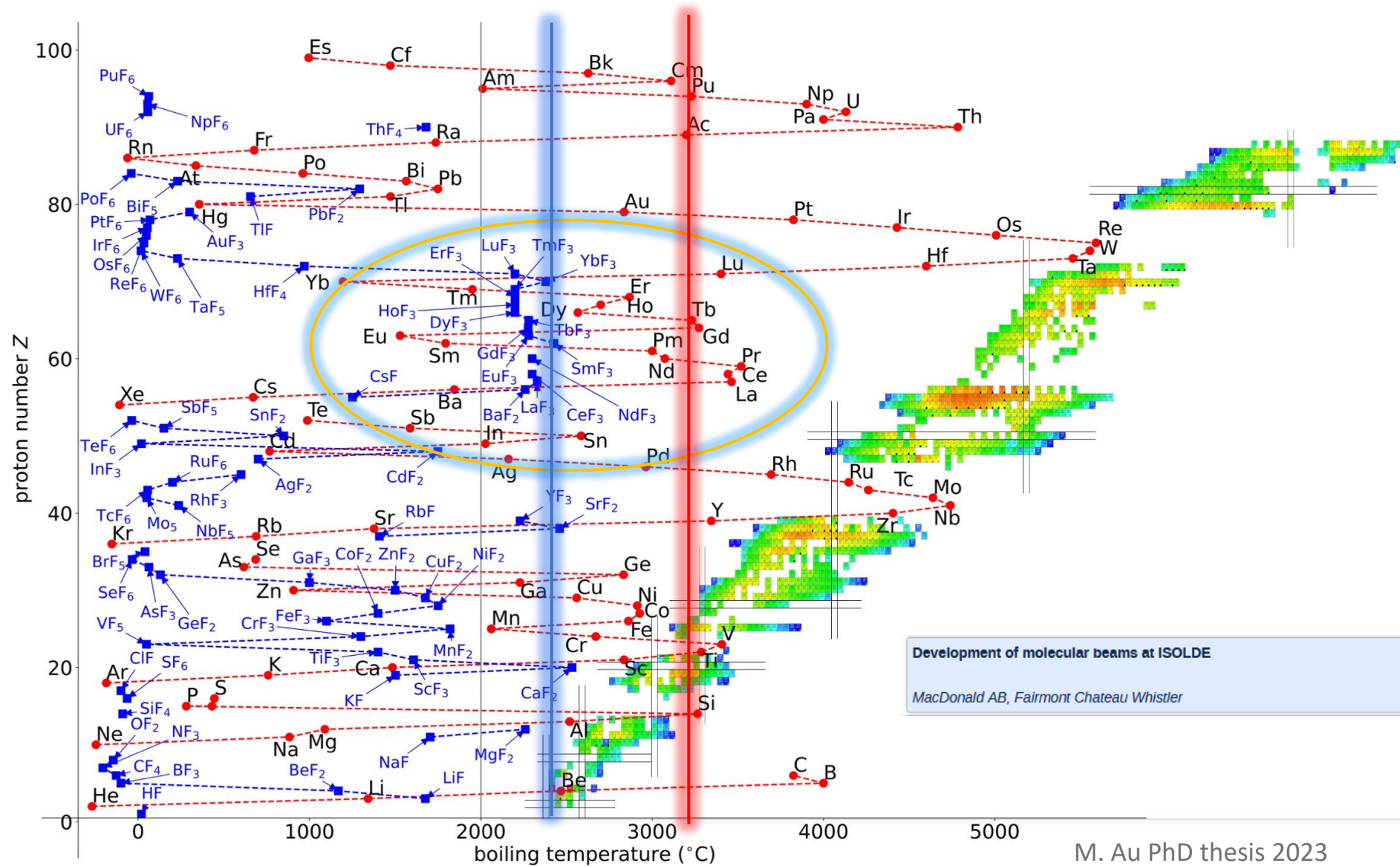




How can we produce more
Tb?

