System improvements to produce astatine-211

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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 made improvements to our ability to reliably produce ^{211}At at the Cyclotron Institute using the (α,2n) reaction at 28.8 MeV on a ^{209}Bi target. In the past year, we have added two graduate students to our team, expanded our collaborative footprint, improved the amount and stability of alpha beam available to produce astatine-211, made a detector to help monitor the beam current on target, experimented in target production methods (see McCann's contribution to this report), and improved detection methods to support a safe target extraction.

We produced astatine-211 on six occasions over the past year. A summary of the amount of beam available, length of irradiation, and total amount of astatine-211 produced during each of the runs is shown in Table I. The asterisk for the amount produced in December 2020 is because the target melted during this irradiation, and the amount of activity had to be estimated by a different means than the other runs. The targets were transferred to Radiochemical Lab 118 within the Cyclotron Institute, where the target was dissolved in HNO_3 and radiochemical experiments were carried out, which are described in reports by Burns and Tereshatov.

Table 1. Bombardments and amount of astatine-211 produced in each bombardment in the past year. The irradiations shaded blue occurred with the target 10 degrees from the beam, and the green rows occurred with the target at 80 degrees from the beam.

Irradiations	Highest Instantaneous Beam Current (pμA)	Average Beam Current (pμA)	Irradiation Length (h)	At-211 Activity at EoB (mCi)
June 2020	4.5	2.1 (Unstable)	9.4	8.0 ± 1.3
August 2020	2.6	2.4	9.6	21 ± 2
September 2020	7.4	5.1	7.3	22 ± 2
October 2020	5	4 .0	7.9	12 ± 1
November 2020	7.2	4.2	9.7	24 ± 2
December 2020	6.8	4.8	13.6	47 ± 5*

To investigate the uniformity of the beam at the target position, a segmented Faraday Cup-Viewer was assembled. The body is made of 3D-printed plastic, with 37 brass screws arranged at regular intervals, as shown in the right of Fig. 1. Each of these screws acts as a small Faraday Cup, from which beam current can be read via a LabView program, as shown on the left in Figure 1. The body of the viewer was coated with adhesive and CdS, which caused it to phosphoresce in the presence of beam (right of Fig. 1). This gives a much more detailed view of where the beam is situated on the target. A more uniform beam on the target should lead to fewer melted targets.

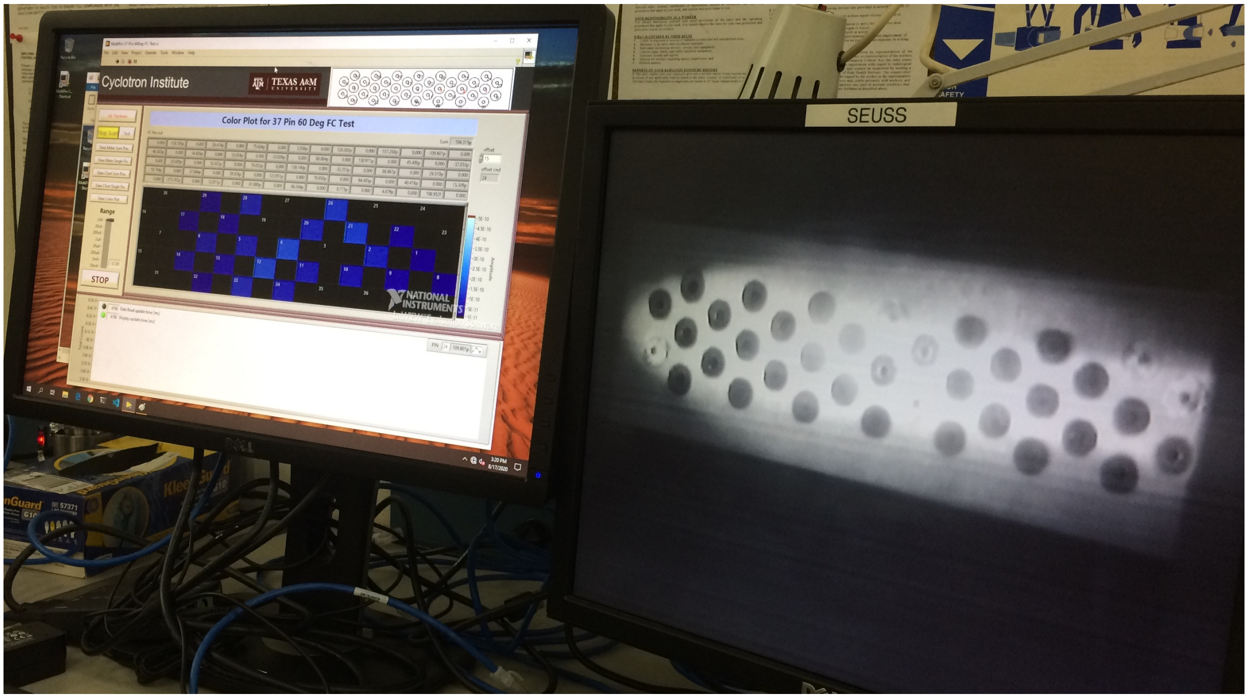

Fig. 1. Photograph of Segmented Faraday Cup-Viewer (SFCV) being used to tune the alpha beam. The SFCV is 3D printed, with 37 screws which are wired to read the beam current at each disparate position across the target position. The surface has material adhered to it which phosphoresces in the presence of the beam. On the right is a video feed of the SFCV with alpha beam on the target position. On the left is the LabView program reading in the beam current off of each of the disparate screws.

