Development of Alpha Spectrometry for Diagnostics of TAT on Cancer Cells *in Vitro*.

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Background

Radiopharmaceuticals have been utilized for almost a century for various treatments. In the last couple of decades, cancer treatment has become an increasingly important element of this. Through Targeted Alpha Therapy (TAT), Alpha-emitting isotopes, such as Ac-225, are used to systematically target cancerous cells in the body. This approach enables the targeting of cancer at closer ranges with minimal damage to surrounding tissues.

Motivation

The goal of the project is to improve investigative methods of TAT on cells *in vitro* through the design of a new detector and measurement protocols. This is done so that we can measure uptake efficiencies of the primary isotope and its decay products while incubated in cancerous cell cultures. Commercial Alpha Detectors cannot be used for biological cases due to a variety of difficulties, but predominantly the need to operate under a vacuum. This project intends to solve that problem.

Experimental Procedure

- Seed pancreatic rat tumour cells in Mylar foil cups
- Incubate the seeded cups with [225Ac] Ac-CROWN-TATE or a similar biomolecule (Figure 1)
- Wash cells several times with PBS and save the resulting supernatant.
- Take reference measurements by performing the identical procedure without cells (Figure 3)
- As well as CROWN TATE [225Ac] PSMA is used for comparison (Figure 7)

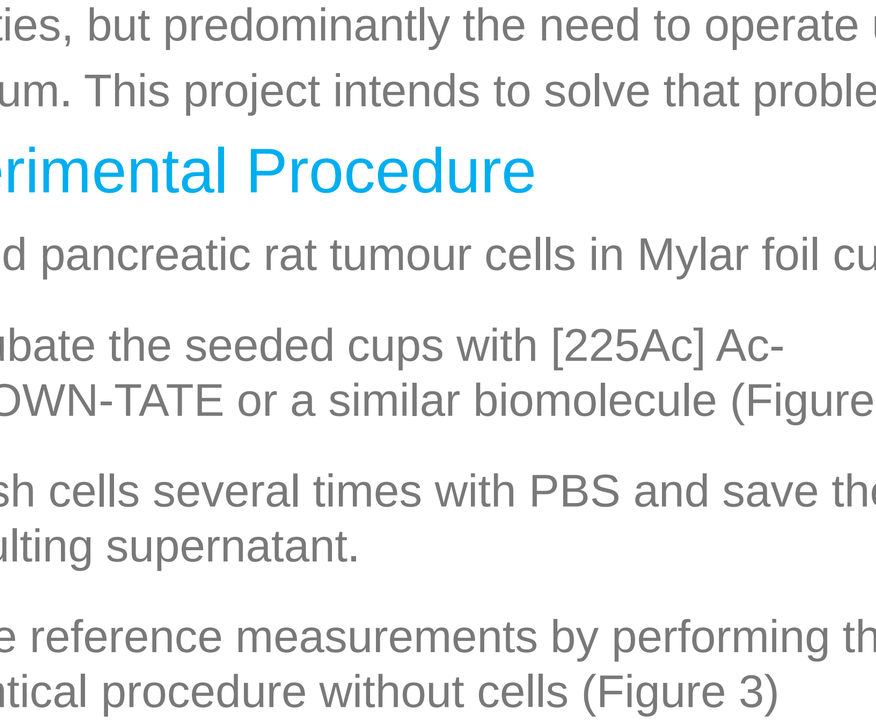
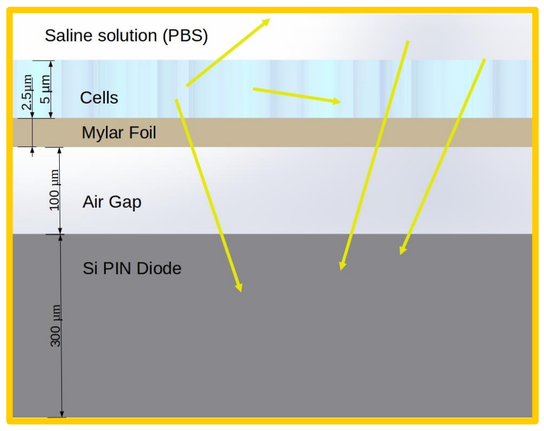


