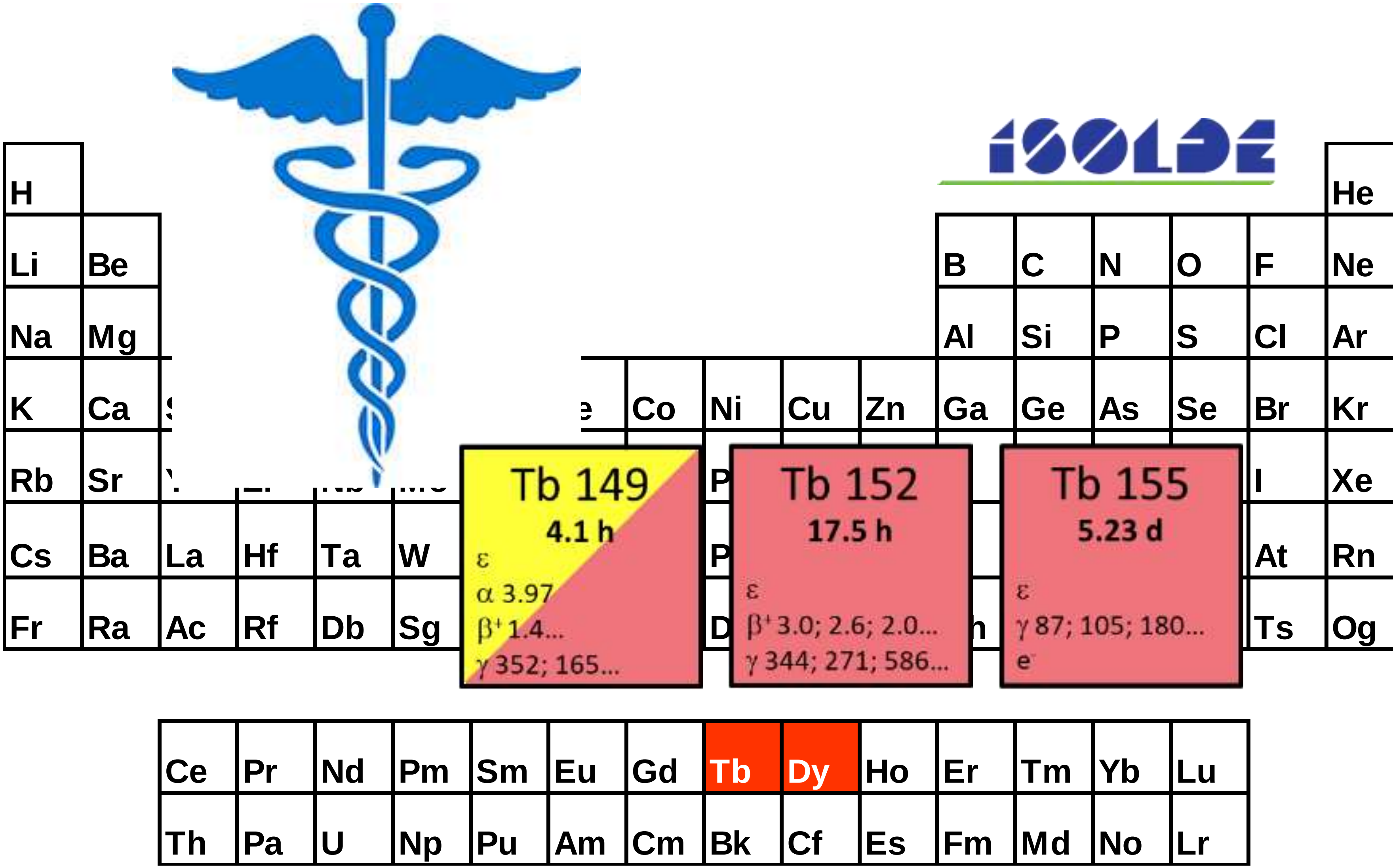
Characterization and optimization of ISOLDE beams of Dy/Tb isotopes for medical applications



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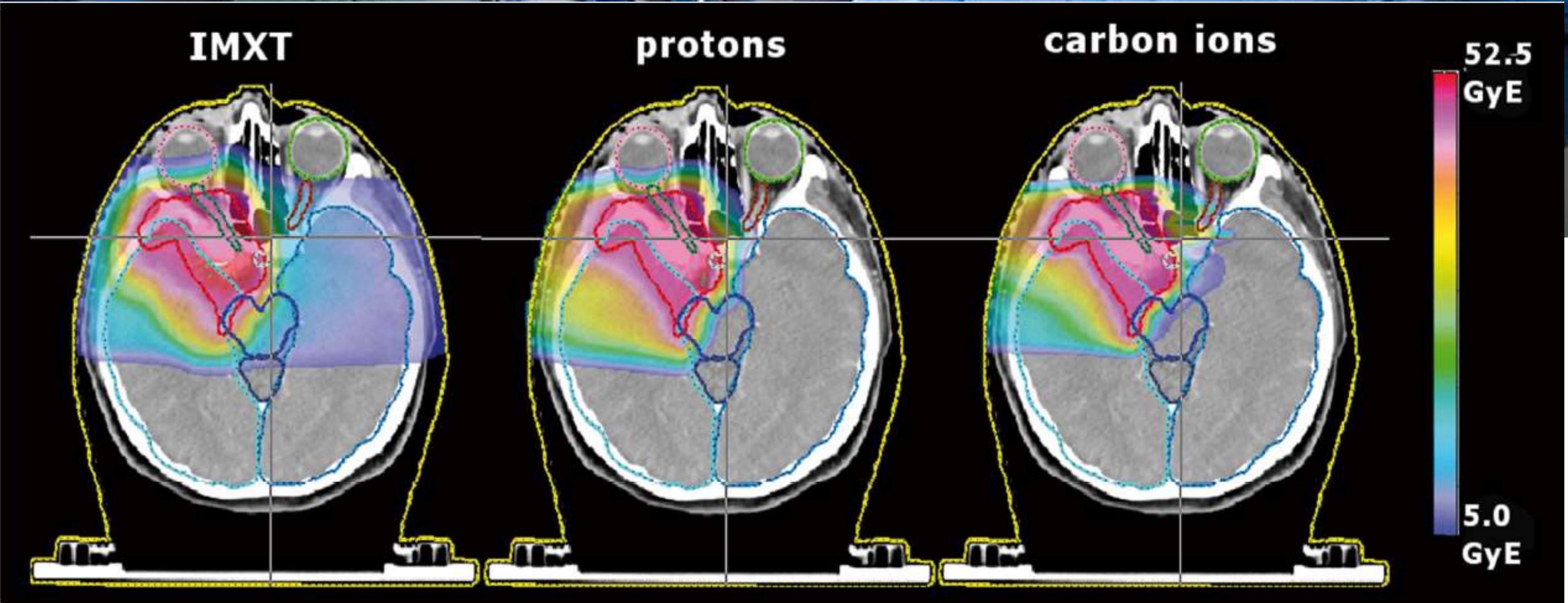
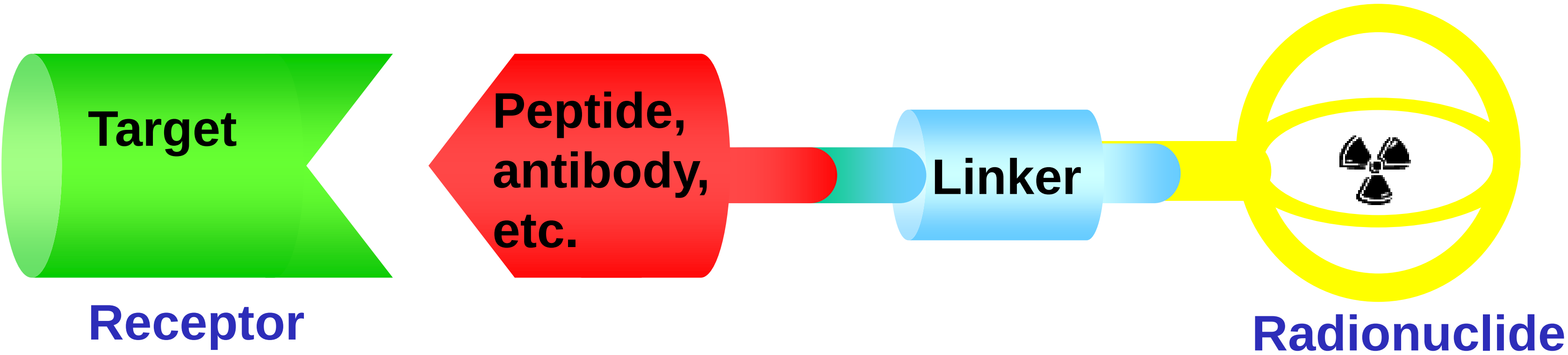
Progress in cancer treatment



How to treat such patients?