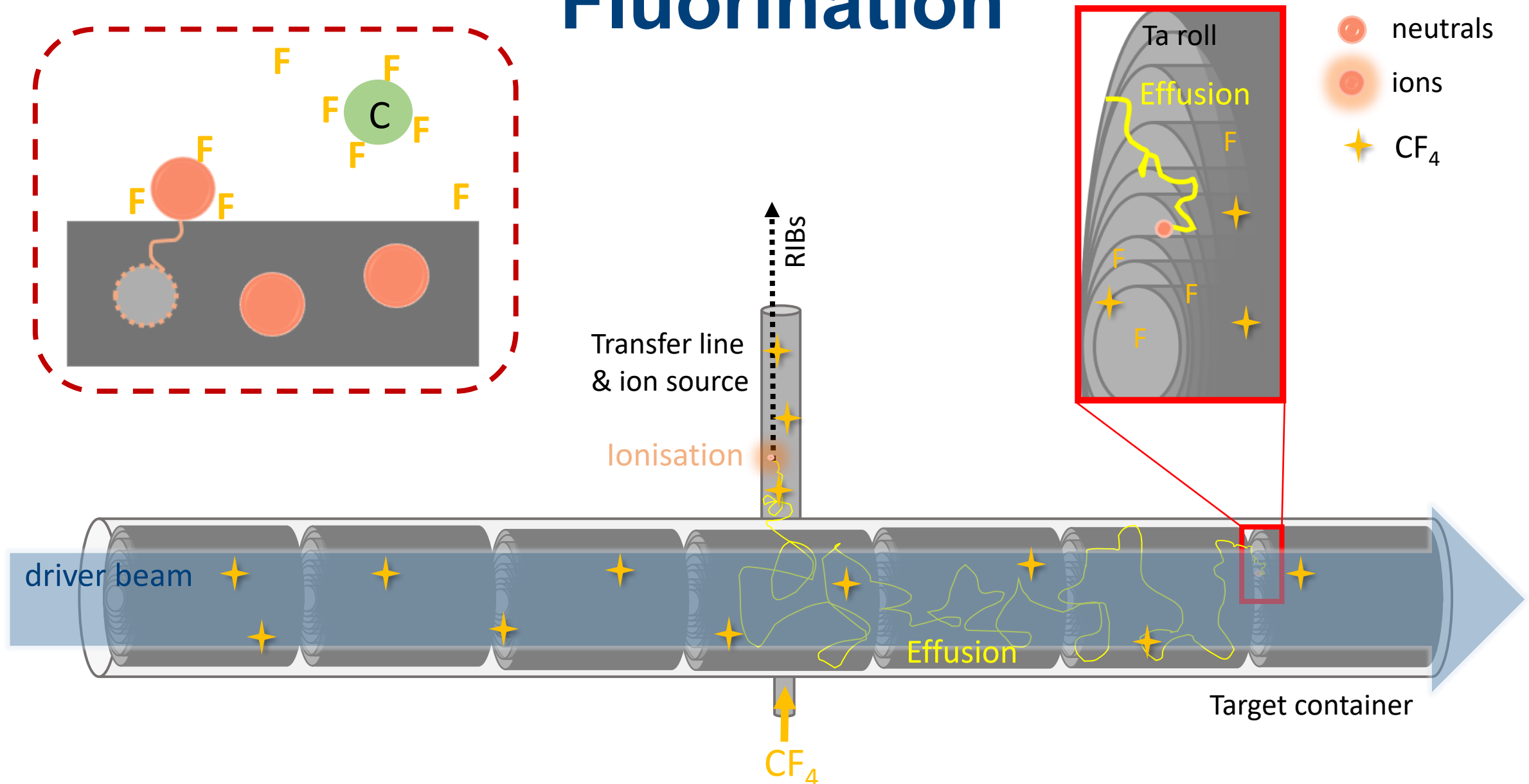
Isotopically pure 149,152,155Tb





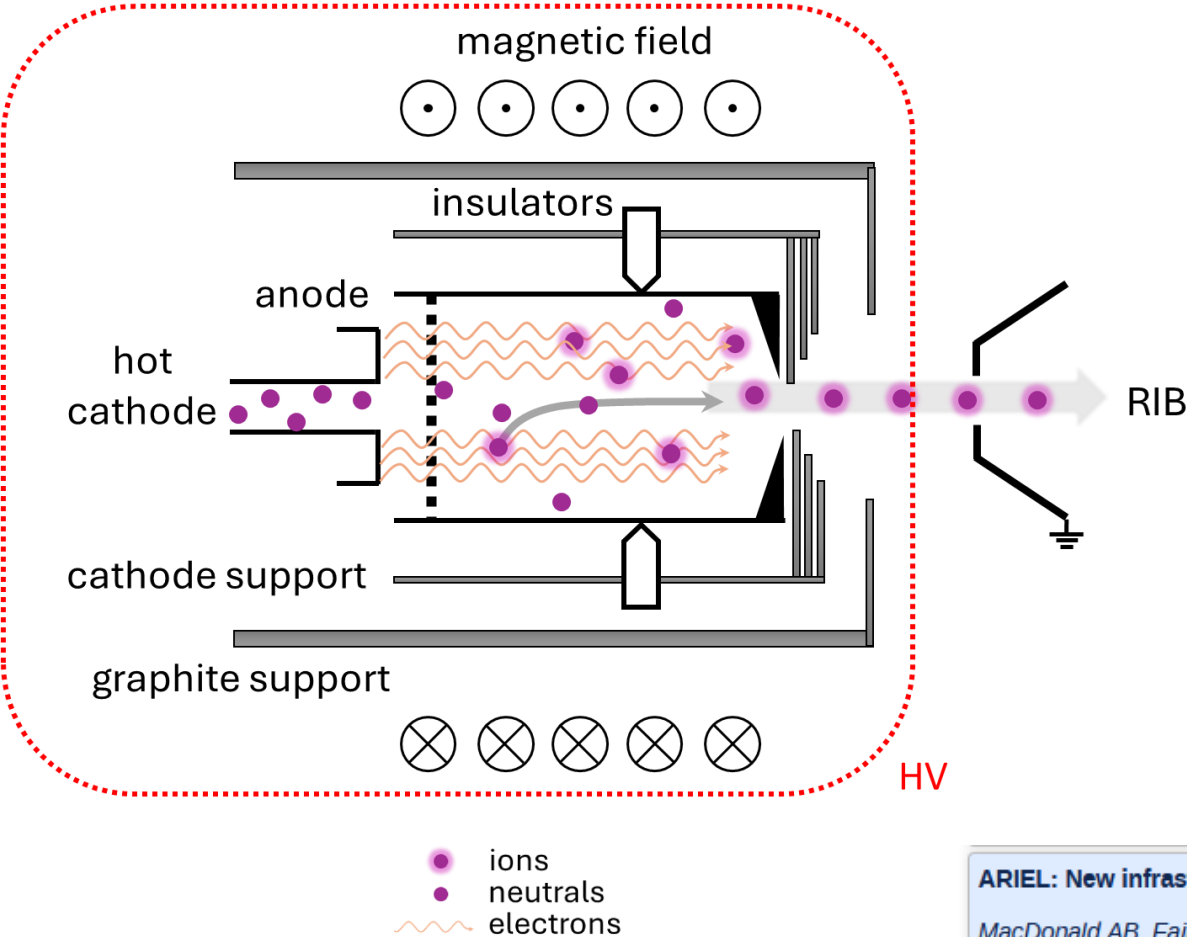
M. Au PhD thesis 2023

Fluorination



Forced Electron Beam Induced Arc Discharge

At ISOLDE referred to as VADIS (Versatile Arc Discharge Ion Source)



What can we optimise?

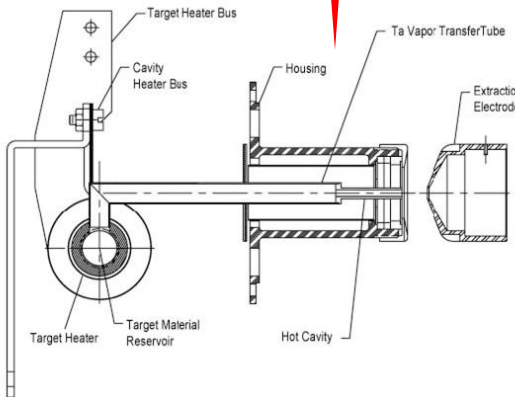
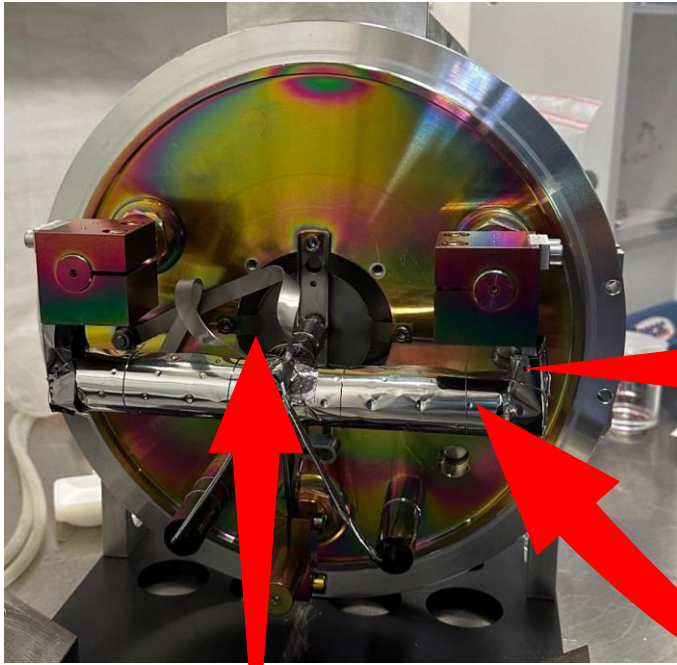
	Variable parameter	Effect
target	temperature	release ion load neutral load equilibrium point for chemical reactions over long times: target microstructure evolution
ion source	anode voltage magnetic field cathode temperature	electron energy electron trajectories electron density ion survival dissociation\ionisation plasma conditions beam shape (extraction and transport efficiency)
gas injected	composition partial pressure time since fluorination	fluorine availability neutral species pressure fluorine saturation chemical equilibrium on target surfaces

ARIEL: New infrastructure, new opportunities for target and ion source development *Fernando Alejandro Maldonado Millan*

