Mass separation of ^{225}Ac for medical applications

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Metastases and Targeted Alpha Therapy

Over the last decades, cancer has become one of the leading causes of death. The vast majority of these happen due to cancer cells breaking away from the tumor and forming metastases. Subsequently, they spread throughout the body colonizing and growing on new sites. Due to the non-locality of the cancer, techniques such as surgical removal or localized external beam therapy are no longer effective. Because of this, doctors have to move towards alternative methods, such as chemotherapy. However, these treatments are usually very damaging to healthy tissues.

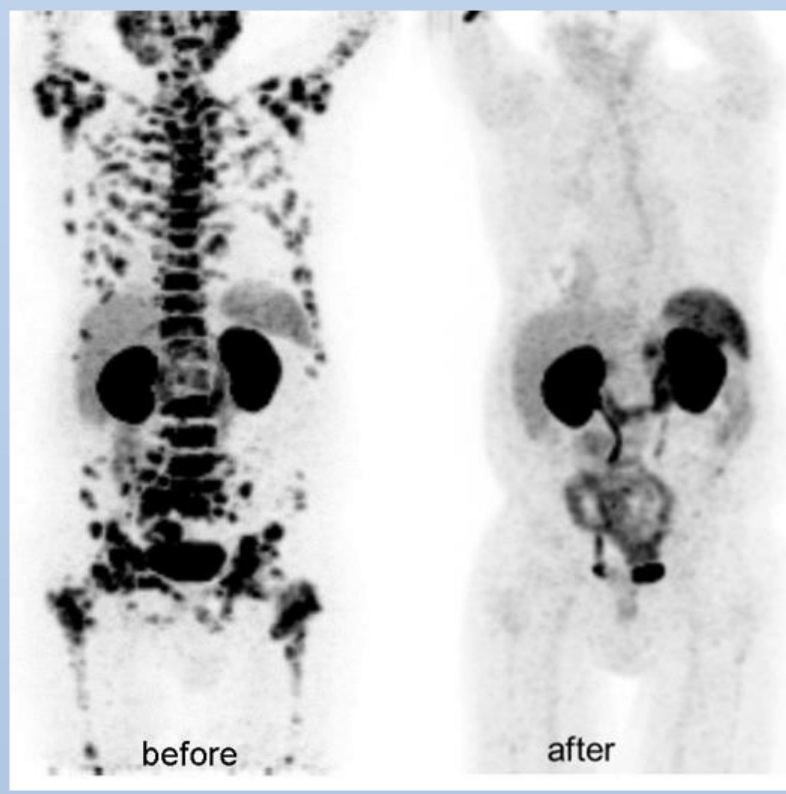


Image courtesy: [1]

A lot of promise lies in Targeted Alpha Therapy (TAT), which makes use of the small stopping range and large linear energy transfer of alpha emitters decaying close to the cancer cells. The radioisotope is chelated to targeting molecules that circulate in the body and have preferential binding to receptors on the malignant cells, where they accumulate. Unfortunately, the need for a relatively specific half-life, low radiotoxicity and lack of excreted long-lived waste products, only leaves a handful of viable candidates. One of these is ^{225}Ac, which has a half-life of about 10 days and no long-lived radioactive daughters. There are two downsides to using this isotope, namely the limited availability and contaminants of the non-favorable isotope ^{227}Ac, which is present in unpurified accelerator produced ^{225}Ac.

Laser ionization and mass separation

- Long term goal: Production via proton induced spallation of thorium and uranium targets.
- Campaign goal: Quantification of the efficiency contributions for the collection process.
- Isotopic purity obtained via:
  - Element specific laser ionization
  - Magnetic mass separation

Present contributions for production:

$$\epsilon_{tot} = \epsilon_{diff}\,\epsilon_{eff} \times \epsilon_{ion} \times \epsilon_{sep}\,\epsilon_{trans}$$