Multidisciplinary collaboration to fight cancer



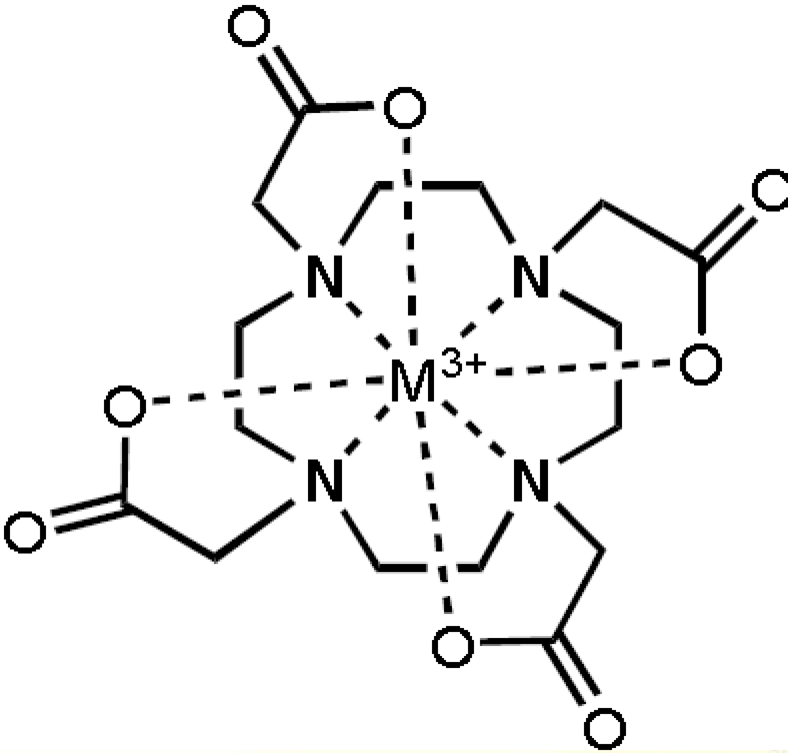
Immunology
Structural biology

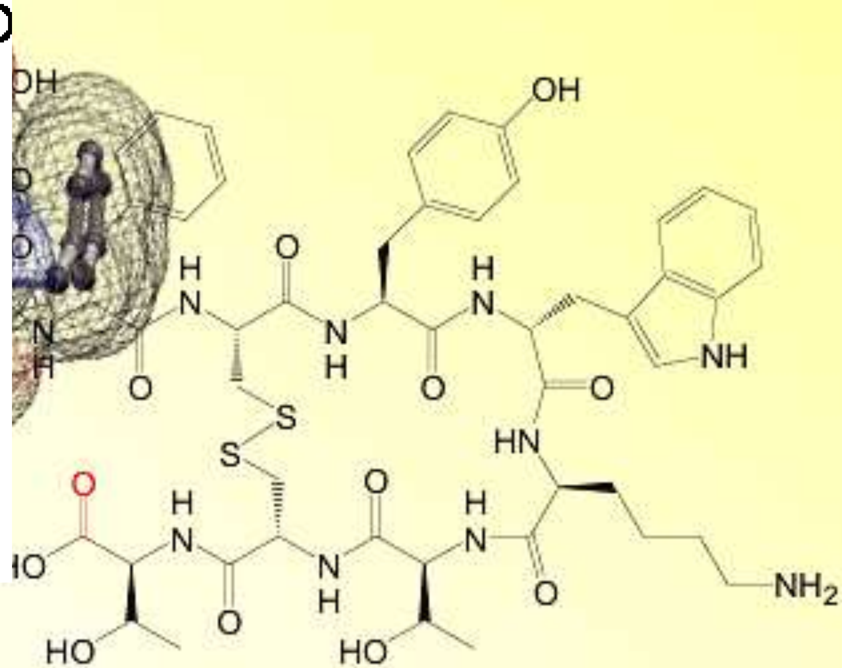
Coordination chemistry

Nuclear physics and radiochemistry

Nuclear medicine and medical physics

Structural Formula of DOTA-TOC/TATE





DOTA-TATE

1,4,7,10-tetraazacyclododecantetraacetate

^{111}In ^{90}Y

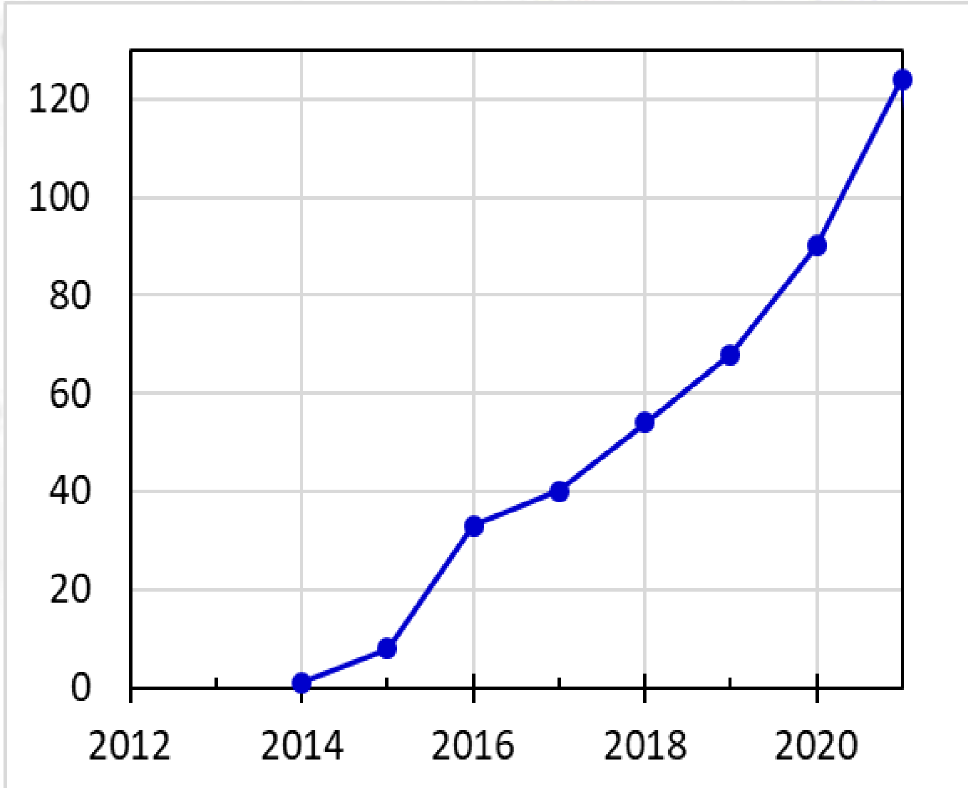
^{67}Ga ^{177}Lu

^{68}Ga ^{213}Bi

IC_{50} (Y^{III}) = 1.6 ± 0.4 nM

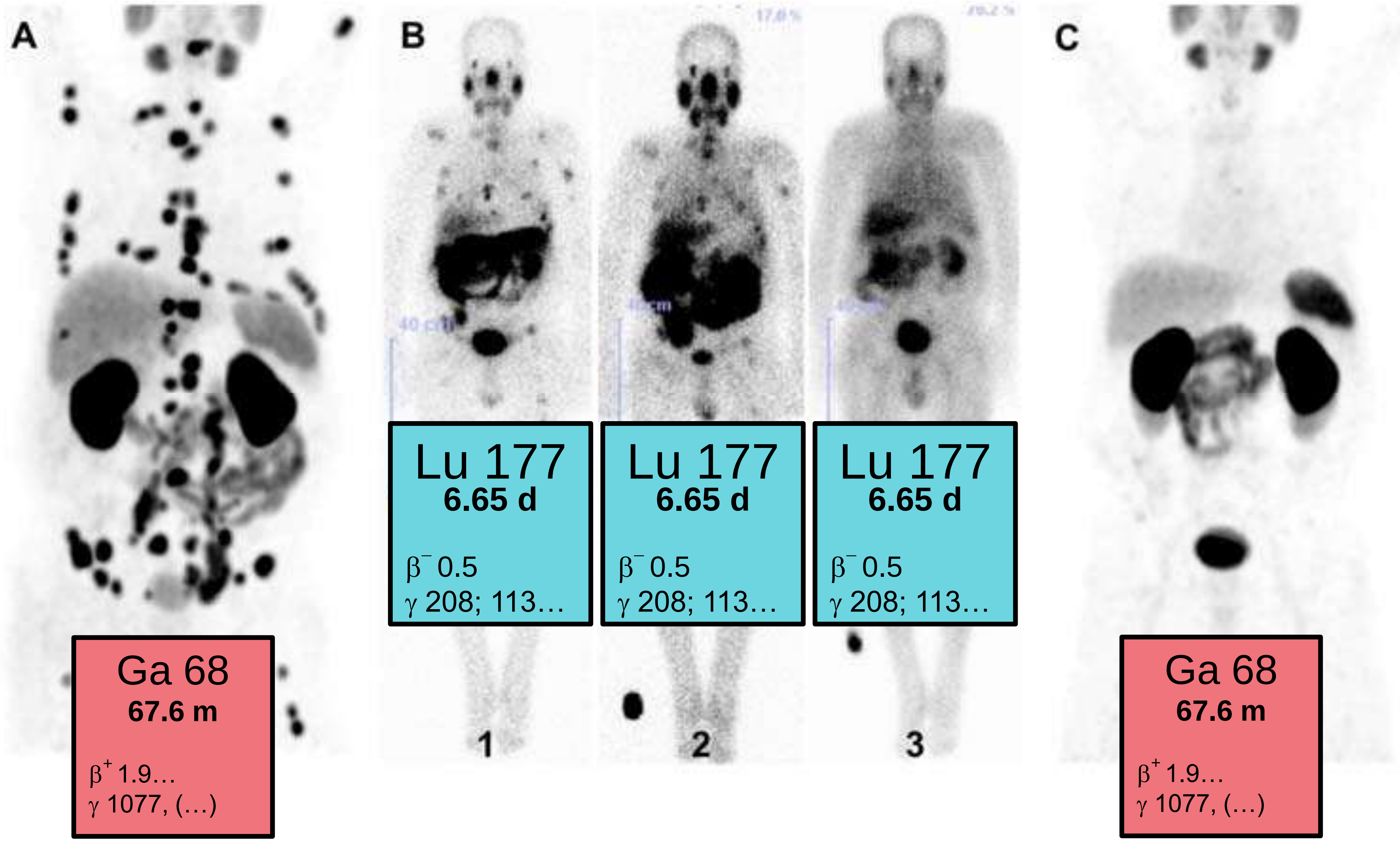
Helmut Maecke, EANM-2007.

^{177}Lu-radioligand therapy of advanced prostate cancer

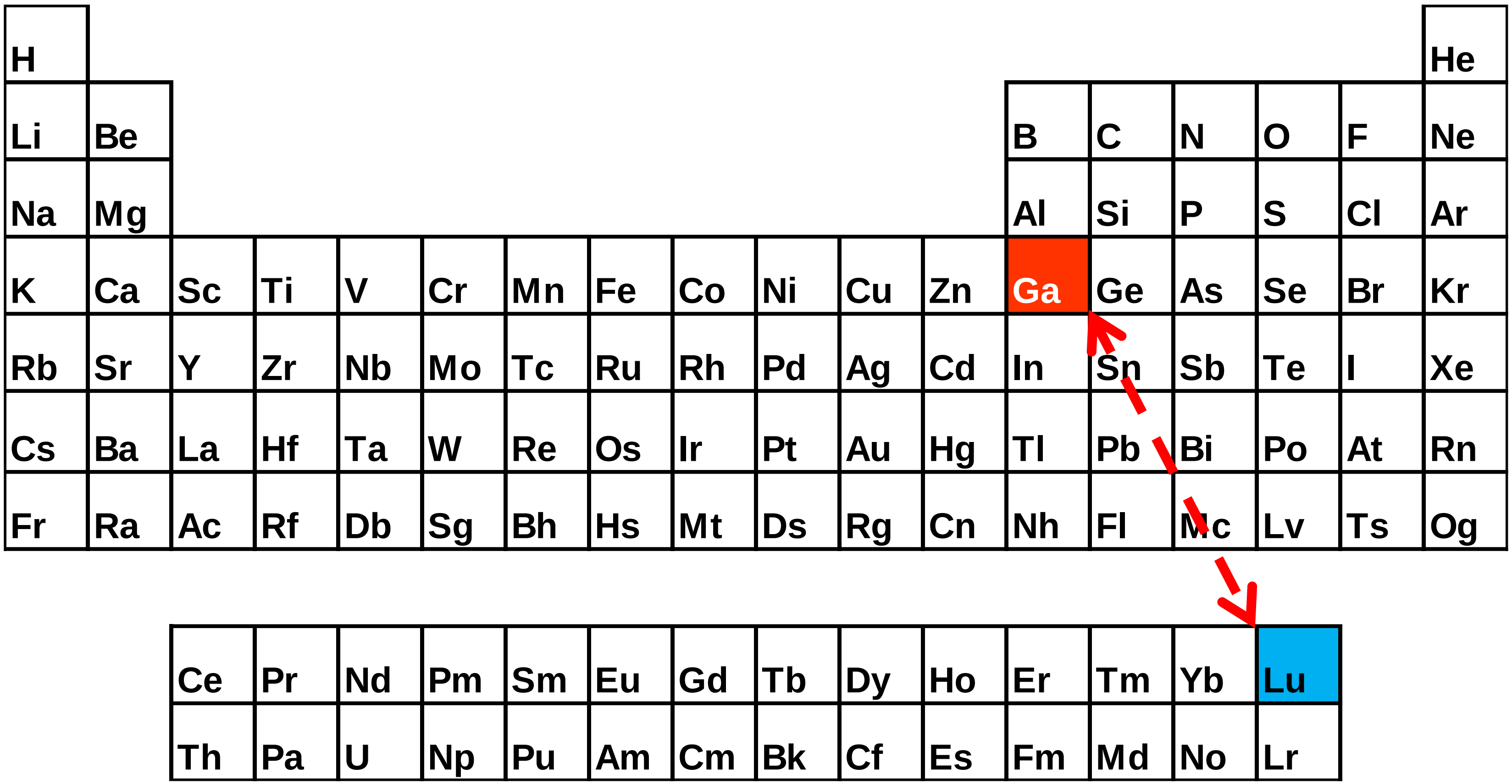


C. Kratochwil et al., Eur J Nucl Med Mol Imaging 2015;42:987.
R.P. Baum et al., J Nucl Med 2016;57:1006.
C. Kratochwil et al., J Nucl Med 2016;57:1170.
K. Rahbar et al., J Nucl Med 2017;58:85.
M.S. Hofman et al., Lancet Oncol 2018;19:825.
O. Sartor et al., N Engl J Med 2021;385:1091.
23 March 2022: Pluvicto® approved by FDA

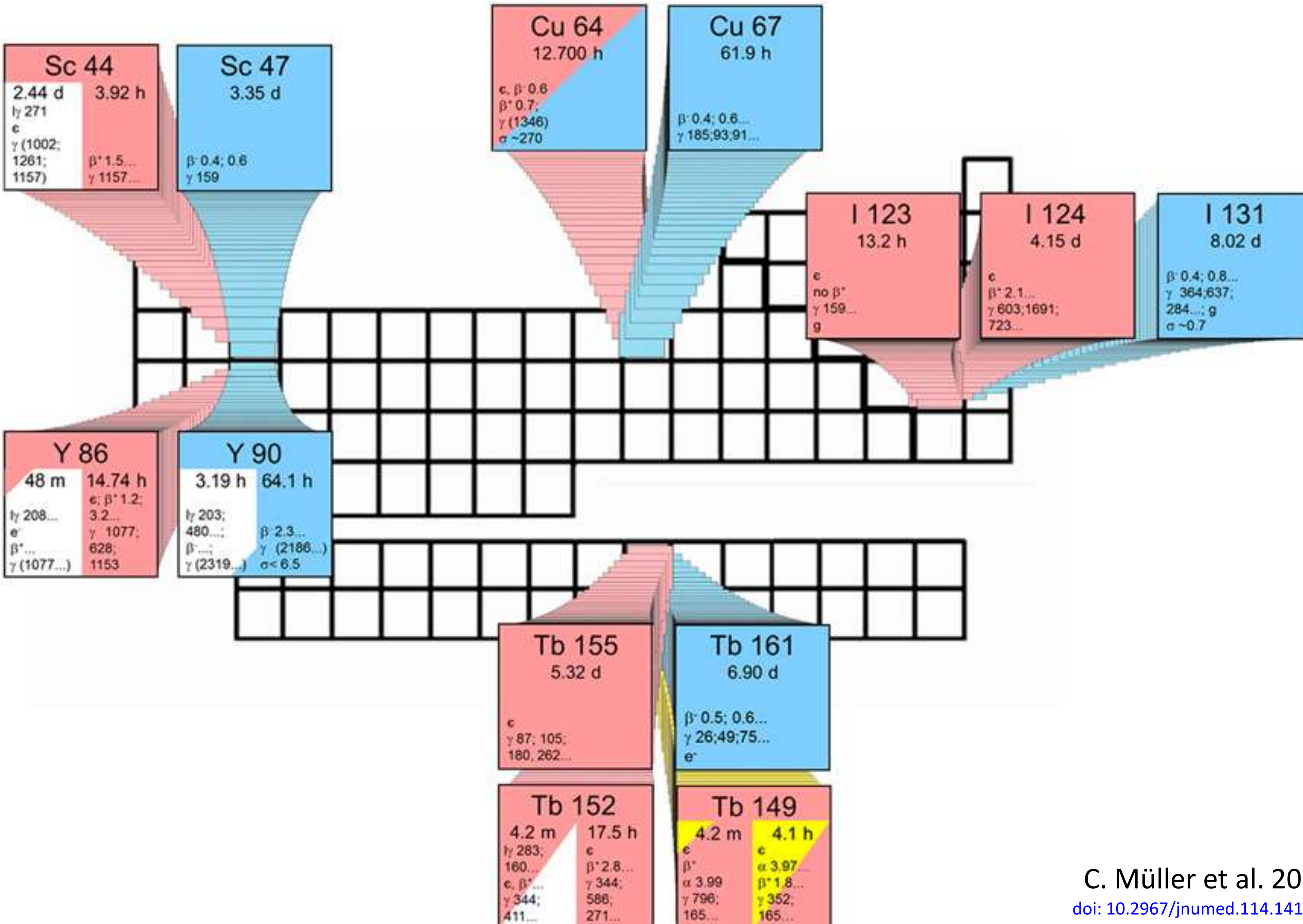
^{177}Lu-radioligand therapy of advanced prostate cancer



Matching of in-vivo behaviour ?