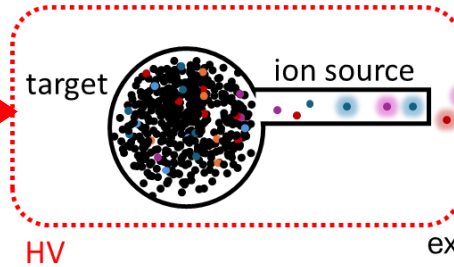
MacDonald AB, Fairmont Chateau Whistler

09:20 - 09:40

Offline tests

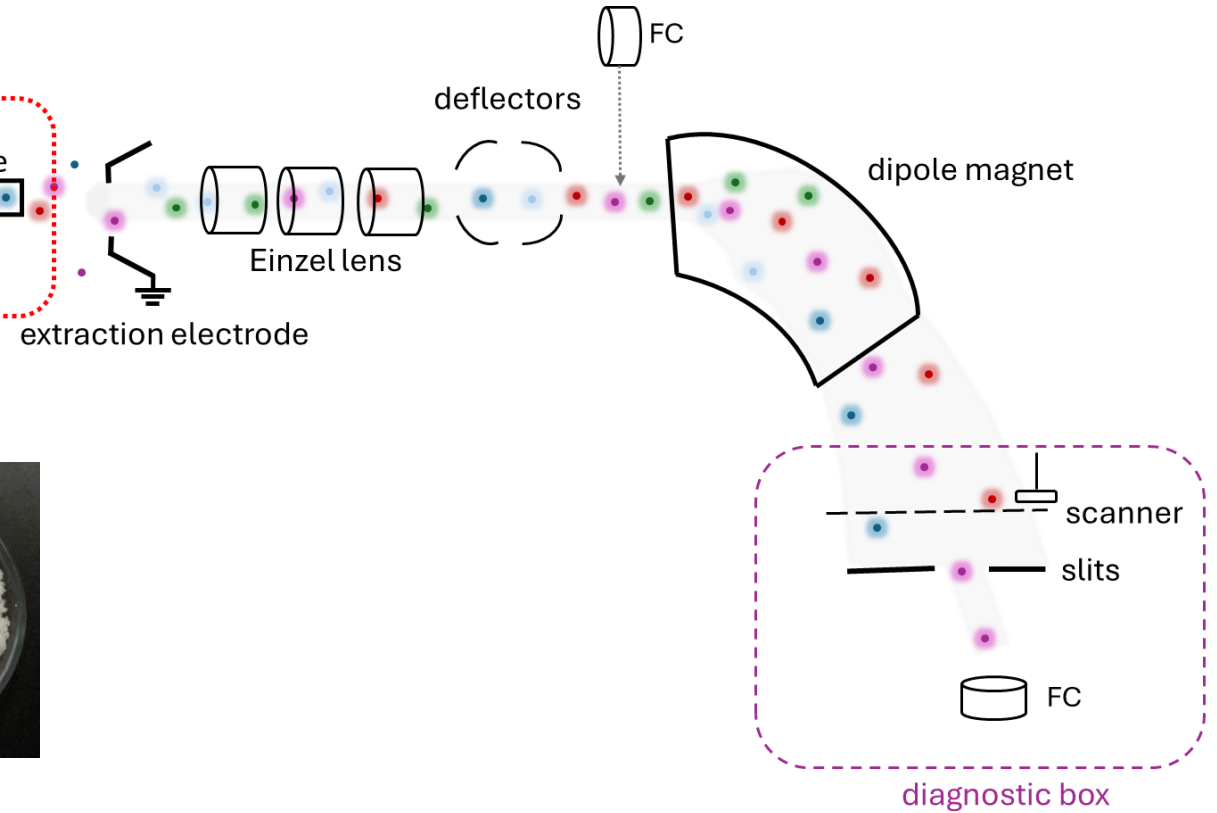


FEBIAD ion source



TbF_3 powder

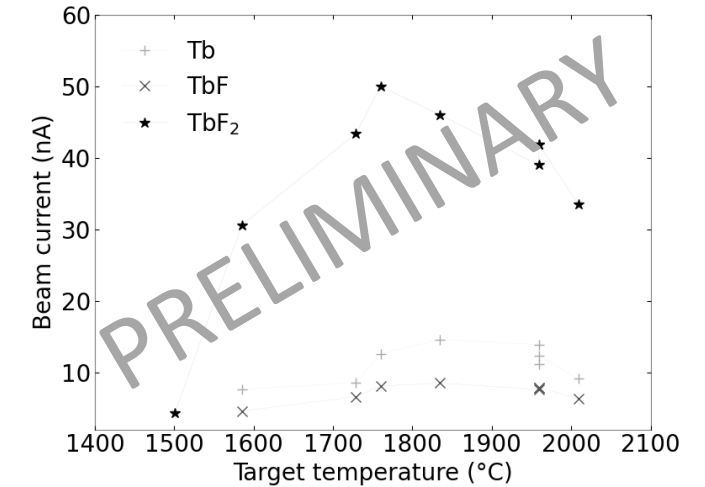
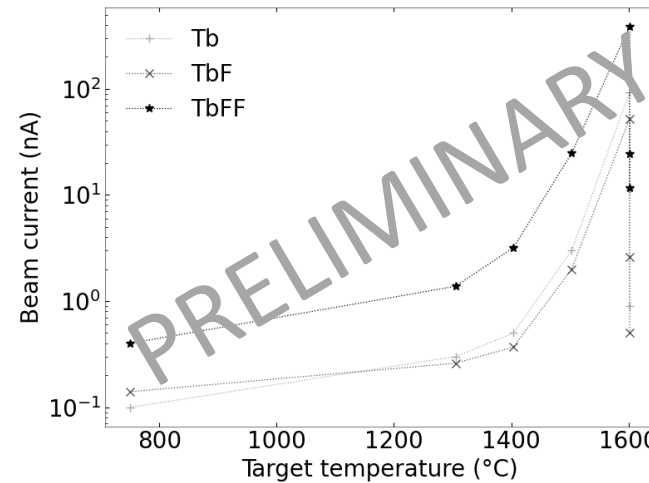
ISOLDE Offline 1



Temperature dependence

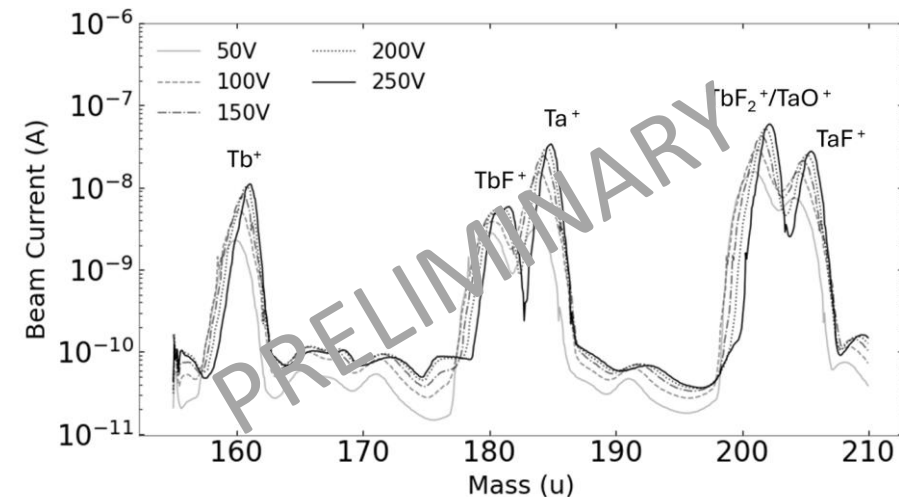
→ Already observed
<1500°C

→ Appearance temp. depends on
oxygen content and CF_4 saturation

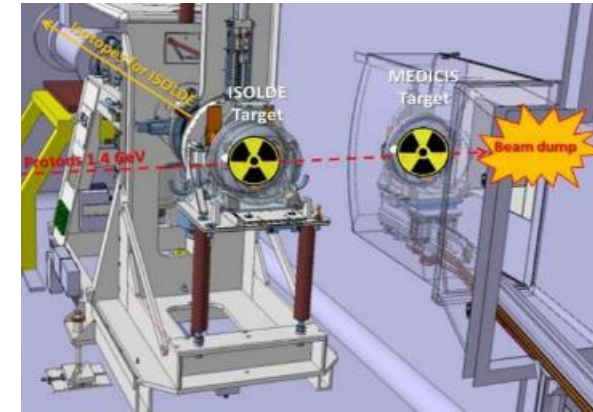
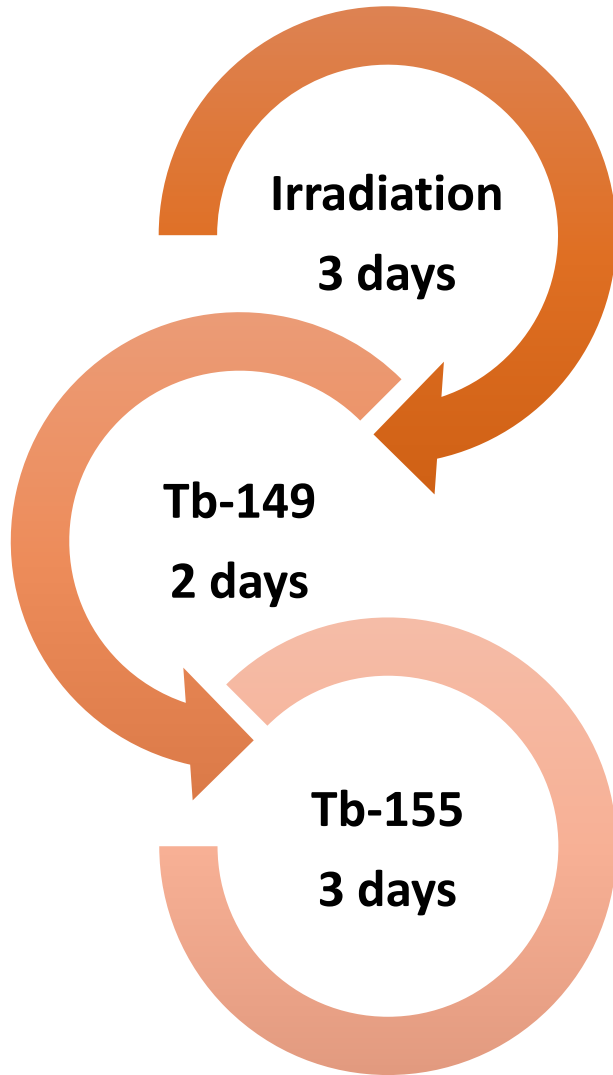