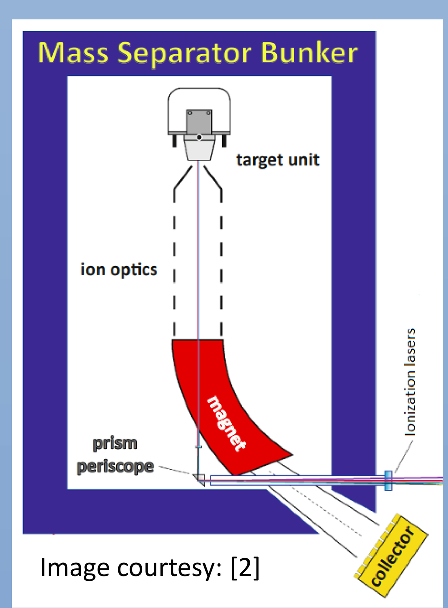
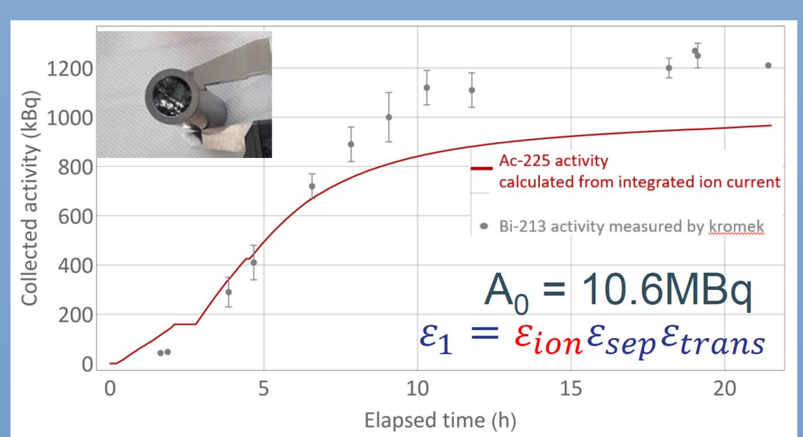
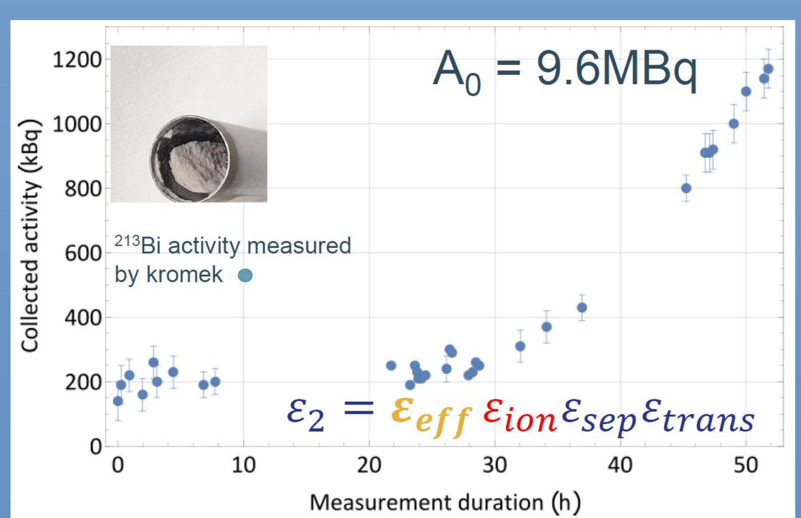


Image courtesy: [2]