Matched pairs for theranostics



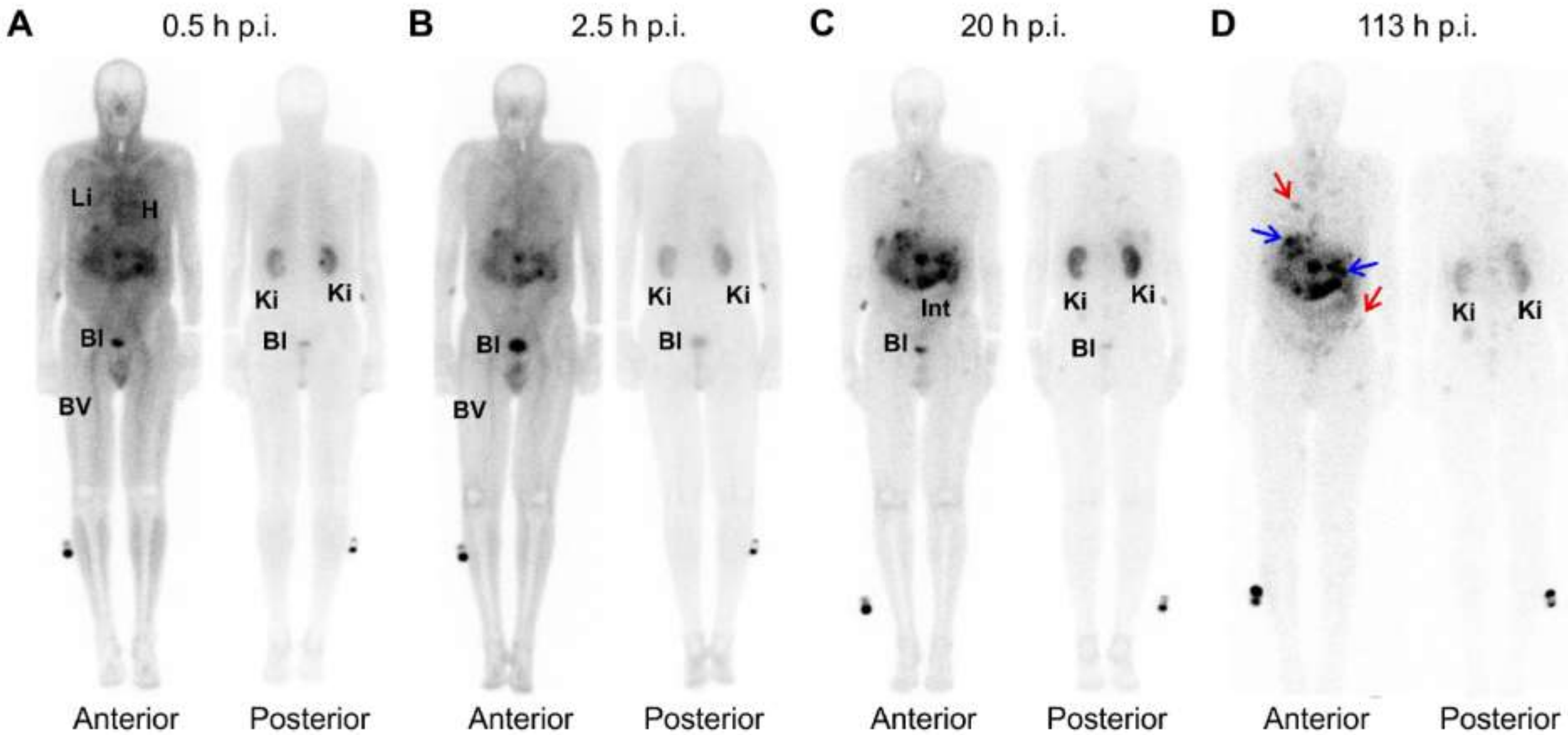
C. Müller et al. 2014

doi: 10.2967/jnumed.114.141614

The ideal beta emitter ?

Tb 161
6.96 d

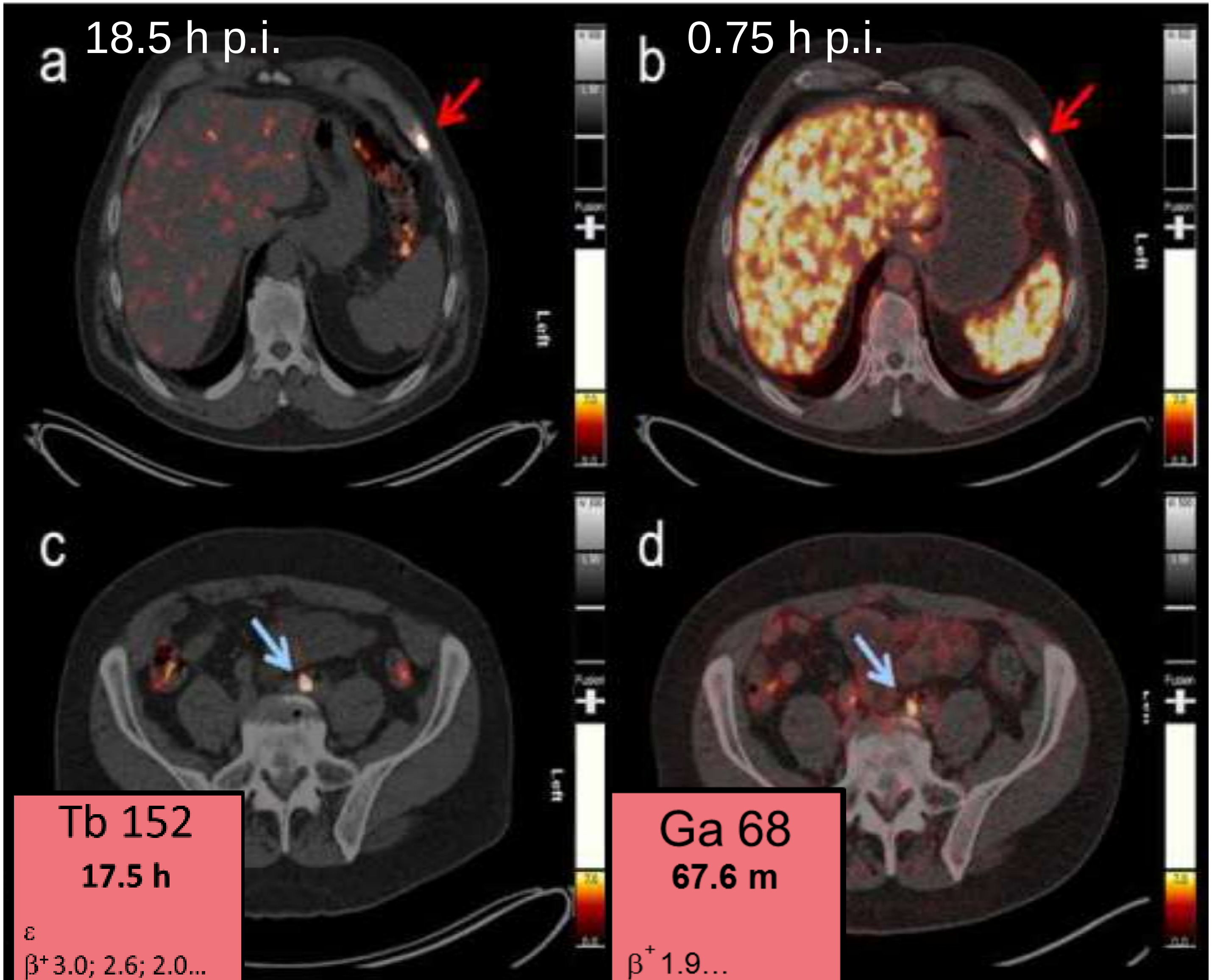
β^- 0.5; 0.6
γ 26; 49; 75…
e^-



R.P. Baum et al. 2021

doi: 10.2967/jnumed.120.258376

First-in-human study with ^{152}Tb-PSMA-617



Tb 152
17.5 h
ε
β^+ 3.0; 2.6; 2.0…
γ 344; 271; 586…

Ga 68
67.6 m
β^+ 1.9…
γ 1077, (…)

Zentralklinik Bad Berka

PAUL SCHERRER INSTITUT PSI

ETH zürich

ISOLDE

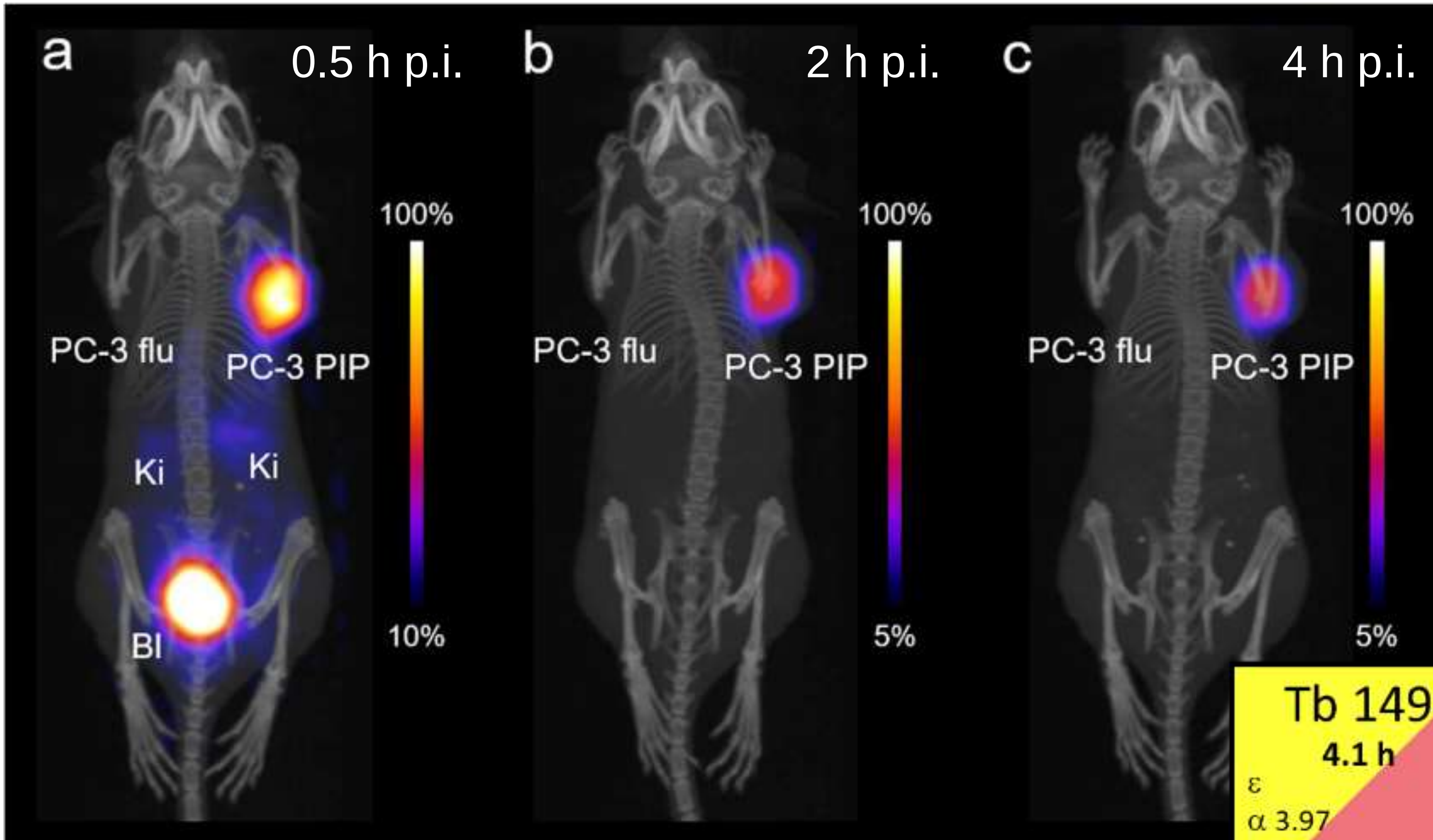
NEUTRONS FOR SOCIETY

ENSAR2

150 MBq ^{152}Tb-PSMA-617

C. Müller et al. EJNMMI Research 2019;9:68.

Alpha-PET with ^{149}Tb



5 MBq ^{149}Tb-PSMA-617

Tb 149
4.1 h
ε
α 3.97
β^+ 1.4...
γ 352; 165...

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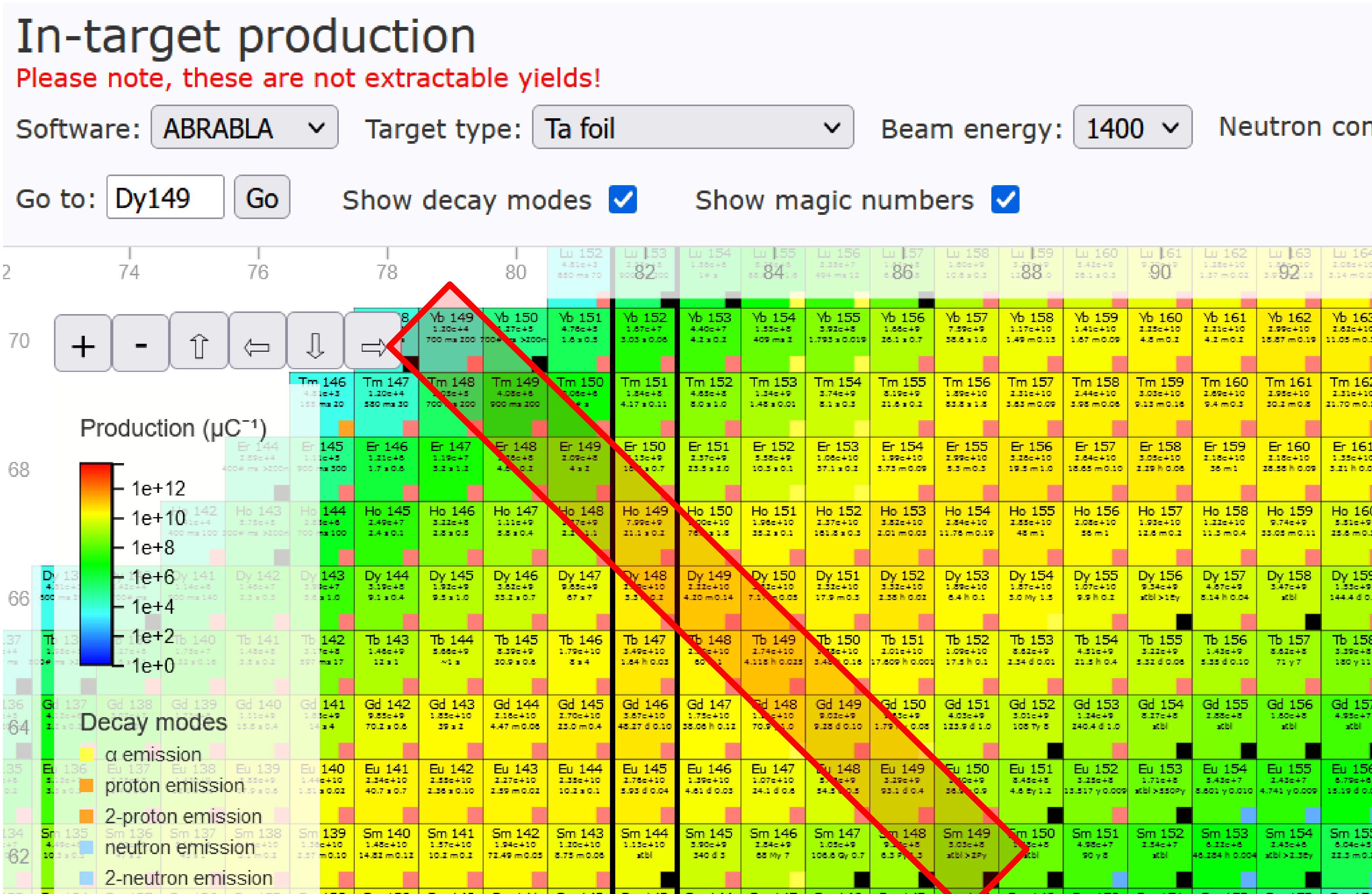
SAHLGRENSKA ACADEMY

C.A. Umbricht et al. Sci Rep 2019;9:17800.