Response to change in electron bombardment energy

→ Cannot shift sideband distribution



Offline extraction at MEDICIS

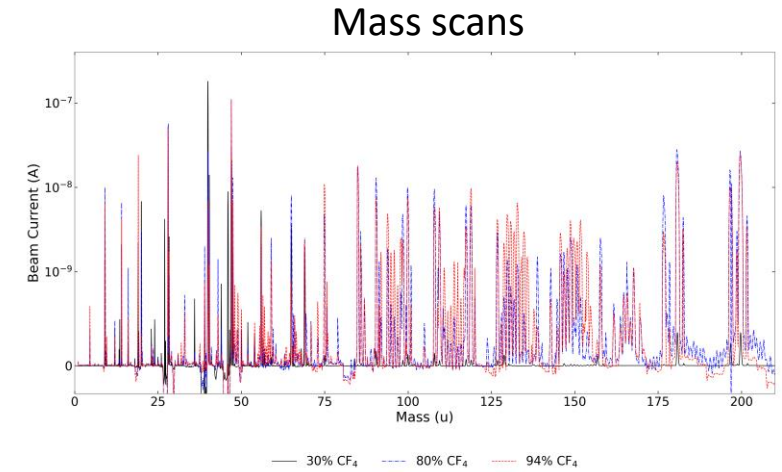
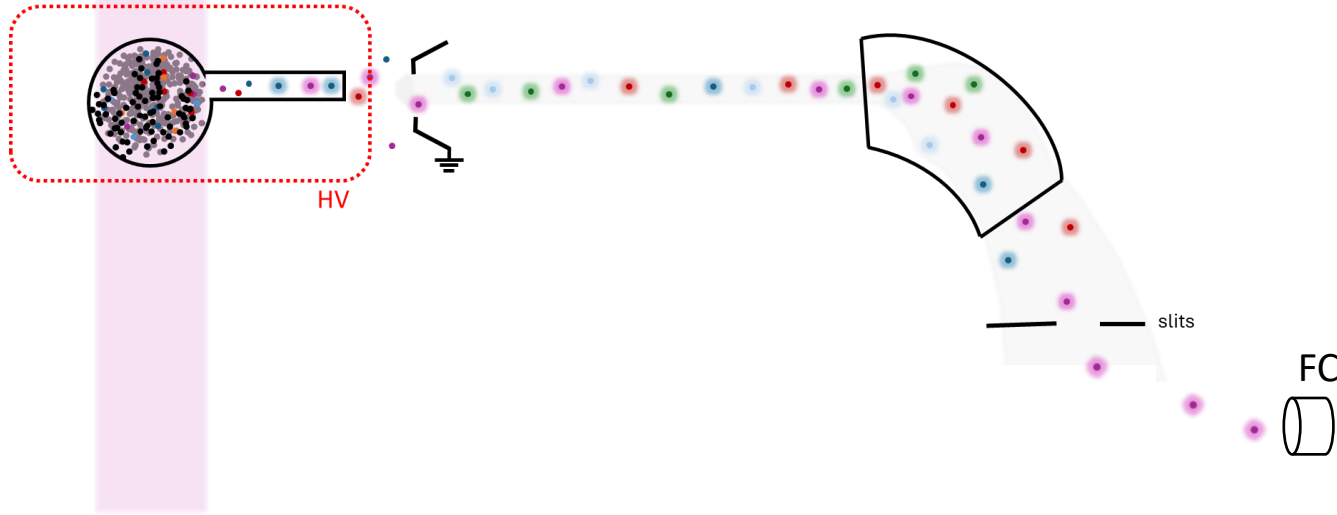


Isotope	Sideband	A/q	A _{in-target} [MBq]	A _{foil} [MBq]	A _{collimator} [MBq]	Efficiency %
Gd-149	GdF ₂	187	748 (11)	1.27 (7)	5.45 (2)	0.17 (1)
Tb-149	TbF ₂	187	3090 (90)	0.015 (3)	0.045 (6)	0.0005 (1)
Tb-155	TbF ₂	193	1130 (20)	1.25 (4)	–	0.11 (3)

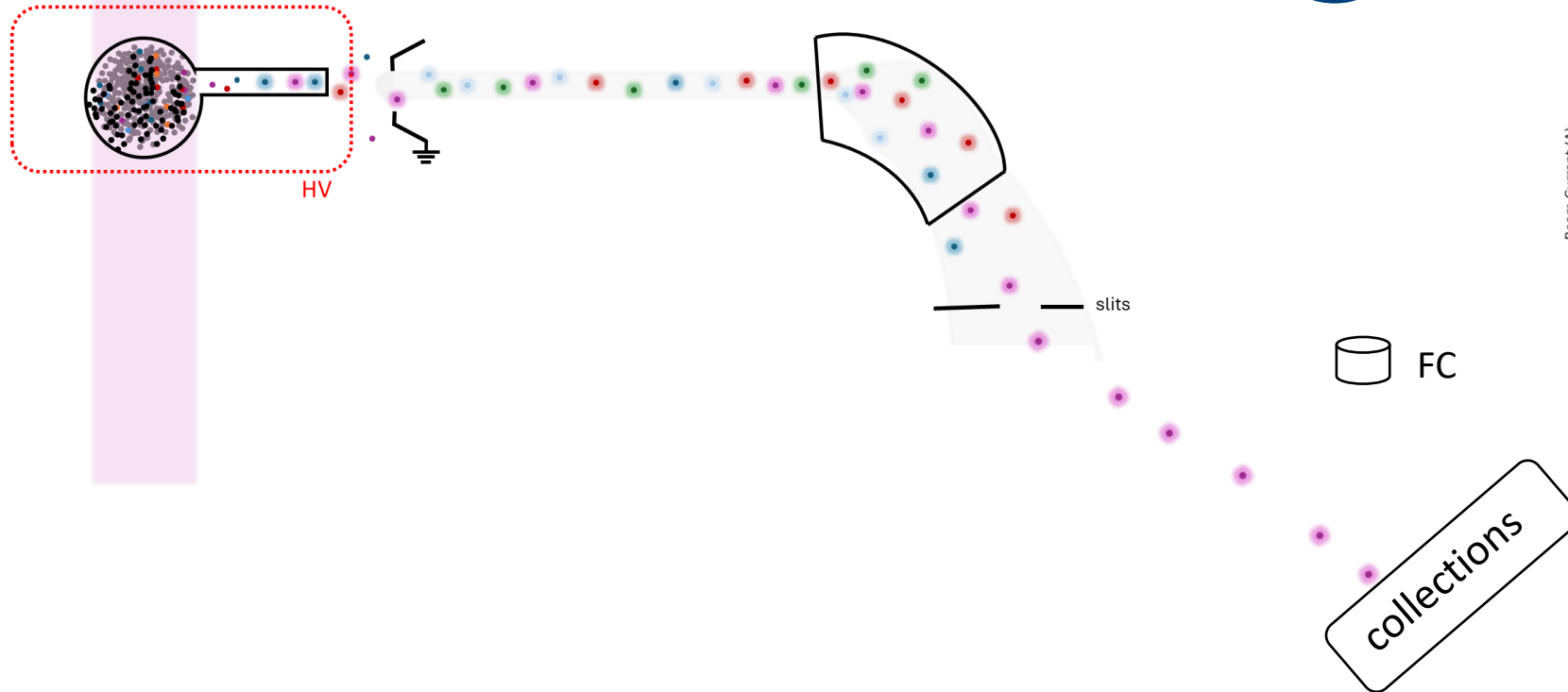
Difluoride extraction
Tb-155 efficiency 0.1%
- comparable to laser ionised Tb @ MEDICIS

