Natural bismuth target production and characterization to produce astatine-211

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Targeted alpha therapy (TAT) is an emerging field in cancer treatment research due to the ability to directly target cancer cells while minimizing damage to surrounding healthy cells. Several radioisotopes have been identified as showing great promise for this research. Astatine-211 is a promising candidate because of its simple alpha decay chain and short 7.2-hour half-life, ideal for biological systems. It is primarily produced via the ^{209}Bi(α,2n)^{211}At reaction using a 28.8 MeV alpha beam [1]. Keeping the bismuth target intact poses one of the greatest challenges for astatine production. Bismuth has a relatively low melting point—only 270°C—which means the energy deposited by the beam can melt the target during irradiation [1]. This melting process alters the geometry of the irradiated bismuth (reducing total astatine production) and can cause the astatine to volatilized. To prevent melting of the bismuth targets, we have made significant advancements in the cooling of the bismuth target during irradiation by removing interfaces between the chilled water and the target. The current design uses a single jet, chilled water system flowing directly on the back of the target frame. Additionally, many efforts are being made to produce the optimal targets for irradiation and subsequently characterize them for integrity and impurities.

Bismuth targets are produced in-house by astatine production facilities and are made by a variety of facility-dependent methods. In an effort to develop a target-making procedure compatible with our

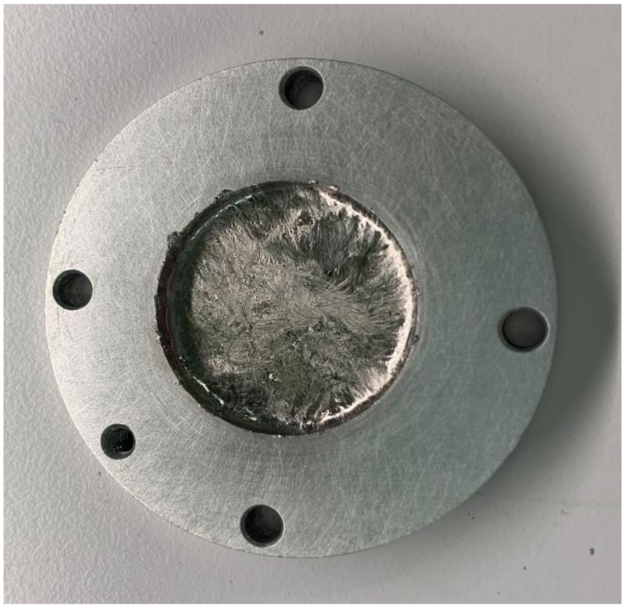

Fig. 1. Bismuth target produced by melting bismuth pellets into the aluminum frame at 310°C and spread with a ceramic spatula to evenly cover the surface. This is a thicker target, with a mass of 2.425 g of bismuth and an average thickness of 625 microns. This target was not used for irradiation.

facility, bismuth was molten into a solder pot (initially containing flux to aid in the melting. The flux was eventually discontinued due to potential impurities) and then pressed into the target frame with a machine press. Additional bismuth was removed through machining the surface of the target. While the use of a solder pot to melt bismuth and the use of the machine press to flatten the targets is still being explored, alternate methods based on procedures in use at other programs were also attempted.

In accordance with the procedure used at the University of Washington [2], another target-making process involved the melting of bismuth metal on a thin aluminum target frame on a hot plate. The bismuth is then spread evenly around the frame using a ceramic spatula (completed target shown in Fig. 1).

Another method attempted was adapted from the procedure used at the University of Pennsylvania [3], in which a heated block is pressed onto the molten bismuth to spread it into the target frame on the hot plate, rather than spread with a ceramic spatula. This method resulted in very uneven targets with a bismuth oxide crystalline surface when it was attempted at our facility (shown in Fig. 2).

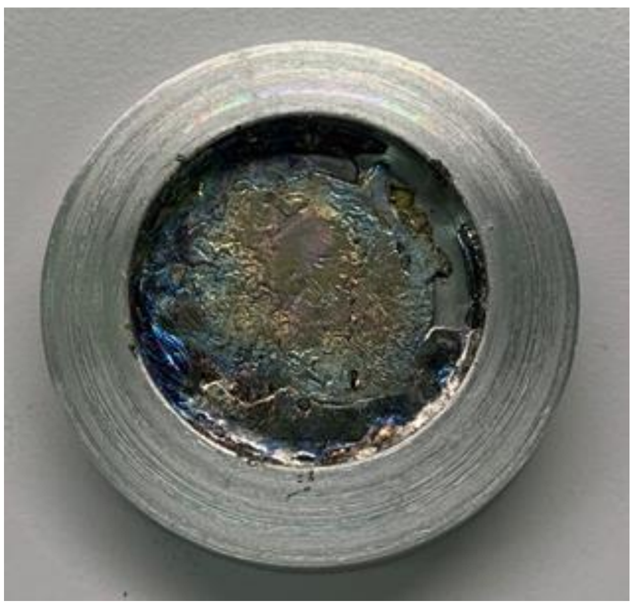

Fig. 2. Bismuth target produced by melting bismuth pellets into the aluminum frame at 310°C and pressed with a heated stainless-steel weight with aluminum foil in between the weight and melted bismuth. The weight and foil were removed while the target was still hot, to prevent adhesion to the surface. The bismuth did not spread fully over the surface, and a colorful bismuth oxide crystalline layer formed on the surface. The total mass of bismuth is 2.649 g, with an average thickness of 210 microns. This target was not used for irradiation.

