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FIRST PRODUCTION OF ASTATINE-211 AT CROCKER NUCLEAR LABORATORY AT UC DAVIS*

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Abstract

There is a great deal of interest in the medical community in the use of the alpha-emitter ^{211}At as a therapeutic isotope. Among other things, its 7.2 hour half life is long enough to allow for recovery and labeling, but short enough to avoid long term activity in patients. Unfortunately, the only practical technique for its production is to bombard a ^{209}Bi target with a 29 MeV alpha beam, so it is not accessible to commercial isotope production facilities, which all use fixed energy proton beams. The US Department of Energy is therefore supporting the development of a "University Isotope Network" (UIN) to satisfy this need. As part of this effort, we have developed an ^{211}At production facility using the variable-energy, multi-species cyclotron at Crocker Nuclear Lab the University of California, Davis. This effort relies on a beam probe which has been modified to serve as an internal ^{209}Bi target, to avoid problems with alpha particle extraction efficiency. We have recently performed the first production and recovery run, in which we recovered on the order of 50 μCi of ^{211}At in solution. Now that production has been demonstrated, we plan to increase capacity to 10s of mCi per run for use in local research.

INTRODUCTION

The detailed motivation for this project was discussed IPAC19 [1], but it is summarized here for completeness.

Radionuclides are an important component of medical diagnosis and therapy. Broadly speaking, they fall into two categories: positron (β^+) emitters to be used for PET scans and α or β emitters to be used for treatment. α emitters are particularly attractive for treatment, because all of the energy is deposited in close proximity to the update site. In this context, there has recently been a great deal of interest in ^{211}At as a therapeutic α-emitter. Unfortunately, sources of ^{211}At are limited, because the only practical method that has been demonstrated for production is to bombard a ^{209}Bi target with α particles of roughly 29 MeV kinetic energy to produce ^{211}At through the reaction

$$^{209}\mathrm{Bi}(\alpha, 2\mathrm{n})^{211}\mathrm{At}$$

Most medical isotope production facilities rely on either nuclear reactors or proton accelerators, with low energy (10-40 MeV) proton cyclotrons being the most common commercial production tool. Such cyclotrons are designed to accelerate only protons to a fixed energy, as designing them for variable energy and/or multiple species acceleration would increase the cost and complexity, threatening their commercial viability. Thus, they are unable to produce the α beam necessary to create ^{211}At.

We have been funded to develop the capability to produce ^{211}At at the Crocker Nuclear Laboratory cyclotron at the University of California Davis [2]. This is a research cyclotron built in the mid-1960s, which can accelerate protons, deuterons, helions ($3He^{++}$), or alpha particles to variable energies, with a maximum energy of 67 MeV for protons.

EXPERIMENTAL TECHNIQUE

An excellent overview of ^{211}At production can be found in reference [3]. Its production cross section is a strong function of the energy of the α beam incident on the ^{209}Bi; however, care must also be taken to avoid the the production of ^{210}At, because that decays to ^{210}Po, which poses a serious health risk. The production rates for both are shown in Fig. 1 (See Figs. 2.3.2 and 2.4.3 in [4]). We see that while the production rate for ^{211}At peaks at about 31 MeV, that is above the turn-on threshold for ^{210}At, so we will plan to use a beam of about 28-29 MeV, a point at which production is still significant.

UC Davis is uniquely positioned to provide such a service. The Crocker Nuclear Cyclotron has been used to produce isotopes in the the past [5], and has demonstrated the currents required. Figure 2 shows the layout of the cyclotron. Extracted beam goes through a switch magnet, where it can be directed to one of 7 beam lines. Three of these are internal to the cyclotron vault and four go to three external caves, as shown in. The external lines are limited to 100 nA for radiation safety reasons, while currents can go to at least 100 μA inside the vault.

Historically, isotopes were produced in “line 0", as indicated in the figure; however, while high currents have been demonstrated in the cyclotron, the efficiency of extraction is

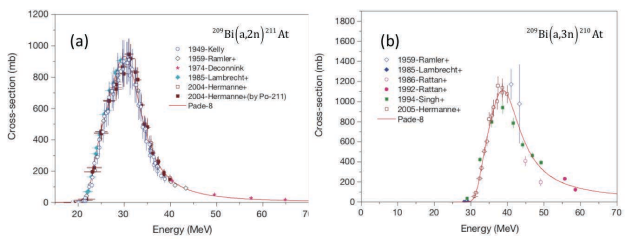

Figure 1: Production cross-section as a function of beam energy for (a) ^{209}Bi(α,2n)^{211}At and (b) ^{209}Bi(α,3n)^{210}At. (Cyclotron Produced Radionuclides: Physical Characteristics and Production Methods, Technical Reports Series Number 468, International Atomic Energy Agency: Vienna, 2009, pp. 33-40 with permission from the IAEA)