Difficult to disentangle influence of different parameters

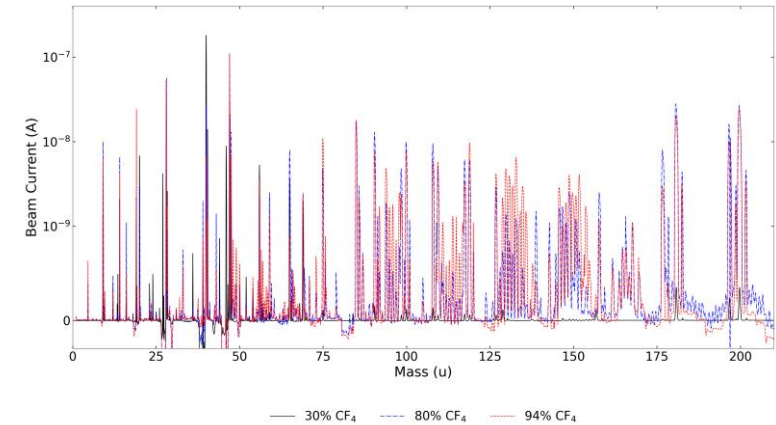
Online extraction @ ISOLDE



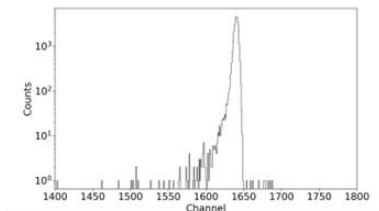
Online extraction @ ISOLDE



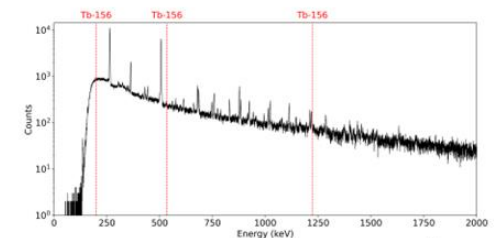
Mass scans



Alpha spectrometry

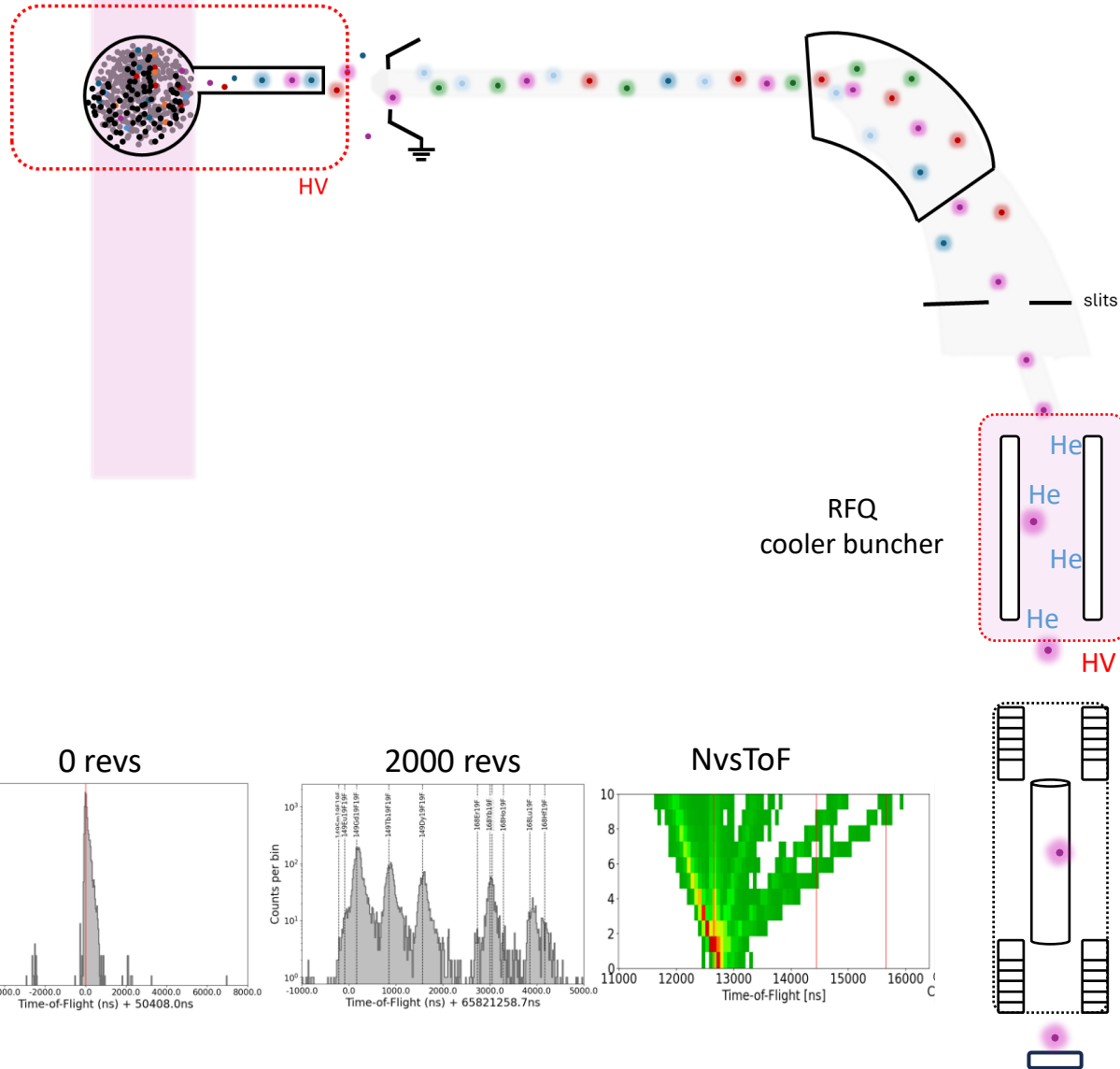


Gamma spectrometry



41

Online extraction @ ISOLDE



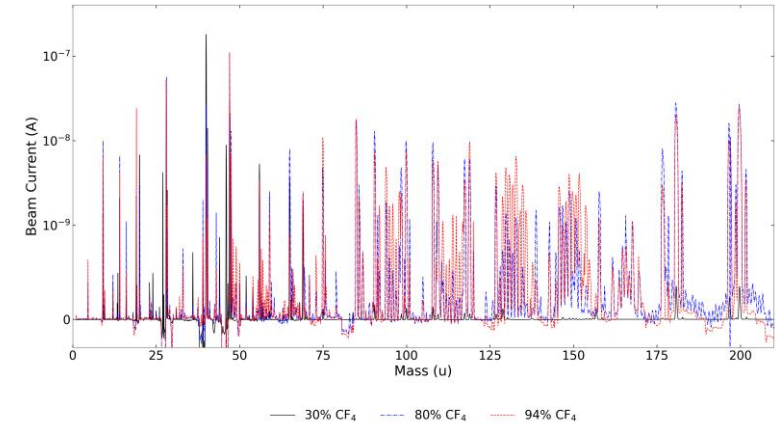
FC

collections

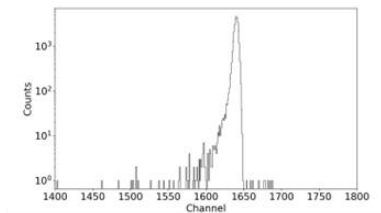
ISOLTRAP
MR-ToF MS

MagneToF
detector

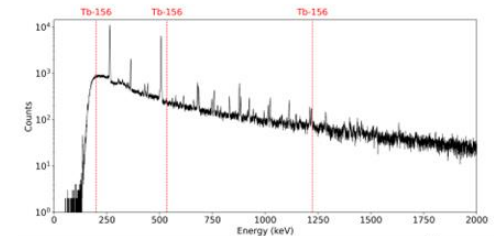
Mass scans



Alpha spectrometry

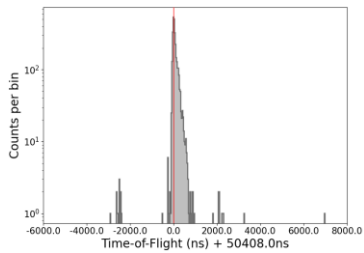


Gamma spectrometry

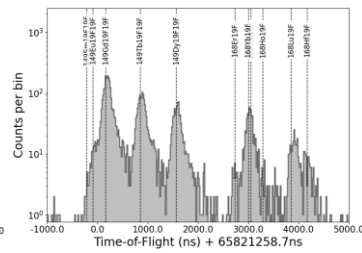


41

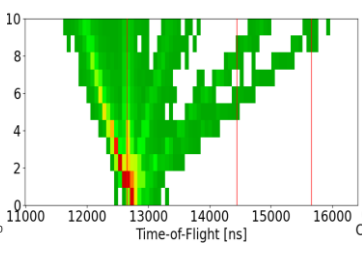
0 revs

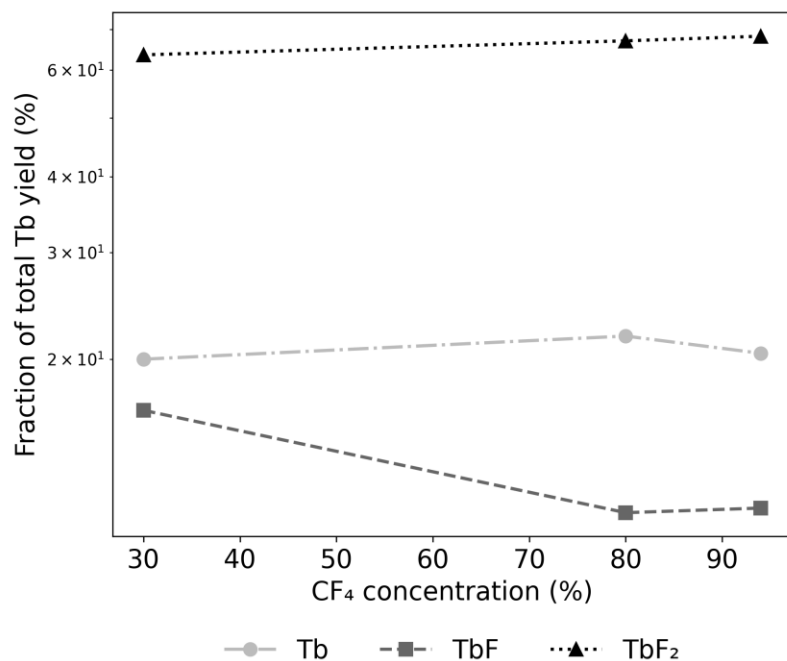
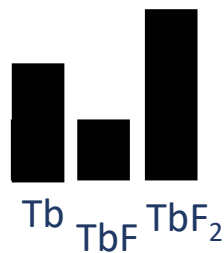
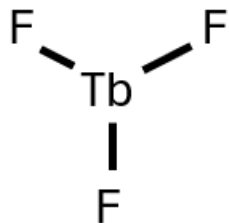


