"Characterization of a commercial gamma counter for pre-clinical use: First steps on the quantification of ^{225}Ac and its gamma emitting daughters"

PhD topic: "Dosimetry aspects of recoiling daughter nuclides of ^{225}Actinium in Targeted Alpha Therapy"

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Introduction

Targeted alpha-therapy (TAT) have shown promising results when overcoming resistance to β-emitters in clinical applications. In terms of α-emitters, Actinium-225 (^{225}Ac) is considered a promising candidate for TAT due to its relatively long half-life (10 days) and because it is a highly cytotoxic radionuclide in view of the high α-particle emission energies produced in its decay chain. However, the emission of an α-particle can lead to the recoil of the resulting daughter (recoil daughter effect), loosing affinity to the molecular carrier which will lead to a redistribution of recoiling daughters within the patient's body and associated side effects.

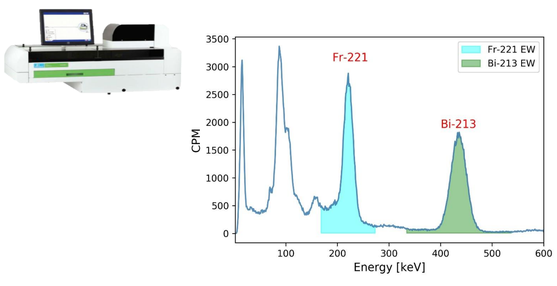
Gamma counters (GC) are considered the gold standard and most used technique for ex-vivo quantification on preclinical level. In order to quantify ^{225}Ac and its recoiling daughters (^{221}Fr and ^{213}Bi) it is crucial to properly calibrate and optimize the GC protocols in pre-clinical applications, where quantification and biodistribution assessment of new developed radiopharmaceuticals require precise and accurate results.

Objectives

- Characterize a commercial well-type gamma counter (2480 Wizard2, PerkinElmer, Waltham, MA, USA) to be used for the ex-vivo quantification of ^{225}Ac (i.e. through its gamma emitting daughters ^{221}Fr and ^{213}Bi, when they are in secular equilibrium) and radiopharmaceutical QA measurements.
- Obtain isotope-specific calibration factors for both ^{221}Fr and ^{213}Bi energy window settings.

Materials & Methods

- Acquisition protocol creation for ^{225}Ac: Energy window configurations corresponding to ^{221}Fr and ^{213}Bi gamma peaks.



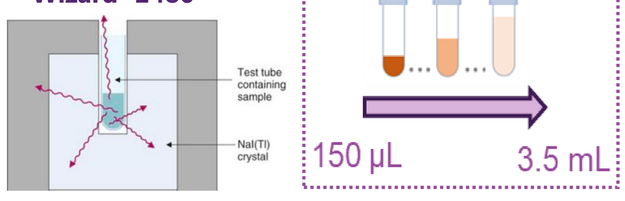
Gamma counter characterization

➢ Cross-talk test

High activity sample ~500 kBq → Low activity sample

➢ Volume effect test

Well-type GC Wizard² 2480

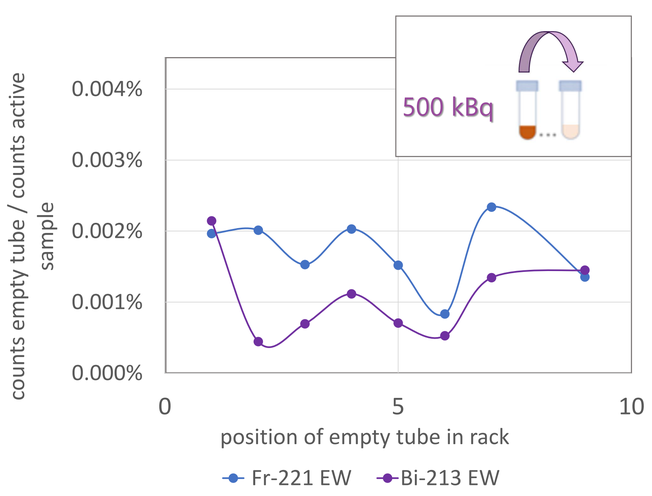


Volume (=Activity) ⇕ Counts loss

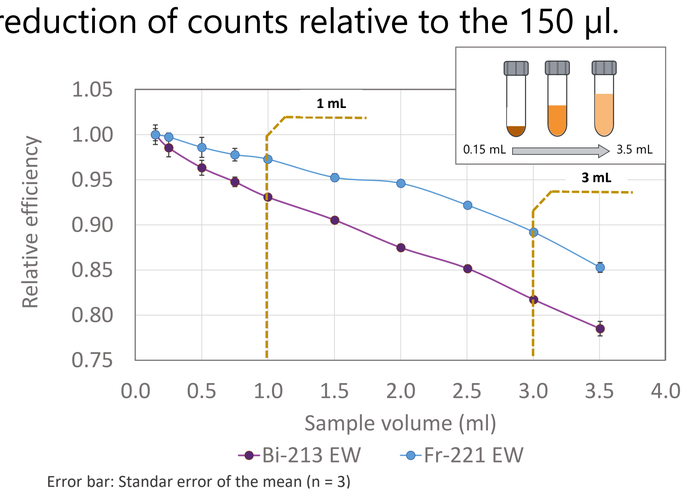
➢ Linearity of the detector response

Results

- No significant **cross-talk** effect is expected for these GC model (<0.002%).

