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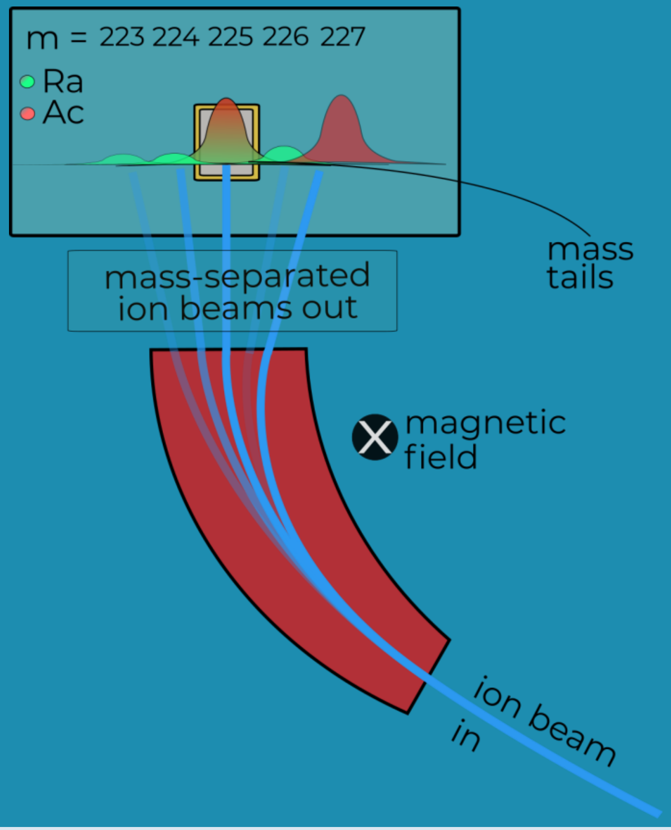
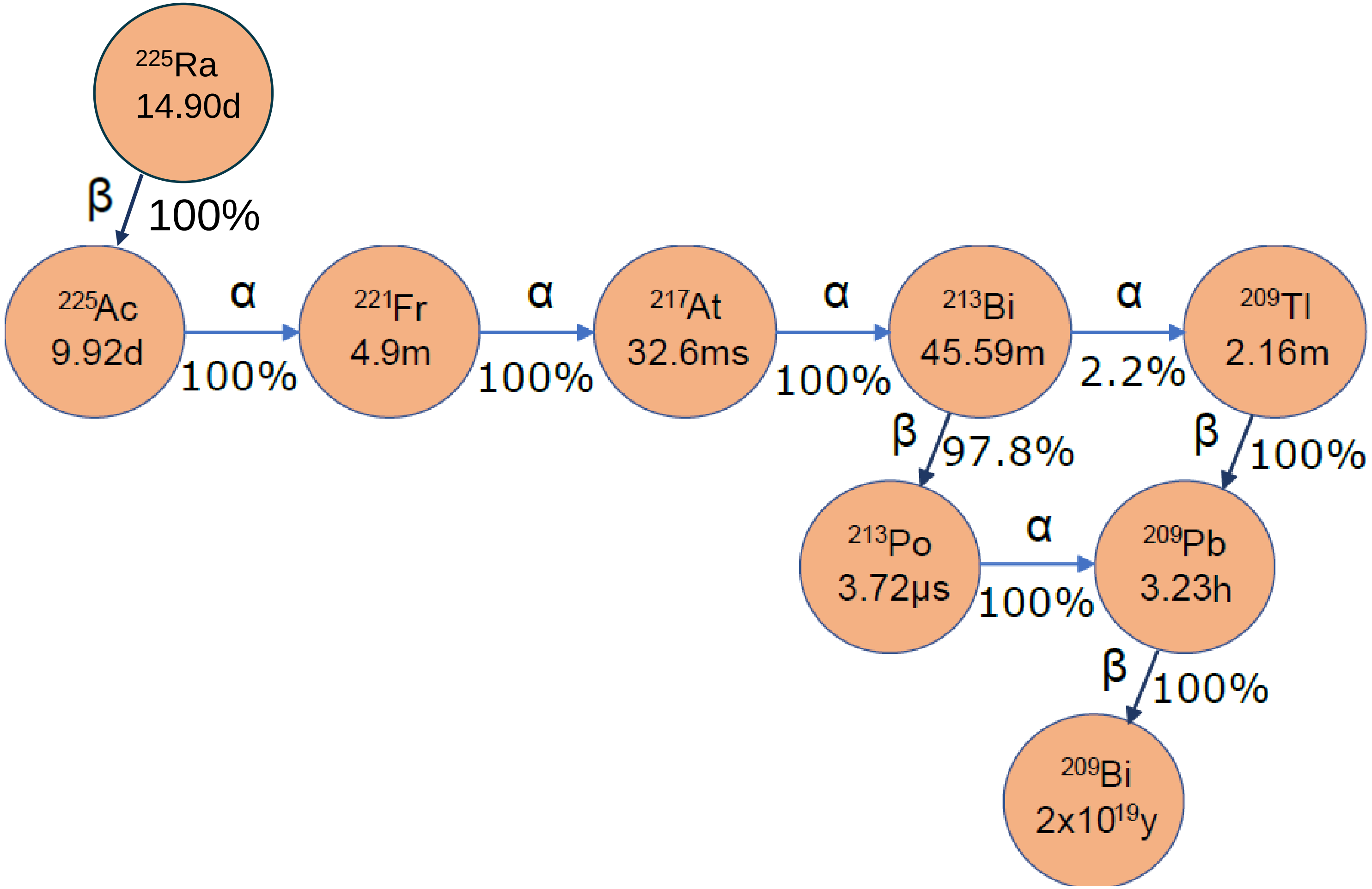


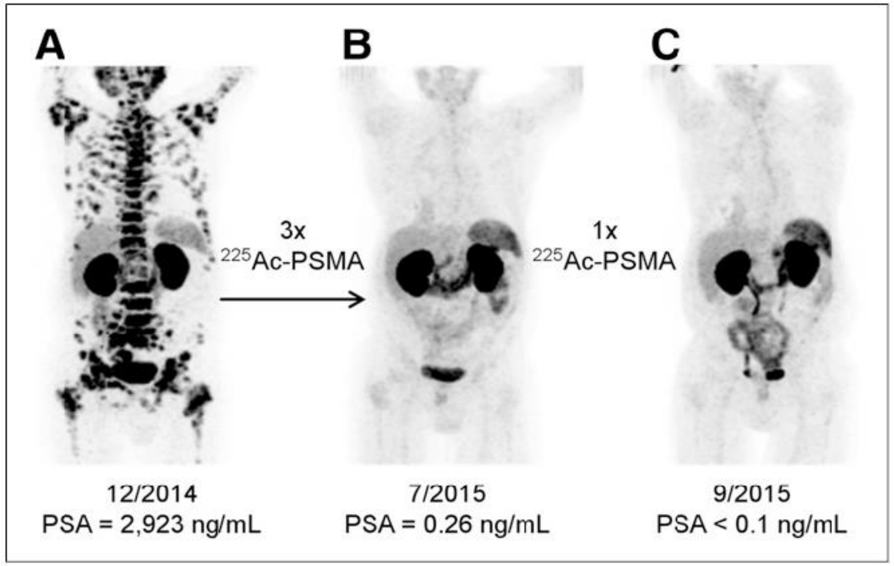
MEDICIS collaboration board July 2024

^{225}Ac in Belgium: Sample purity and ^{225}Ra / ^{225}Ac collection efficiencies

Jake Johnson

^{225}Ac interest



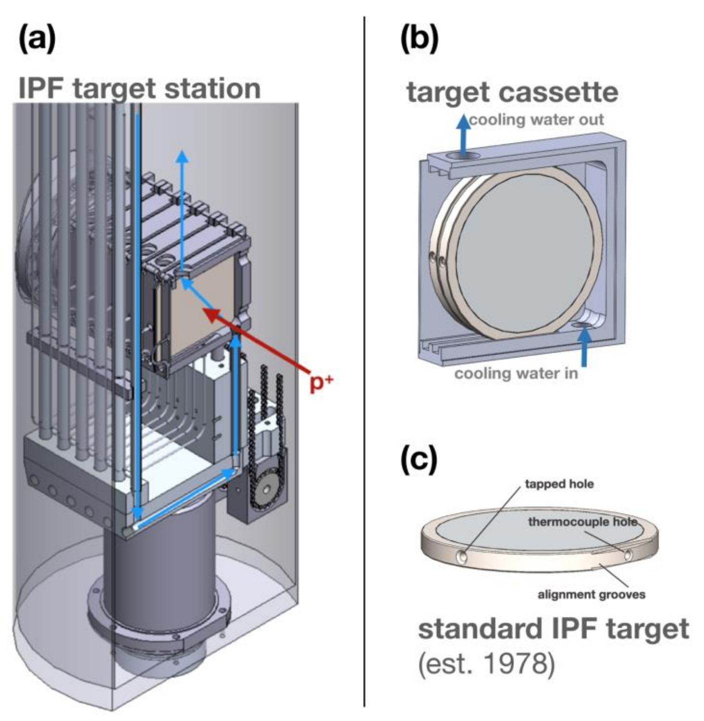


Kratochwil, C. et al.J. Nucl. Medicine 57, 1941–1944 (2016).

- 10 MBq patient doses.
- 7000 patient doses only produced WORLDWIDE via ^{229}Th generators[1]
- New production methods needed

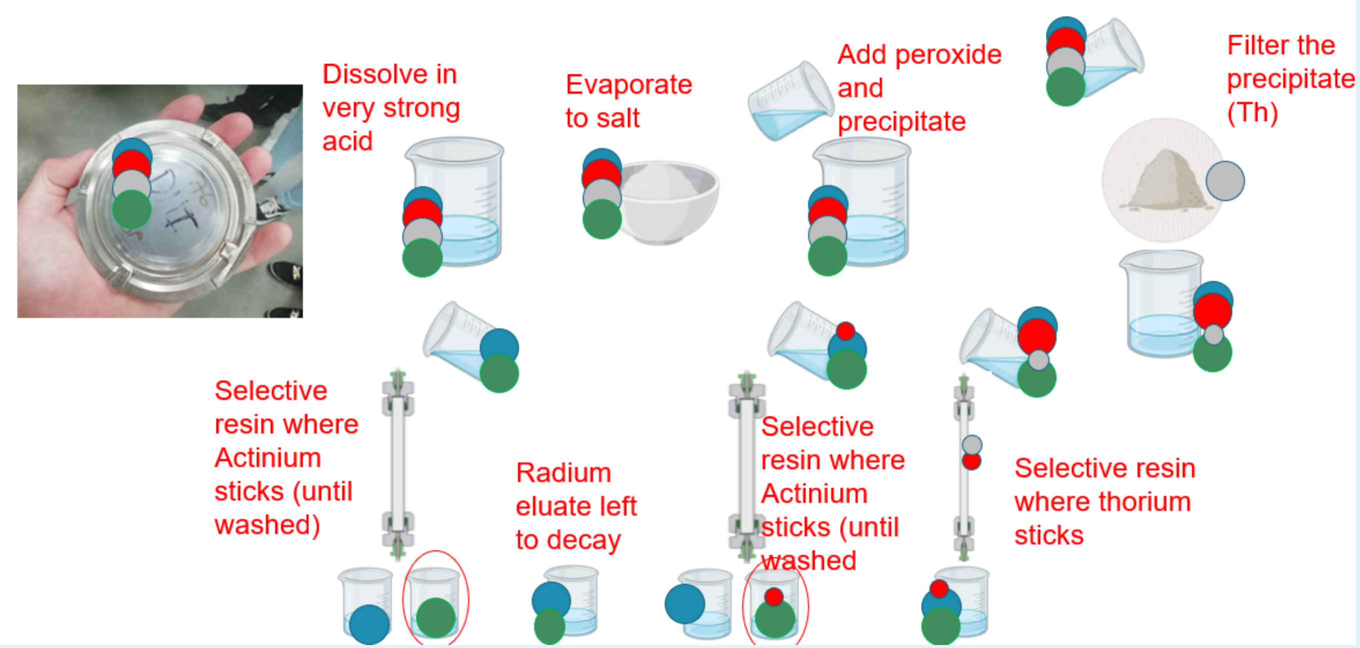
^{nat}Th (p , X / X') ^{225}Ac / ^{225}Ra production route (1)

Production



Robertson, Andrew KH, et al. *Instruments* 3.1 (2019): 18.

Separation



Robertson, Andrew KH, et al. *Inorgan. Chem.* 59.17 (2020): 12156-12165.

44-98% efficient…

127.7 – 11267 GBq production of ^{225}Ac per month[1]

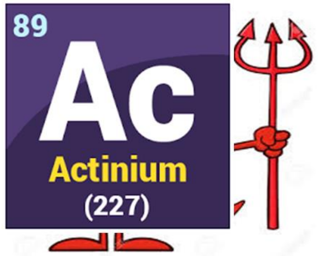
40.77 GBq of ^{225}Ac in five years from tri lab effort[2]

[1]Robertson, Andrew KH, et al. *Curr. Radiopharm.* 11.3 (2018): 156-172.
[2] https://www.isotopes.gov/information/actinium-225.

^{nat}Th (p , X / X’) ^{225}Ac / ^{225}Ra: The problem

^{227}Ac ($t_{1/2}$ = 21.8 y) co-produced ~equal cross section
> ~0.1 % of ^{225}Ac activity

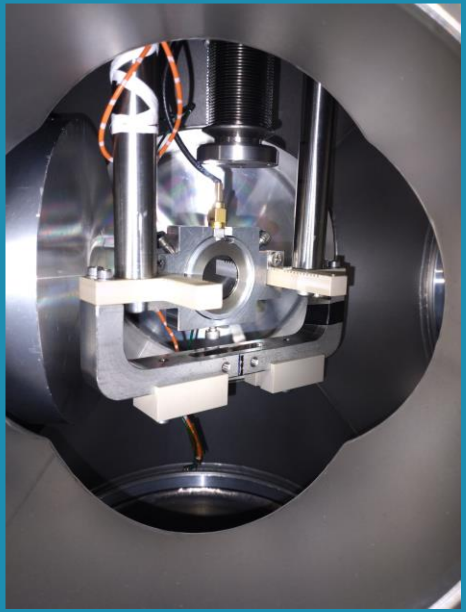
Measured in samples:
[1] 0.15%
[2] 0.142%



Mass separation enhances ^{225}Ac/^{227}Ac activity ratio with competitive efficiency to radiochemistry?

→ 3 samples collected to analyse **purity**
→ **Collection efficiency** analysis performed

[1] Tollefson, A. D. et al. Appl. Radiat. Isot. 172,109693 (2021)
[2] Robertson, A. K. et al. Inorg. Chem. 59, 12156–12165(2020).