2000 revs



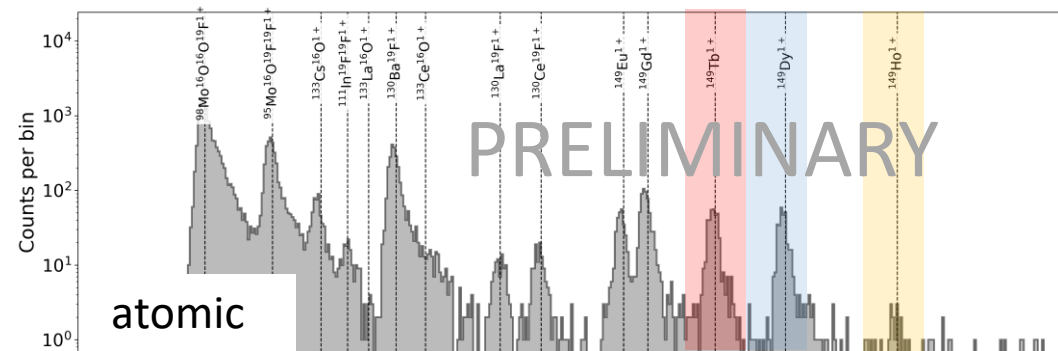
NvsToF



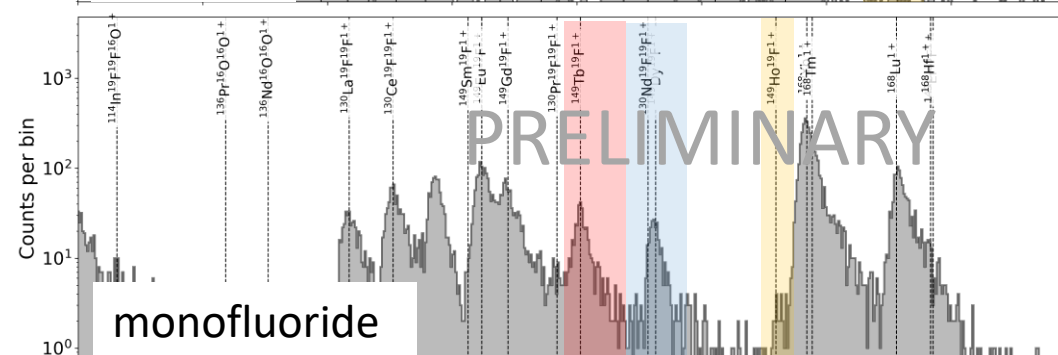


TbF₂ strongest
(and cleanest)
sideband

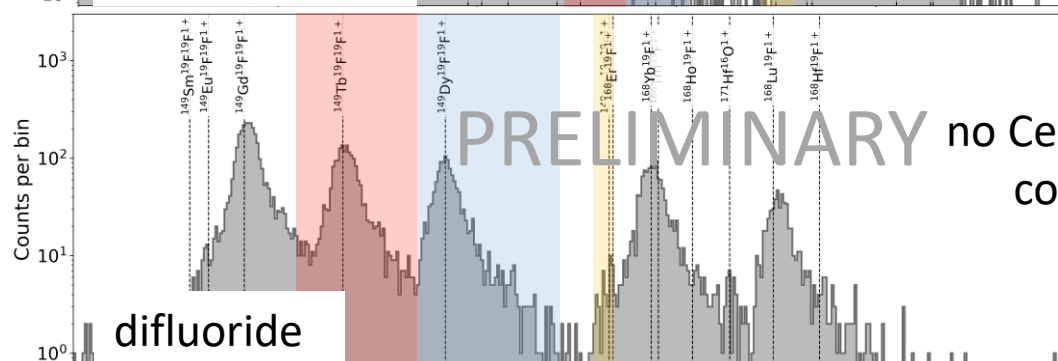
A=149



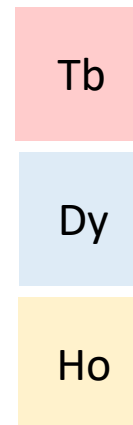
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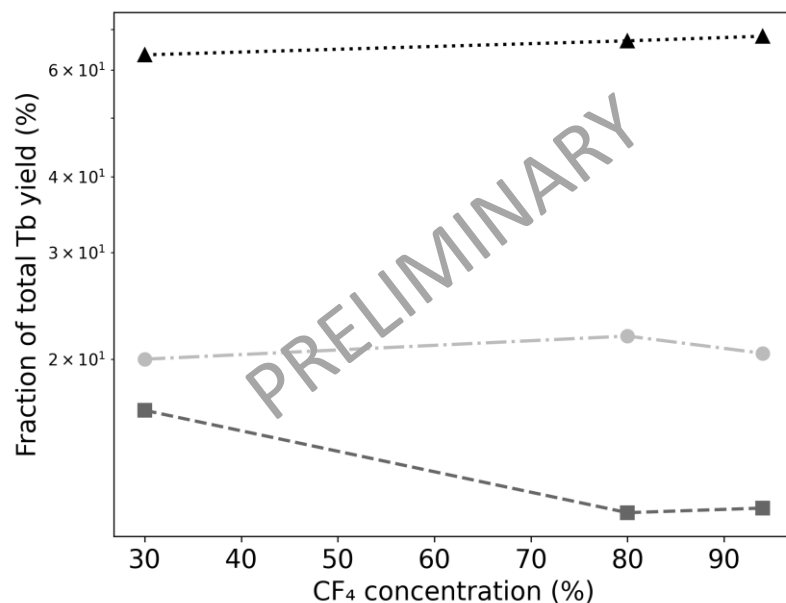
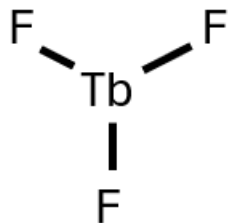