Another innovation was electrically isolating the target mounting structure from the rest of the beamline, so that the beam current can be read directly off the target throughout the entire overnight irradiation. This means other Faraday Cups do not need to be dropped in to know how much beam is being delivered to the bismuth target during the irradiation. The resulting beam on target from the December 2020 run is shown in Fig. 2.

Another new aspect of the isotope production set upwas focused on the safety of those who remove the target from the beamline post-irradiation. Astatine-211 is known to be able to volatilize, particularly if the bismuth target melts during the irradiation. To determine whether this has occurred with any given target, the Air Handling Monitoring System depicted in Fig. 3 was developed. The top of the system attaches to the target chamber. A pump is attached to the bottom of the system, as shown. A fiberglass filter to catch At-211 can be inserted and removed below the silicon detector, as shown. If there is astatine in the air, the silicon will show a characteristic alpha energy, which will alert the team that it is unsafe to open the chamber at this time. As a double-check, the filter can be removed and counted by a radiation probe, to see whether or not it is clean.

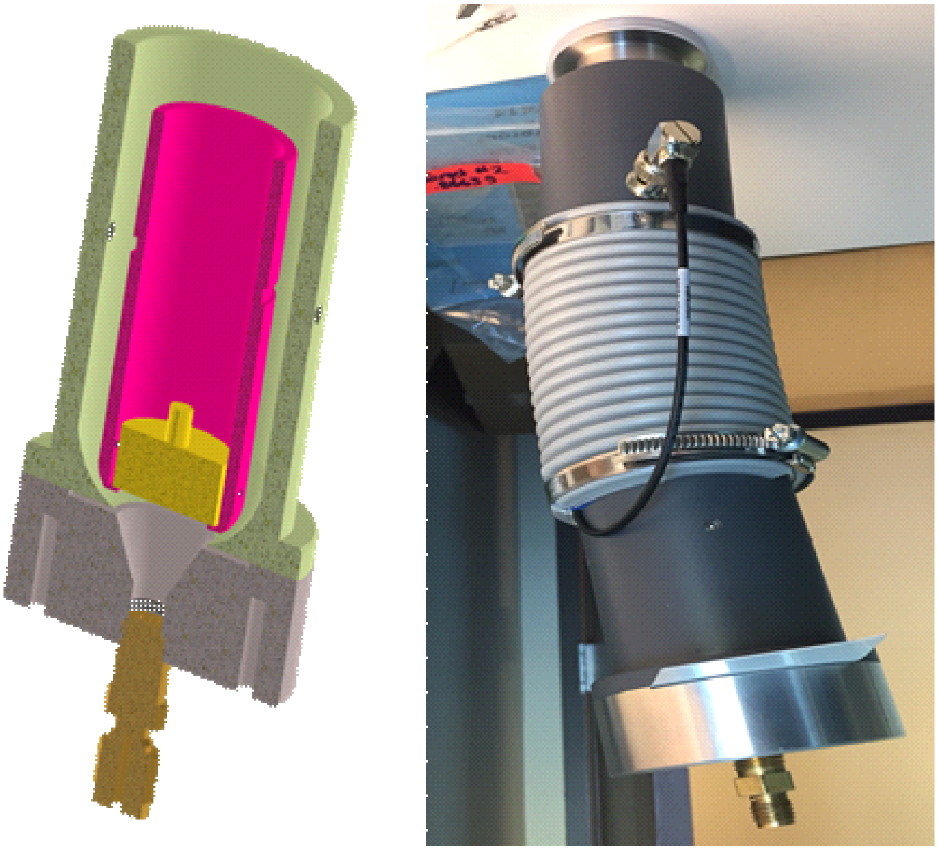

Fig. 2. Air Handling Monitoring System. Left panel shows a cutaway of the system, where air from the isotope production chamber enters from the top and flows around the pink cylinder, pulled by a pump attached to the gold nozzle. The yellow cylinder indicates the presence of a silicon PIPS detector which detects alpha particles emitted from isotopes caught by the fiberglass filter (not depicted here). Right panel shows a photograph of the actual device. The white card is the fiberglass filter.