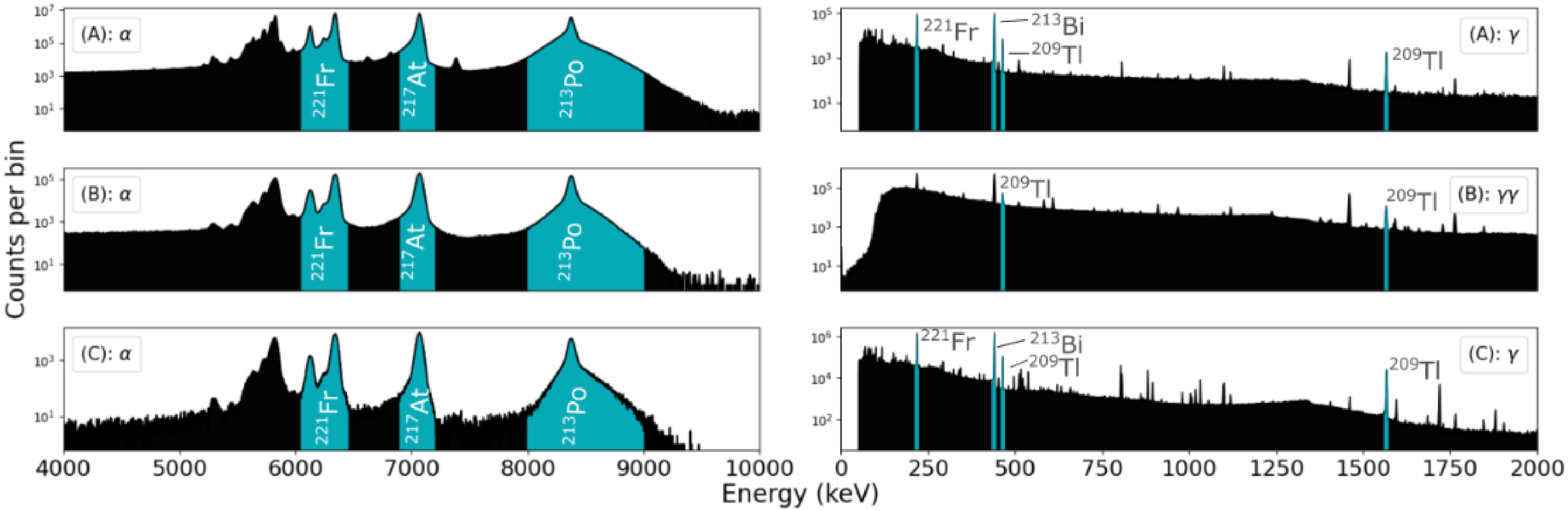
Purity

^{227}Ac content of resonance-laser-ionized and mass-separated ^{225}Ac samples from proton spallation of thick Th-based targets at CERN-MEDICIS

3 samples collected from 3 "sources"

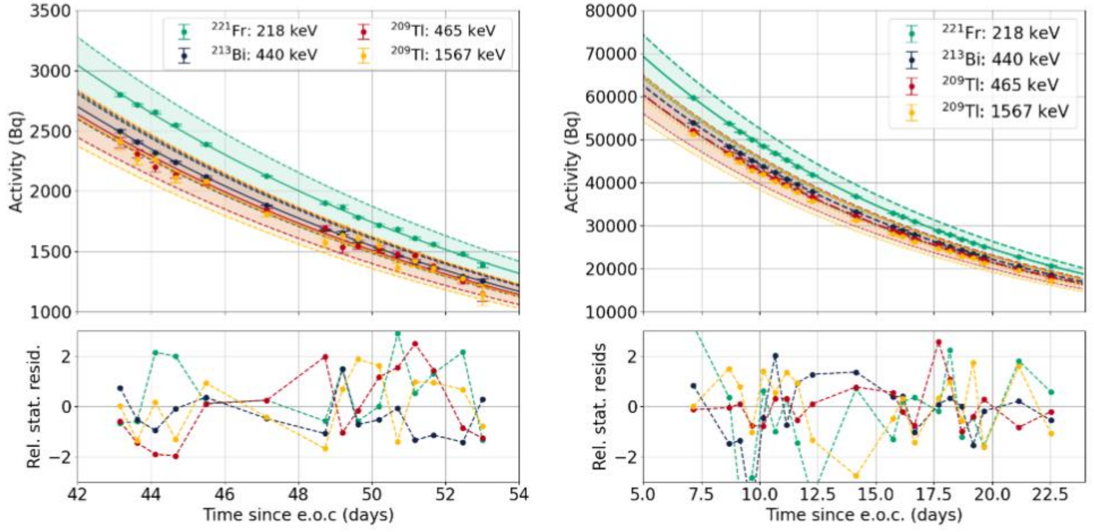
Source	**A**	**B**	**C**
Preparation method	$[^{227}Ac/^{225}Ac]Ac(NO_3)_3$ solution deposition + evaporate + dry	Direct irr.	Direct irr.
Collection time	Dec 2022	Nov 2021	May 2023
Target material	15.08 g ThO_2	14.65 g ThO_2 fibre felt	98.9 g ThC_x pellets
s.o.c $A(^{227}Ac)$ (MBq)	$100(5) \times 10^{-3}$	$4.7(2) \times 10^{-3}$	1.64(2)
s.o.c $A(^{225}Ac)$ (MBq)	10.8 (6)	2.37(7)	$1.03(3) \times 10^{3}$

^{225}Ac / ^{225}Ra activity through nuc. decay spec.

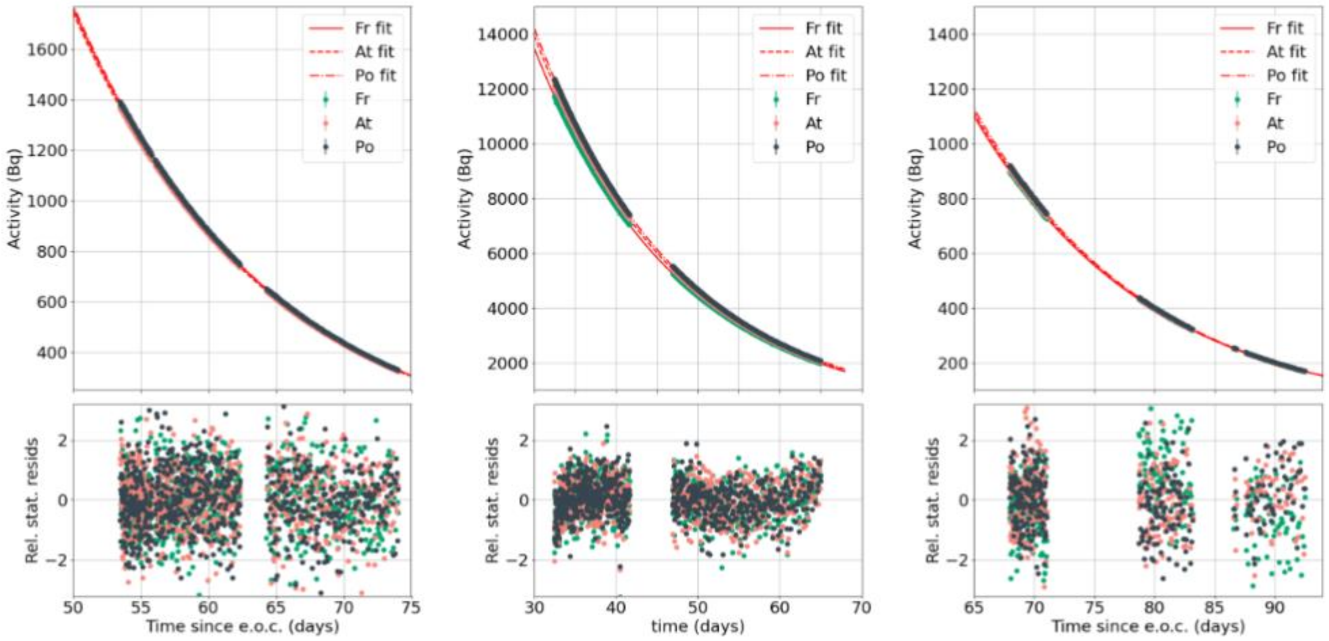


- γ-singles
- $\gamma\gamma$ –coincidence
- α-singles

E.O.C activities: ^{225}Ac and ^{225}Ra



(a) Sample A **(b)** Sample C



(a) Sample A **(b)** Sample B **(c)** Sample C

sA: $A^{(ii)}(t) = A^{(ii)}_{e.o.c} e^{-\lambda_{ii} t}$ *

sB+C: $A^{(ii)}(t) = A^{(ii)}_{e.o.c} e^{-\lambda_{ii} t} + A^{(i)}_{e.o.c} \frac{\lambda_{ii}}{\lambda_{ii} - \lambda_i} \left(e^{-\lambda_i t} - e^{-\lambda_{ii} t} \right)$ *

Sample	A	B	C
$A_{e.o.c}$(^{225}Ac) (kBq)	52.9(12)	79.0(10)	91.2(21)
$A_{e.o.c}$(^{225}Ra) (kBq)	-	11.3(12)	0*

* $ii = 225Ac$, $i = 225Ra$

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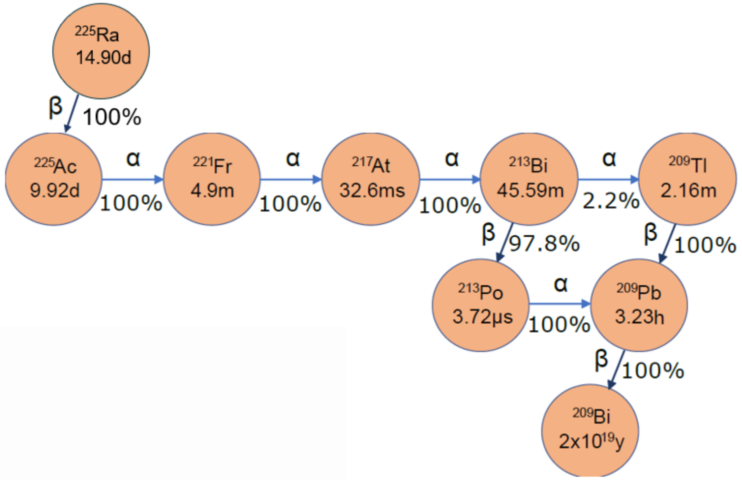
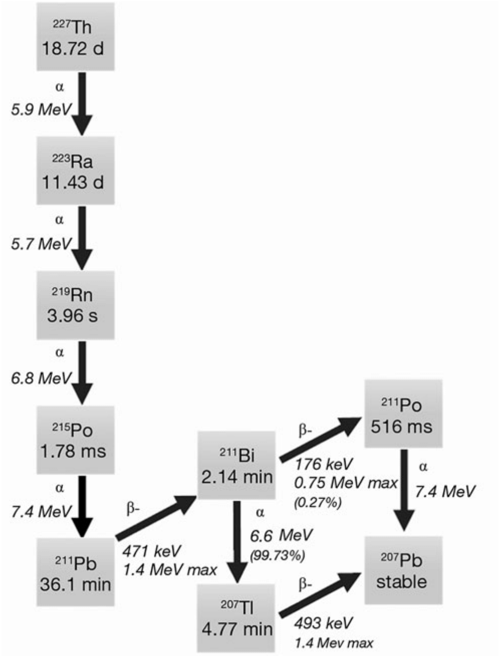
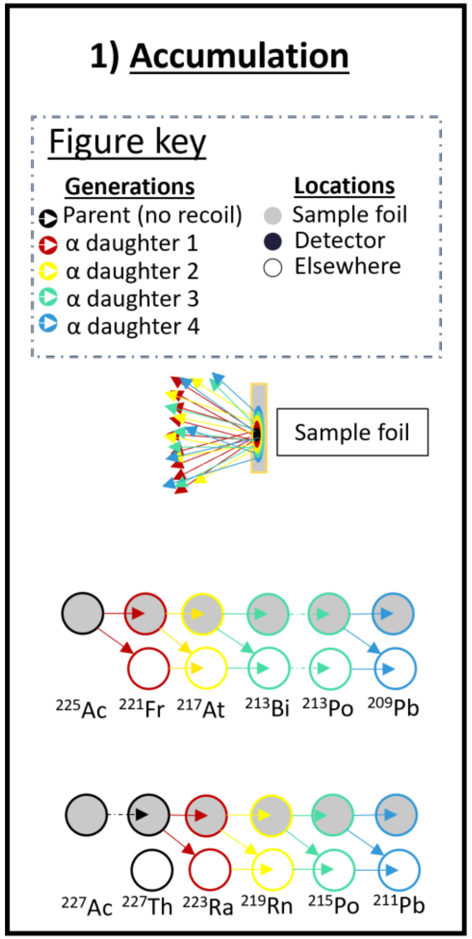
^{227}Ac activity measured using α-recoil spectroscopy





Frantellizzi, Viviana, et al. *Cancer biother. radiopharm.* 35.6 (2020): 437-445.



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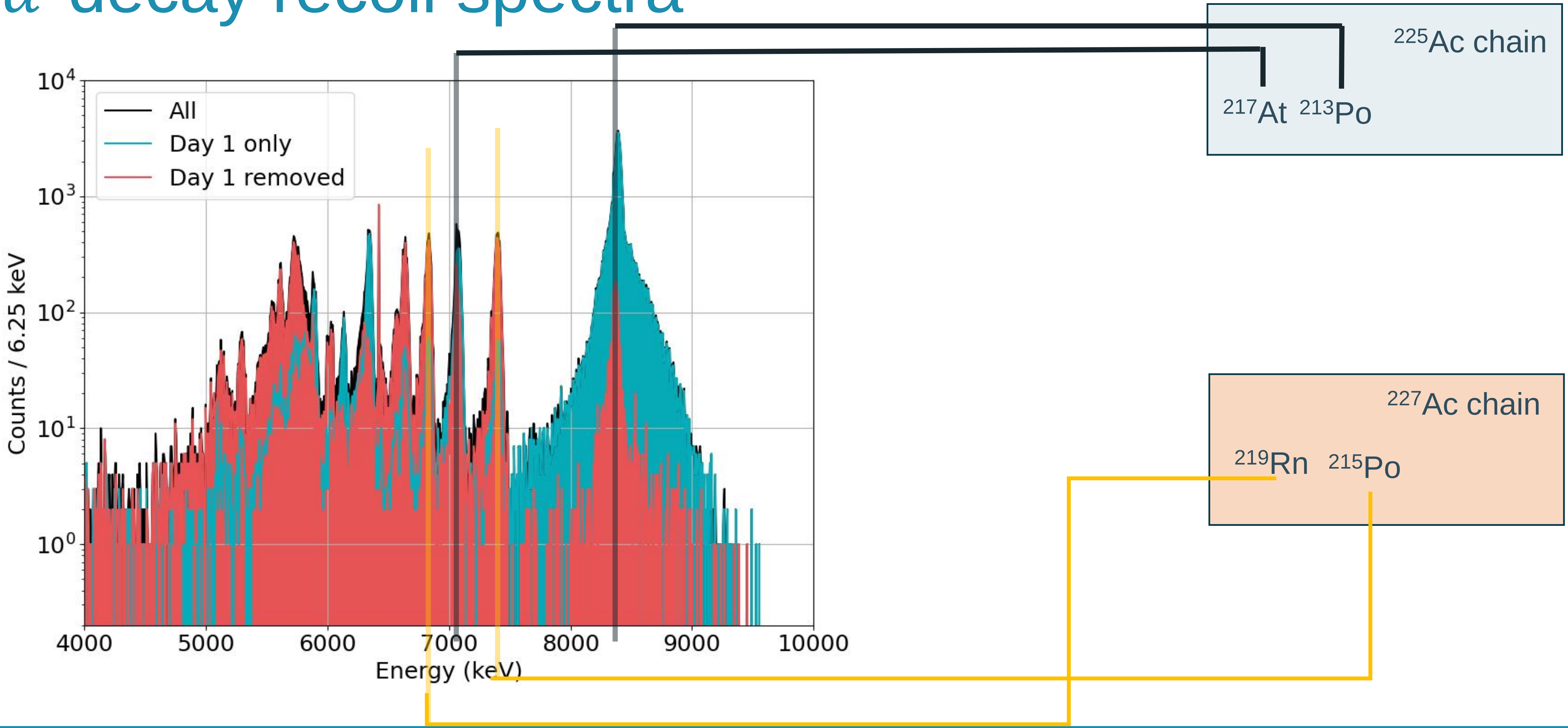
α-decay recoil spectra



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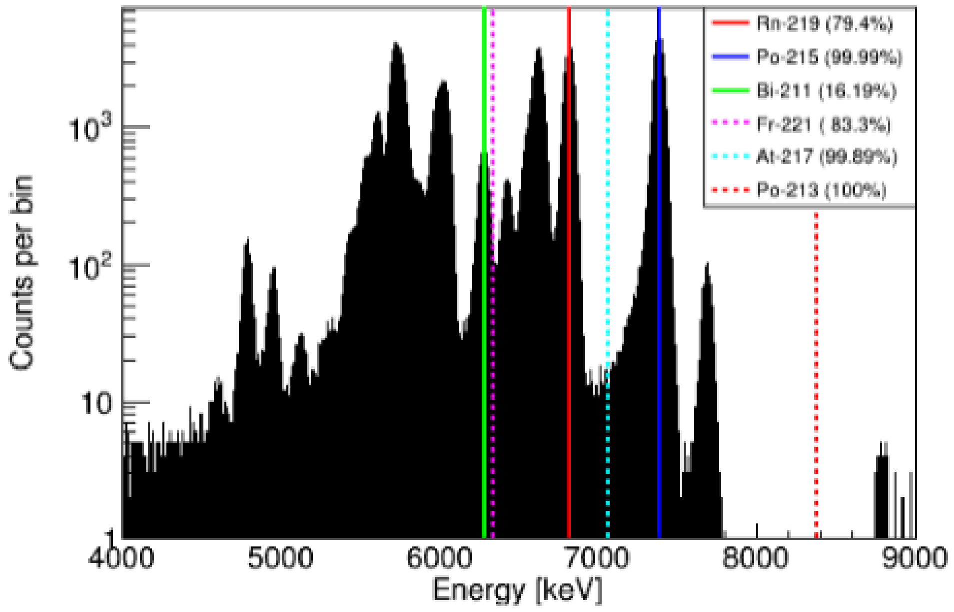
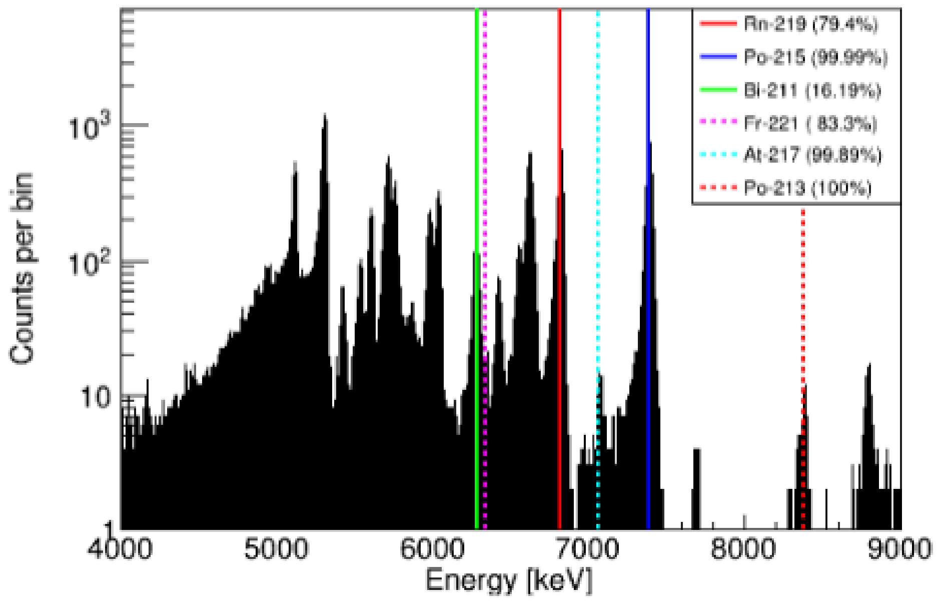
Direct alpha decay spectrometry validation



