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DEVELOPMENT OF ASTATINE-211 PRODUCTION IN THE CROCKER NUCLEAR LABORATORY CYCLOTRON

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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. Our prposoal is to retrofit the variable-energy, multi-species cyclotron at the Crocker Nuclear Laboratory at the University of California Davis with an internal ^{209}Bi, such that we can put at least 100 μA of 29 MeV alpha particles on target without concerns about extraction efficiency. Using very conservative assumptions, we are confident we will be able to produce 60 mCi of ^{211}At in solution in an eight hour shift, which includes setup, exposure, and chemical recovery. This poster will cover the design of the target, as well as the required chemical processing and reliability upgrades.

INTRODUCTION

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

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

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.

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We are proposing the development of the capability to produce ^{211}At at the Crocker Nuclear Laboratory cyclotron at the University of California Davis [1]. 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 [2]. 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 Figure 1 [3]. 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.

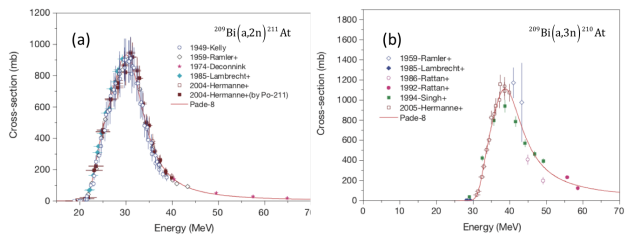

Figure 1: Production cross-section as a function of beam energy for (a) ^{209}Bi(α,2n)^{211}At and (b) ^{209}Bi(α,3n)^{210}At. (Cyclotron Produced Radionuclides: Physical Characteristics and Production Methods, Technical Reports Series Number 468, International Atomic Energy Agency: Vienna, 2009, pp.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

UC Davis is uniquely positioned to provide such a service. The Crocker Nuclear Cyclotron has been used to produce isotopes in the the past [4], 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 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

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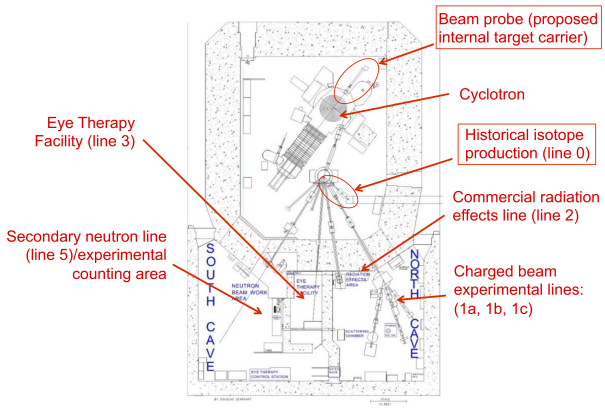

Figure 2: Layout of the Crocker Cyclotron, showing the internal lines, as well as the three external experimental areas. Current in the external caves is limited to 100 nA, while in principle, up to 1 mA could be run in the cyclotron vault itself. The decommissioned historical isotope production line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

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.

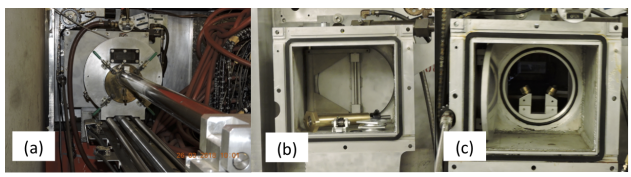

Figure 3: Retractable probe assembly. The complete assembly is shown in (a), including the screw drive. In (b), the probe and outer flange have been removed to show the inner "airlock" hatch. This hatch is shown open in (c).

The cyclotron has a retractable probe, used to tune the adjust trim coils as the beam evolves to larger radii. Figure 3(a) shows the probe assembly, including the screw drive used to retract the probe. Our plan is to develop an alternate probe that will incorporate our internal target.