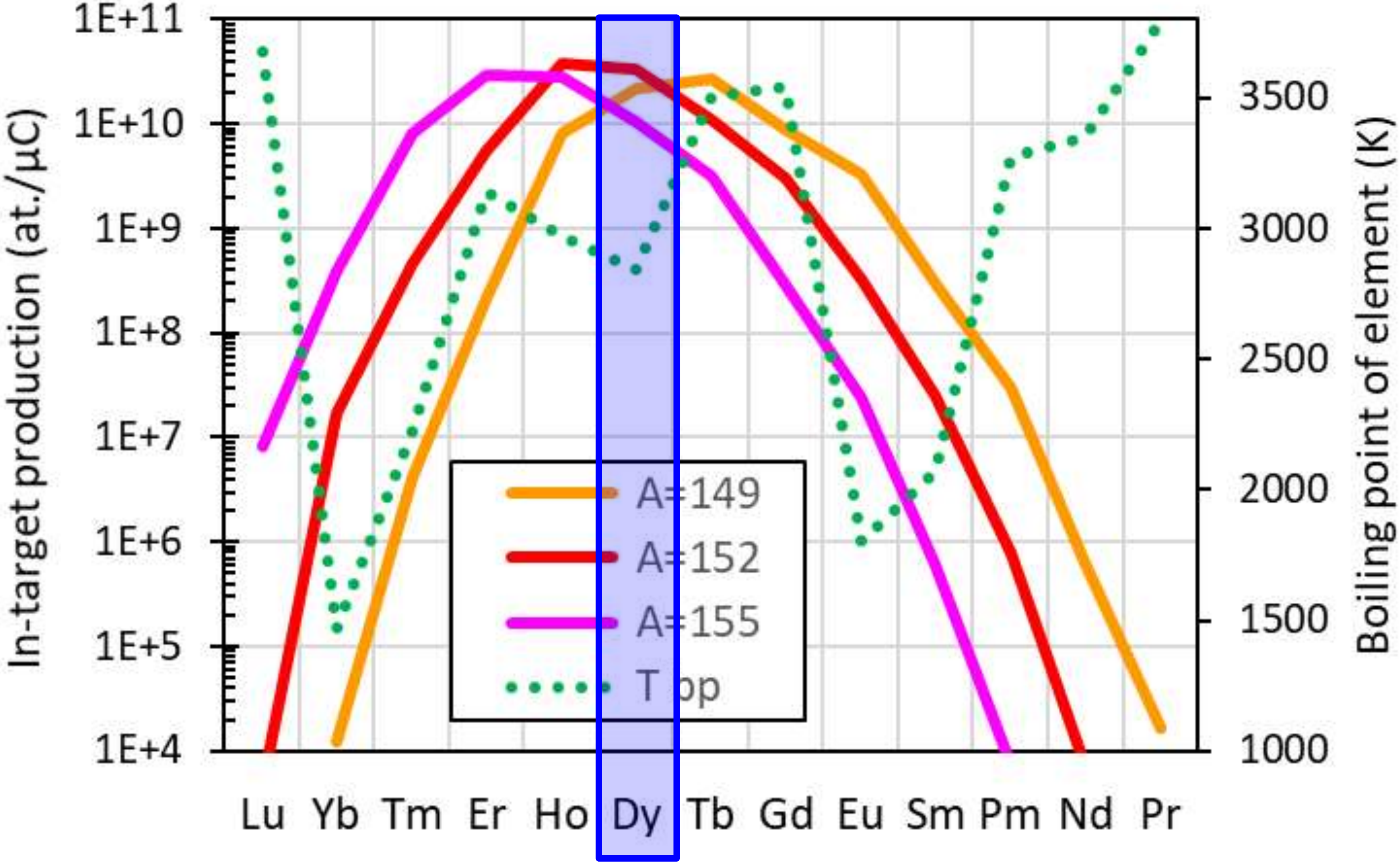
Terbium: a unique element for nuclear medicine

Predicted production rates



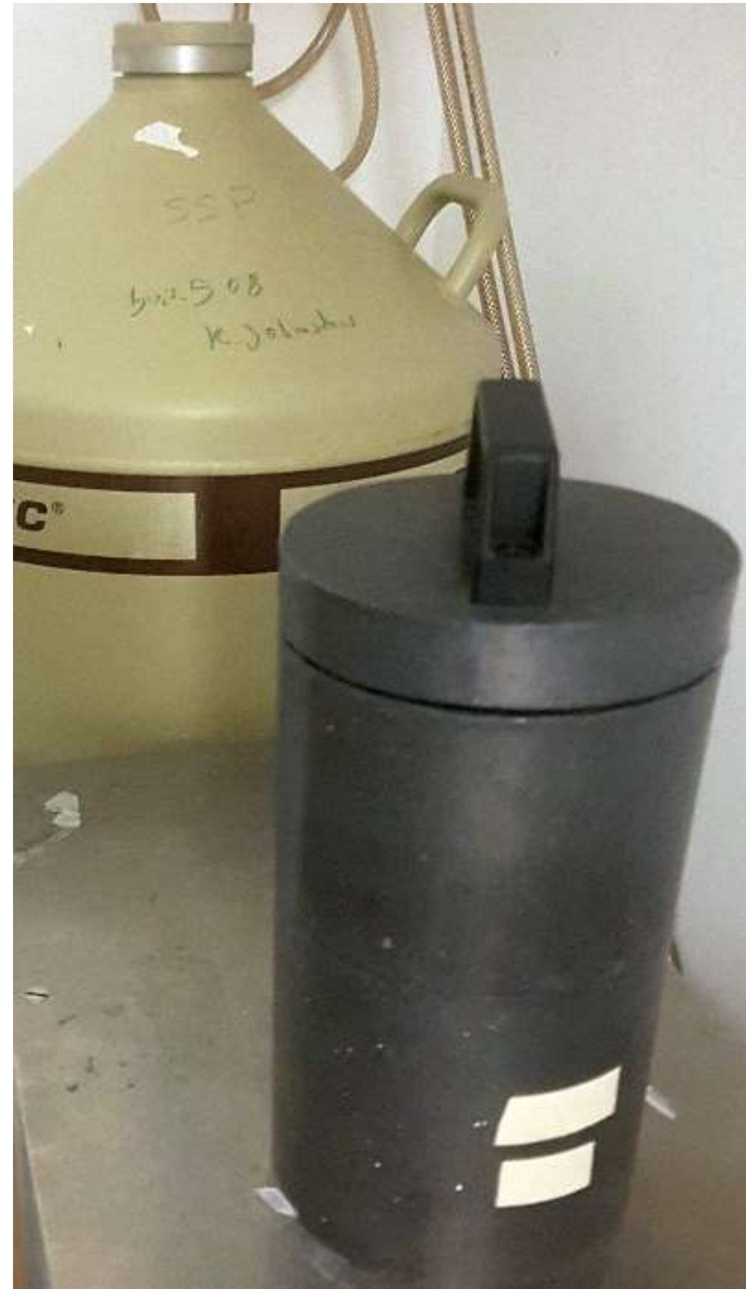
https://isoyields2.web.cern.ch/InTargetProductionChart.aspx