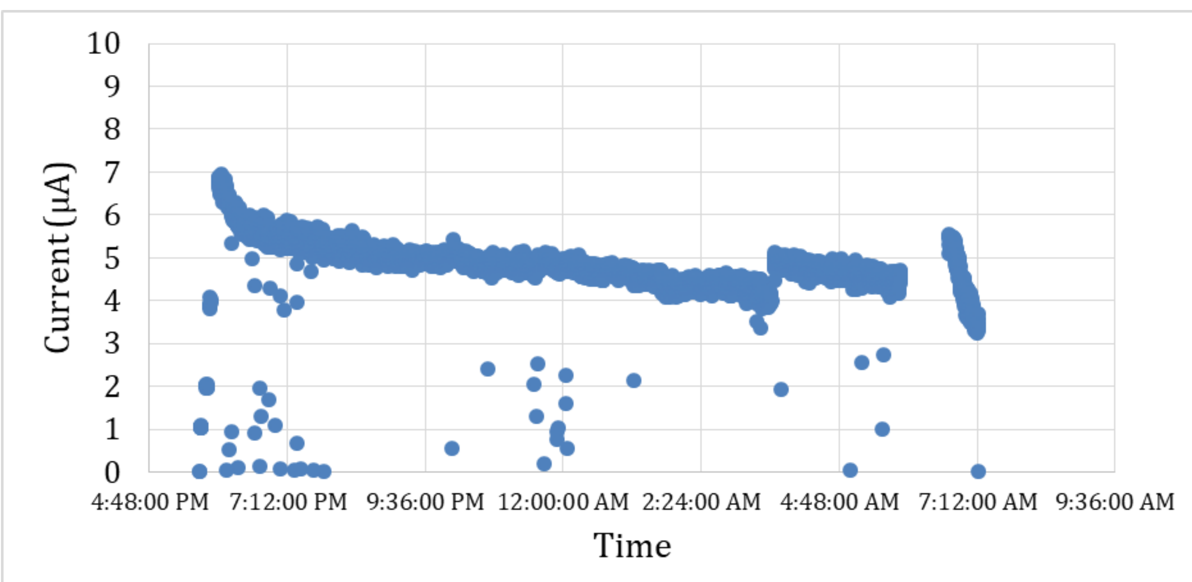

Fig. 3. Integrated alpha beam current on targetduring the overnight irradiation, December 2020.

Two High Purity Germanium (HPGe) detectors are used to measure the hundreds of liquid samples that are produced during the separation chemistry. A spectrum of one sample containing astatine-211 is shown in Fig. 4. 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.

The astatine-211 team plans to build on this success and continue to expand our collaborations within TAMU and outside of the University in the next year.

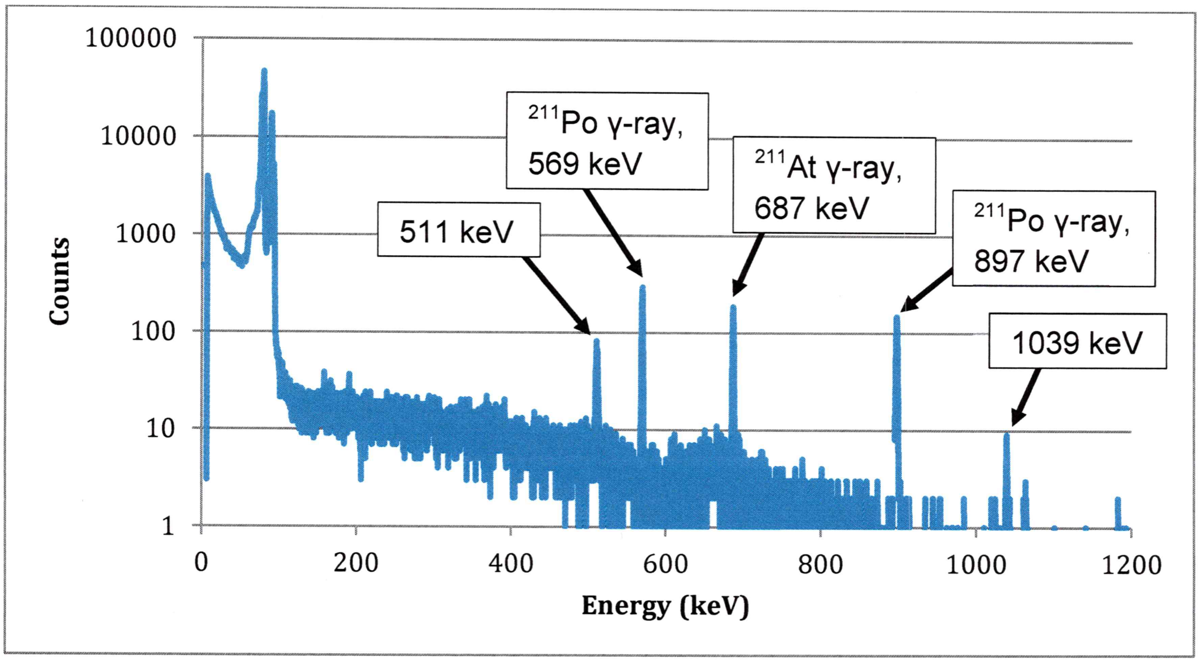

Fig. 4. HPGe spectrum of an aliquot of target dissolved solution, containing the characteristic gamma-rays from astatine-211 and its decay daughter polonium-211. The gamma-rays at 511 and 1039 keV are contributed to by gallium-66.

[1] J. Elgqvist, S. Frost, J. Pouget, and P. Albertsson, Frontiers in Oncology **3**, 1 (2014).

[2] M.R. Zalutsky and M. Pruszynski, Current Radiopharmaceuticals **4**, 177 (2011).

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