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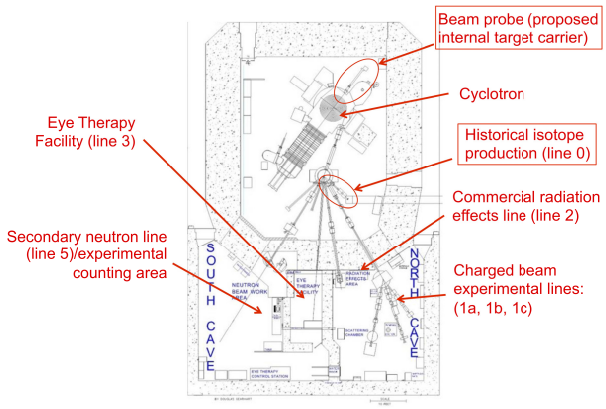

Figure 2: Layout of the Crocker Cyclotron, showing the internal lines, as well as the three external experimental areas. Current in the external caves is limited to 100 nA, while in principle, up to 1 mA could be run in the cyclotron vault itself. The decommissioned historical isotope production line is highlighted, as is the retractable beam probe that will be used for the new target.

rather low, particularly for α particles, for which it can be as low as 15%. Therefore, to achieve the maximum α flux on target and to minimize the unwanted loss and activation in the vault, we will be pursuing the development of an internal target for our ^{211}At production, thereby restricting most the activation to the target itself and the interior of the cyclotron.

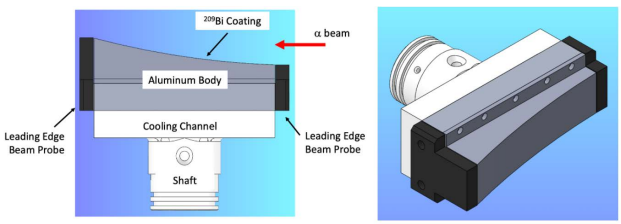

Figure 3: Target design. Beam is incident on the bismuth coated target aluminum target, which has been machined to match the orbit shape. The target assembly and the upstream and downstream beam probes are all electrically isolated and monitored.

The use of an internal ^{209}Bi target for ^{211}At production has been well established at Duke University [6] and elsewhere, and our plan is to leverage their experience as much as possible. One key difference is that Duke university uses separate probe and target insertions, but the design of our cyclotron will not allow this. We have therefore designed a hybrid probe/target assembly, which can be swapped in place of our usual target. This task is made significantly easier by the fact that the probe assembly already has an "airlock", to allow the probe to be removed without breaking the vacuum of the machine.

During ^{211}At production, it serves as both the beam probe and the production target. To get the best targeting efficiency, we want the target to be at the largest possible radius. We determined that the optimum configuration is to configure the cyclotron for 35 MeV α extraction and then position the probe at a radius corresponding to an energy of roughly 29 MeV, to be well away from the ^{210}At threshold.

The design is shown in Fig. 3. An aluminum target has been machined such that the final turn will uniformly deposit beam, to prevent sputtering. In operation, current is measured from the target itself, as well as leading and trailing beam probes. The preliminary curvature was determined based on beam studies and calculations, then it was refined after beam tests with a blank (uncoated) target, with the goal of maximizing the beam on the target and balancing the beam on the leading and trailing probes. The target body is attached to a copper cooling channel with bolts and an o-ring to esablish the water seal.

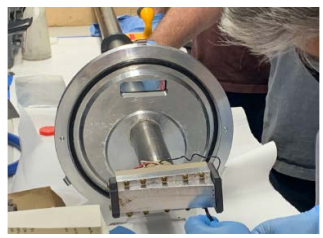

Figure 4: A target that has been coated with ^{209}Bi and attached to the probe shaft. Note the sealing flange that will mate to the airlock.

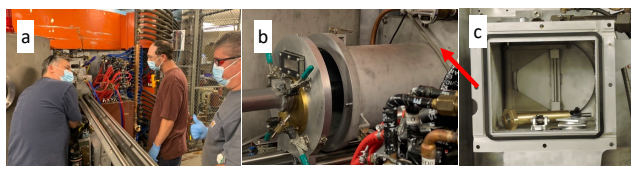

Figure 5: Target installation. The installation of the target and shaft is shown in (a), (b) shows the flange just before sealing, and (c) shows the details of the inner "airlock" flap with the outer flange removed.