Our 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. This is shown in 3(b) and 3(c). The external flange is designed to allow the removal of a probe for which the head is larger than the probe shaft. It's envisioned that this airlock will accommodate our target assembly with no modifications whatsoever.

The use of an internal ^{209}Bi target for ^{211}At production has been well established at Duke University [5] and elsewhere, and our plan is to leverage their experience as much as possible. Figure 4 shows a schematic view of the target, based on the Duke design. An aluminum carrier plate has a relieved channel, into which the ^{209}Bi is introduced by melting it. The channel will be machined to match the curvature of the beam, and a thin layer of bismuth will be

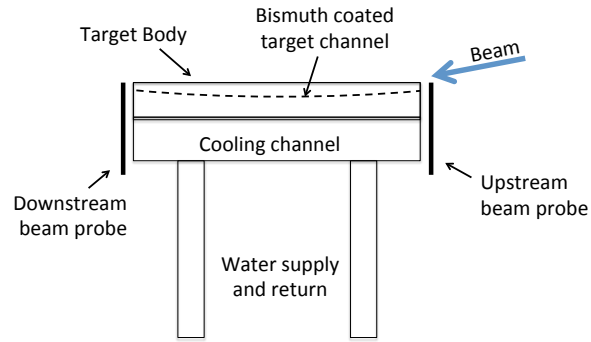

Figure 4: Schematic illustration of the target. Beam is incident on the bismuth coated target channel, which has been machined to match the orbit shape. The target assembly and the upstream and downstream beam probes are all electrically isolated and monitored. The currents induced on them by the beam will be used for targeting and alignment.

melted and applied. The target body will be held to a copper cooling channel by means of a clamp, and an o-ring will establish the water seal. Beam probes at the upstream and downstream ends of the target will be used for alignment. The target assembly itself will also be electrically isolated and read out.

This target assembly will be bolted onto a water cooling fixture, and the aluminum will have cooling channels to aid in the heat transfer.

We are designing approximately a 10 mrad range of adjustment into the head itself, implemented with a pivot point, bellows, and a push rod linkage to correctly align the target with the incident beam. An integrated design will allow the assembly to serve as both the target and the beam probe. During astatine production, we will use the target itself as the beam probe, and when we are not producing astatine, we will load a blank target to seal the water channel, and extent the leading edge carbon probe to act as the beam probe. This approach will eliminate possible problems with repeatability that might occur if we switched probe heads between astatine production and normal operation.

Operational Considerations

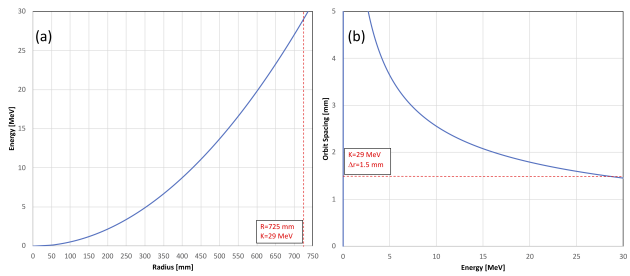

Figure 5: (a) shows beam energy vs radius for the machine configured to extract at 30 MeV. In this configuration, the beam is at 29 MeV approximately 22 mm inside of the extraction radius. The orbit separation is shown in (b) and is about 1.5 mm at K=29 MeV.

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To simplify the targeting of the beam, it's advantageous to have the cyclotron orbits spaced as far apart as possible. This achieved by configuring the cyclotron to extract α particles at an energy slightly above the desired 29 MeV energy, and then placing the target just inside this radius, at a point corresponding to 29 MeV, such that the beam will hit the target before getting to the extraction septum. There is an established cyclotron configuration for 30 MeV α particles, which will use as the basis of our operational model. Figure 5(a) shows the energy vs. radius curve for this configuration. The 30 MeV beam is normally extracted at 736.6 mm (29"). If we set the target about 22 mm further in, it will intercept 29 MeV beam. As shown in Figure 5(b), the orbital spacing at this radius is about 1.5 mm, which should allow for a clean separation of orbits.