A=187



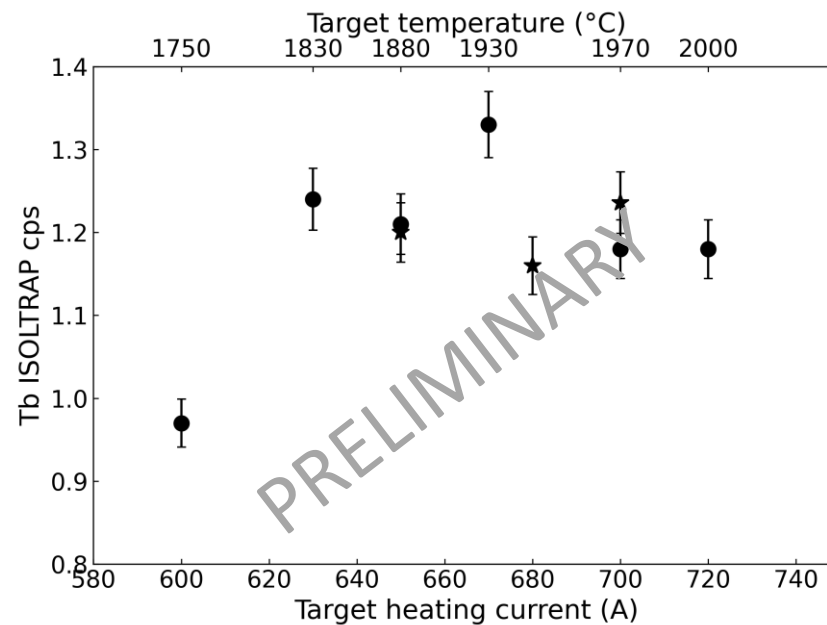
no CeO but different
contaminants



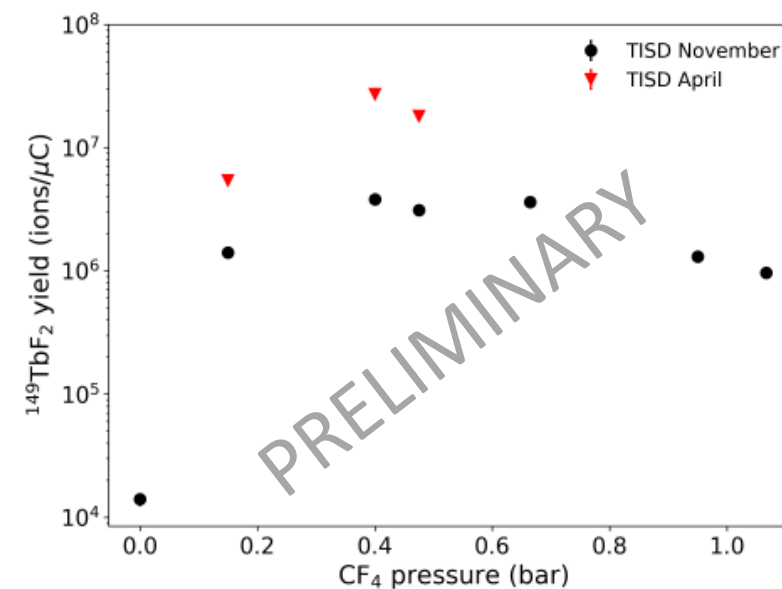


—●— Tb -■- TbF ···▲··· TbF₂

TbF₂ strongest
(and cleanest)
sideband



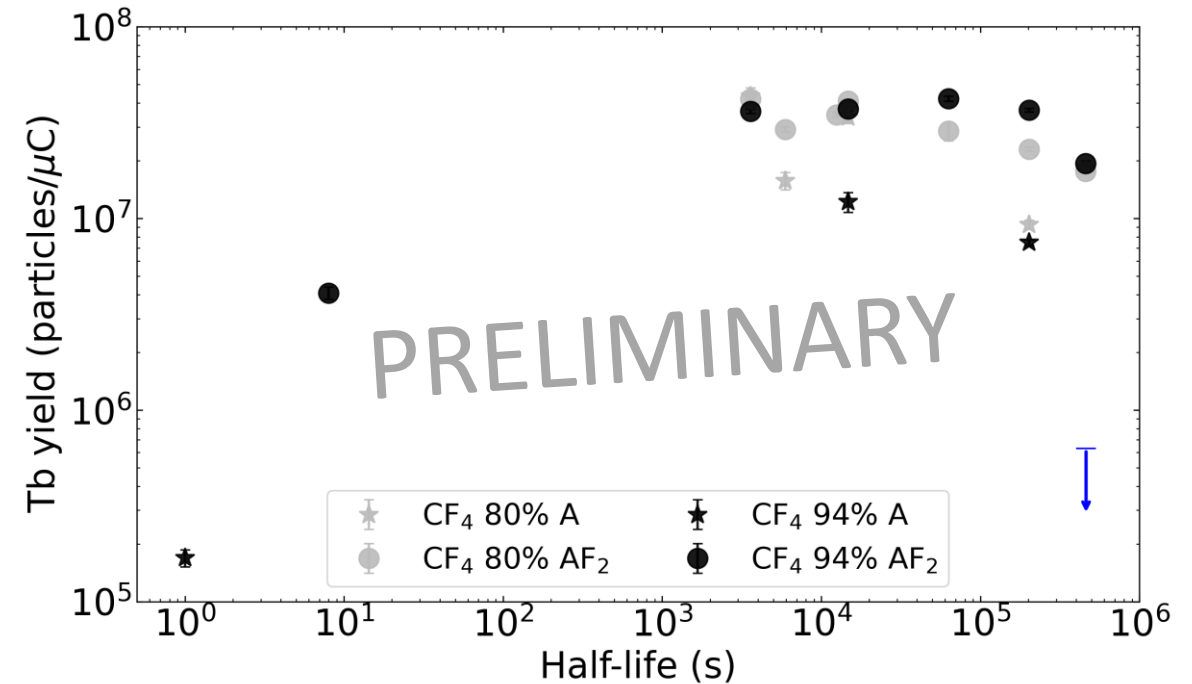
Tb beam <1900°C



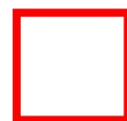
Optimal fluorine
concentration

What we saw, what we didn't see

- Higher yields than RILIS Tb
- No neutron rich Tb observed
- No Tb on Dy shielded masses
 - 154, 156, 158, 159 not observed



Dy 144 9.1 s	Dy 145 145 s 6 s	Dy 146 33.2 s	Dy 147 55.2 s 67 s	Dy 148 3.3 m	Dy 149 0.490 s 420 m	Dy 150 7.17 m	Dy 151 17 m	Dy 152 2.38 h	Dy 153 6.4 h	Dy 154 3.0-10 ¹⁰ s	Dy 155 9.9 h	Dy 156 0.056	Dy 157 8.14 h	Dy 158 0.095	Dy 159 144.4 d	Dy 160 2.329	Dy 161 18.889	Dy 162 25.475	Dy 163 24.896	Dy 164 28.260
Tb 143 <21 s 12 s	Tb 144 4.25 s ~1 s	Tb 145 30.9 s ?	Tb 146 24.1 s 8 s	Tb 147 1.83 m 1.65 h	Tb 148 2.29 m 60 m	Tb 149 4.2 m 4.1 h	Tb 150 5.8 m 3.40 h	Tb 151 25 s 17.609 h	Tb 152 4.2 m 17.5 h	Tb 153 2.34 d	Tb 154 2.7 h 194 h 21.8 h	Tb 155 5.32 d	Tb 156 5.3 h 14 h 1.8 d	Tb 157 71 s	Tb 158 10.70 s 10 s	Tb 159 100	Tb 160 1.3 d	Tb 161 6.89 d	Tb 162 7.76 m	Tb 163 1.5 m



Positive ID



Negative ID



Unable to ID

What's limiting Tb release?

Production limit

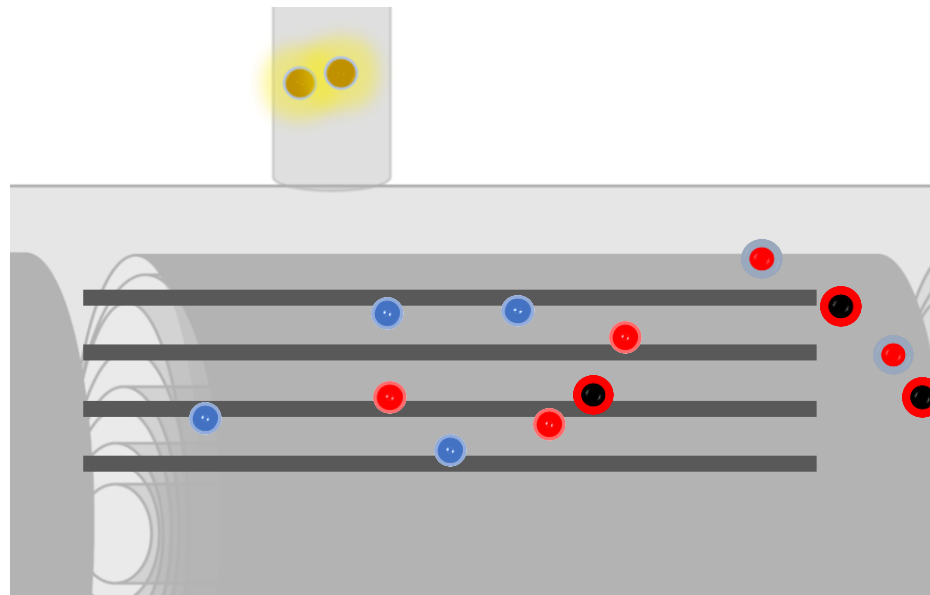
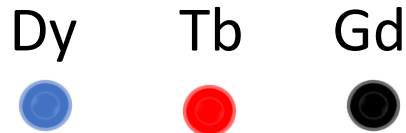
- Not a lot of Tb is directly produced in the foil
→ most of the Tb is a decay product of Dy

What's limiting Tb release?