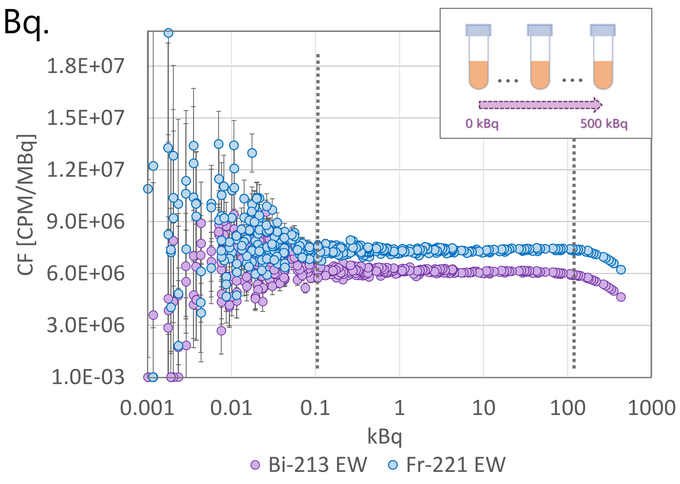


- **Volume effect** for a 3mL sample: detector efficiency results in 12% (^{221}Fr) and 20% (^{213}Bi) reduction of counts relative to the 150 µl.



Error bar: Standar error of the mean (n = 3)

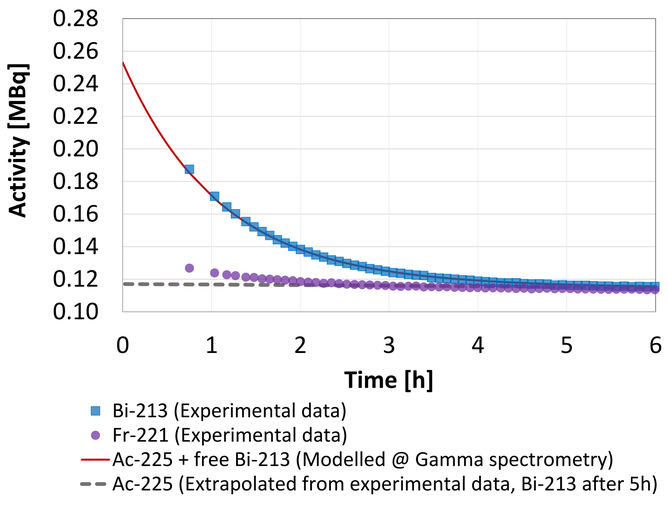
- **Linearity** range: 0.1kBq -> 150 kBq
- Underestimation of the counts of up to 17% (^{221}Fr) and 25% (^{213}Bi) for activities around 0.5 MBq.



Ongoing investigation

For this study the GC was characterized with respect to cross-talk, linearity of the detector response and sample volume effects. As a result the isotope-specific calibration factors for both EW settings were obtained. Currently, further protocol optimization and validation are being performed in order to:

- **Quantify** ^{225}Ac and gamma emitting daughters under **non-secular equilibrium** conditions relying on ^{213}Bi and ^{221}Fr EW.
- Optimize the **^{221}Fr** peak **quantification** to be used for early assessment of ^{225}Ac activity under **non-secular equilibrium** conditions (e.g. excess of ^{213}Bi).
- Investigate the **recoil daughter effect** on the **stability** of different radiolabeling **prior to secular equilibrium** (i.e. ^{225}Ac + peptide: DOTA/DEPA)



Conclusions

Correct characterization and further optimization of the acquisition protocols

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IMPROVED ex-vivo quantification of ^{225}Ac

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Pre-clinical applications like ***quantification*** and ***biodistribution*** assessment of new developed radiopharmaceuticals

[1] Castillo Seoane D, de Saint-Hubert M, Crabbe M, Struelens L, Koole M. "Targeted alpha therapy: A critical review of translational dosimetry research with emphasis on actinium-225. Q J Nucl Med Mol Imaging. 2020;64:265–77. DOI: 10.23736/S1824-4785.20.03266-5.

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