To increase the surface interaction and conductivity between the bismuth and aluminum interface, an ultrasonic soldering iron (S-Bonder SB-9210, *S-Bond Technologies, LLC, Hatfield, PA 19440*) was used in addition to the hot plate. This method resulted in a noticeably stronger adhesion of the bismuth to the aluminum surface and allowed thinner targets, on the order of 50-100 microns, to be produced (shown in Fig. 3). Since the alpha particles only have enough energy to produce astatine in the first 70 μm of the bismuth, targets thicker than this are absorbing the alpha energy as heat, further contributing to melting. The thinner targets produced by the ultrasonic soldering iron show promise for maximum production as well as decreased melting due to the strong bismuth-aluminum interface and 70 μm target depth.

Fig. 3. Bismuth target produced by melting bismuth pellets on a hot plate at 300°C and spreading the bismuth using an ultrasonic soldering iron. The surface is mostly smooth with some ridges and valleys. It has a mass of 0.258 g of bismuth and an average thickness of 66 microns. This target was not used for irradiation.

The presence of air bubbles and holes throughout the bismuth targets is another potential initiator of the melting process, as they can create hot pockets within the target when irradiated. Additionally, the presence of any impurities with lower melting points may also lead to melting of the target. To identify some of these imperfections, characterization of the targets via scanning electron microscopy coupled with energy dispersive x-ray spectroscopy (SEM-EDS) was performed. Figures 4a and 4b show some of the topographical imperfections in the target surface taken via SEM imaging. These images demonstrate the variability in the target surface within the same target. A subsequent EDS analysis indicates primarily the presence of oxygen, carbon, bismuth, and aluminum on the target. The most important of these elements is oxygen, which could indicate the presence of bismuth or aluminum oxide within the target. This oxide is particularly unwanted due to the nuclear reaction of oxygen with the alpha particles, resulting in the production of fluorine-18. These oxide impurities will likely be reduced through the use of the ultrasonic soldering iron.

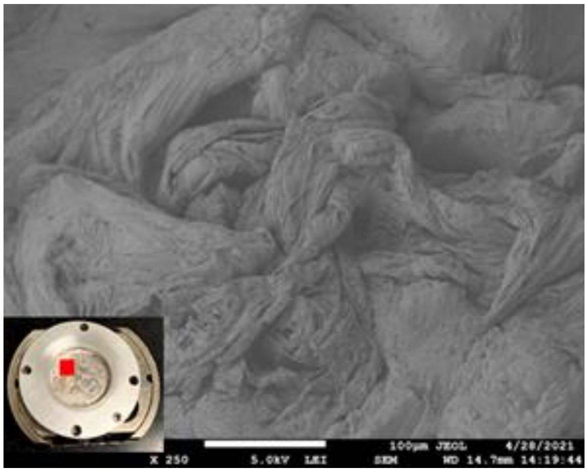

Fig. 4a. SEM image of part of the surface of a target produced by the spatula spreading method. The ridges and nonuniformities in the target surface from spatula spreading can be seen clearly.

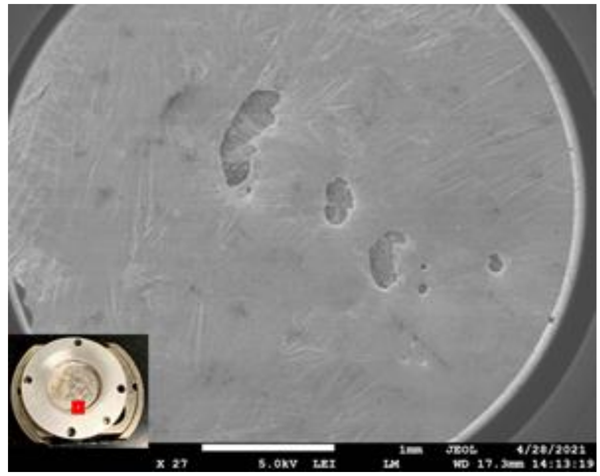

Fig. 4b. SEM image of another part of the surface of the same target produced by the spatula spreading method. A clear image of holes in the target surface that cannot be seen with visual inspection.

Many advancements in target production and characterization have been made to increase the total production of astatine-211. To combat the melting of bismuth targets, many improvements to the cooling and the integrity of the targets have already been made. The targets and the production process are continually being studied and optimized to forward the isotope production capabilities of the Cyclotron Institute.

[1] M.R. Zalutsky and M. Pruszynski, Curr. Radiopharm. **4**, 177 (2011).
[2] K. Gagnon *et al.*, J. Labelled Compd. Radiopharm. **55**, 436 (2012).
[3] University of Pennsylvania, personal communication.

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