Production of astatine-211 at the Cyclotron Institute

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Astatine-211 shows promise for cancer treatments when connected to a targeting agent such as a monoclonal antibody, especially for non-localized cancers [1]. With the advent of such targeting agents, the major impediment to its use in clinical trials remains the availability of production and reliable separation chemistry [2]. We have produced ^{211}At at the Cyclotron Institute using the (α,2n) reaction at 28.8 MeV on a ^{209}Bi target. In the past, astatine-211 has been successfully produced in small quantities at the CI [3-5]. However, the dry distillation method used to separate out the astatine-211 from the target was laborious and not very efficient [5]. In the past year, a new team has been assembled, and novel chemistry is being used for the separation.

Successful production, recovery, and experimentation of ^{211}At were achieved at the CI using this new team. Two irradiations have been conducted, producing approximately 24 ± 2 mCi and 40 ±4 mCi of ^{211}At on December 12, 2019 and March 3, 2020, respectively. The average beam current of the 28.8 MeV α-particle beam was 5.3 μA (4.0–8.7 μA) for 8 h during the first campaign and 6.3 μA (5.5–7.0 μA) for 9 h during the second campaign. The targets were transferred to Radiochemical Lab 118 within the Cyclotron Institute, where a portion (roughly 30% in December 2019 and 46% in March 2020) of the target was dissolved in HNO_3 and experiments into a number of new separation systems were carried out. For the first campaign a series of solvent extraction system were studied, with the goal of direct extraction of ^{211}At out of HNO_3, and a promising system was identified to produce a rapid and efficient separation. In the second campaign, the promising system was adapted into extraction chromatography separation system and was shown to have an ^{211}At recovery yield of ≥ 95% with a decontamination factor from Bi of ≥ 100,000 by direct loading of the dissolved target on the column. These results are promising from both the practical side of being able to make and purify ^{211}At, but also for the scientific standpoint of discovering and understanding the unique chemistry of ^{211}At.

Improvements were made between the December and March runs, including the introduction of a sealed dissolution container, scrubber, and charcoal filter, which reduced the amount of astatine-211 detected by the Continuous Air Monitor, or iCAM (an alpha and beta particle detector and monitor) connected to the exhaust of the biosafety cabinet, where the target dissolution was performed. Air is drawn through the instrument by means of an external pump, and airborne particulate material is deposited on a filter. The filter is monitored by a Canberra PIPS ion-implanted silicon radiation detector, which allows simultaneous measurement of energy of both alpha and beta particles deposited on the filter. Data is recorded every 15 seconds.

The counts in the appropriate alpha energy range for astatine-211 were integrated in 10-minute increments before, during, and after the target dissolution and separation chemistry. Alpha particles of the appropriate energy are shown in Fig. 1 (December 2019 run) to increase at the time of target dissolution, and then drop off, congruent with astatine-211's short half-life ($t_{1/2}$=7.2 hours). In the March