(a) Sample A



(b) Sample C

Δt since E.O.C:	297 days	276 days
Recoil method	3.90 (13) Bq	0.244 (33) Bq
Direct α spec	3.70 (25) Bq	0.248 (17) Bq

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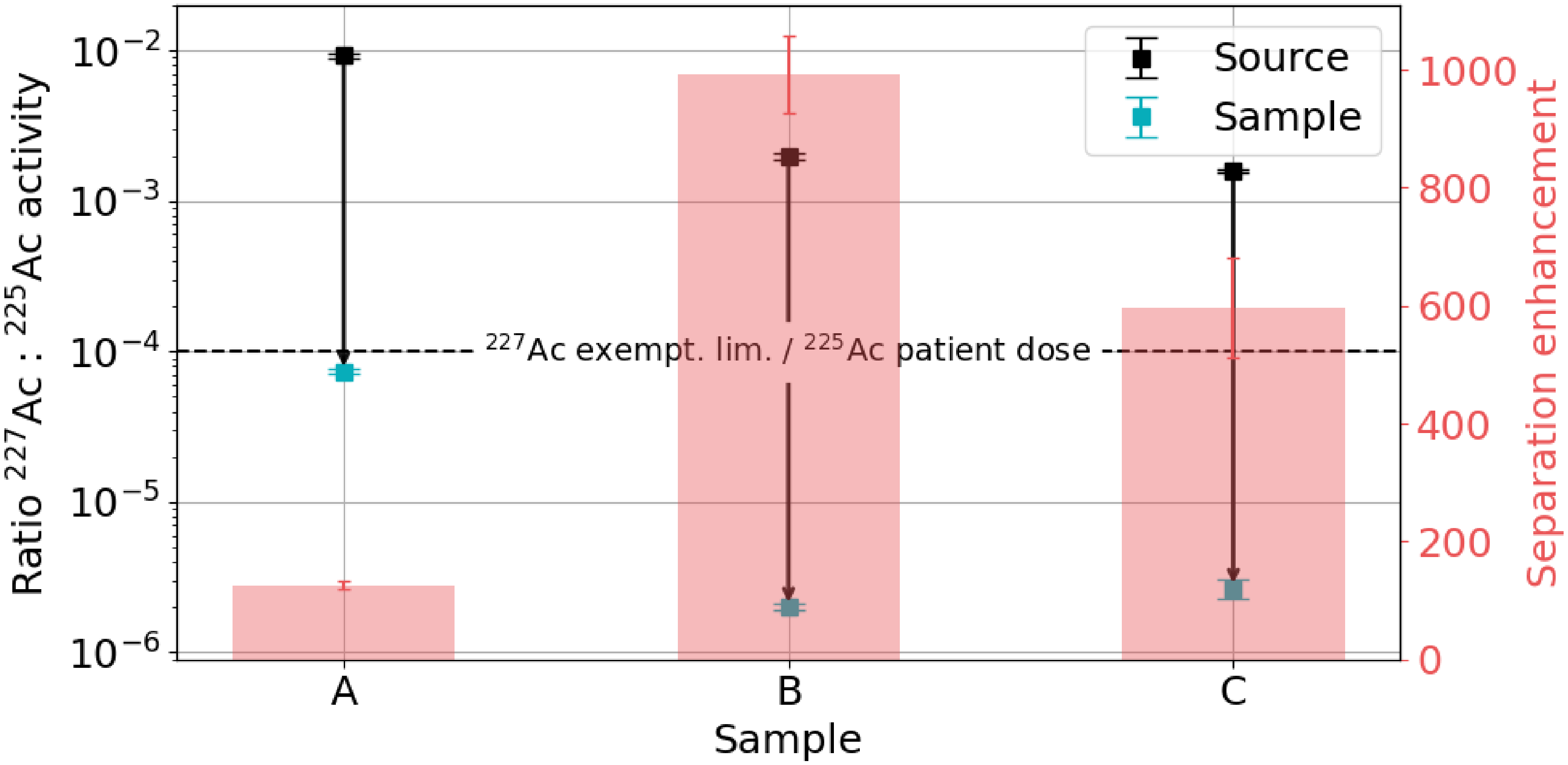
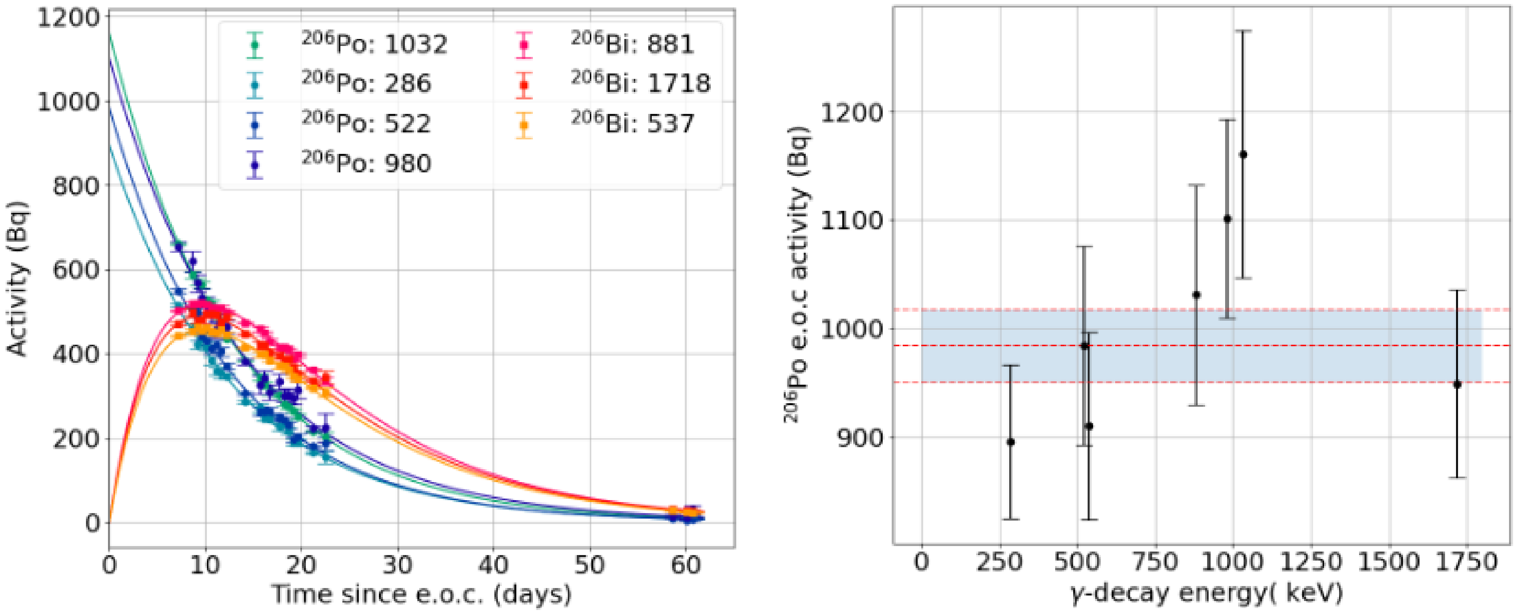
^{227}Ac / ^{225}Ac activity ratio result

Mass separation enhances the ^{225}Ac / ^{227}Ac by a factor of ~500 – 1000.

Isotopic purity ~O(10) > than reasonable limit.



Other contaminants?



(a) Sample C decay curves

(b) Sample C mean e.o.c. activity

Figure 12. Gamma decay spectroscopy activities of ^{206}Po and daughter ^{206}Bi.

^{206}Po^{18}O^{+}

→ 1% of ^{225}Ac activity at e.o.c

→ Not seen in all samples

→ Implies even more (#) ^{209}Po in collected sample.

→ ^{208}Po, ^{210}Po seen in alpha spec…

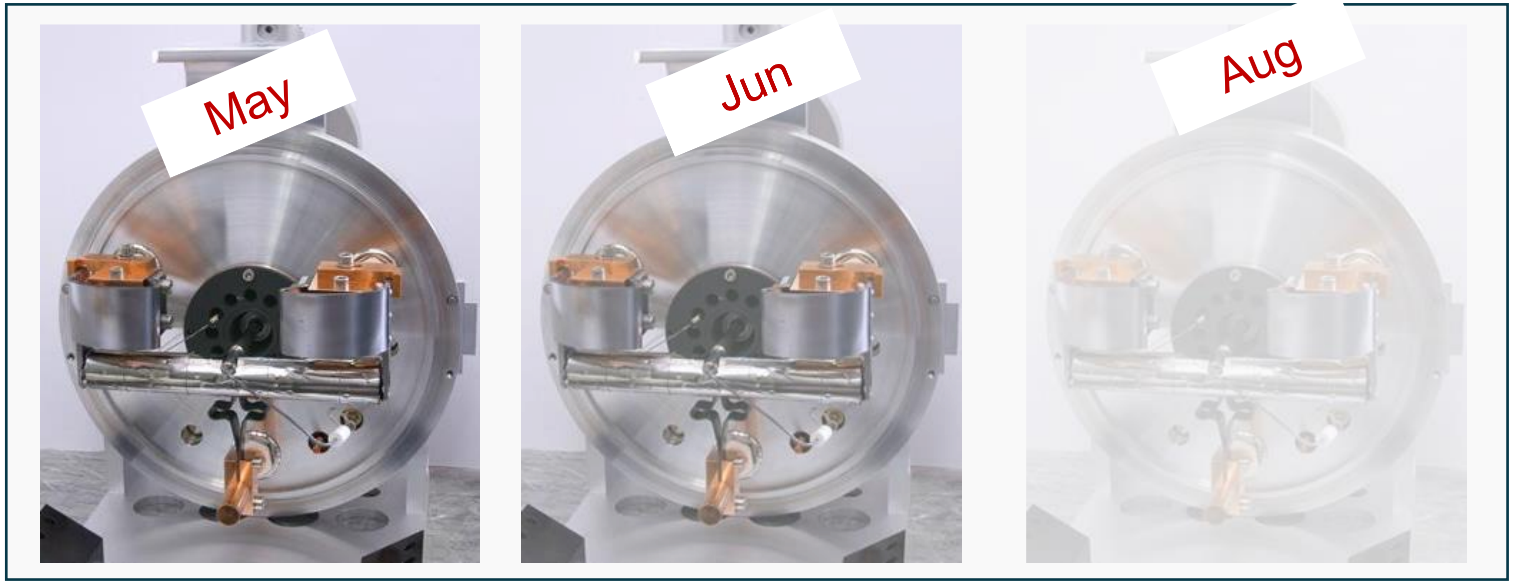
Also…

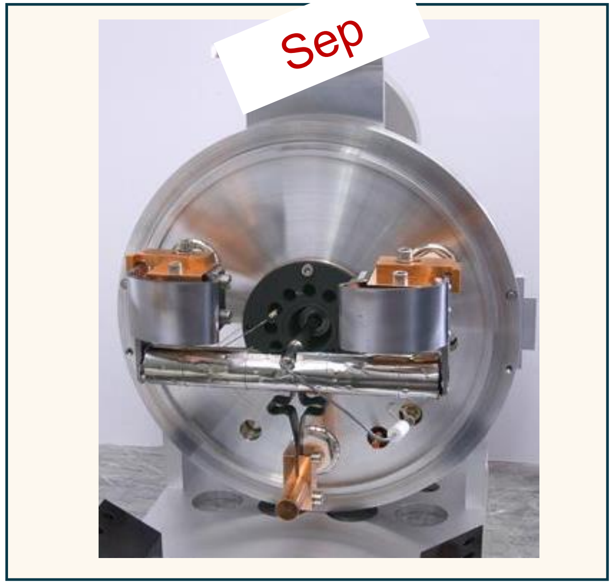
→ ^{214}Po and ^{218}Po seen in alpha spec… ^{226}Ra daughters…

Collection efficiency

ThC_x targets irradiated in 2023

Proton charge (μAh)	42	40.7	159	95



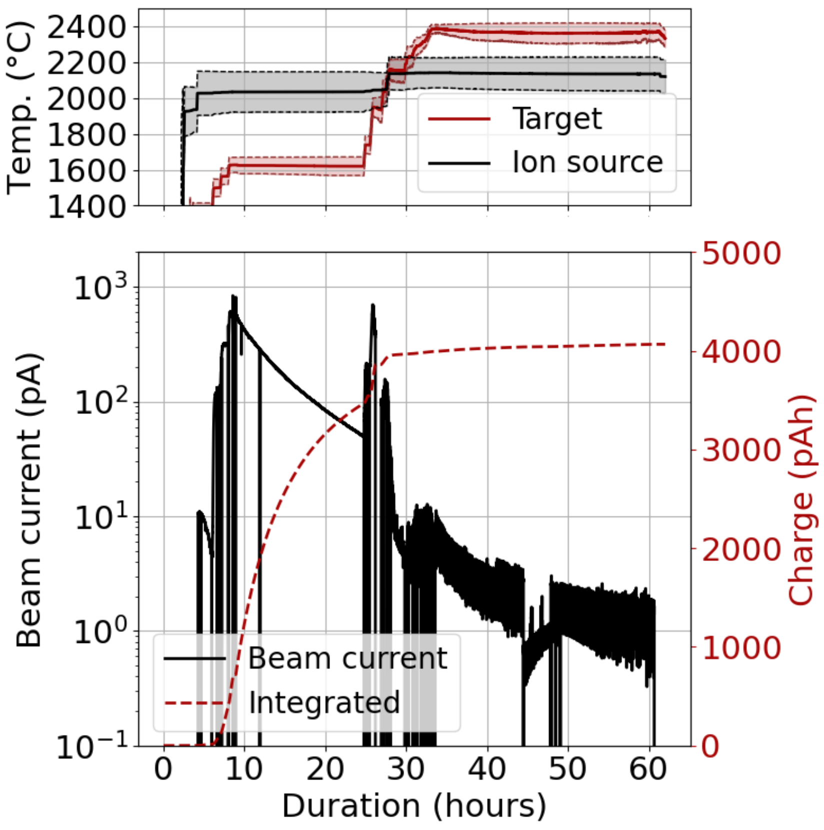


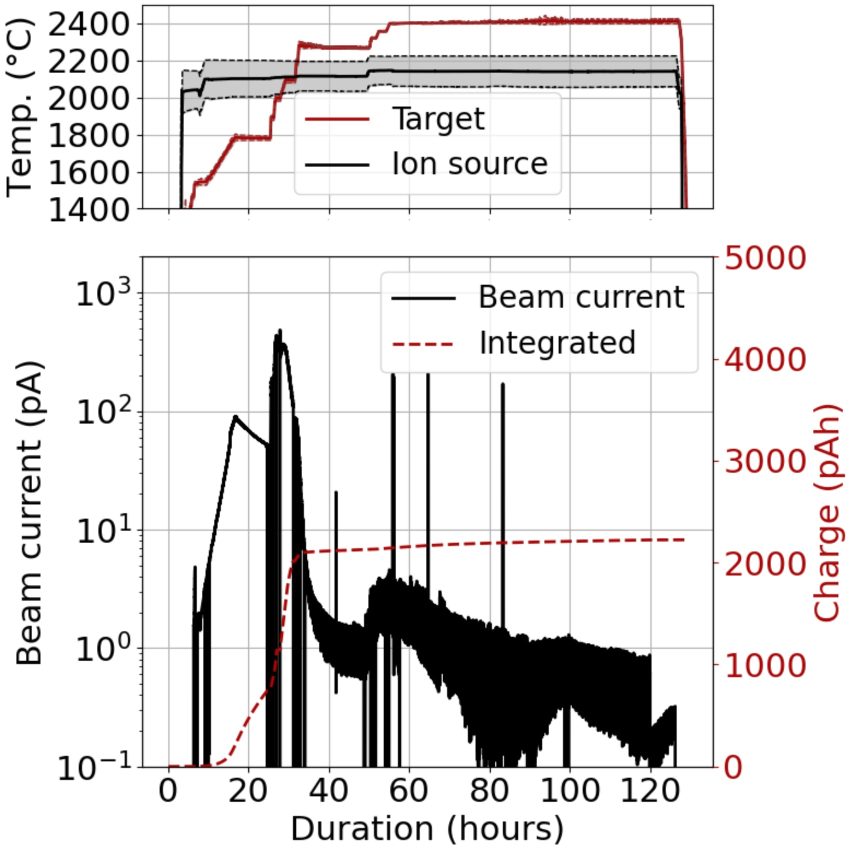
In target ^{225}Ac (MBq)	1030	997	611	2400
In target ^{225}Ra (MBq)	149	144	100	348