Predicted production rates

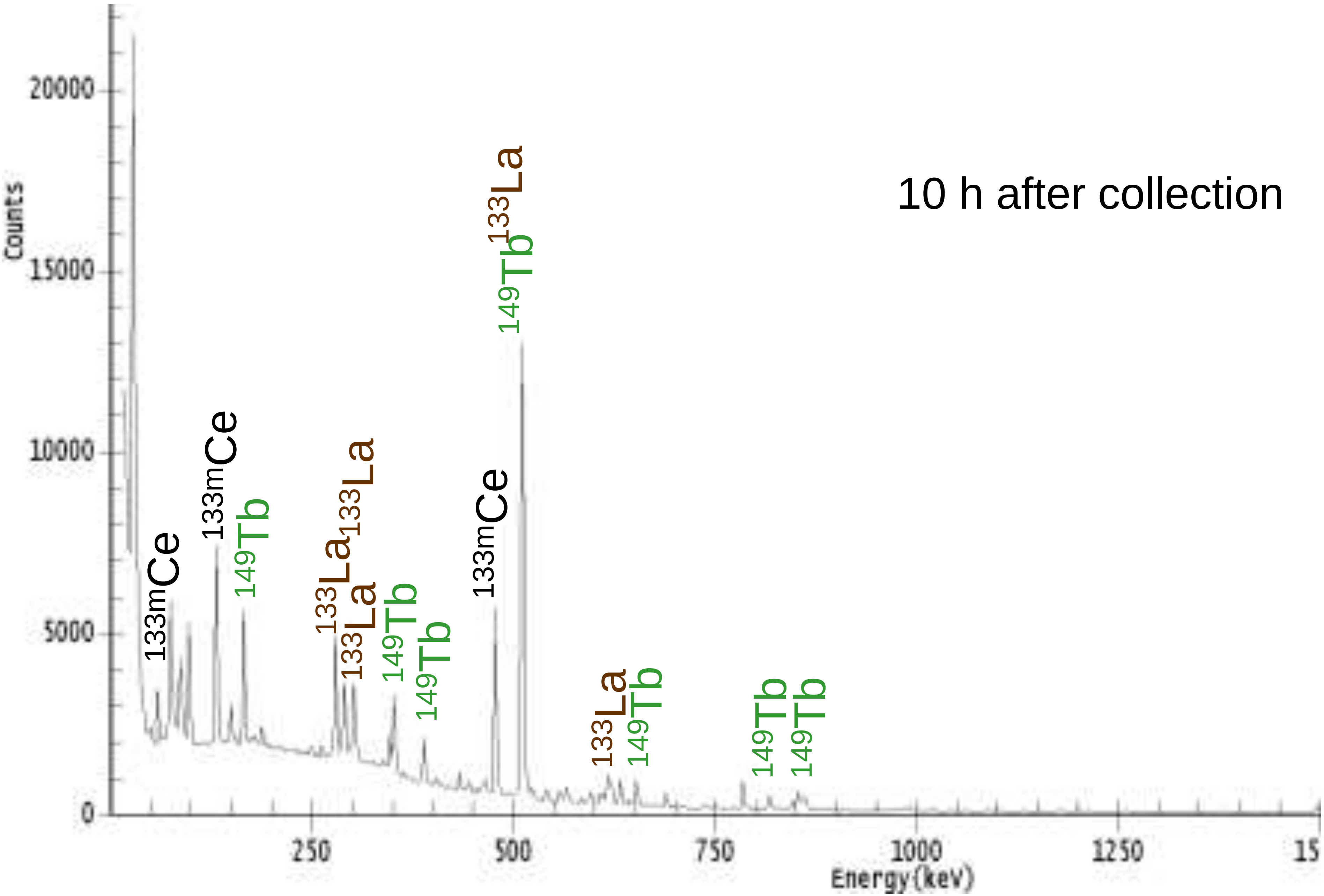


Off-line gamma ray spectroscopy

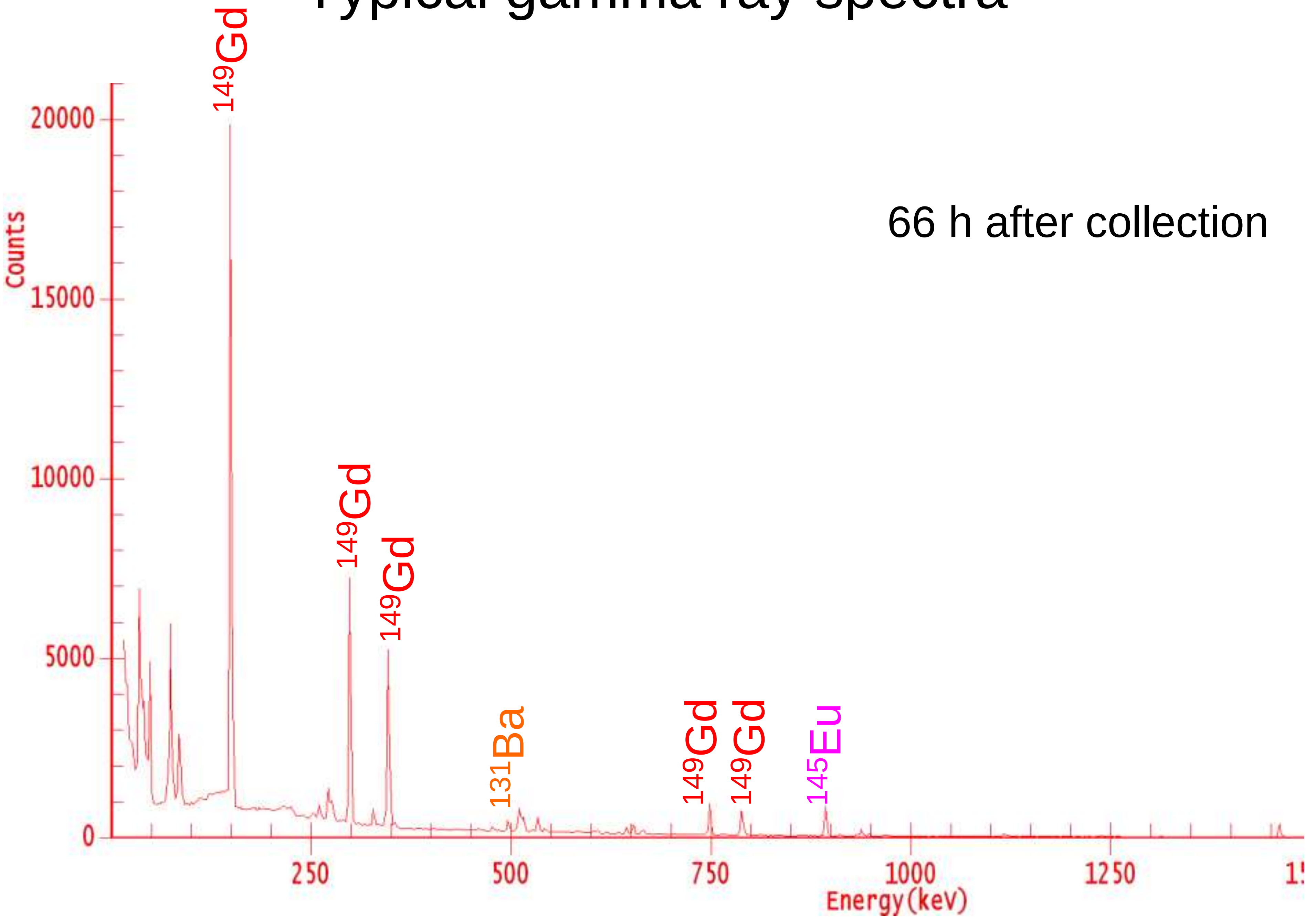
Implant test samples



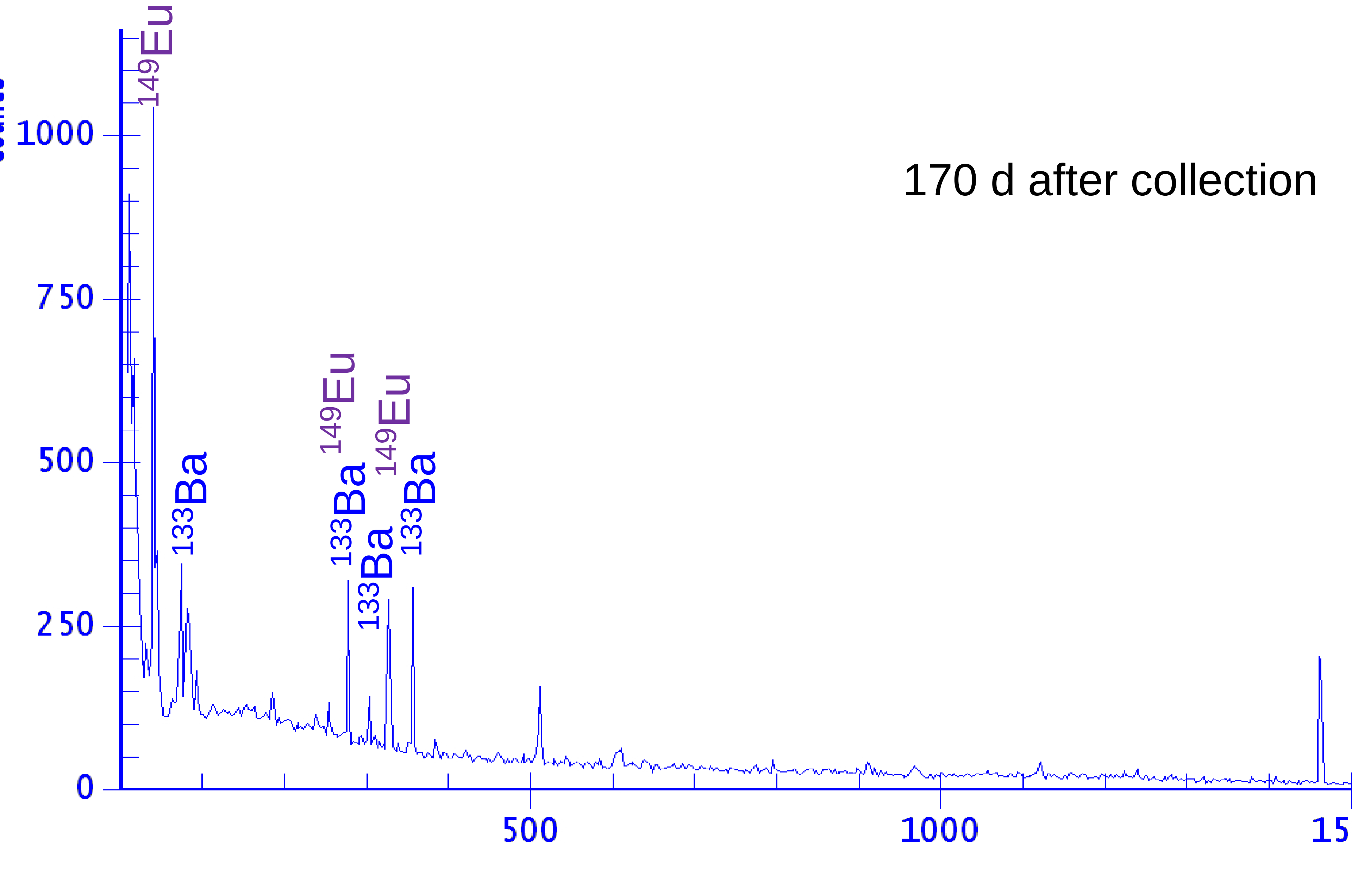
Typical gamma ray spectra



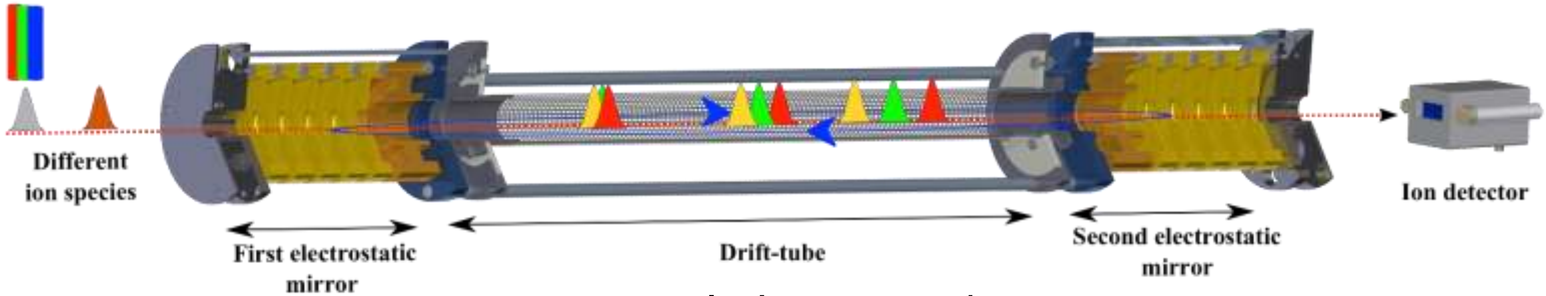
Typical gamma ray spectra



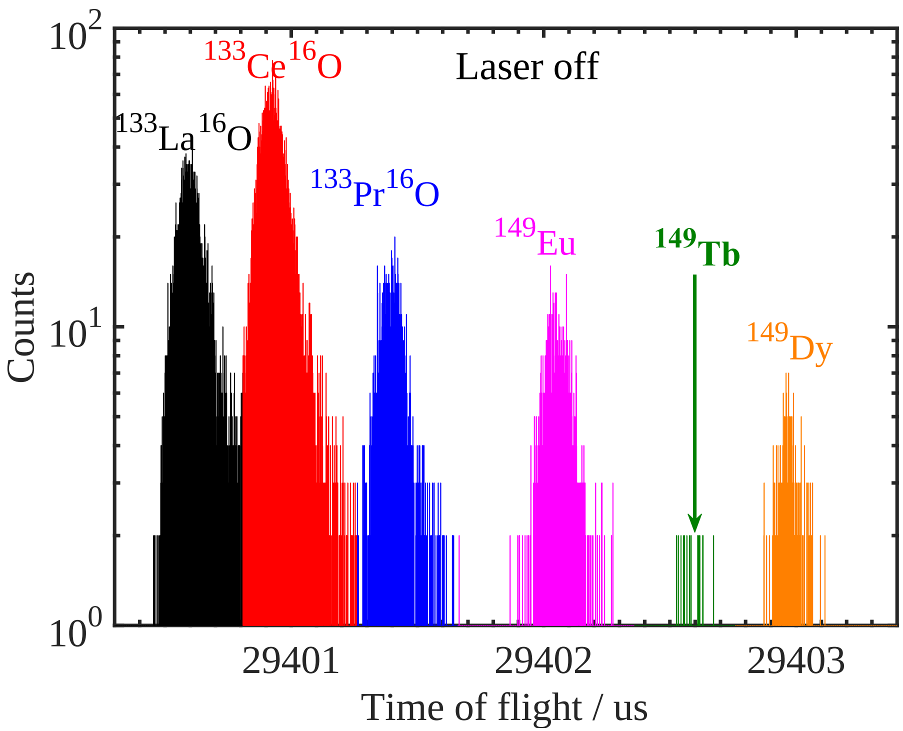
Typical gamma ray spectra

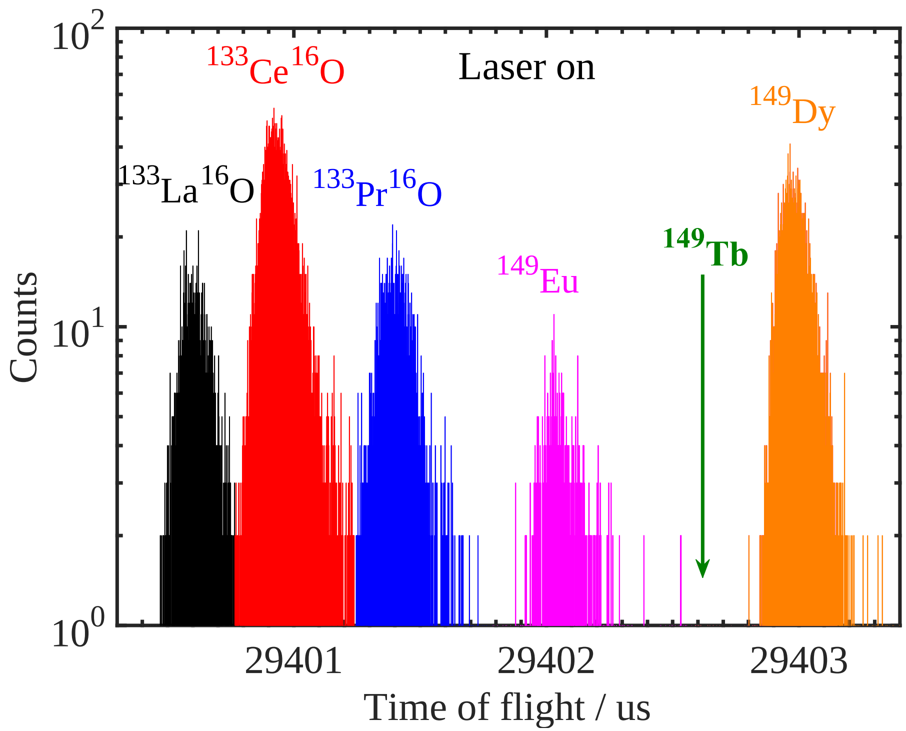


Beam optimization with ISOLTRAP's MR-ToF-MS



1000 revolutions $\Rightarrow$ $m/\Delta m \approx 115000$

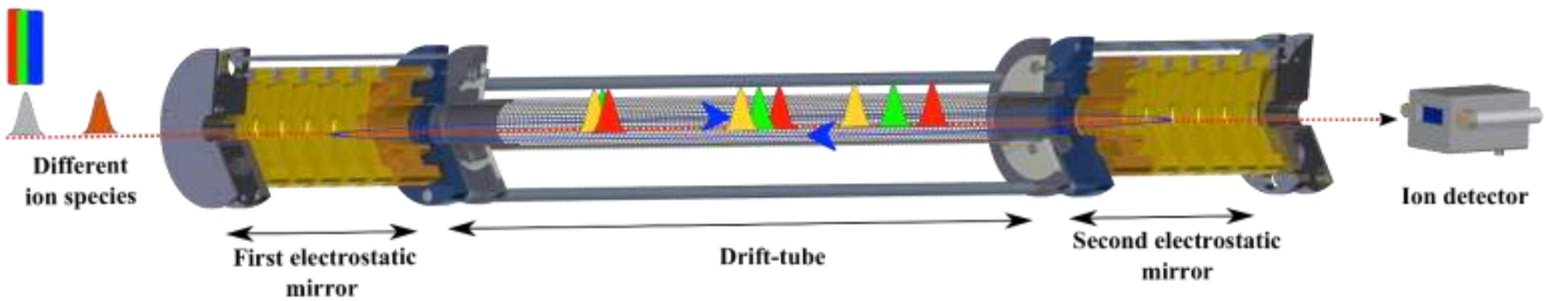


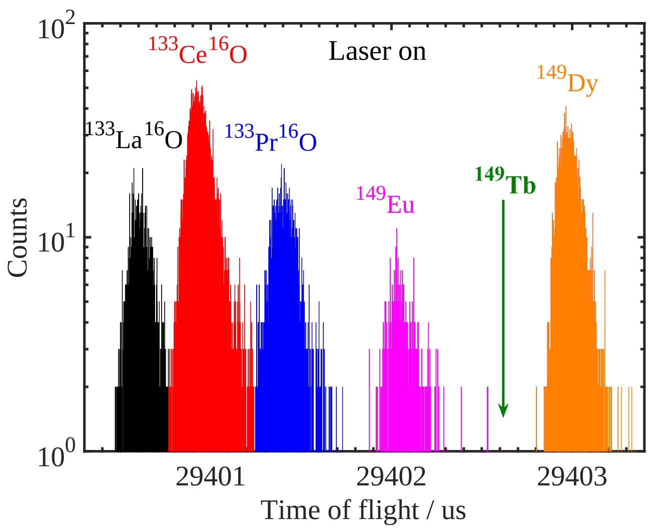


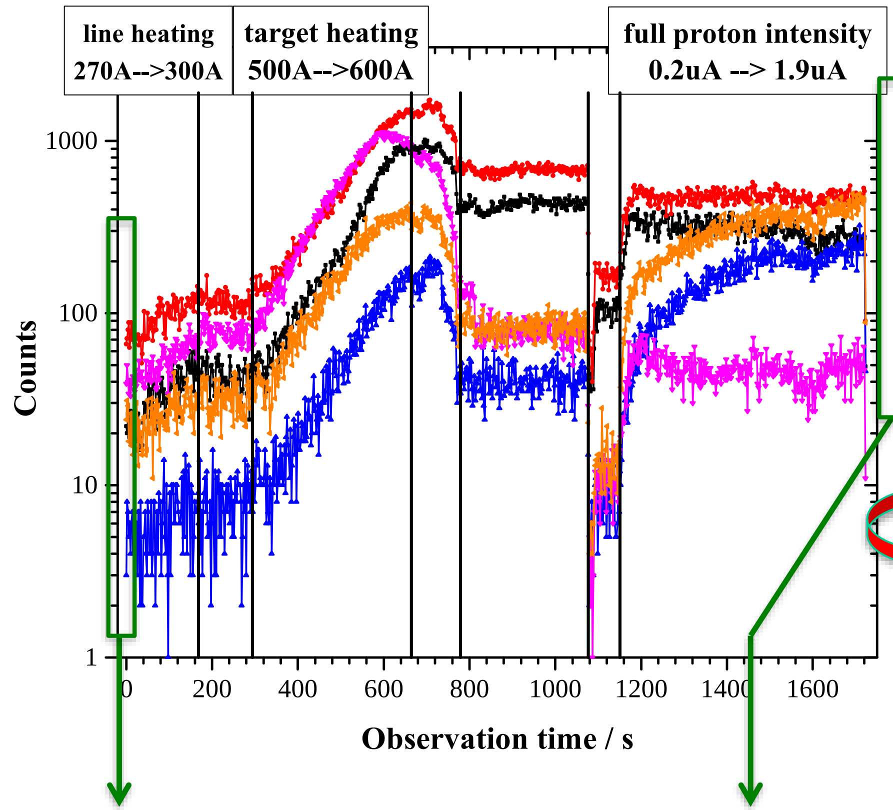
Much more Dy than Tb

Laser on/off ratio ≈ 10

Beam optimization with ISOLTRAP's MR-ToF-MS







Isotope	Half life
^{133}La	3.9 h
^{133}Ce ^{133m}Ce	97 m 5.1 h
^{133}Pr	6.5 m
^{149}Eu	93 d
^{149}Dy	4.2 m
^{149}Tb	4.1 h