The aluminum target is coated with molten ^{209}Bi with a wire brush, to a depth of roughly 50 µm. The target is then attached to the cooling channel, which is already attached to the probe shaft, and the electrical connections are made. Figure 4 show a target that has been prepared, mounted and is ready for installation. Figure 5 show the details of the target and probe shaft installation. This process is reversed to remove the target at the end of exposure.

PRODUCTION RUN

The hardware needed for production has been ready for some time, but our original schedule was significantly delayed by the Covid-19 pandemic and by technical difficulties with the cyclotron. We were finally able to get a period of dedicated running at the end of March, 2022. We used the first day to run with an uncoated target to verify that the beam distribution was acceptable, and then did a full initial production run on March 27, with the beam configured for 29 MeV on target, as described.

We exposed the target to the beam current of roughly 2.5 µA for a little over three hours, for a total beam on target of 8.4 µAh.

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TARGET REMOVAL AND ASTATATINE RECOVERY

One attractive aspect of this reaction is that there are negligible amounts of undesirable γ and β emitting isotopes produced that would necessitate complex handling procedures.

After exposure, the probe assembly was removed from the cyclotron. The target was removed and carried by hand to the processing area, which is nearby in the same building.

Two techniques have been successfully used to separate ^{211}At from ^{209}Bi target following exposure: "dry distillation" [7] and "wet distillation" [8]. Both have advantages and disadvantages, and ultimately we would like to explore both; however for our initial run, we chose to focus on wet distillation.

Figure 6: Recovered ^{211}At from our first production run.

The details are in the reference, but the approximate procedure is:

1. Immerse the coated face of the target in nitric acid to fully dissolve both the astatine and the bismuth.
2. Boil away the liquid to leave a combined astatine/bismuth salt.
3. Disolve the salt in hydrocloric acid
4. Add diisopropyl ether (DIPE), which cases the ^{211}At and ^{209}Bi to separate, with the latter floating to the top.
5. Pipette out the lighter ^{211}At containing solution into a scintillation flask.

Figure 6 shows our first recovered ^{211}At solution.

RECOVERY ESTIMATE

We assayed the recovered ^{211}At sample using an EG&G Ortec high purity germanium (HPGe) detector. which we calibrated using a ^{152}Eu source. To get as accurate a measurement of our initial production as possible, we did a "destructive" assay by measuring the spectrum of the sample for several half lives to get maximum statistics. This allowed us to use not only the decaying 687 keV ^{211}At line, but also the 568 keV and 1063 keV lines from the long-lived ^{207}Bi daughter product, they appeared. The final spectrum is shown in Fig. 7. In the future, we will use these reading to calibrate a dose calibrator, for fast measurement.

The analysis is ongoing, and there are still inconsistencies, but our initial estimate is that we recovered 42 µCi.

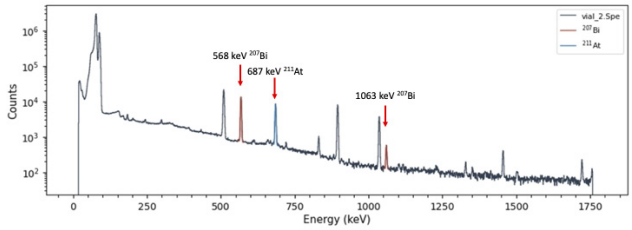

Figure 7: The HPGe spectrum used to determine the amount of ^{211}At recovered in our initial run. The estimate was based on both ^{211}At peaks and peaks from the long lived daughter isotope ^{207}Bi, as indicated in the figure.

STATUS AND PLANS

This initial production run satisfied the goals of our scope of work, but questions remain. Referring to our original proposal, our ultimate goal estimated that we could recover 60 mCi of ^{211}At after 800 µAh of exposure. Scaling this to 8 µAh, we see that our recovery appears to be about a factor of ten too low, even correcting for the extended processing time. We need to understand this discrepancy.

In addition to increasing the efficiency of the recovery, we will need to work to increase the current on target, with the combined goal of being able to produce at least 10 mCi of ^{211}At in solution.

Once we have achieved this, we plan to seek out those on campus and in the surrounding area who are interested in carrying out research using ^{211}At.

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