Fluka simulations for in-target activity performed by C. Duchemin

Collections in 2023

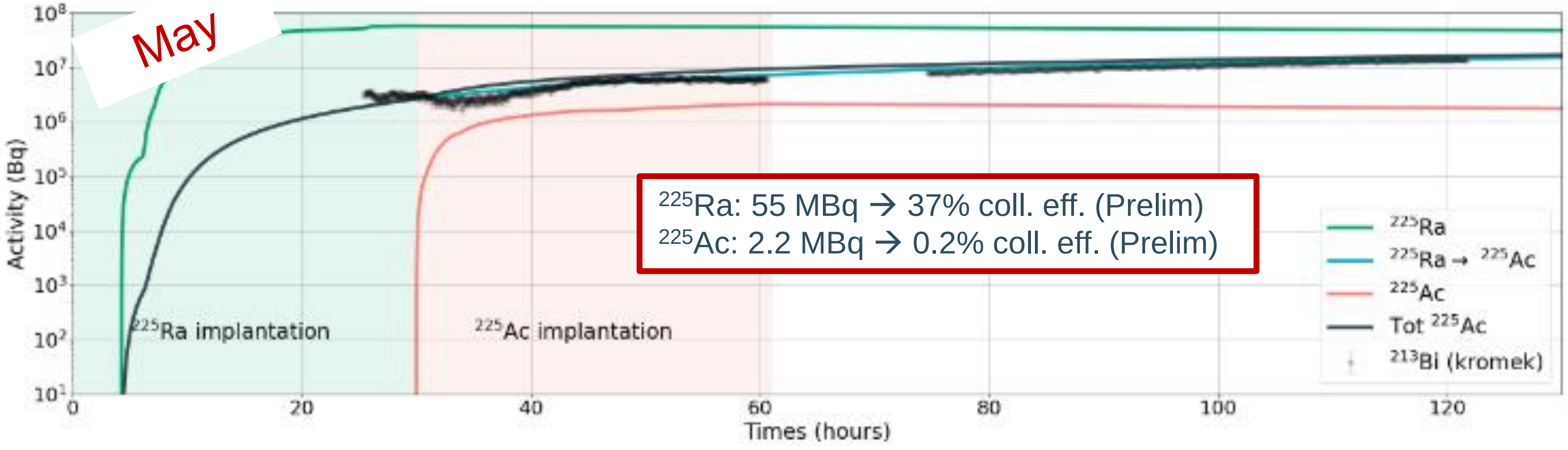
- ^{225}Ra release:
  T > 1600°C
- ^{225}Ac release
  T > 2240°C



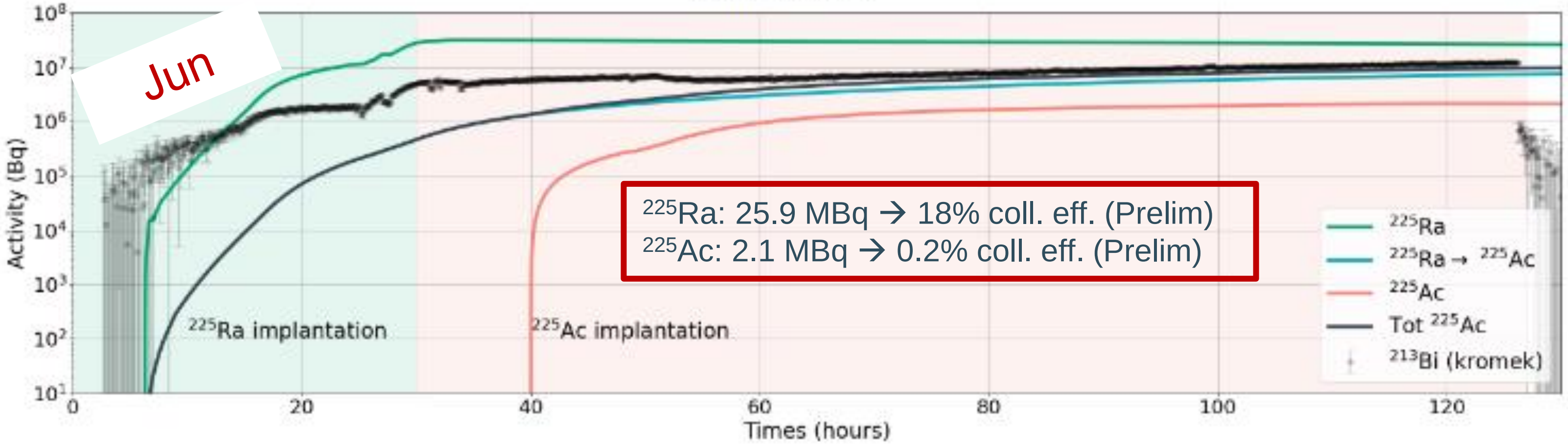


Preliminary collection efficiency estimate from beam current

- Assign beam current to ^{225}Ra and ^{225}Ac regions
- Integrate + convert to activity (accounting for feeding $^{225}Ra \rightarrow ^{225}Ac$)
- Normalise to γ-spec activity

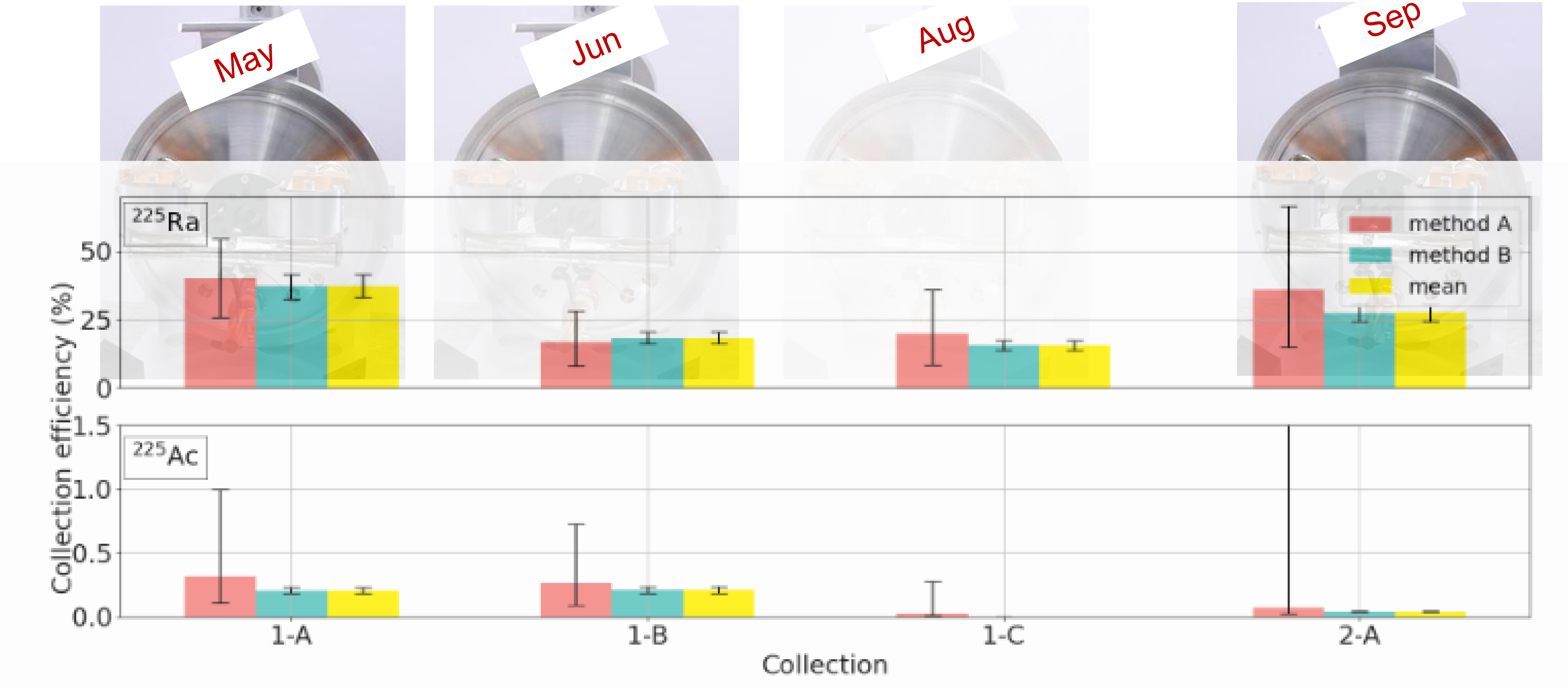


(a) Sample A



(b) Sample B

All ^{225}Ac / ^{225}Ra collection efficiencies (2023)



Conclusions:

- ^{225}Ac and ^{225}Ra has been produced at MEDICIS
- The isotopic purity of the collected ^{225}Ac samples has ^{227}Ac content below a reasonable limit for medical use
- Most ^{225}Ac can be produced from ^{225}Ra implantation and decay
- Target reuse is possible, but efficiency is reduced if target is ‘punished’

Outlook:

Possible “Best” ^{225}Ac production:

- Irradiate ^{232}Th metal target
- Radiochemistry to separate Ra and Ac fractions
- Use the Ra fraction as ^{225}Ac generator
- Perform mass separation on the Ac fraction

More research:

- Ionize Ra using Raman laser at MEDICIS
- Re-use of target at lower temperature, collecting $^{225}Ra/^{224}Ra$ only, not ^{225}Ac
- …

Thanks to wonderful colleagues

Mia Au[2], Cyril Bernerd[1,2], Frank Bruchertseiffer[3], Thomas E. Cocolios[1], Marie Deseyn[1], Charlotte Duchemin[2], Michael Heines[1], Max Keppens[1], Laura Lambert[2], Nathan Meurrens[1], Ralf E. Rossel[2], Thierry Stora[2], Viktor Van den Bergh[1], Wiktoria Wojtaczka[1]
MEDICIS collaboration, CERN SY-STI group…

[1] KU Leuven
[2] CERN
[3] JRC Karlrushe

LISA
LASER IONISATION AND SPECTROSCOPY OF ACTINIDES
This Marie Sklodowska-Curie Action (MSCA) Innovative Training Networks (ITN) receives funding from the European Union's H2020 Framework Programme under grant agreement no. 861198

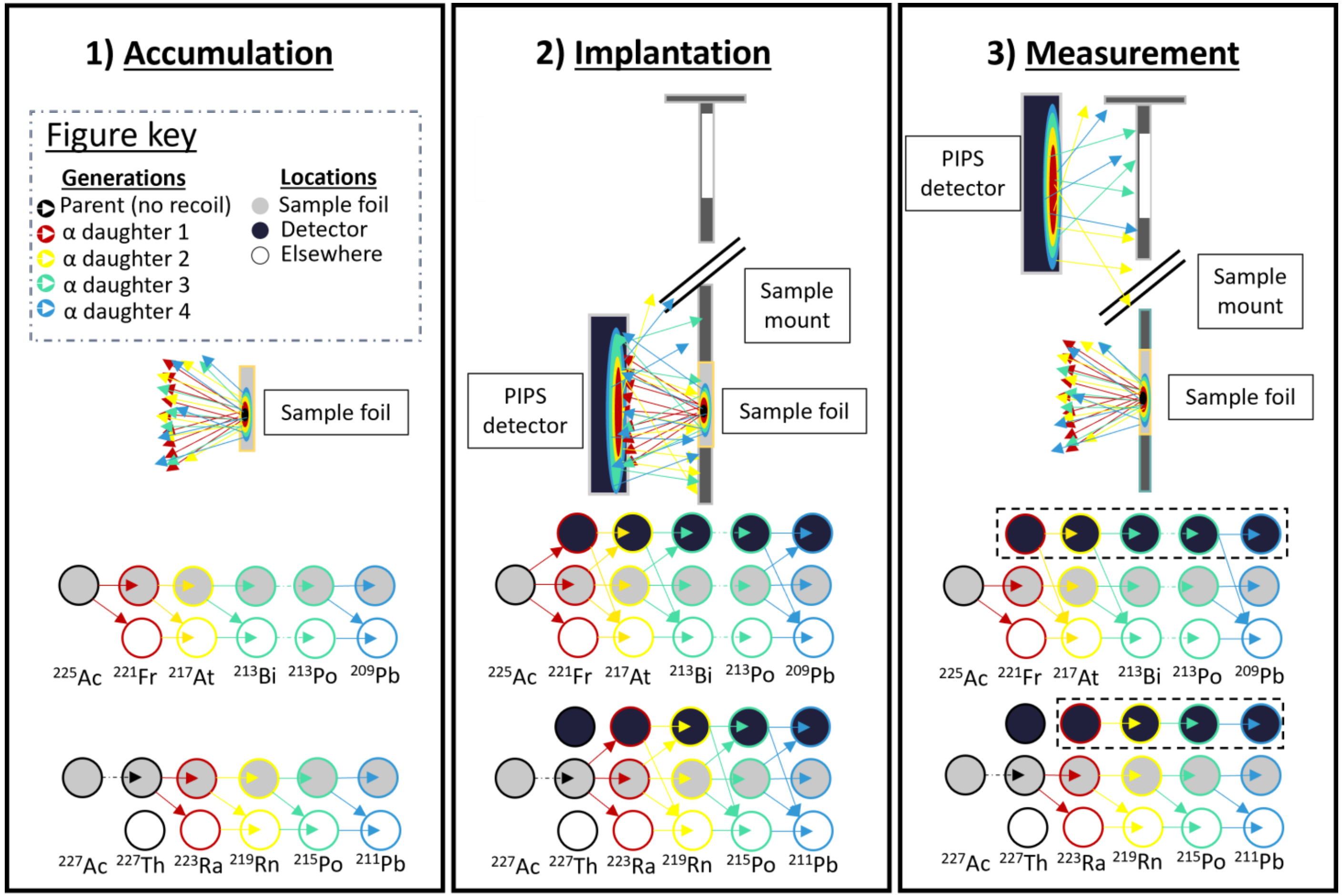
Backup slides…

How to get Ac-227 activity from recoil spectrum (1)

$$R_X(t_{out}) = A(t_{e.o.c}, Ac)\mathscr{F}_B(t_{in}, t_{out}, Y)\varepsilon_{\alpha}^{d\rightarrow d}(X)\varepsilon_{X}^{d\rightarrow d}(Y)\varepsilon_{Y}^{f\rightarrow d}(P)$$

~Same for same generation daughters in ^{227}Ac and ^{225}Ac chains

$$A(t_{e.o.c.}, {}^{227}Ac) = \frac{R_{X_{227}}(t_{out})}{R_{X_{225}}(t_{out})}\frac{\mathscr{F}_B(t_{in}, t_{out}, X_{225})}{\mathscr{F}_B(t_{in}, t_{out}, X_{227})}A(t_{e.o.c.}\, {}^{225}Ac)$$



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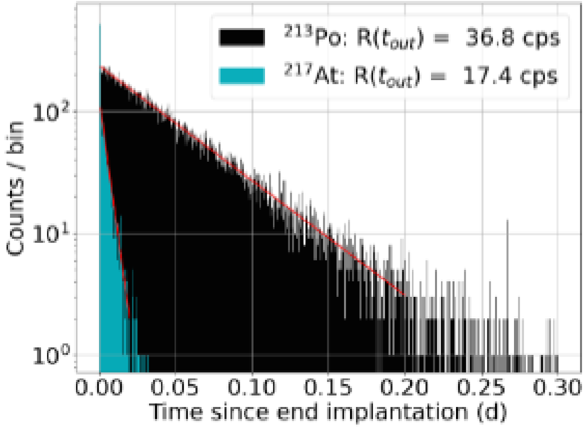
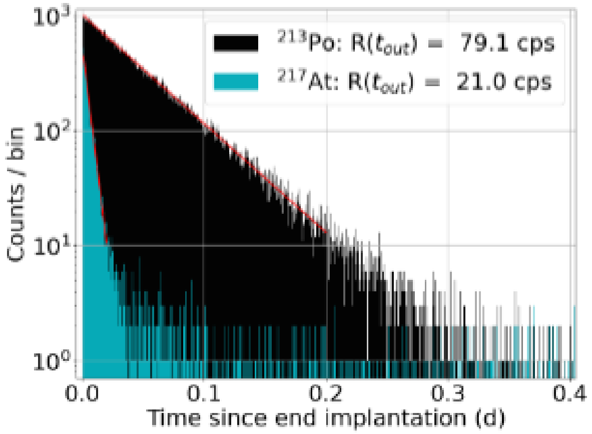
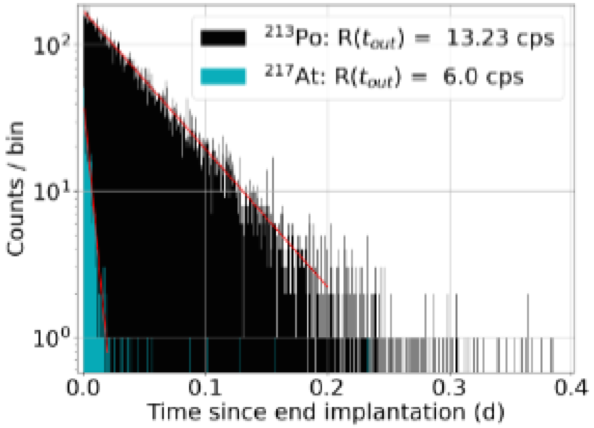
How to get Ac-227 activity from recoil spectrum (2)