Run 1: Determine ionization efficiency



Run 2: Determine effusion efficiency



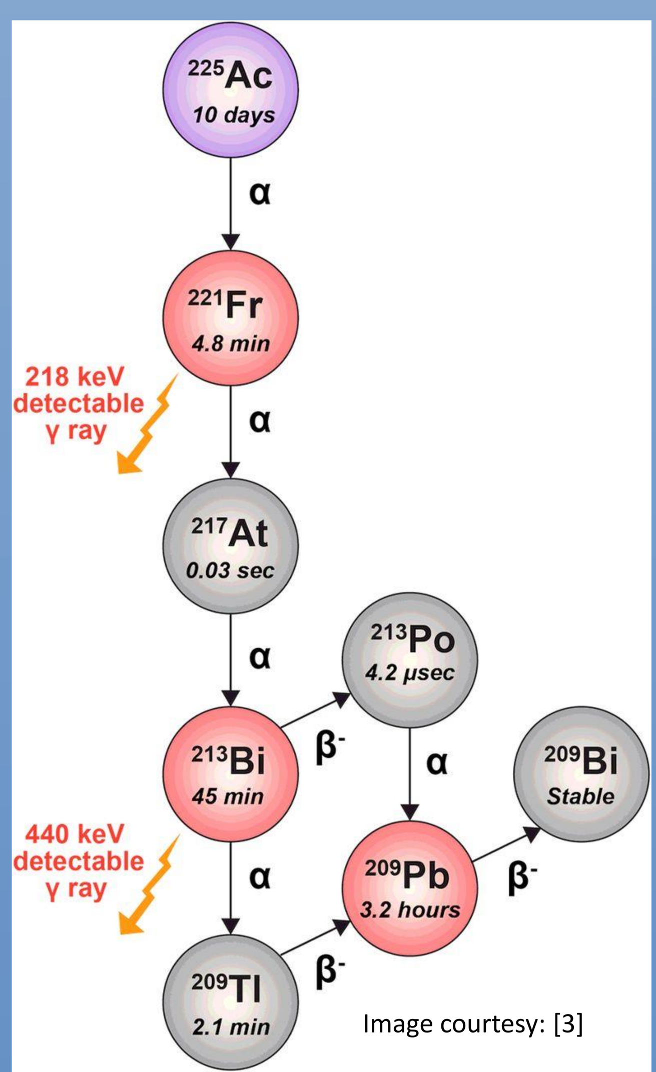


Image courtesy: [3]

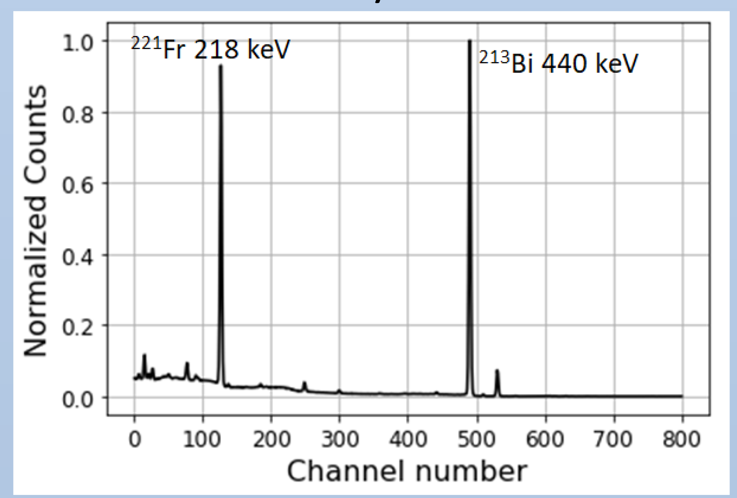
Conclusion

- The collection efficiency is heavily dominated by the ionization efficiency.
- Optimization and mass scans performed during collection → Actual ionization efficiency estimated to be 12.8%
- The required temperature for extracting ^{225}Ac is much larger for the second collection (2400 °C) than for the first collection (1920 °C).
- This approach could be suitable for large-scale production of this isotope in the future in facilities such as at ISOL@MYRRHA in SCK CEN

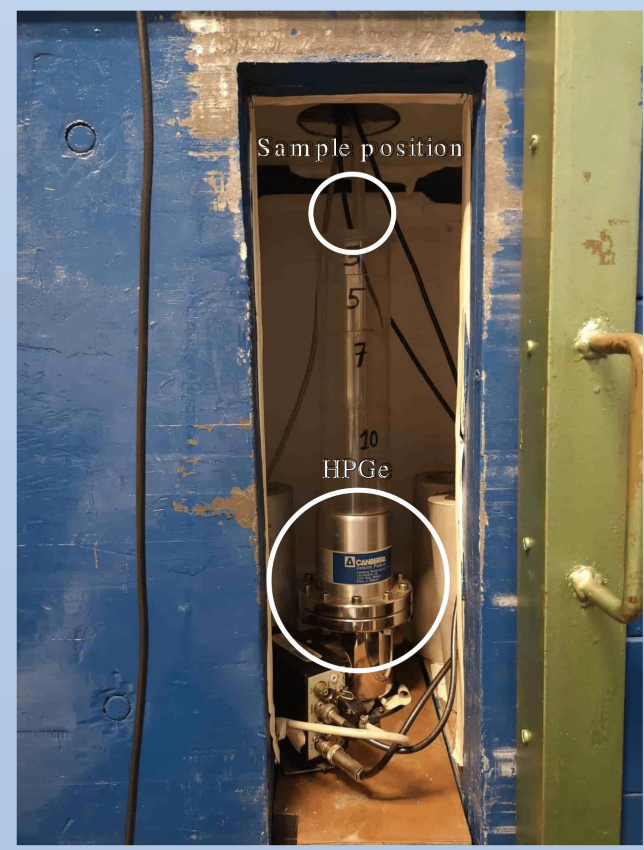
Spectroscopy

Lead castle setup:

- Detect single gamma-rays
- Low background
- Systematic uncertainties due to the detector efficiency

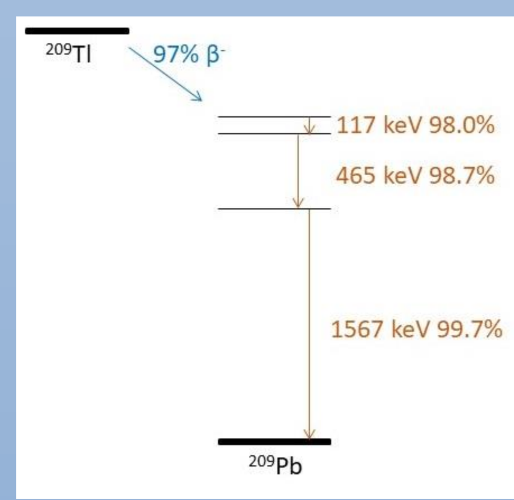


Gamma energy spectrum for the lead castle setup



Coincidence setup:

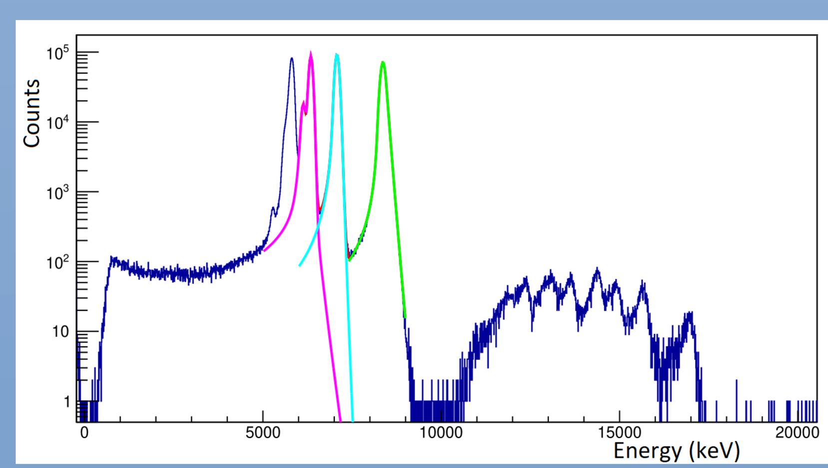
- Detect coincidence photons
- Efficiency free → No systematic uncertainties due to efficiencies
- Requires relatively high activities
- Unknown multipolarity for bismuth coincidences



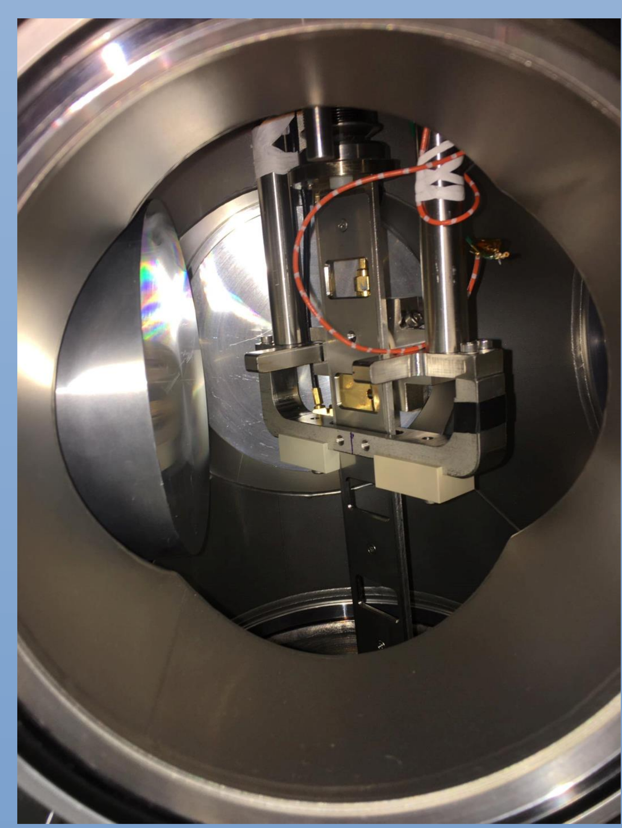
Simplified ^{209}Tl decay scheme

Alpha chamber setup:

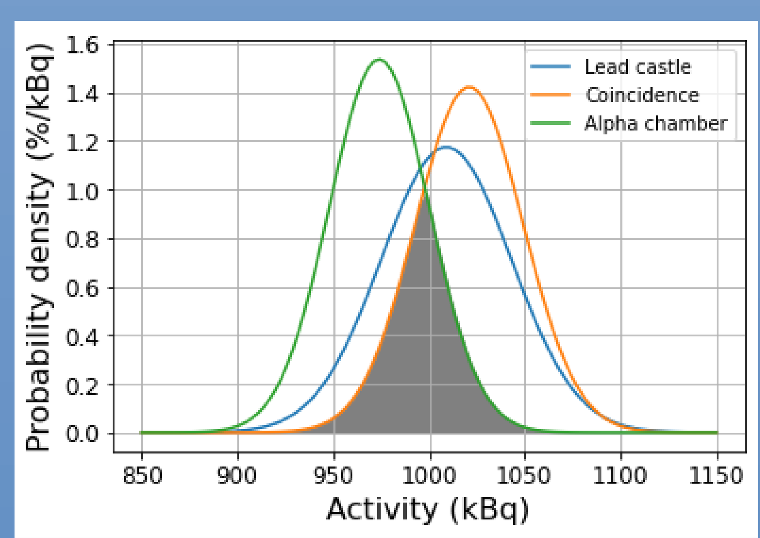
- Detect alpha particles
- Systematic error on the geometric efficiency
- Detector degrading during experiment



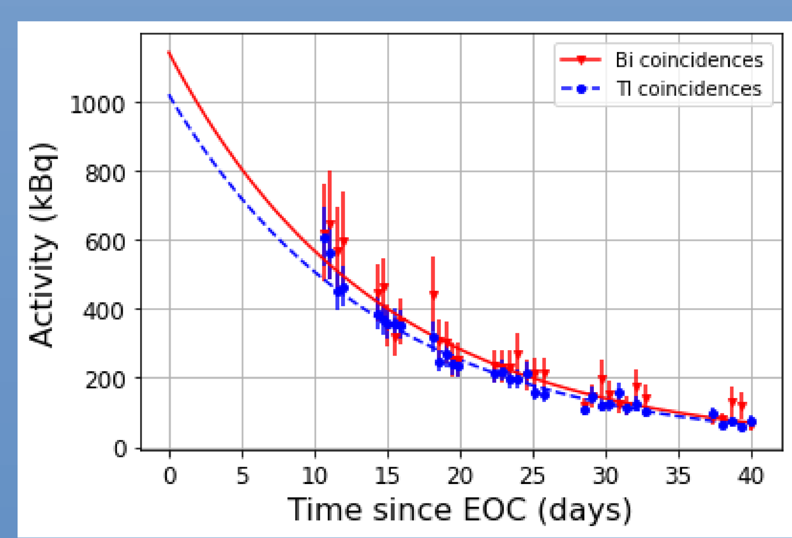
Alpha energy spectrum for the alpha setup



Resulting activities



Comparison of setups on the M108 sample (first run) activity measurements



Exponential decay fit for the M108 sample (first run) coincidence setup measurements

Collection activities:

- M108 (First run): 999(17) kBq
- M118 (First run): 62.8(8) kBq
- M120 (Second run): 861(24) kBq

Collection efficiencies:

- First run: 10.02(16)%
- Second run: 9.23(25)%

References

[1]: KRATOCHWIL, Clemens, et al. 225Ac-PSMA-617 for PSMA-targeted α-radiation therapy of metastatic castration-resistant prostate cancer. *Journal of Nuclear Medicine*, 2016, 57.12: 1941-1944.
[2]: GADELSHIN, V. M., et al. MELISSA: laser ion source setup at CERN-MEDICIS facility. Blueprint. *Nuclear Instruments and Methods in Physics Research Section B: Beam Interactions with Materials and Atoms*, 2020, 463: 460-463.
[3]: POTY, Sophie, et al. Leveraging bioorthogonal click chemistry to improve 225Ac-radioimmunotherapy of pancreatic ductal adenocarcinoma. *Clinical Cancer Research*, 2019, 25.2: 868-880.