Figure 1. AR42J cells after incubation with [225Ac] Ac-CROWN-TATE

Detector and Sample Preparation

- Si PIN Photo diode detector suspended in a shielded metal box (Figure 2)
- Pressure-sealed opening keeps light out
- Holds a SpectroMicro XRF sample cup with a 2.5µm Mylar foil substrate for the cells in very close proximity to the detector surface
- Detector sends a signal to a preamp/shaping unit and then to a 12-bit MCA
- Spectra are saved at regular intervals



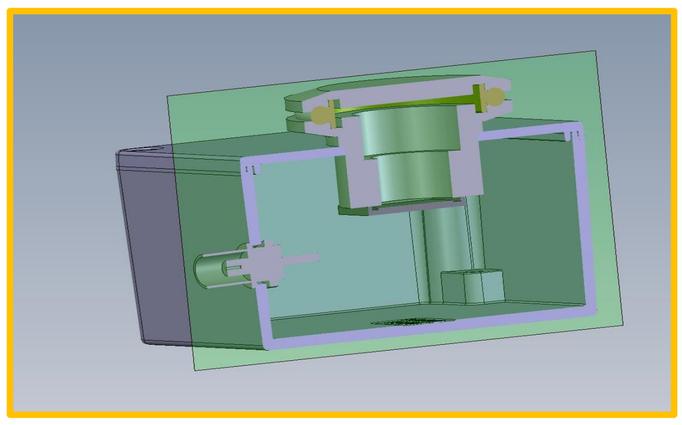


Figure 2. Schematic view of detector assembly. Figure 3. Model of Bio-sample Alpha Detector. Alpha particles from a layer of cells are absorbed in the substrate of a Si PIN diode after passing through a small air gap and thin Mylar foil, separating cells and detector.

Preliminary Results

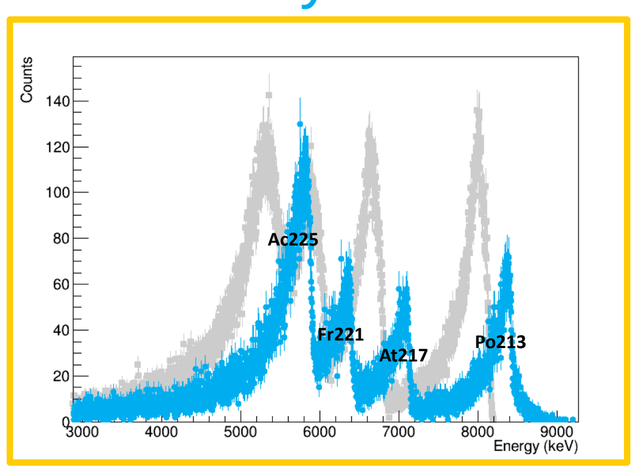


Figure 4. [225Ac] Ac-CROWN-TATE Reference Sample (no cells) – (blue) Geant4 Simulation (grey) Normalized to Activity, Measurement

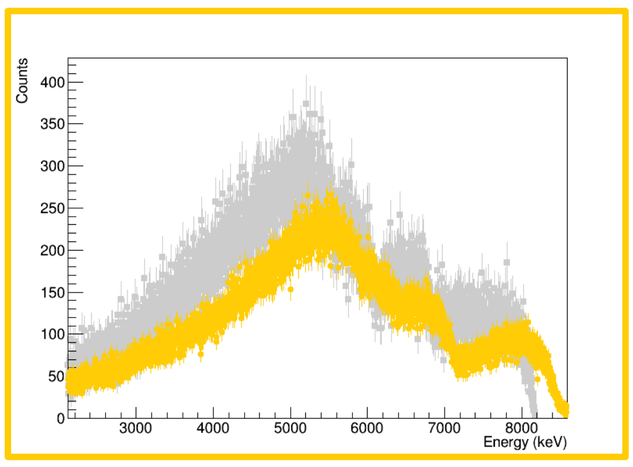


Figure 5. [225Ac] Ac-CROWN-TATE Cell Sample – Geant4 Simulation (grey) Normalized to Activity, Measurement (orange)