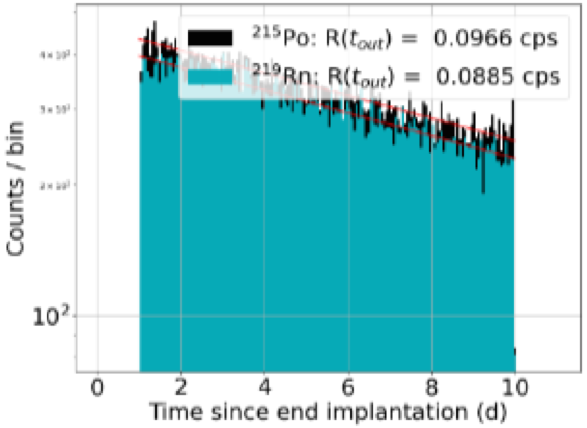
(a) Sample A: ^{225}Ac chain



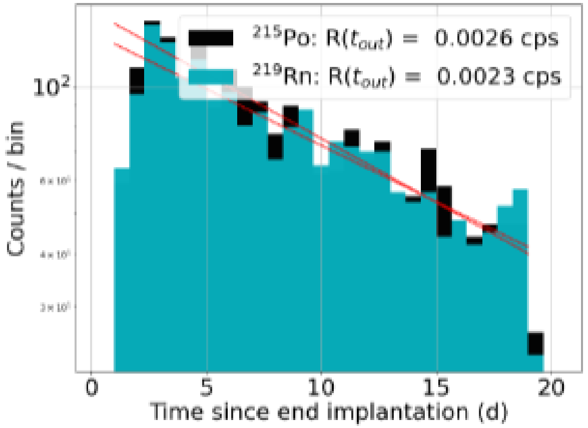
(b) Sample B: ^{225}Ac chain



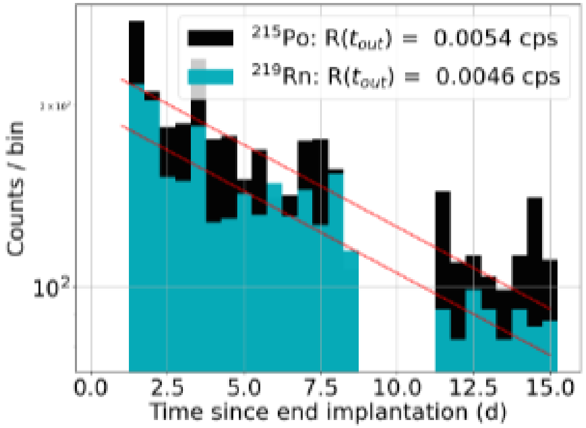
(c) Sample C: ^{225}Ac chain



(d) Sample A: ^{227}Ac chain

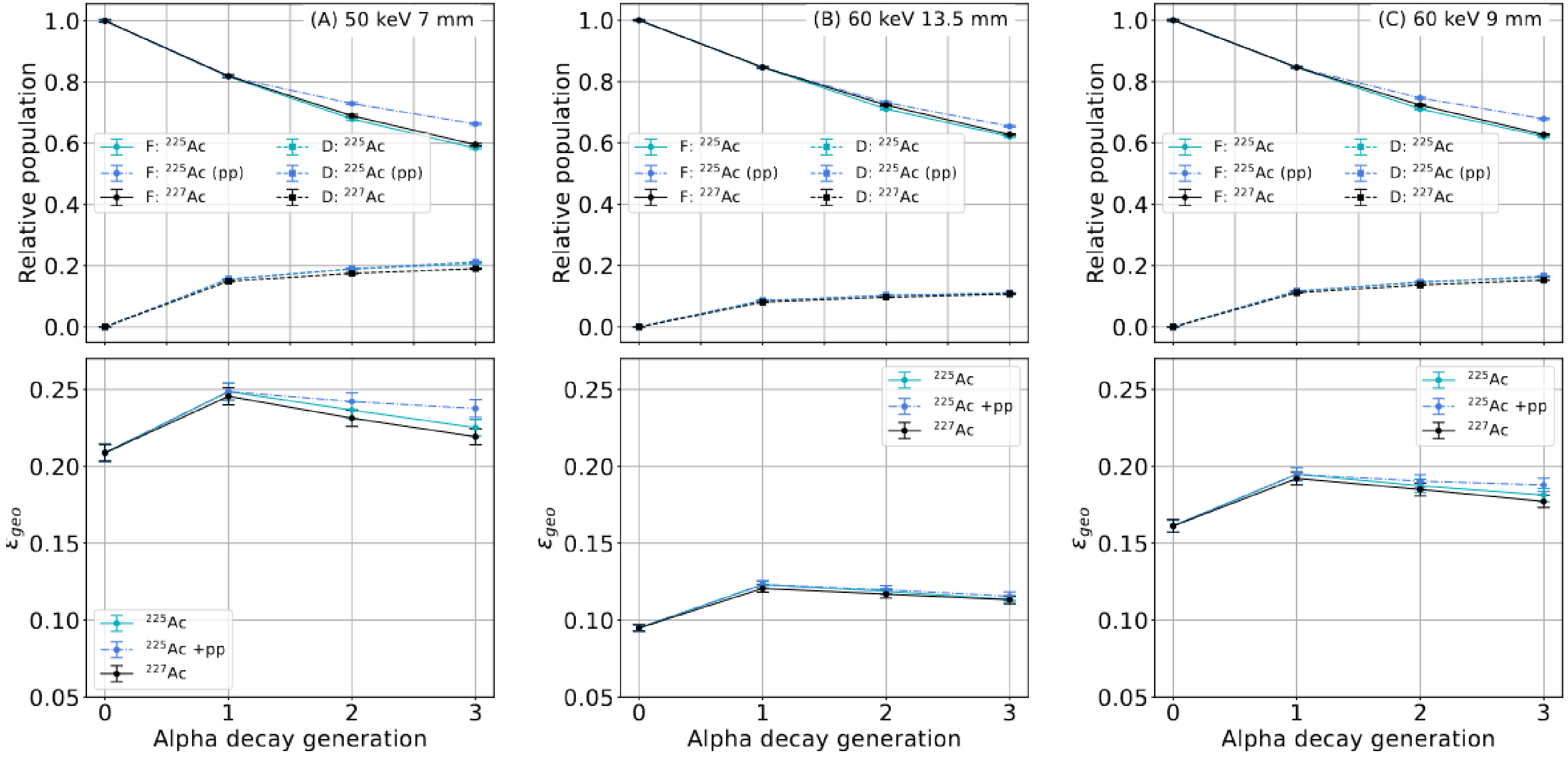


(e) Sample B: ^{227}Ac chain



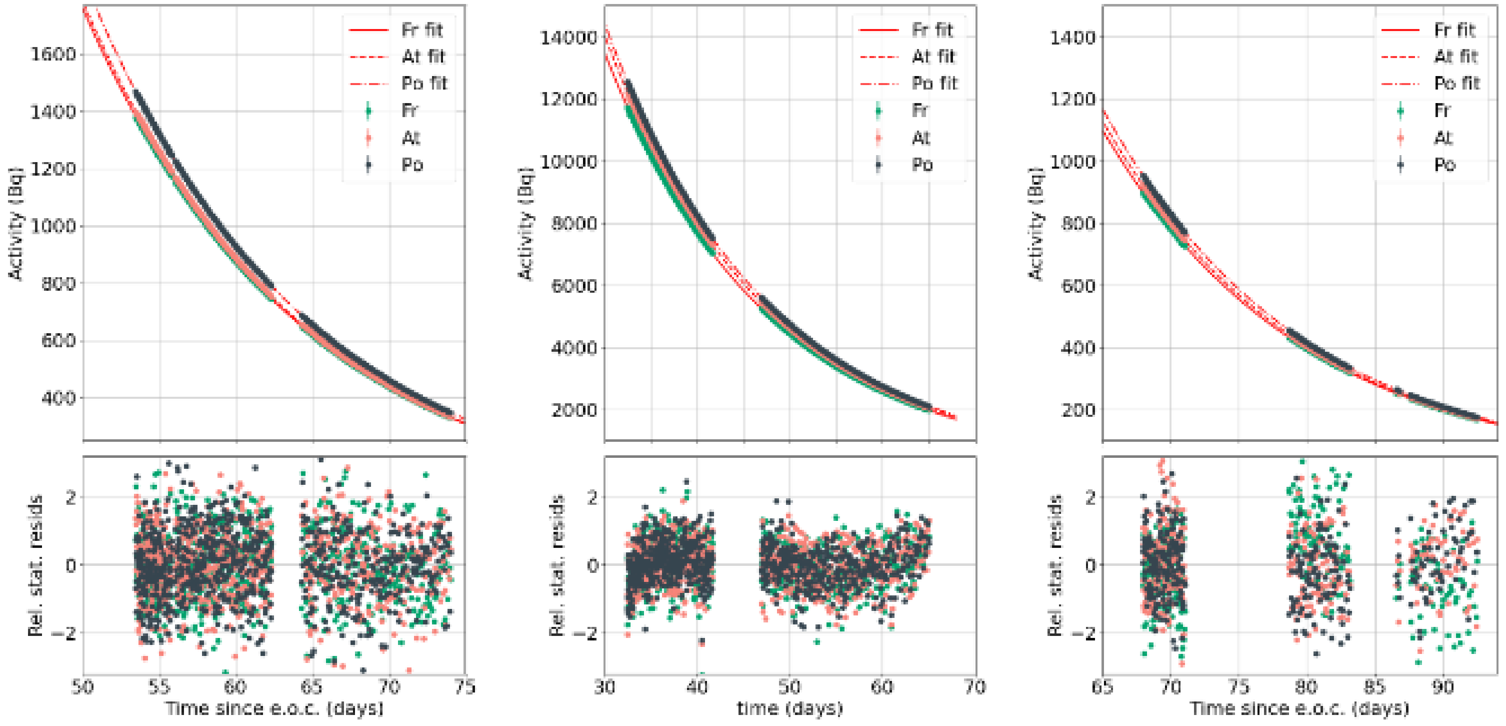
(f) Sample C: ^{227}Ac chain

Geometric corrections due to recoil + ping pong

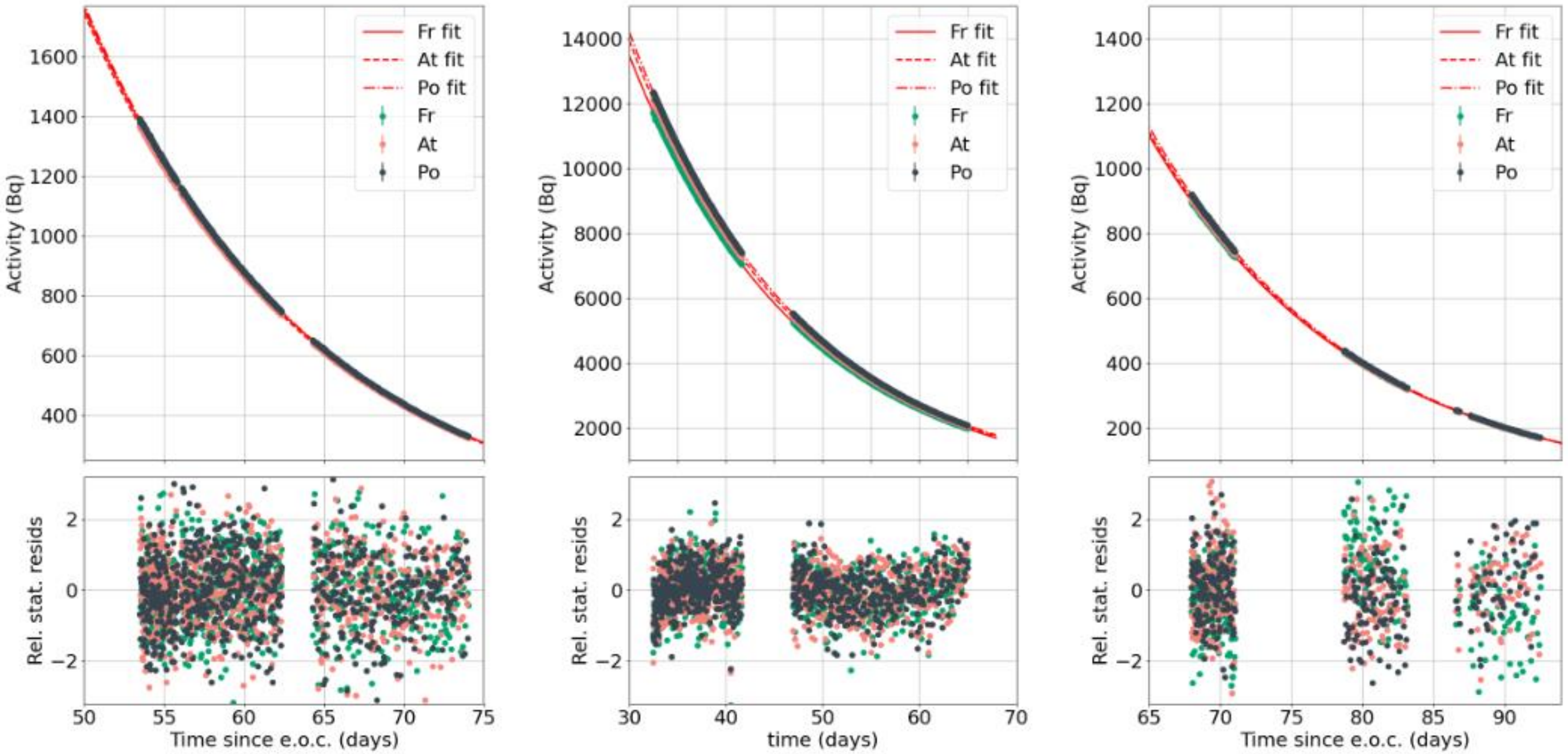


(a) Sample A (b) Sample B (c) Sample C

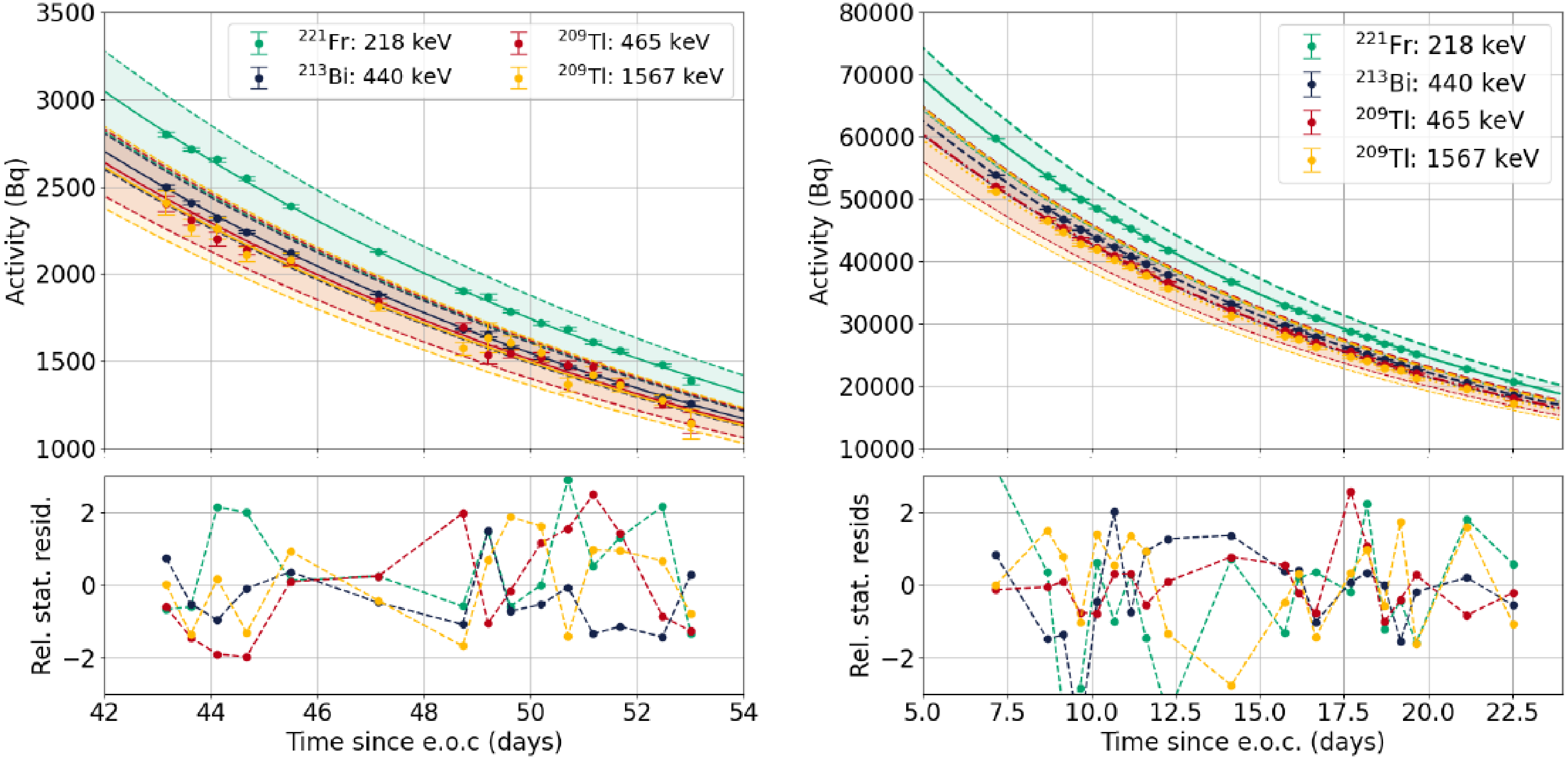
Alpha decay activities of Fr, At, Po with and without ping pong