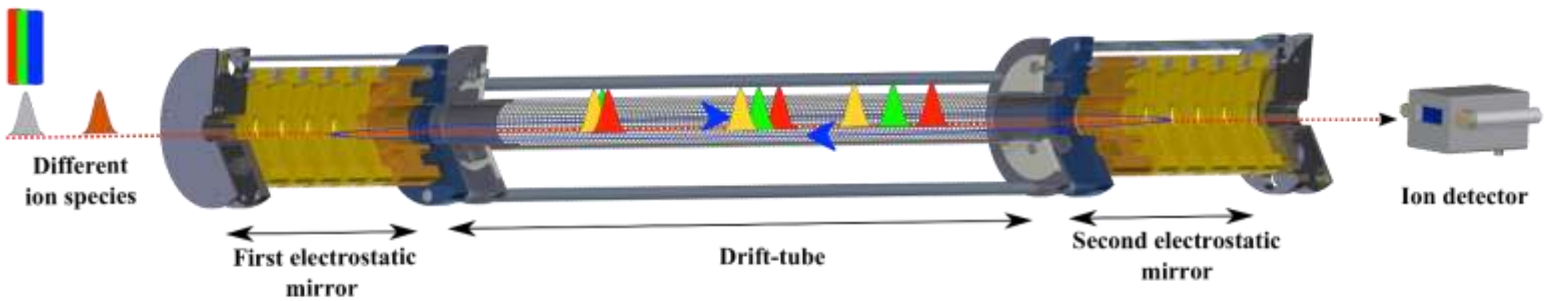
^{149}Dy release-limited

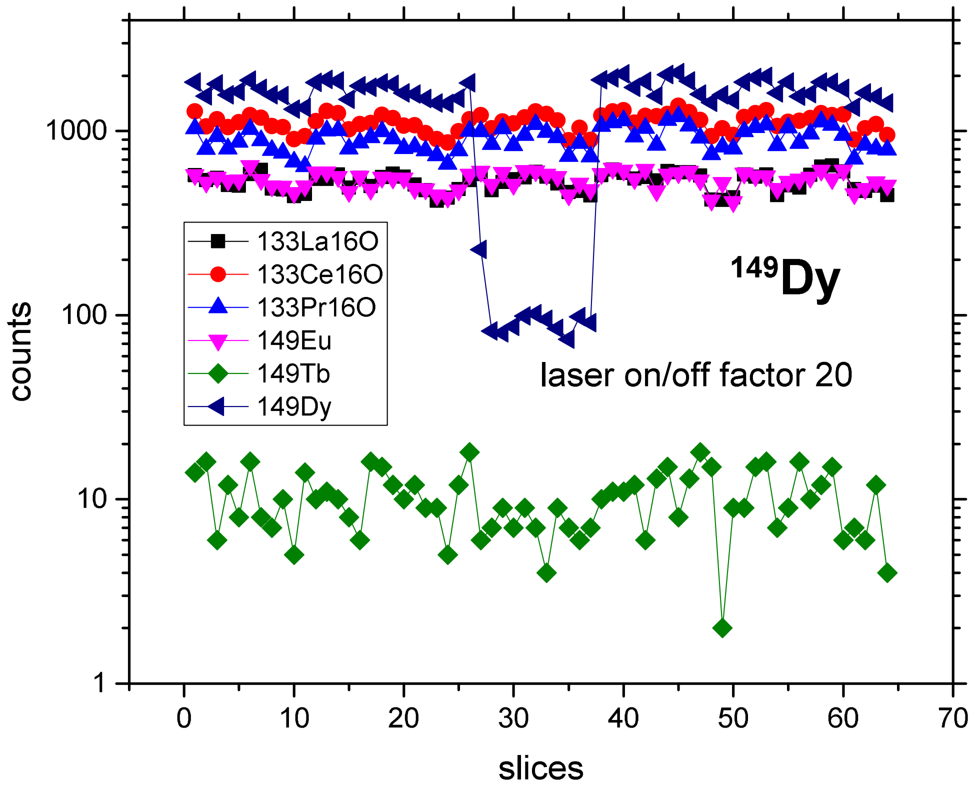
⇒ Improves significantly with hotter target

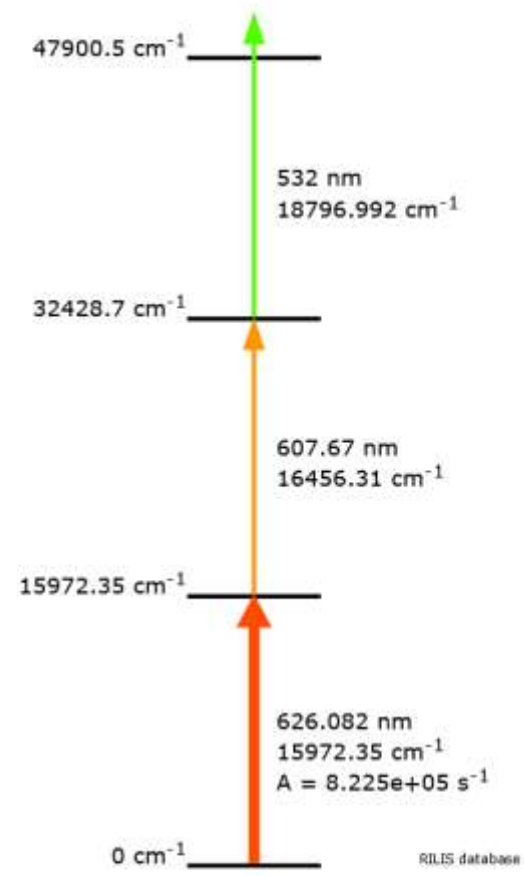
Before optimization: 6.3/1 After optimization: 2.3/1

Tb / contaminants → factor ≈ 3 improvement!