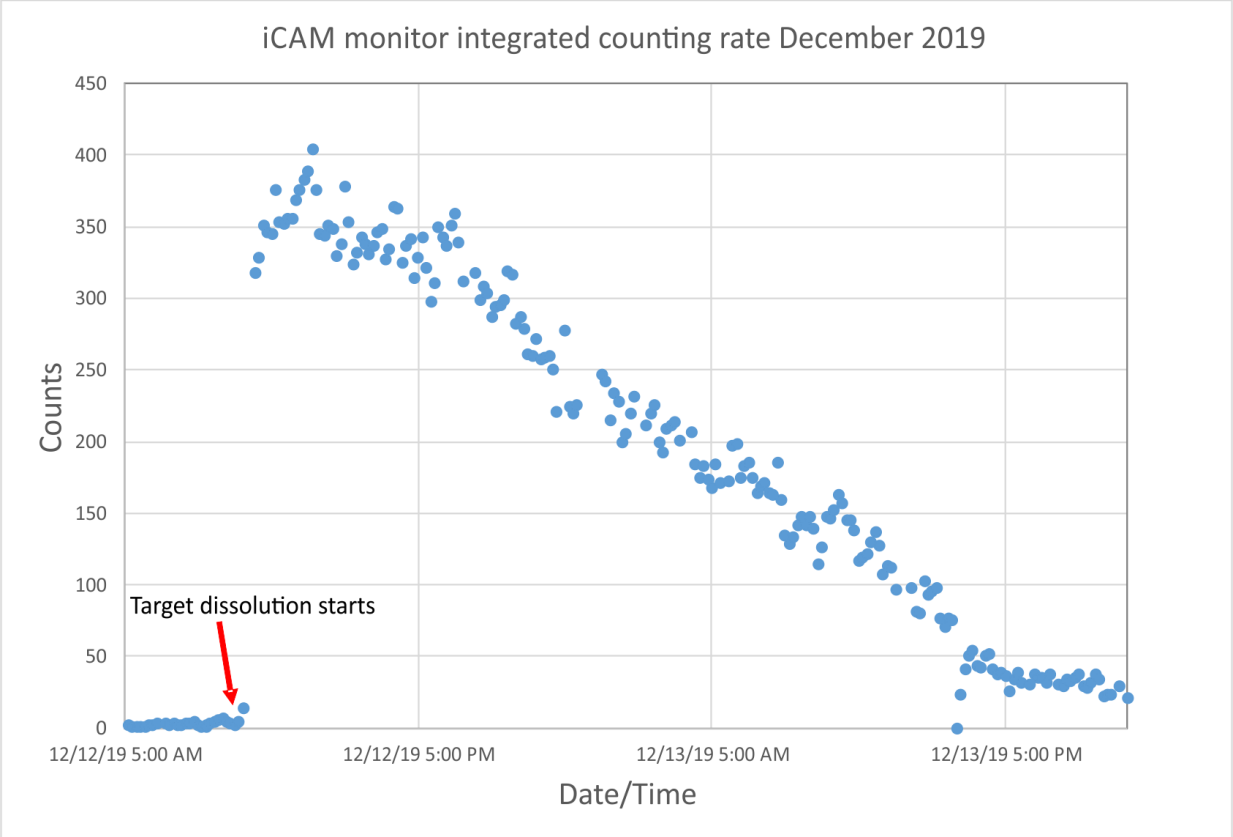

Fig. 1. Integrated iCAM Count Curve for December 12-13 dissolution of bismuth target with produced astatine-211.

run, shown in Fig. 2, the graph has a similar shape, but does not reach the same height of counts, indicating less astatine-211 was volatilized. The March 3-4 runs peaked at 82 counts, while the December 12-13 runs peaked around 375 counts.