(d) Sample A (e) Sample B (f) Sample C


Fr fit
At fit
Po fit
Fr
At
Po
Activity (Bq)
Rel. stat. resids
Time since e.o.c. (days)
time (days)
Time since e.o.c. (days)

Gamma spectroscopy curves



(a) Sample A

(b) Sample C

Gamma-gamma spectroscopy curve

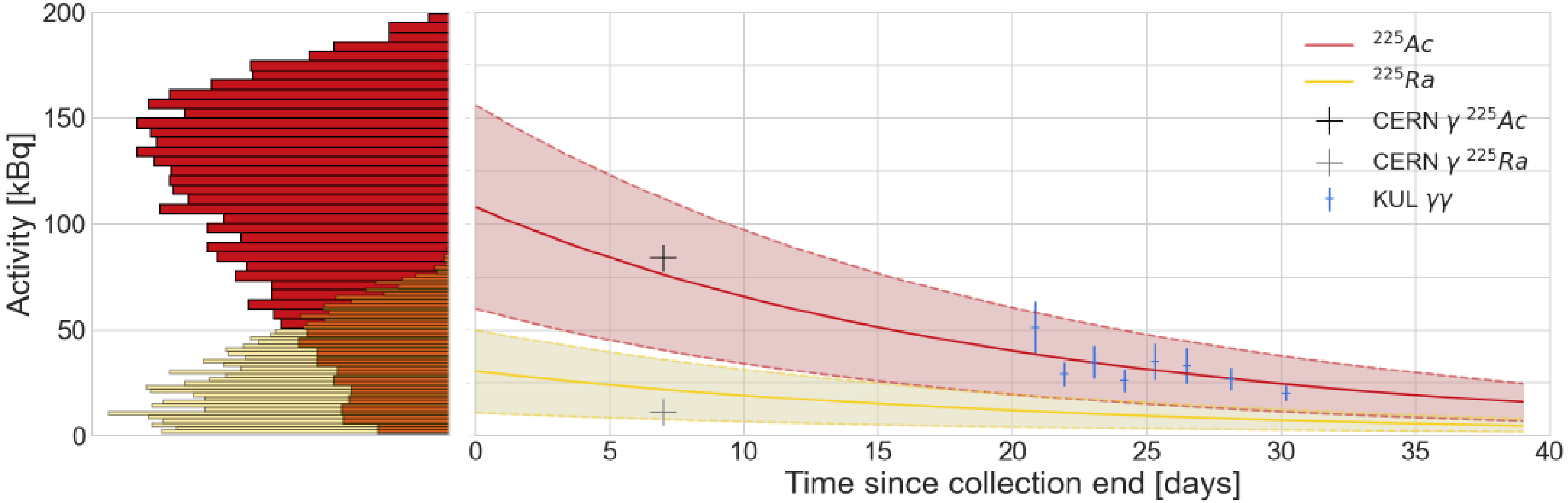
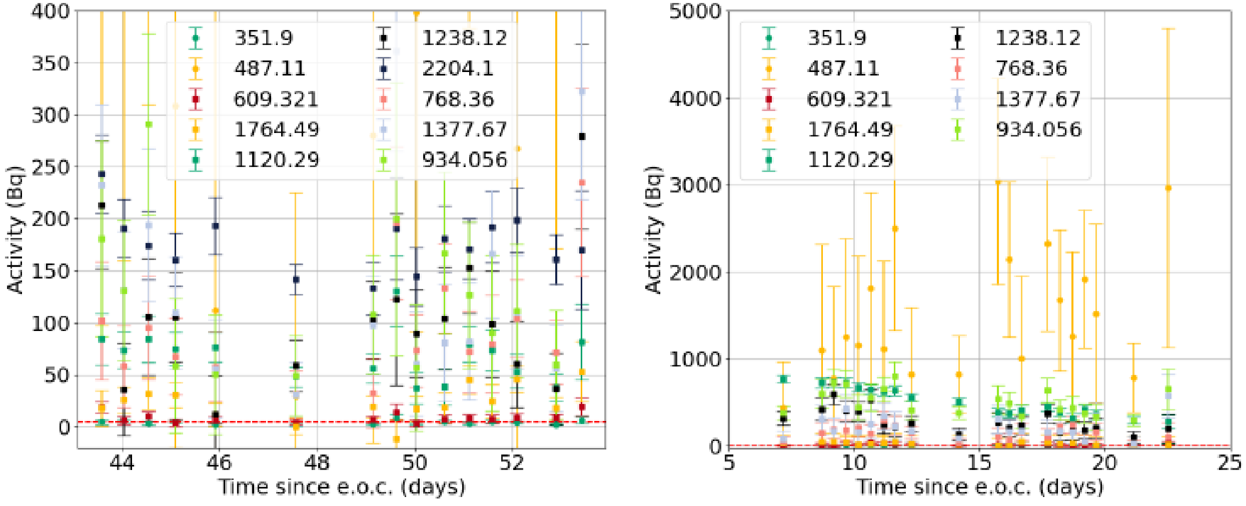


Figure 13. The activity of ^{225}Ac and ^{225}Ra as determined by $\gamma\gamma$ coincidence spectroscopy. The red line represents the ^{225}Ac activity from both ^{225}Ac and feeding from ^{225}Ra present at the end of collection. The yellow line and band is the ^{225}Ra activity calculated from the fitted $A_{e.o.c}(^{225}Ra)$ parameter. The large error bands are due to the large amount of time elapsed from end of collection to measurement meaning a large range of end of collection activity values correspond with measured data within errors. The relatively high statistical errors and limited number of data points amplify this effect.

Ra-226 contamination



(a) Sample A (b) Sample C

Figure 11. Gamma decay spectroscopy activities of ^{226}Ra. The relative statistical uncertainty of the 351.9 keV line of ^{214}Pb was an order of magnitude lower than almost all other lines meaning it gave the highest statistical weight to the calculated mean activity

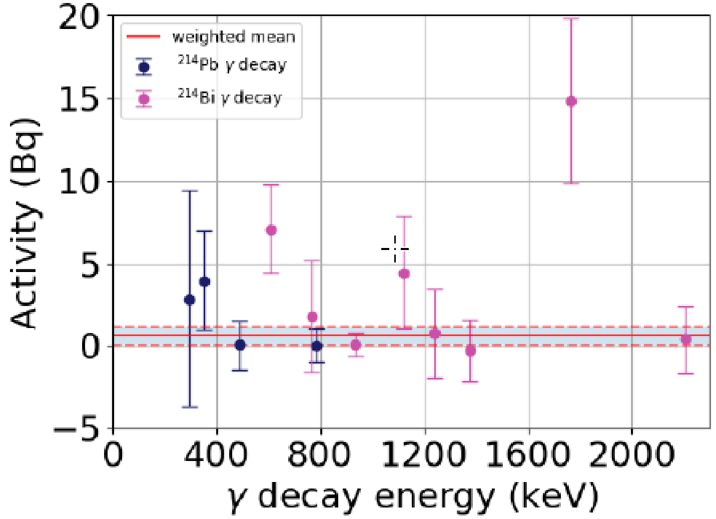


Figure 14. Activities of ^{226}Ra calculated from the progeny with gamma-decay energies shown in the figure. Red line is the mean activity of each analysed gamma decay line. Grey band represents one-sigma confidence interval.

Activities:

A	B	C
4.7 (4) Bq	0.6 (6) Bq	4.1 (7) Bq

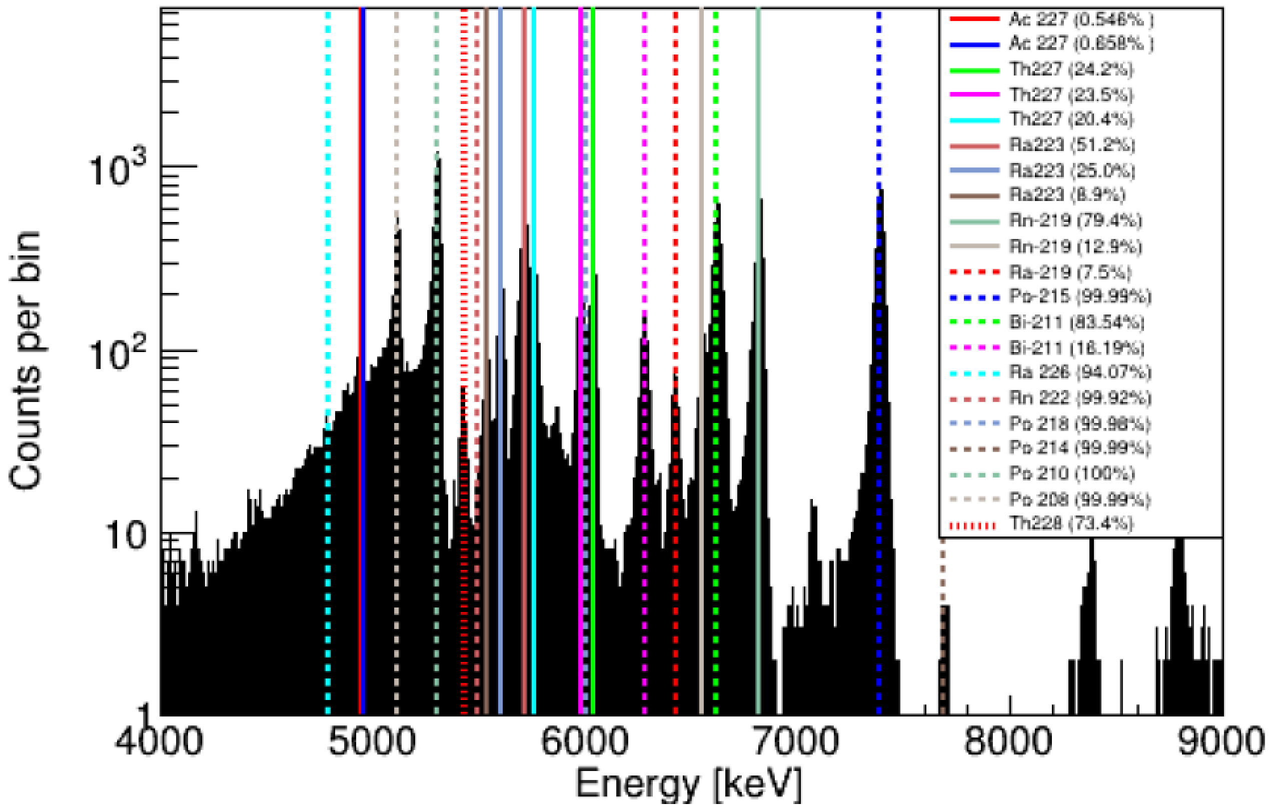
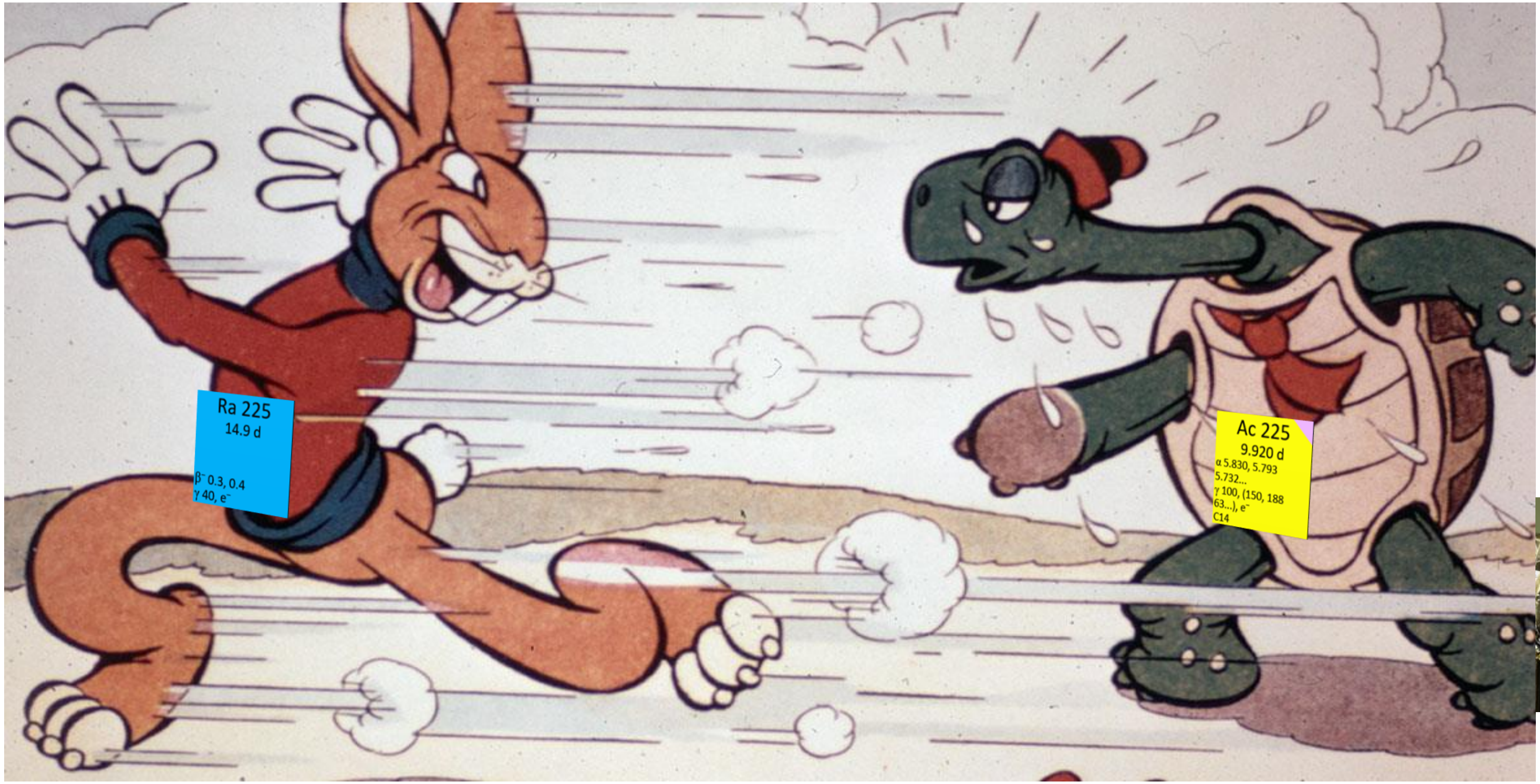


Figure 5.12: Stacked data of all ROOT files from the May source, where the peaks are identified. Full lines represent elements from the decay chain of ^{227}Ac.