Beam optimization with ISOLTRAP's MR-ToF-MS

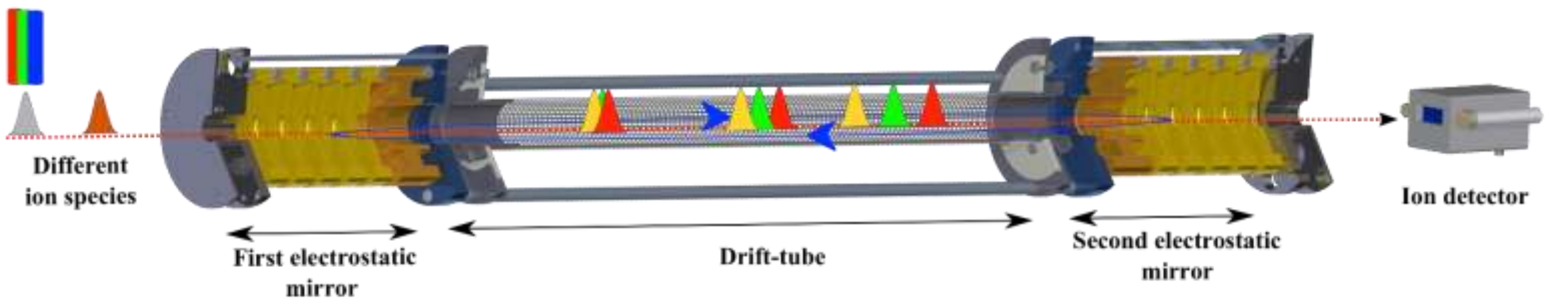


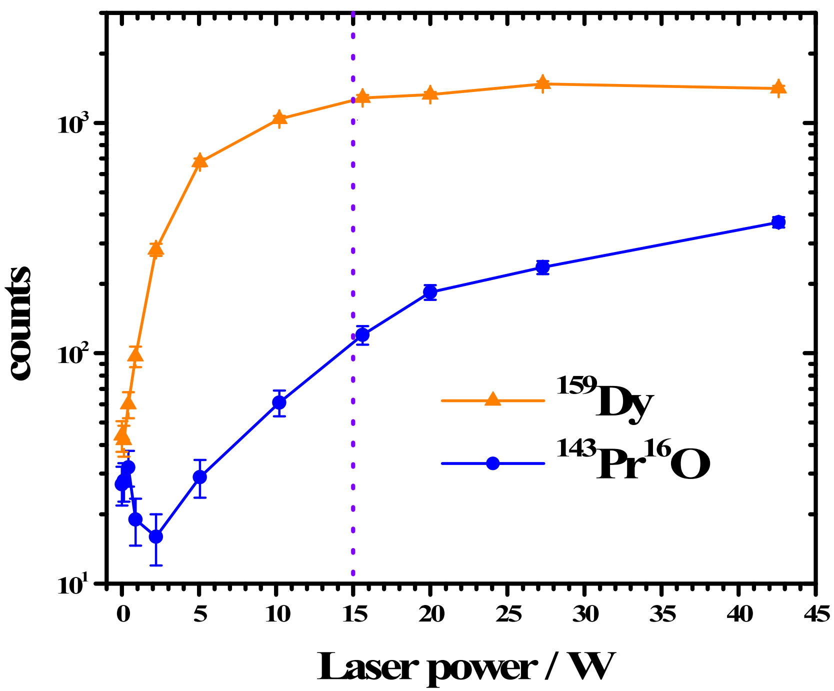


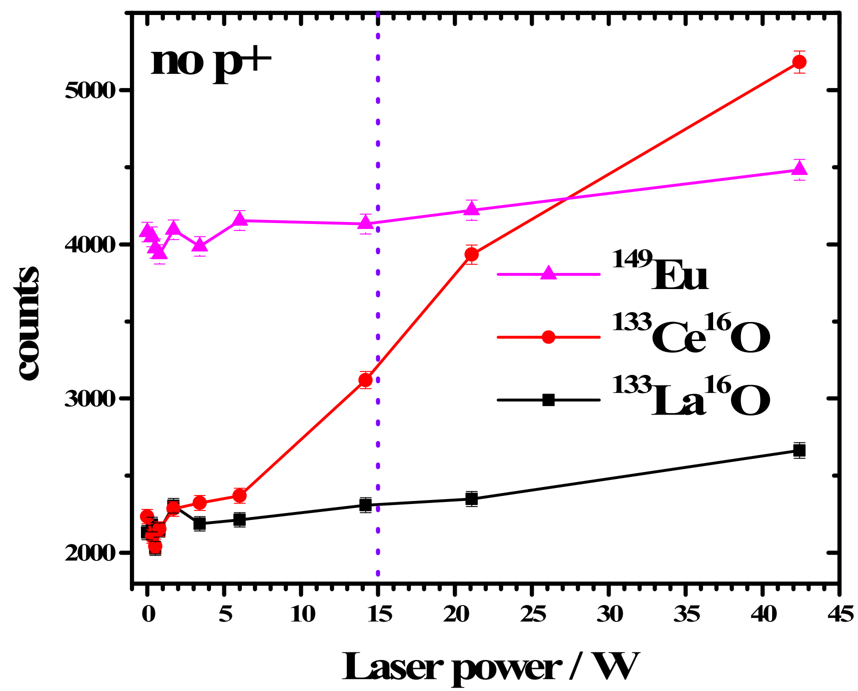


1st step (626 nm) affects only Dy

Beam optimization with ISOLTRAP's MR-ToF-MS



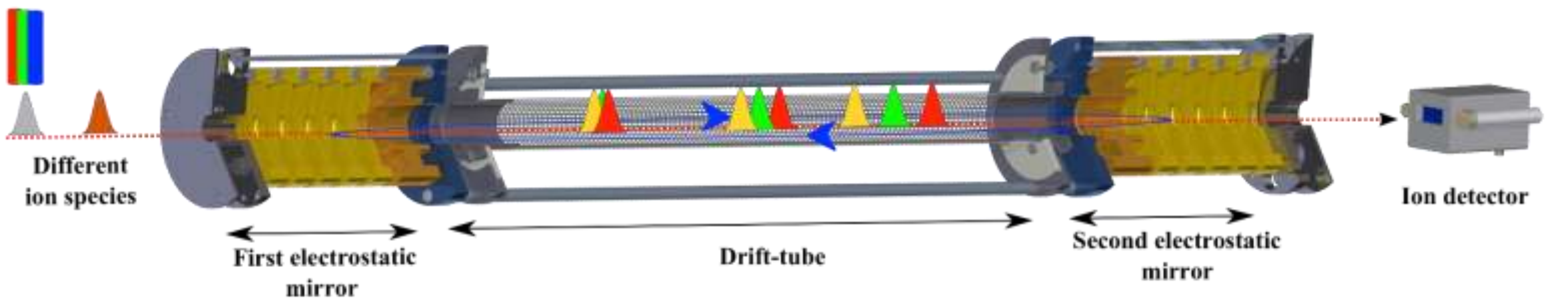


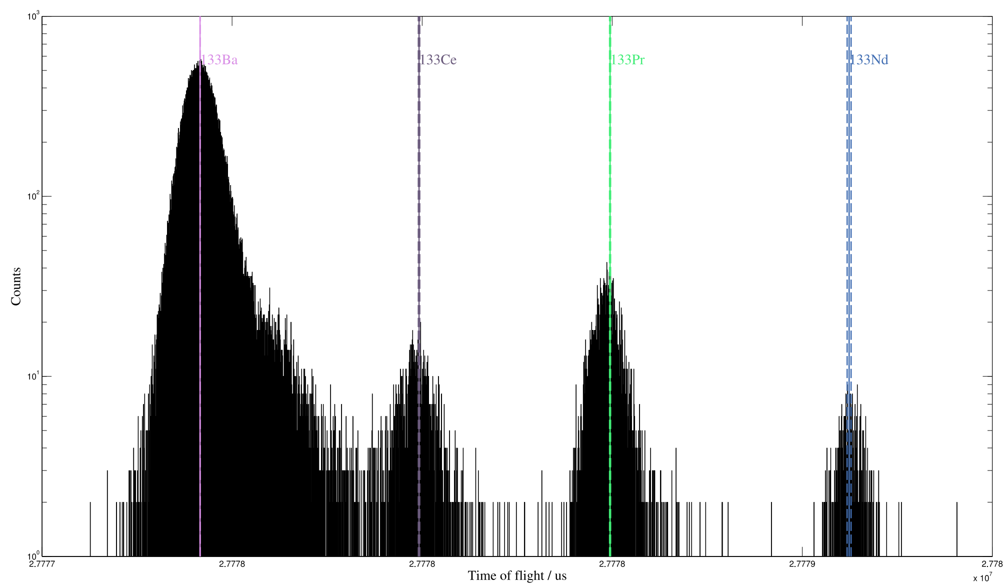


3rd step (532 nm high power) enhances also PrO^+ and CeO^+

⇒ reduction to ≈15 W improves ^{149}Tb/contaminants factor ≈3

Beam optimization with ISOLTRAP's MR-ToF-MS

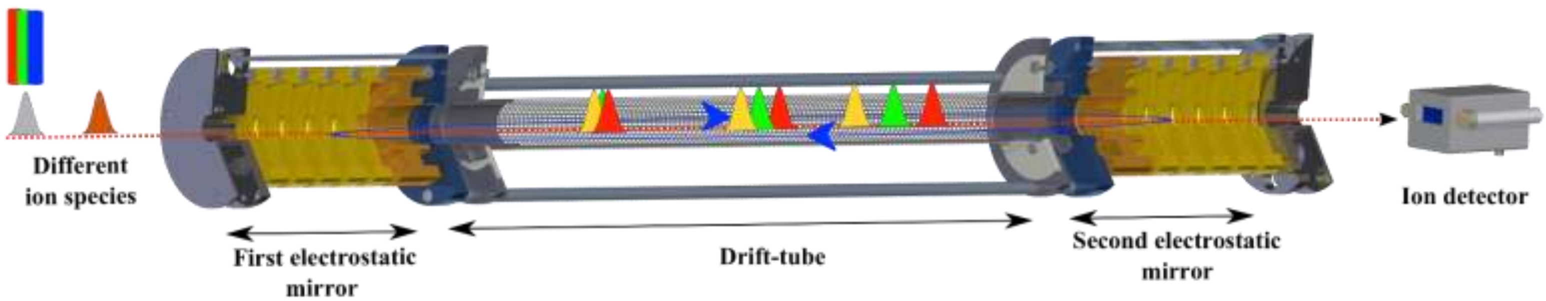




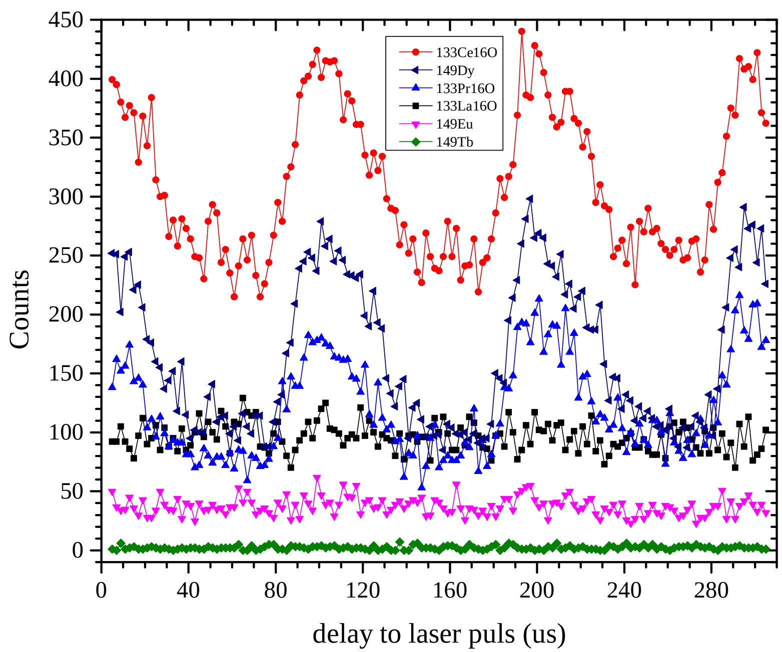
No laser effect on atomic Ba, La, Ce, Pr and Nd,

but on PrO and CeO

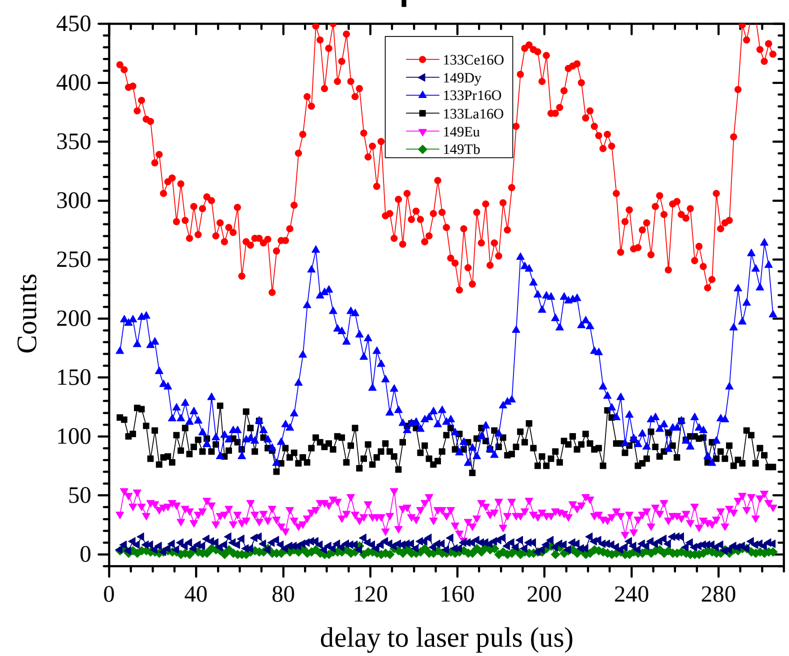
Beam optimization with ISOLTRAP's MR-ToF-MS



All lasers on

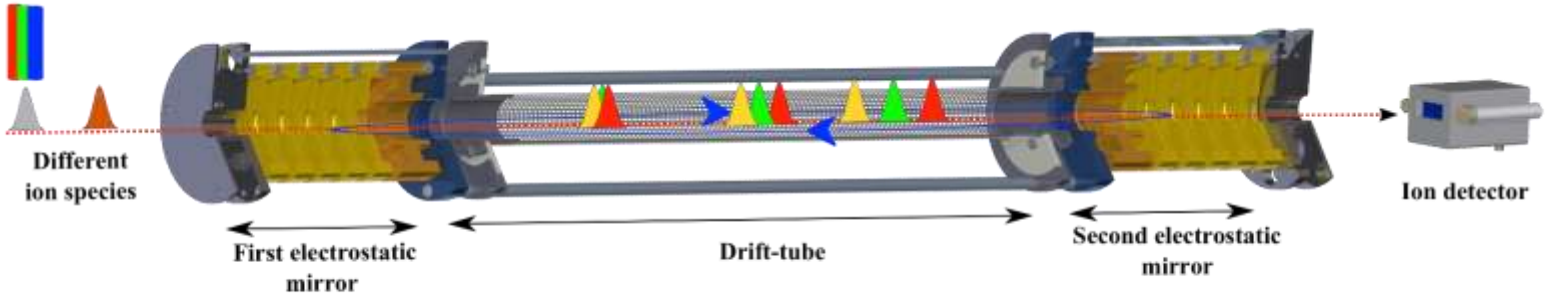


1st step blocked

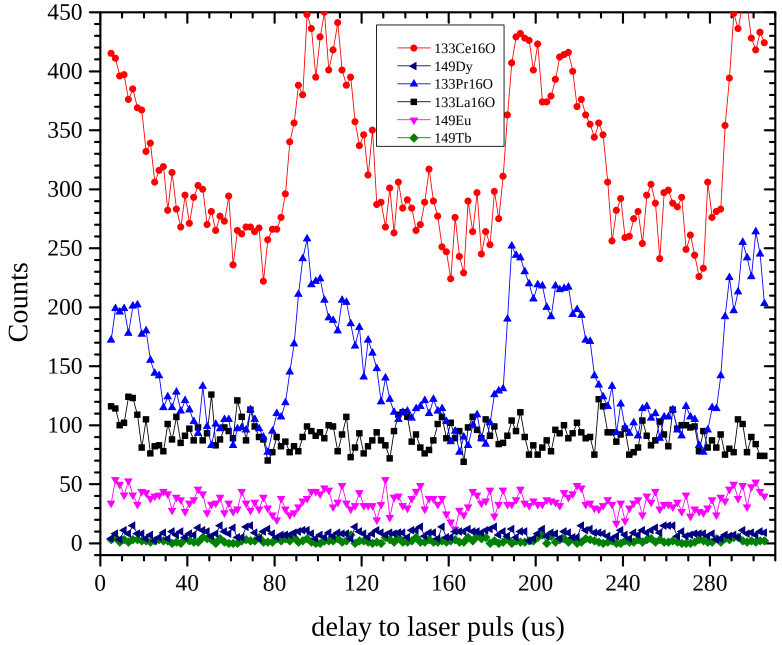


PrO^+, CeO^+ pulsed ⇒ photo-ionized, not only thermo-ionized

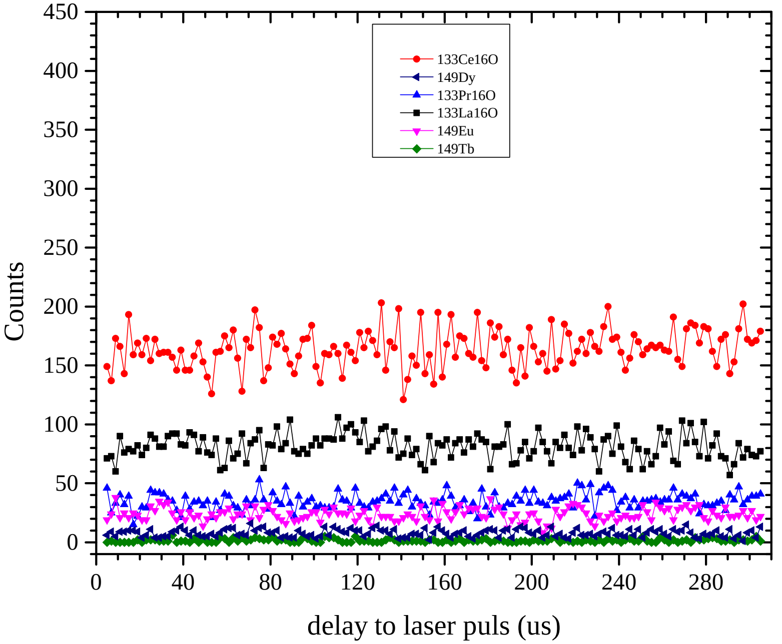
Beam optimization with ISOLTRAP's MR-ToF-MS