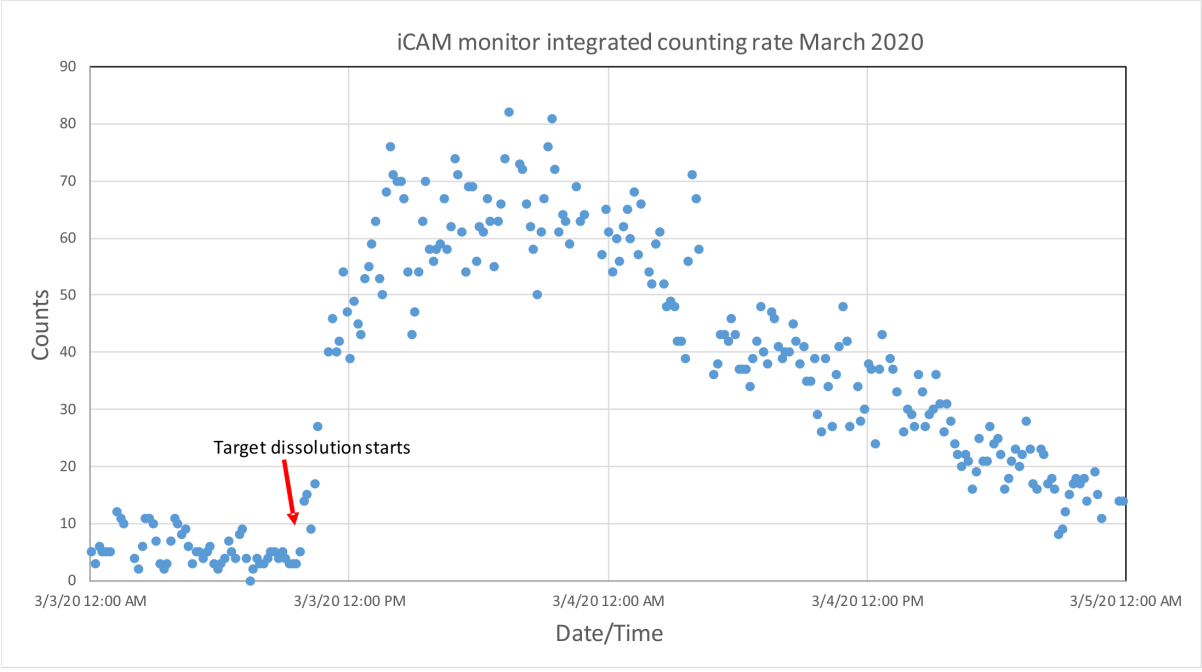

Fig. 2. Integrated iCAM Count Curve for March 3-4 dissolution of target with produced astatine-211.

A High Purity Germanium (HPGe) detector was used to measure the hundreds of liquid samples that were produced during the separation chemistry. A spectrum of one of our samples containing astatine-211 is shown in Fig. 3. Below 100 keV, there are many x-rays. The characteristic γ-ray of ^{211}At is pointed out at 687 keV. The two γ-rays of 211Po are also labeled at 569 and 897 keV. The other two γ-rays belong to unknown radiochemical species, which are separated out by the separation chemistry, but merit further investigation.

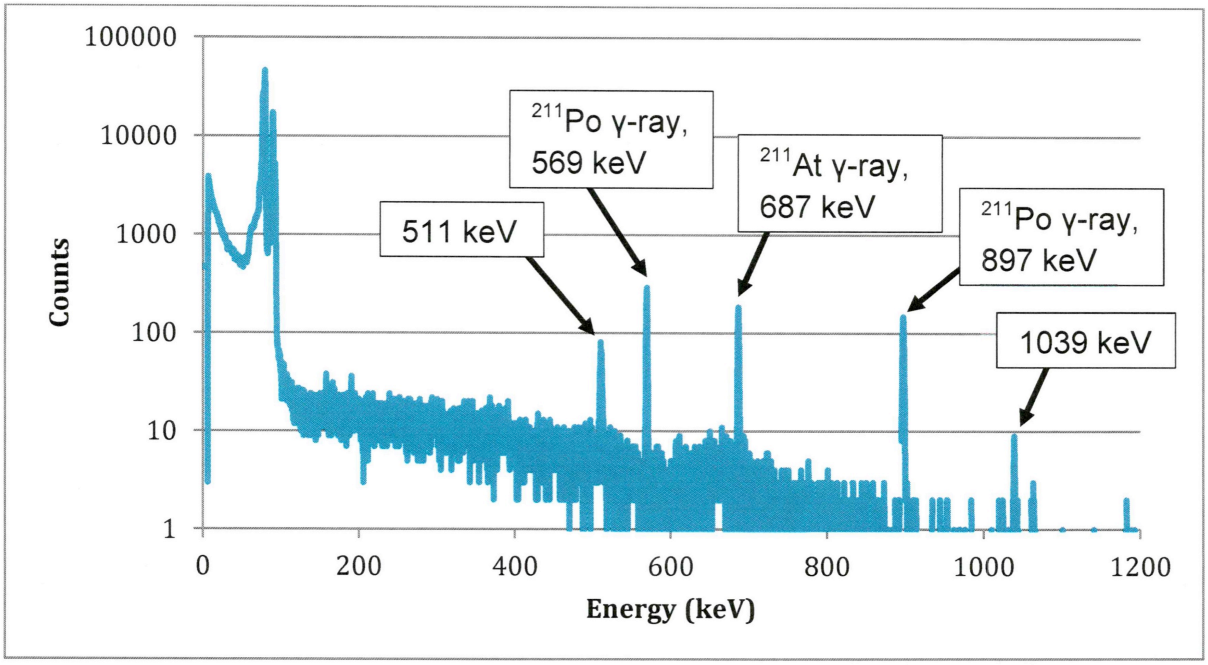

Fig. 3. HPGe spectrum of an aliquot of target dissolved solution, containing the characteristic gamma-rays from astatine-211 and its decay daughter polonium-211. The gamma-rays at 511 and 1039 keV merit further investigation.

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