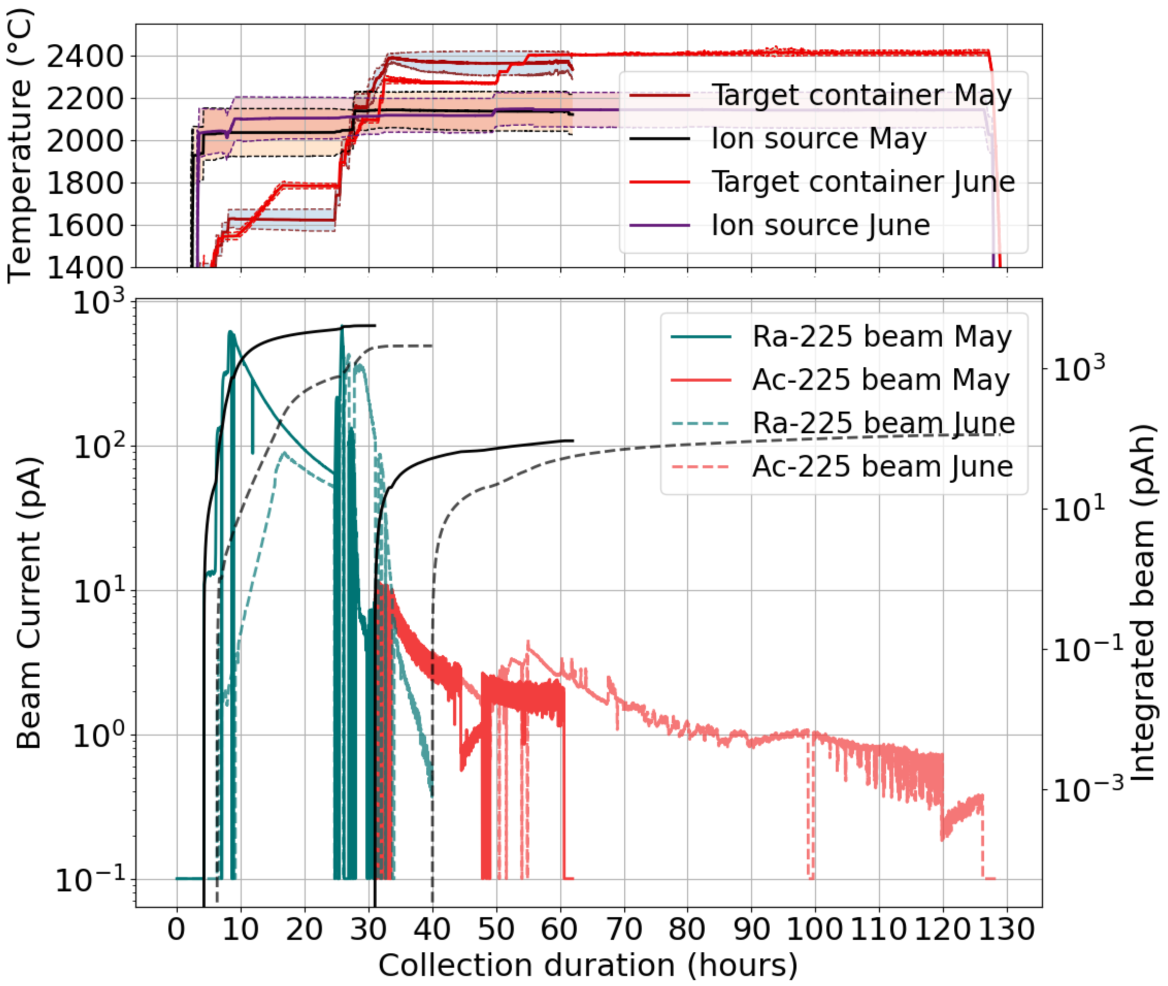
Production

Activity prod. Rate ^{225}Ac (MBq /μAh / g)	p^+ Beam energy (MeV)	Facility
0.55[3]*	800	LANL
0.026[4]	438	TRIUMF
0.25*	1400	MEDICIS



Ra 225
14.9 d
β⁻ 0.3, 0.4
γ 40, e⁻
Ac 225
9.920 d
α 5.830, 5.793
5.732...
γ 100, (150, 188
63...), e⁻
C14

ThC$_x$ target reuse: effect on collection efficiency



From implanted ion current from fresh target:

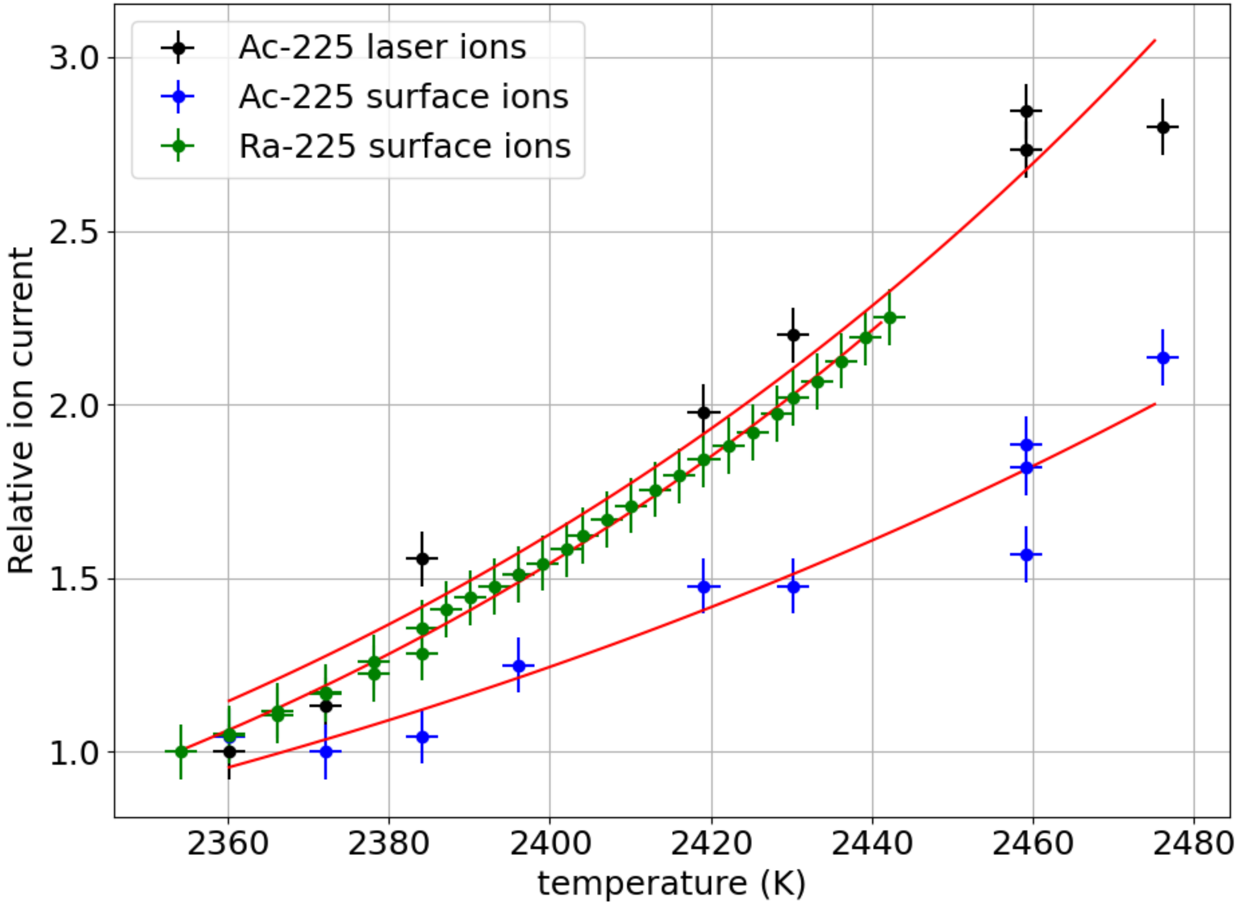
^{225}Ra activity = 50.1 MBq → 34% efficiency
^{225}Ac activity = 1.7 MBq → 0.17% efficiency

Irradiation conditions 2nd time round almost identical.

For re-used target:

^{225}Ra activity = 25.6 MBq → 18% efficiency
^{225}Ac activity = 2.1 MBq → 0.21% efficiency

Influence of ion source temperature on Ra and Ac beam



- Laser ionization efficiency improves with temperature
- Surface ionization efficiency improves with temperature
- Several x improvement in efficiency possible

$$\epsilon_s = \frac{\alpha \exp\left(-\frac{\Phi}{k_b T}\right)}{1+\alpha \exp\left(-\frac{\Phi}{k_B T}\right)}, \alpha = \frac{g_+}{g_0} \exp\left(\frac{\phi - V_{ion}}{k_B T}\right).$$

Φ and normalization constant only free parameters.

Higher temperature → Better ion confinement → higher surface / laser ionization efficiency

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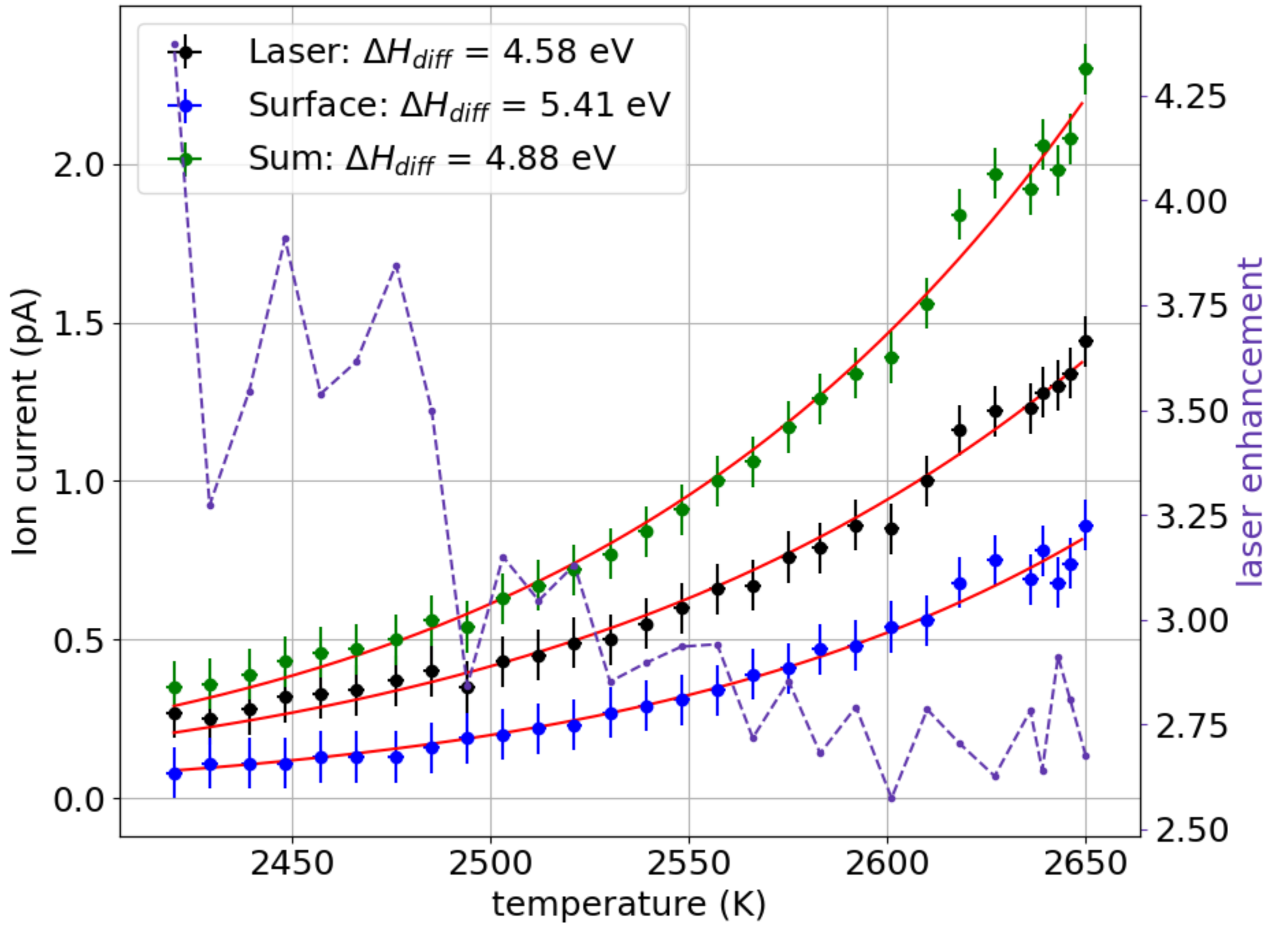
Influence of target temperature on Ac beam



Increase temperature: **Good** for collecting **quicker**, *bad* for collecting more *efficiently*!

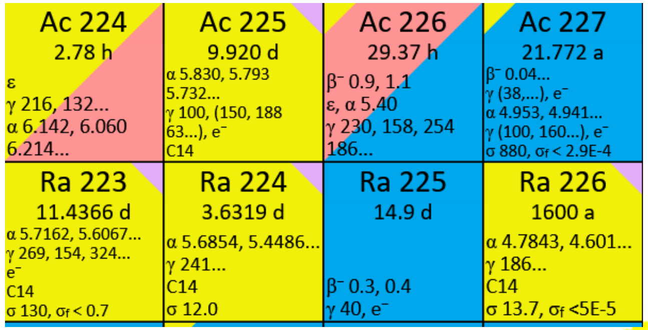
Temperature systematics well described by Arrhenius-law for diffusion…

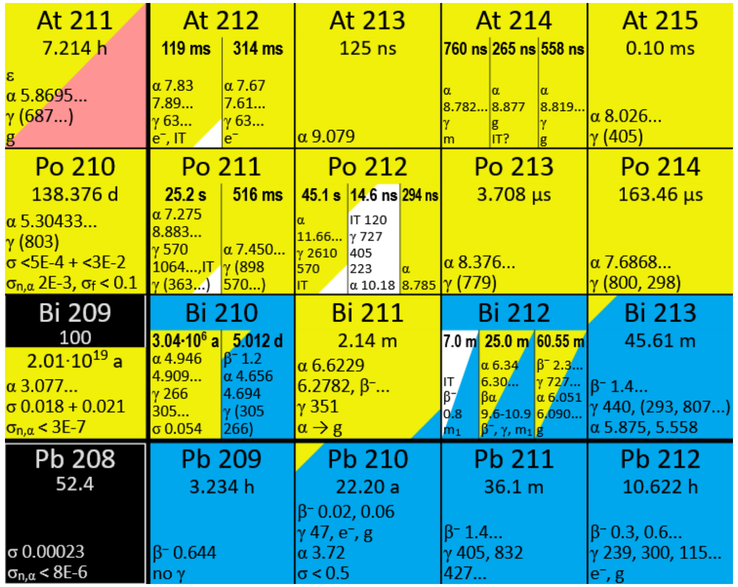
$$I \approx \frac{N_0 \epsilon_{ion}}{a^2} D_0 \exp\left(-\frac{\Delta \mathrm{H_{diff}}}{\mathrm{k_B T}}\right)$$

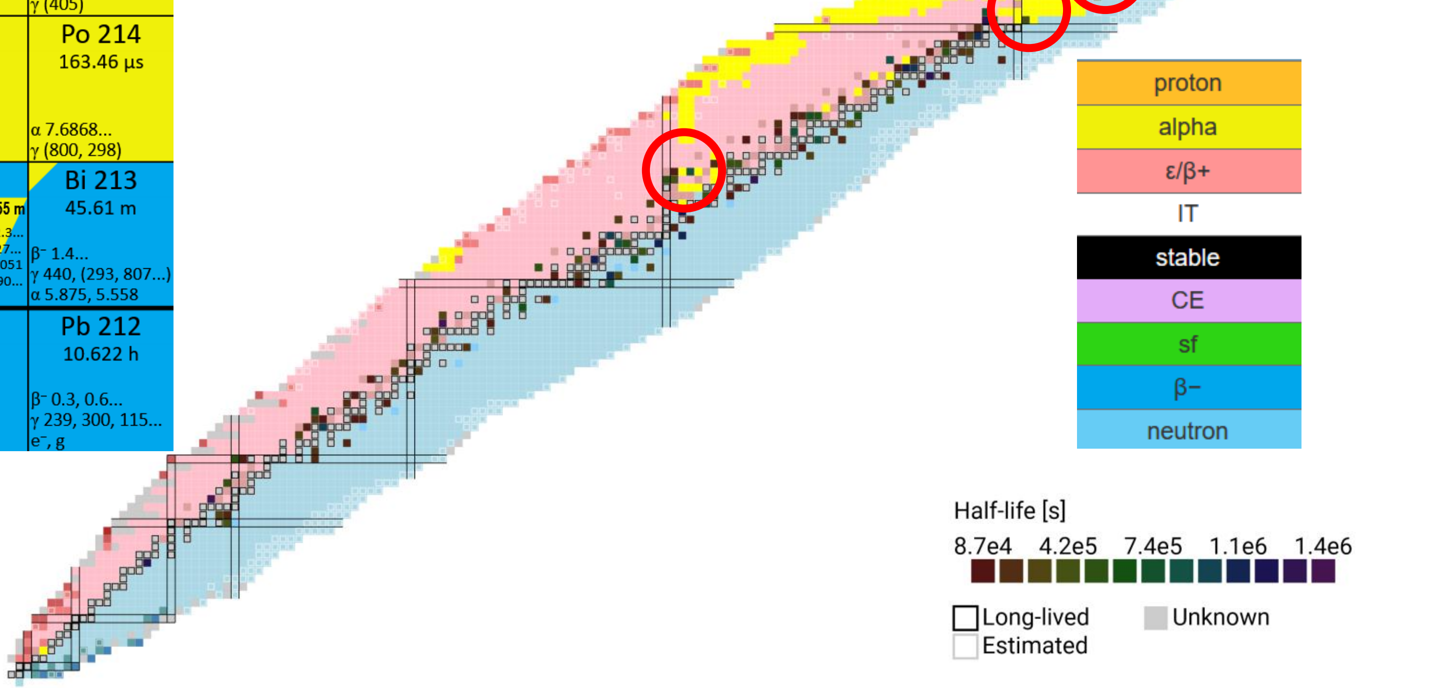
How easy is it to get α-emitters?