1st step blocked

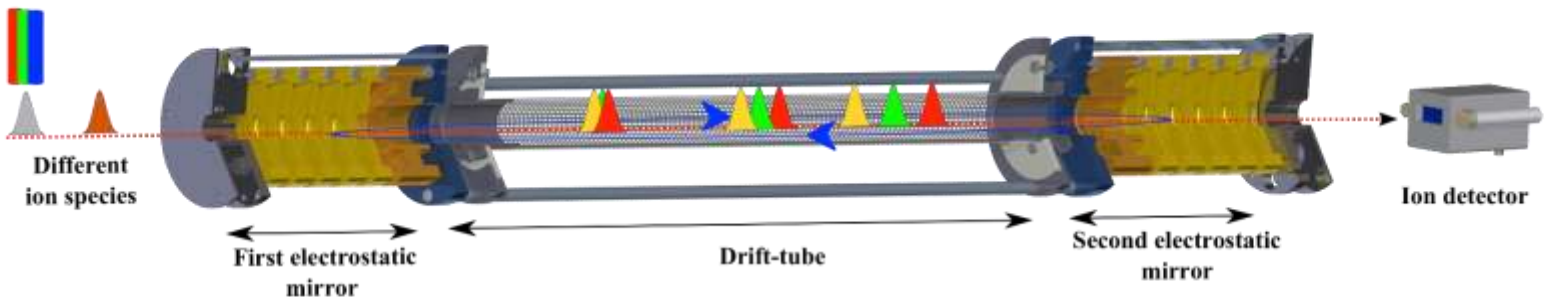


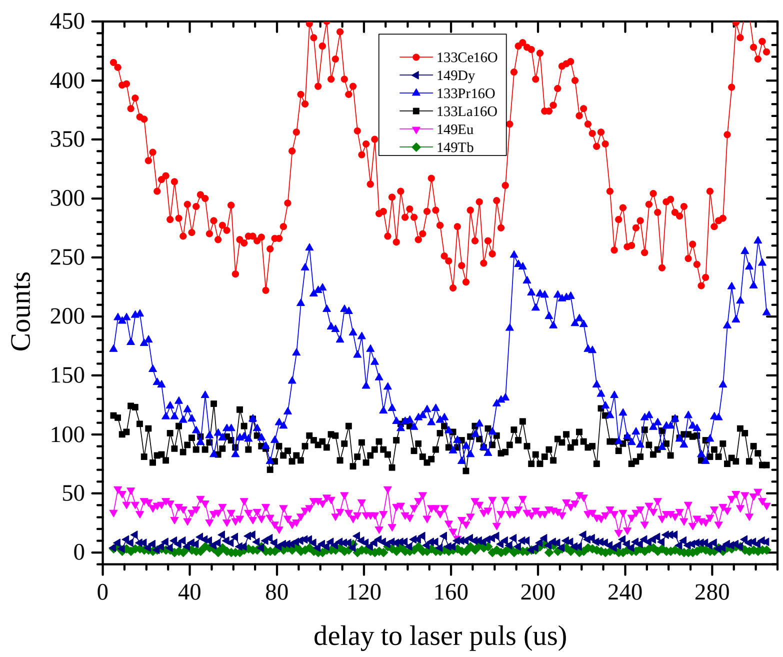
2nd step blocked

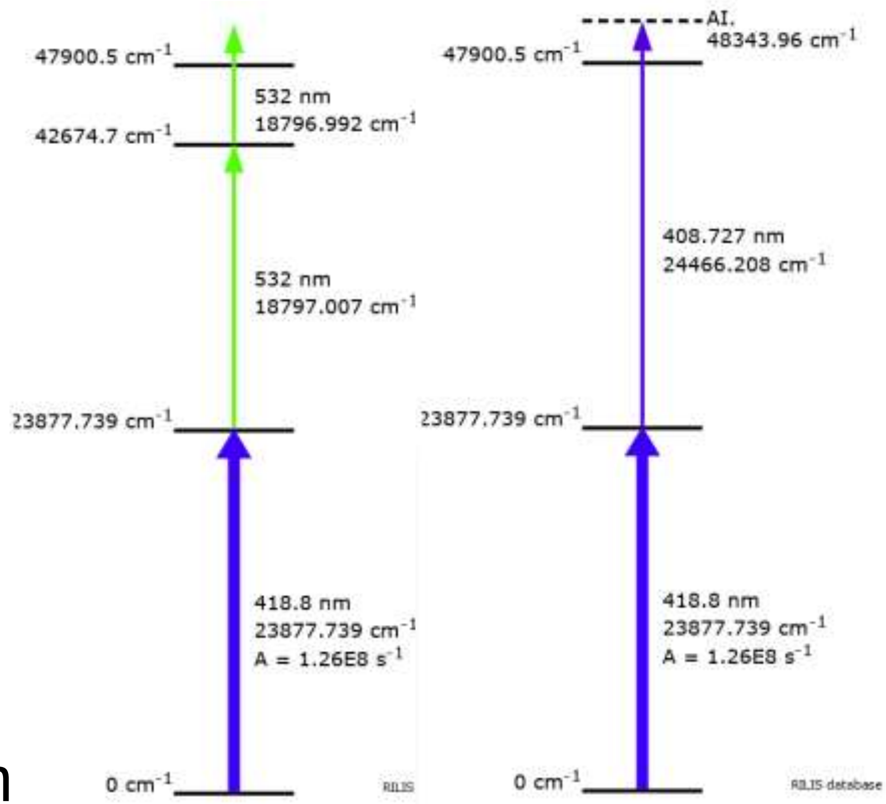


PrO^+ and CeO^+ pulsed ⇒ 608 nm has resonant effect

Beam optimization with ISOLTRAP's MR-ToF-MS



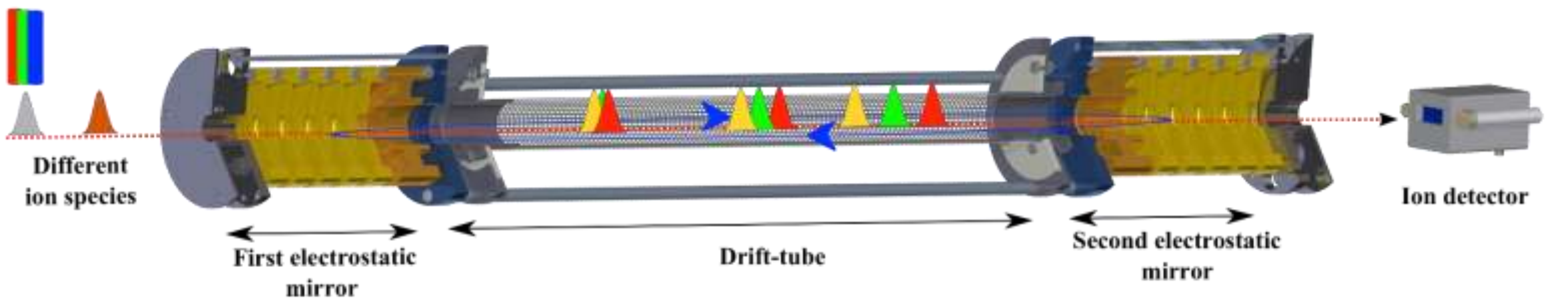


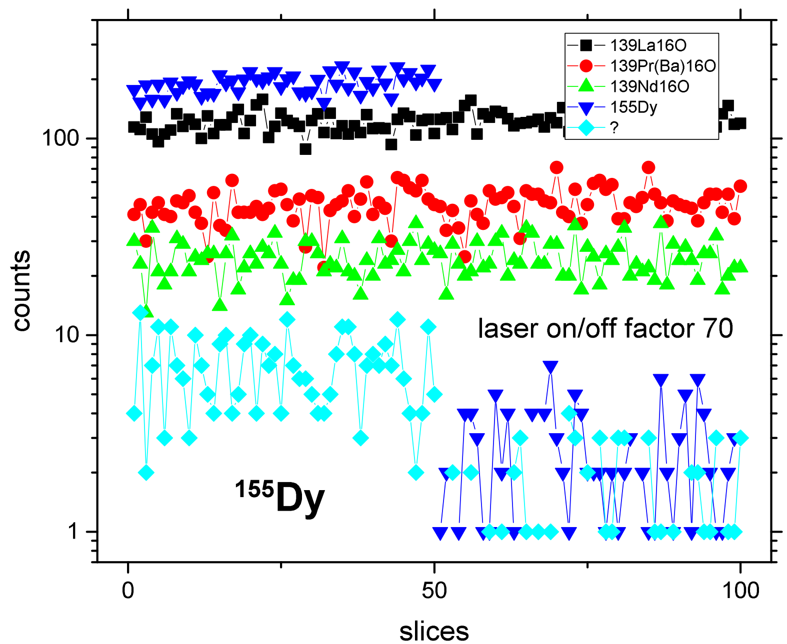


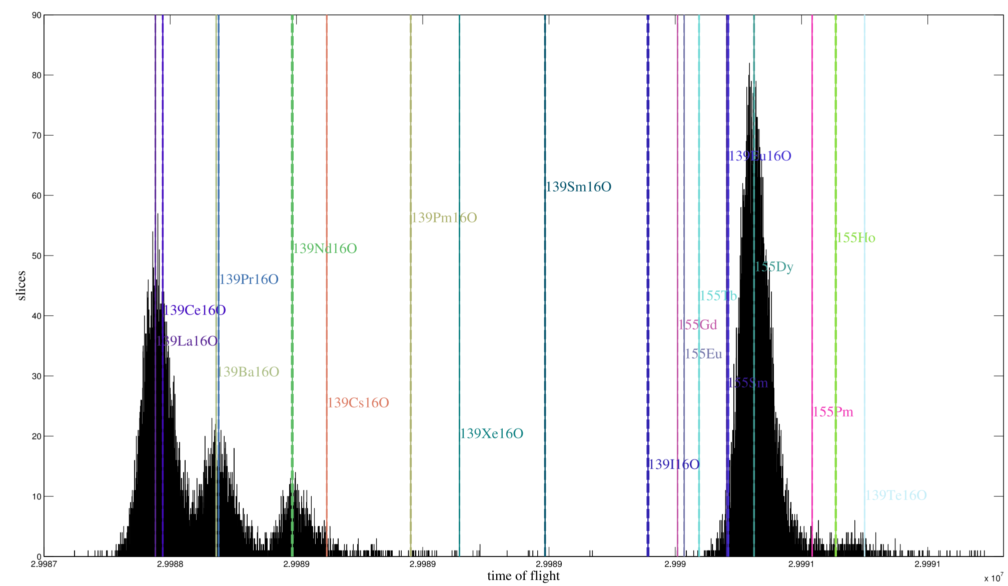
New RILIS schemes avoid 608 nm

(probably) no PrO^+ and CeO^+ enhancement

Beam optimization with ISOLTRAP's MR-ToF-MS





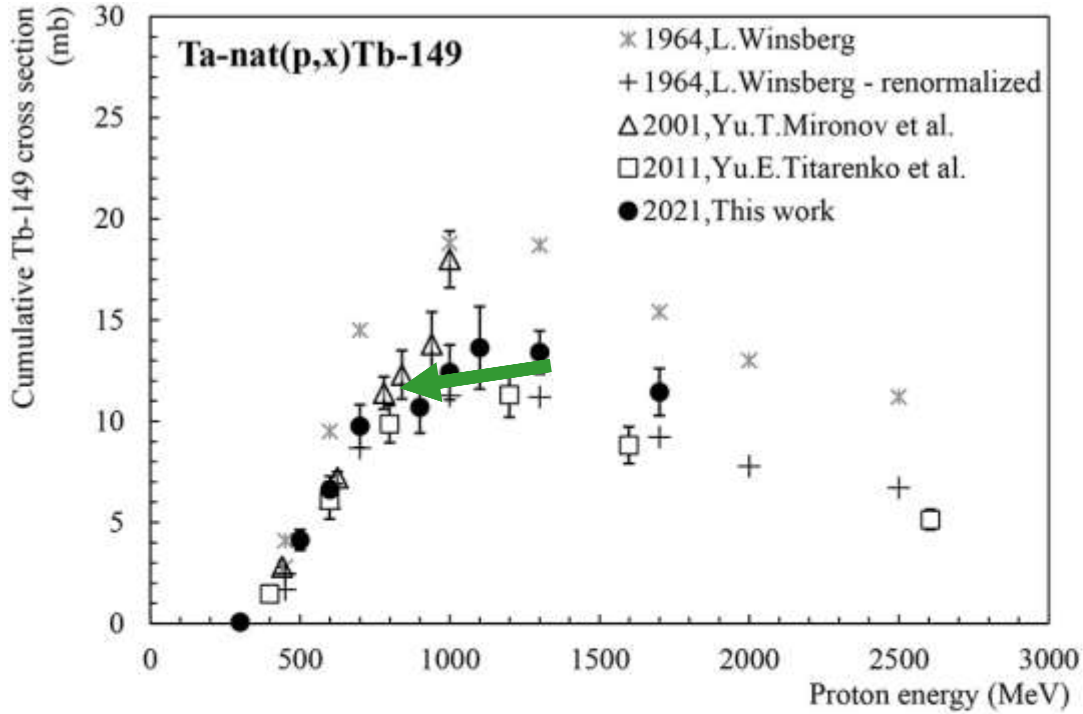


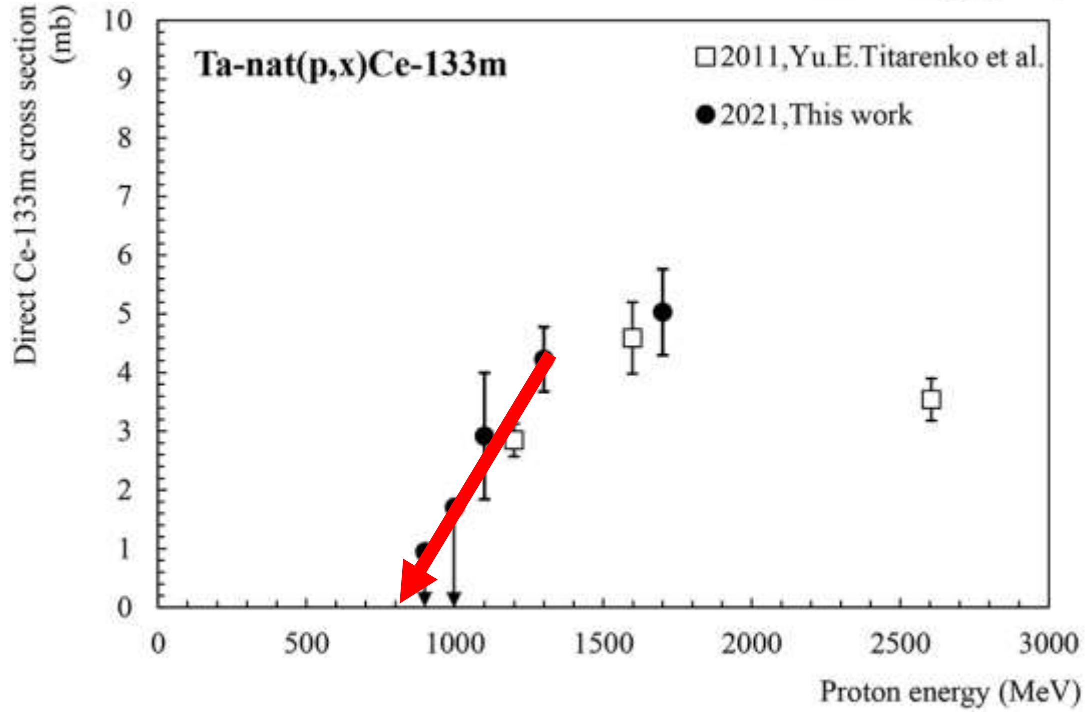
Also for A=155 and A=152 Dy is the dominant isobar

(cf. PS-1-3)

Future improvement of Tb / CeO ratio ?

(cf. Simon Stegemann)





C Duchemin et al,

Frontiers Med 2021;8:625561.

Summary

- MR-ToF-MS is extremely useful for on-line beam optimization

- on-line production of $^{149,152,155}Tb$ best via Dy precursors
- ^{149}Dy yield release limited, ≈2% overall efficiency

  ⇒ hotter target & thinner foils could help
- no laser effect on atomic Pr^+, Nd^+, Ce^+
- PrO^+ and CeO^+ laser-ionized with 608 nm + 532 nm
- RILIS schemes with 1st step 419 nm produce cleaner Dy
- *^{149}Dy laser enhancement smaller than for other Dy isotopes*
- ≈800-1000 MeV p would produce significantly less ^{133}Ce

- off-line production of $^{149,152,155}Tb$ would be different

(cf. next talk)