Accelerator performance is very repeatable, but it will be very important to establish the absolute energy scale to insure that we remain below the production threshold for ^{210}At. This will be done by performing a series of runs with different radial positions, and then assaying the relative amounts of ^{211}At and ^{210}At, using a Ge detector. We will use the 687.8 keV and 897.8 keV γ-rays to identify the ^{211}At and the 245.3 keV and 1181.4 keV γ-rays to identify the ^{210}At, as described in [6]. Once a maximum safe radius is determined, a safety interlock position switch will be implemented during production, such that we cannot target beam at radii beyond that.

Target Handling and ^{211}At Extraction Processing

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. At both the Duke and University of Washington facilities, the exposed target is extracted by hand and placed in a lightly shielded container for transport to the processing area. We intend to do the same.

Two techniques have been successfully used to separate ^{211}At from ^{209}Bi target following exposure. Both have advantages and disadvantages, and it is our intention to investigate them both, as well to investigate other potential methods of separation.

Dry Distillation This is a well established technique that has been used for over 20 years [7]. After irradiation, the target is heated to at least 600 C, causing the ^{211}At to evaporate. The heated chamber is flushed with Argonne to drive the vaporized astatine through a tube that is immersed in chilled methanol. The astatine is then eluted from the tube with a solvent such as methanol. Recovery yields of well over 70% have been observed with this technique, and recovery yields of over 50% are considered typical.

The main advantage of this technique is its extreme simplicity. One disadvantage is that while very high recovery yields have been demonstrated, there are some issues with yield consistency in routine operation. There are also some concerns over the safety of a procedure that involves astatine in a volatile state.

Wet Chemistry In response to some of the issues with the dry-distillation technique, researchers at the University of Washington have developed a wet-chemistry technique that involves multiple steps [8]. Consistent recovery levels of over 60% were achieved over multiple runs, and this has now replaced dry distillation as the standard method of extraction at University of Washington.

The advantage of this technique is the elimination of the volatile ^{211}At and a claimed improvement in the consistency of ^{211}At recovery yield when compared to the dry distillation method. The disadvantage is that is significantly more complicated than the former method, requiring a higher level of training for the technicians performing the process.

Production Estimates

For 29 MeV α particles, in-target production rates of ^{211}At in excess of 1 mCi/(μA·hr) have been demonstrated at several facilities [6]; however, there will likely be some targeting inefficiencies for our configuration, particularly in early operation. We will conservatively assume that 50% of the beam hits the ^{209}Bi target and use .5 mCi/(μA·hr) as our working number. This is consistent with production observed at the Duke facility, on which our target is based. If we set as our goal for standard operation to produce one dose per eight hour shift, then if we assume the following:

- Install target and establish beam: 1 hour
- Exposure: 5 hours
- Extract target and separate ^{211}At: 2 hours

we get 1.6 mCi/μA at the end of the shift, including the decay during processing. Beam currents in excess of 100 μA have been demonstrated in the cyclotron, so we will use this current as our reference, corresponding to 160 mCi in target for a full shift. Extraction efficiencies of > 50% have routinely been demonstrated [5] [8], but we will conservatively assume 40%, giving 64 mCi of extracted ^{211}At.

We therefore set as our initial goal 60mCi of extracted ^{211}At as a maximum standard single shift production dose. Expanding to two shifts with the same setup and processing times increases this number to 120mCi, which we will set as our maximum deliverable dose during initial operation.

STATUS AND PLANS

This project was recently recommended for funding under the US Department of Energy's University Isotope Network program. Over the next two years, we plan to design, build, and commission the internal target, and to demonstrate ^{211}At recovery using existing lab facilities at UC Davis. Once this capability has been established, we plan to ramp up to full production.

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