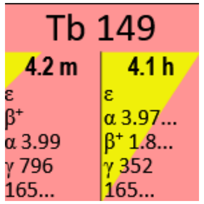
Medical alpha emitters production

- Only few choices
- Often high-Z
- “Difficult” target material or beams

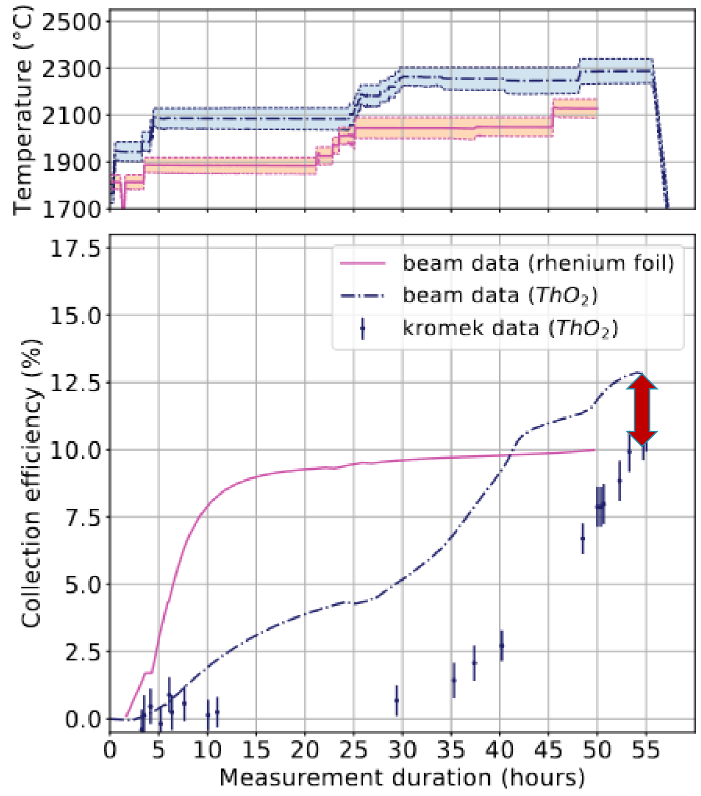


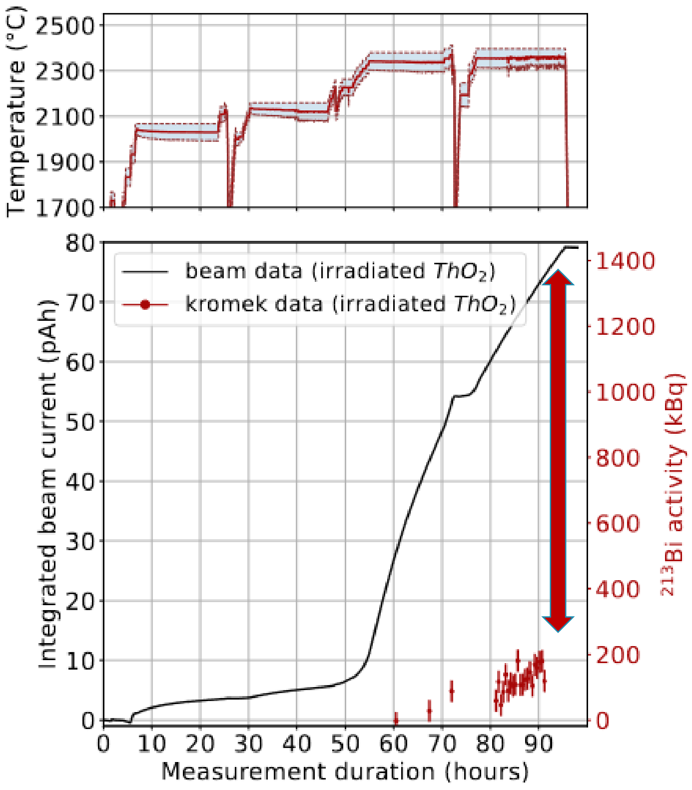






Collections as they happened

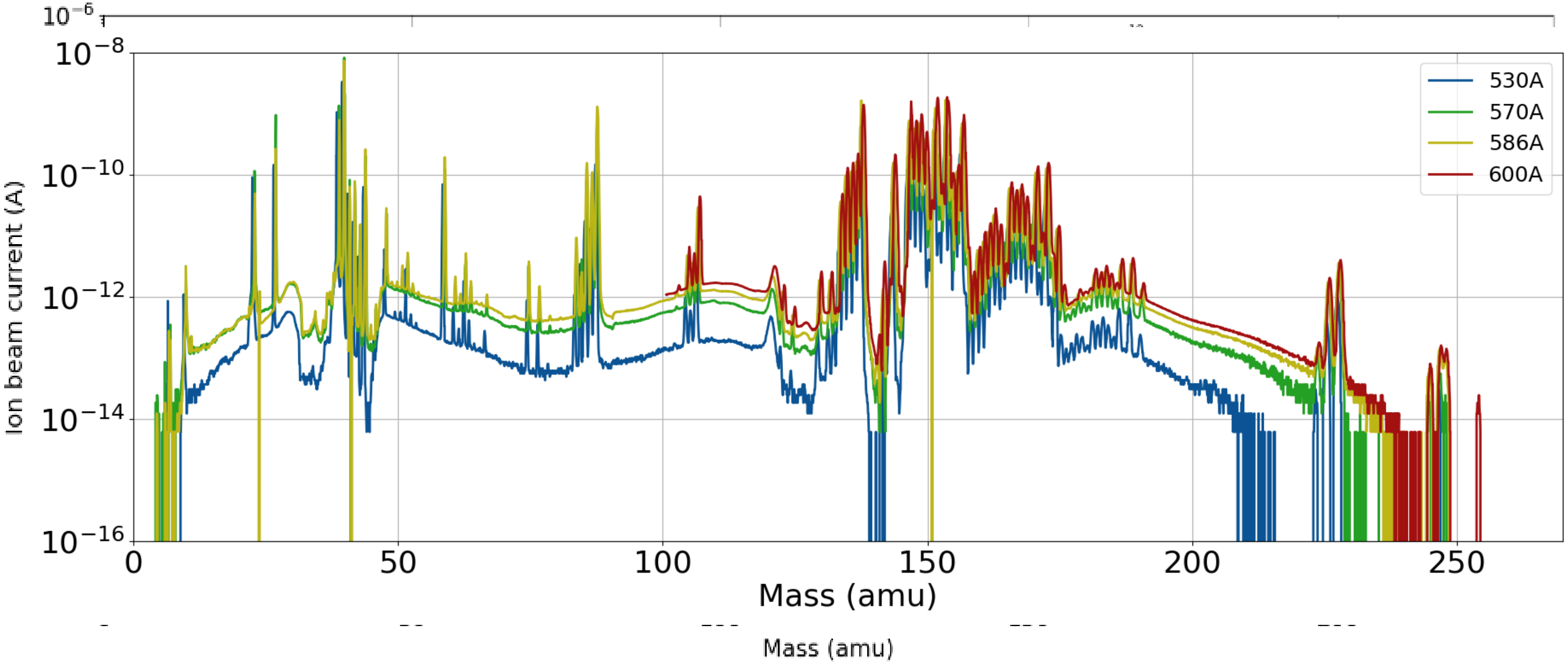




What do we implant on our foils?

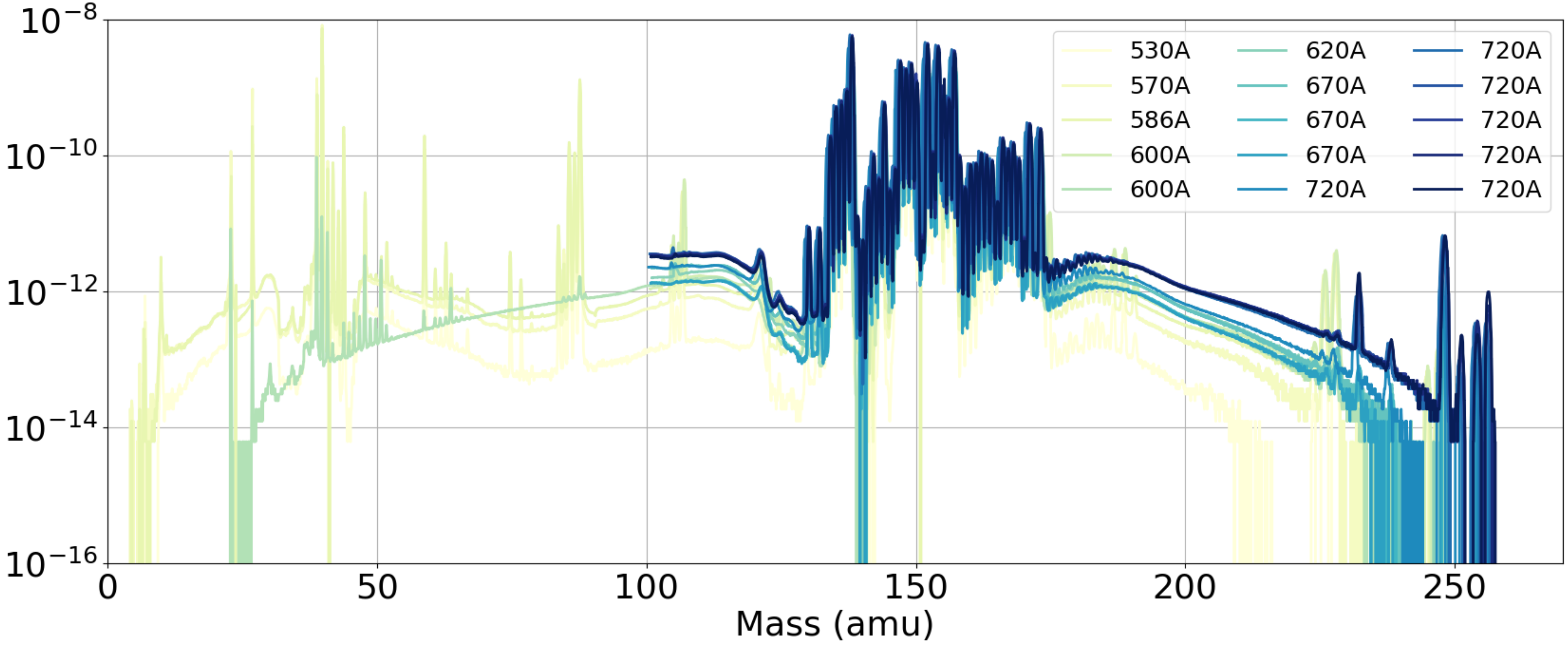
- Exp1: integrated ion current consistent with measured 10% collection efficiency
- Exp2: Integrated ion current overestimates implanted ^{225}Ac activity, Kromek gets it right!
- Exp3: Integrated ion current: wtf? Kromek gets it (mostly) right, but misses implanted ^{225}Ra

A wolf in Sheep’s clothing: The beam at mass 225

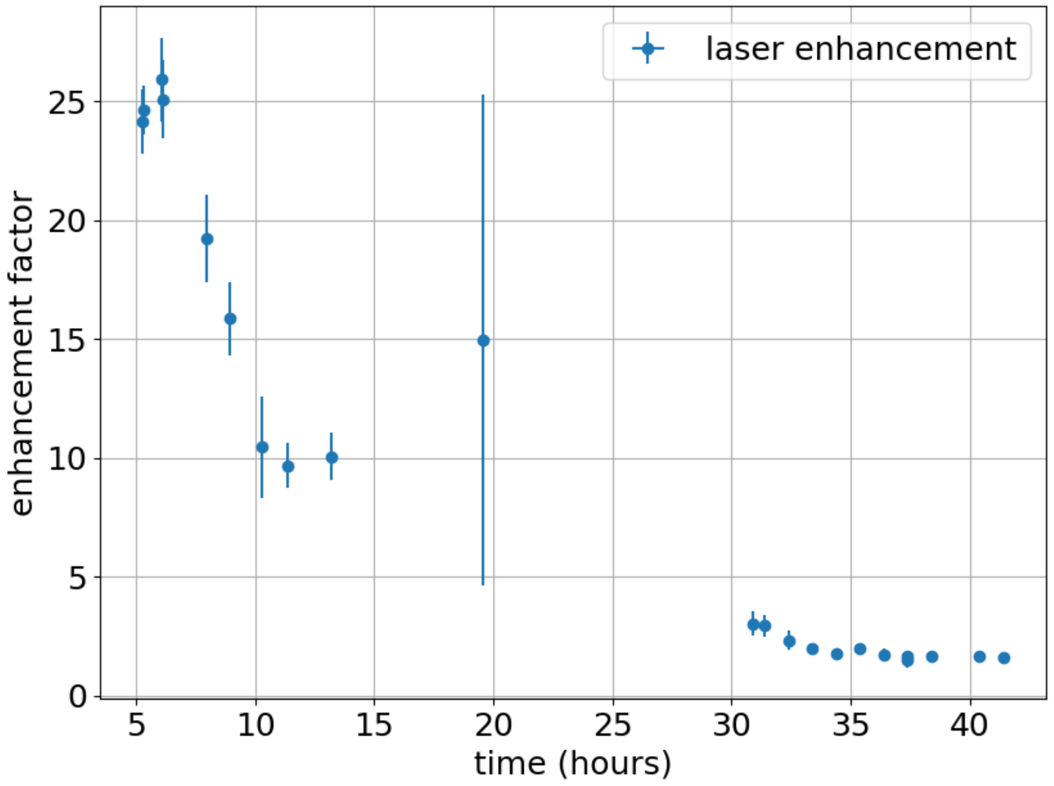


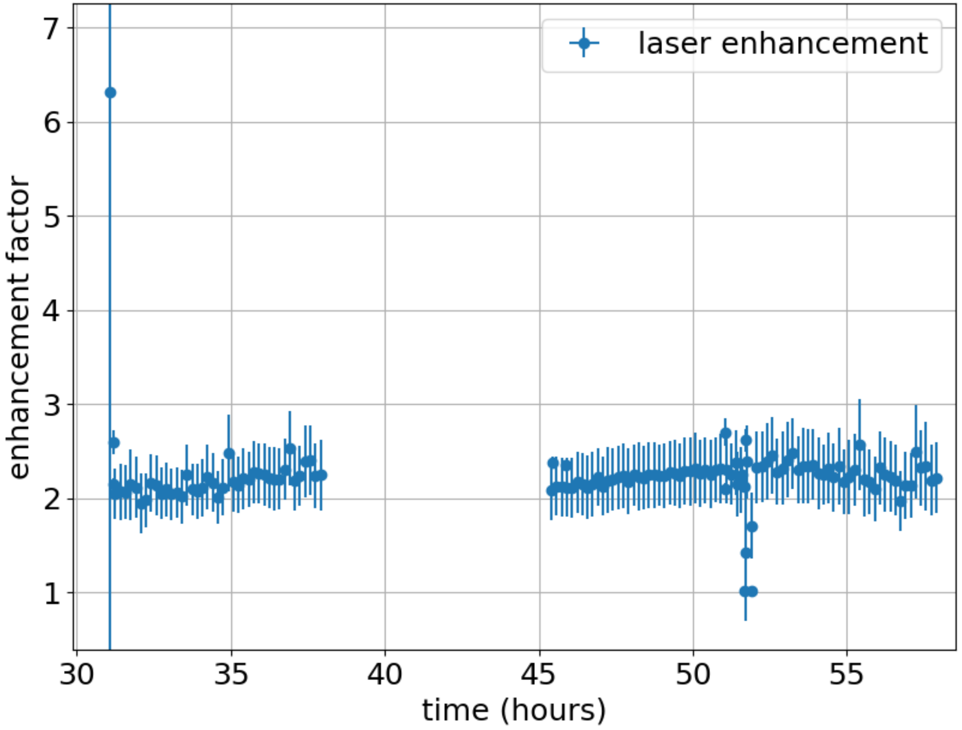
- Intense ion beams of masses have significant mass tailing, in all experiments so far with varying degrees…
- Major contributor to ion beam current at mass 225
- Precludes identification with resonance laser ionization enhancement

Most mass scans ever taken…



Laser enhancement





Ra-225 ID during beamtime