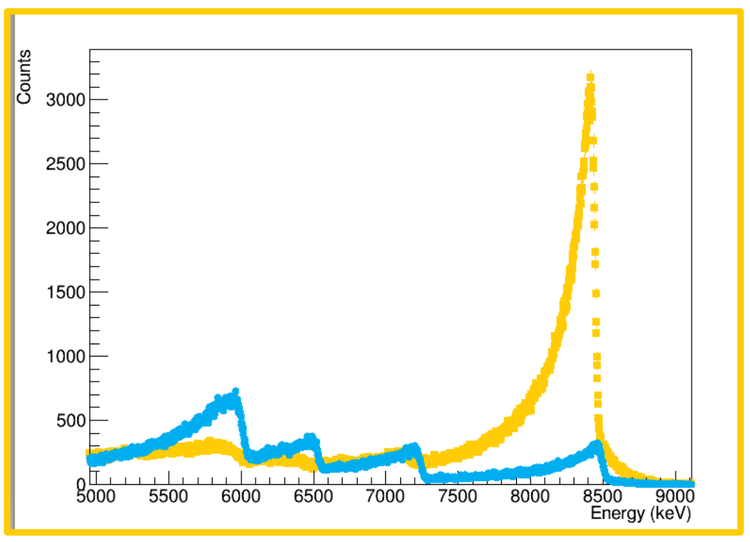
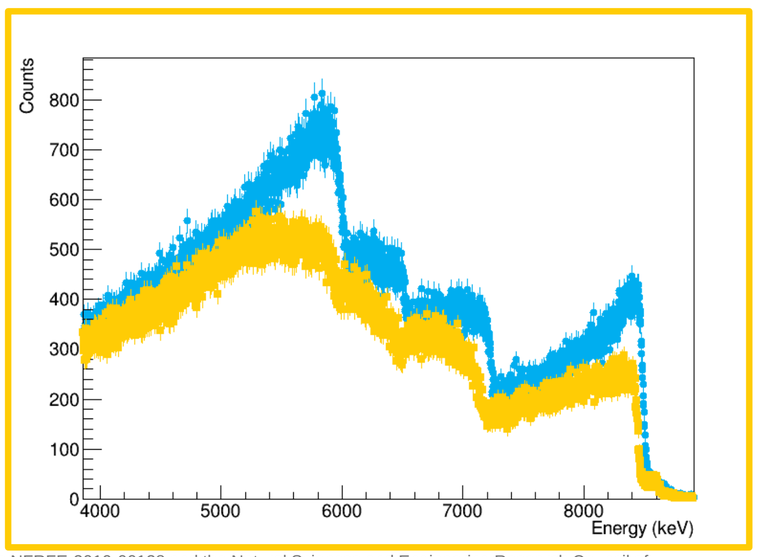


Figure 6 (left). [225Ac] Ac-CROWN-TATE Supernatants - Reference Sample (blue), Cell Sample (orange) . Shows the obvious difference between the unabsorbed actinium in the reference sample and the absorbed actinium in the cell.

Figure 7 (right). [225Ac] Ac-CROWN-TATE Cell Sample (orange) compared with a [225Ac] PSMA cell sample (blue). The PSMA has a larger activity as the biomolecule likely exists outside of the cells while the CROWN-TATE is more attenuated as it has been absorbed.



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