Effusion limit

- Tb produced in the foil is not released
- Tb we see is the decay product of Dy
→ Dy completed part of the pathway

Proposed mechanism:
Dy assisted release

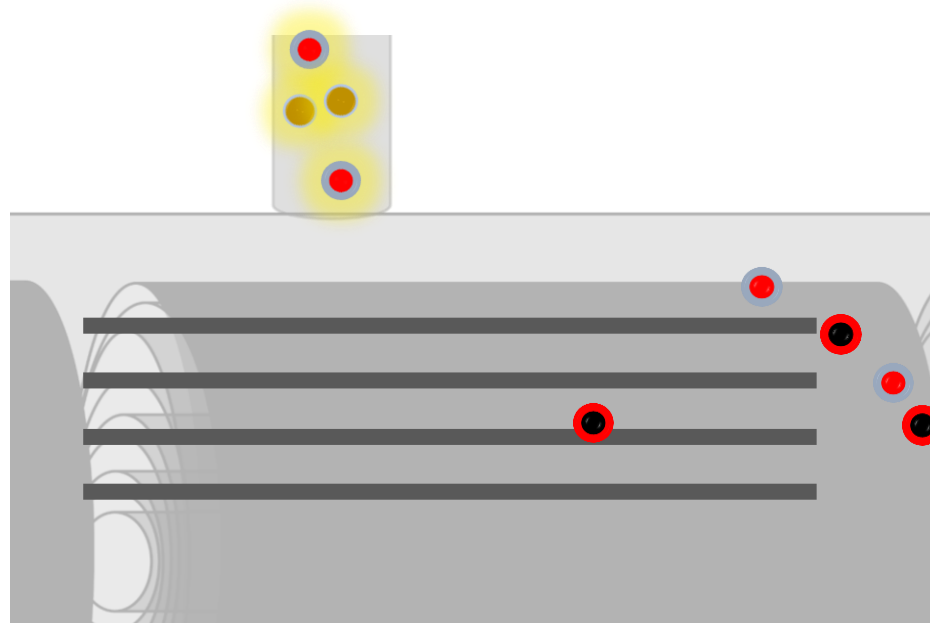


What's limiting Tb release?

Effusion limit

- Tb produced in the foil is not released
- Tb we see is the decay product of Dy
→ Dy completed part of the pathway

Proposed mechanism:
Dy assisted release

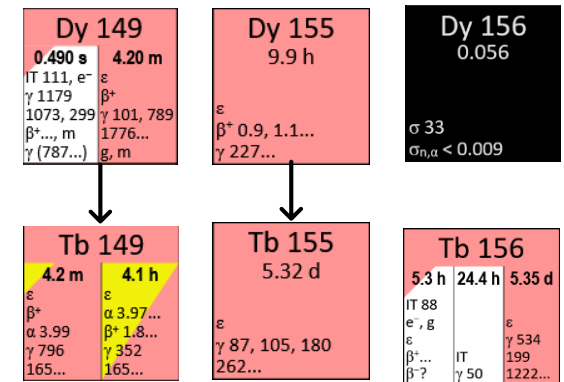
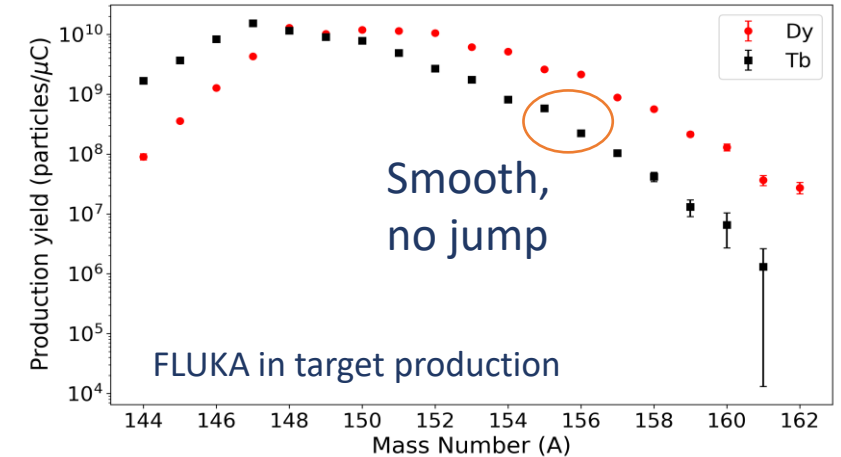


What's limiting Tb release?

Production limit
or effusion limit

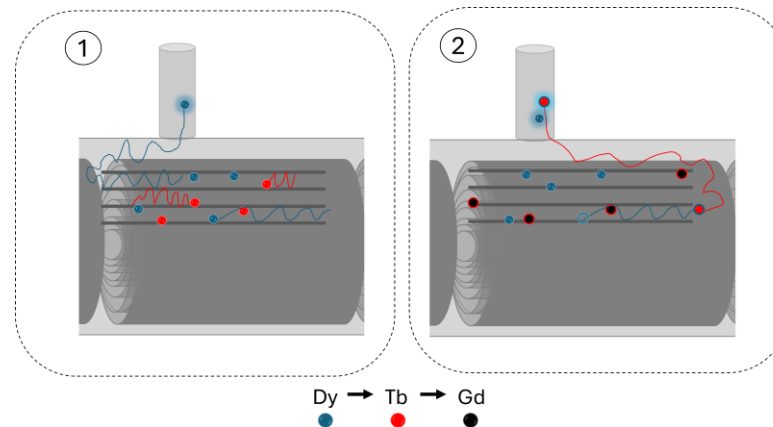
Effusion limit

- No ^{156}Tb observed
- No n-rich Tb observed
- No stable or long-lived Tb observed when there is no feeding from Dy
- Offline extraction:
 $^{149}\text{TbF}_2$ efficiency: 0.0005(1)%
 $^{155}\text{TbF}_2$ efficiency: 0.11(3)%





Molecules allow for co-collection of Tb and its parents $<1900^{\circ}\text{C}$



Dy facilitates release of Tb



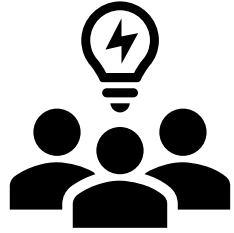
TbF₂ yields not competitive with RILIS Dy for medical isotopes online

$$^{149}\text{Dy RILIS} > \underline{^{149}\text{TbF}_2} > ^{149}\text{Tb RILIS}$$



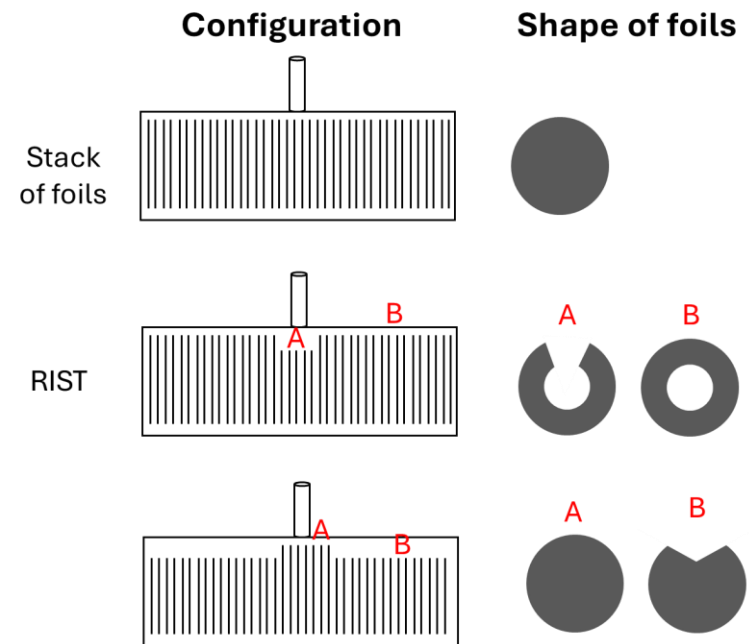
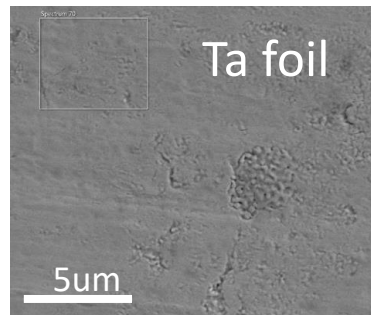
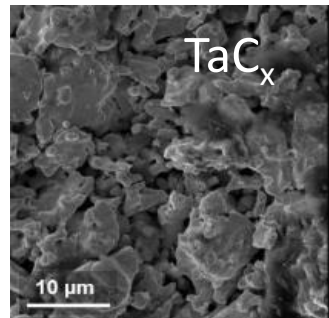
Molecules advantageous for offline extraction

What's next? Short-term



We need to rethink the target itself

- New materials – TaC? Others?
- New geometries



Long term: Tailored systems

Redefine what is needed for medical isotope production

“standard” ISOL

Efficiency

Rapidity

Selectivity

Versatility

medical mass separation

Efficiency

Rapidity

Selectivity

~~Versatility~~

Scalability

New facilities with more powerful proton beams

→ New challenges

There is a lot still to be done.

Acknowledgements

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Thank you for your attention.
Questions?

