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Accelerator Production of Mo-99 Using Mo-100*

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Abstract

Tc-99 m is an essential radionuclide for nearly 40,000 diagnostic nuclear medicine tests in the U.S. each day. Its daily production depends on Mo-99, which must be replenished weekly due to Mo-99's 2.75-day half-life. Mo-99, in the past, was supplied from uranium fission production, depending on overseas nuclear reactors that average 50 years old. Their age in combination with shipment uncertainties make the availability of Mo-99 fragile and subject to severe shortages. The U.S. now has one domestic, FDA-approved supplier that produces Mo-99, NorthStar Medical Radioisotopes. Currently, NorthStar produces Mo-99 via the irradiation of Mo-98 in a nuclear reactor. In the future, NorthStar will also irradiate Mo-100 with accelerator created x-rays to produce Mo-99. This process will use 2 distinct, 40 MeV, 125 kW average electron accelerators, Rhodotrons produced by IBA. Accelerator produced Mo-99 has several advantages over that produced by reactors, including a dual supply and an ability to adjust irradiation timing to meet radiopharmacy demands, such as Sunday delivery. NorthStar is currently installing and commissioning this accelerator based system, entering production in late-2022.

INTRODUCTION

NorthStar Medical Radioisotopes (NMR), with the support of the NNSA and several national laboratories, including ANL, LANL, ORNL, and PNNL, has been working to develop an accelerator based method to produce Mo-99. This method utilizes the Mo-100(γ,n)Mo-99 reaction. An accelerator produces a high energy electron beam, which is then used to create the x- rays needed to convert the Mo-100 into Mo-99 via neutron knock off. A proof-of-concept of this process was performed at ANL [1], and developments [2] needed for this proof-of-concept were used as the basis for NMR's production designs, which are further detailed below.

NorthStar Medical Radioisotopes is a commercial-stage nuclear medicine company that develops, produces and manufactures reliable and environmentally-friendly diagnostic and therapeutic radiopharmaceuticals. Its first FDA-approved diagnostic imaging product is technetium-99m (Tc-99m), which is used in 40,000 patient imaging studies per day in the United States as standard of care to assess extent and severity of heart disease and cancer. Tc-99m is generated by NorthStar's novel RadioGenix® System (technetium Tc-99m generator) which uses U.S.-produced, non-uranium based molybdenum-99 (Mo-99) as its source material.

PRODUCTION PROCESS DESIGN

NMR's production process is centered around two key pieces of enabling technology, the targetry and the accelerators, which when combined with unique supporting equipment creates a reliable, industrial-scale, medical radioisotope production process. The general layout of the production space is shown in Fig. 1.

Targetry and Irradiation Concept

The first piece of enabling technology is the target. NMR's target consists of a cylindrical stack of isotopically enriched Mo-100 disks, which are separated via spacers. These disks are manufactured to very tight tolerances by pressing and sintering Mo-100 powder, a process which was developed primarily at ORNL [3], and undergo inspection prior to use to ensure compatibility both with process and FDA requirements. In this target design, the Mo-100 disks serve both as the target, as well as the Bremsstrahlung converters, which create the needed x- rays.

The unique target is designed for two sided irradiation, which generates a symmetric and smooth x-ray flux profile. This symmetry more effectively uses all target material to improve total and specific activities of Mo-99 when compared to a single sided irradiation.

Accelerators and Beam Transport

The next piece of enabling technology was the development of an electron accelerator capable of enough power and energy to produce Mo-99 at satisfactory rates. With requirements input from NMR, Ion Beam Applications (IBA) Industrial developed a first-of-its-kind industrial accelerator capable of meeting the intense demands of efficient Mo-100 production.

IBA's accelerator is of their Rhodotron design [4], and is specifically based on the IBA TT300, which is a 10 MeV, 245 kW design. To meet NMR's needs, IBA developed the TT300-HE, shown in Fig. 2, which is a 40 MeV, 125 kW average power design, as further described in Table 1. NMR's production process uses two of these accelerators to simultaneously irradiate both sides of the target.

IBA also developed the beam transport system, which connects each accelerator with the target. As seen in Fig. 1, each beamline has an effective bend of 90°. This bend allows for the required two-sided irradiation of the target, while simultaneously reducing the exposure of each accelerator to the radiation produced at the target by the other. This bend is accomplished via a series of dipoles which combine to form an achromatic system, ensuring that all of the electron beam hits the target at the same position. Upon exiting the accelerator, the beam is first manipulated to the acceptance of the achromatic bending magnets, and after this bend, the beam is shaped and focused at the target.

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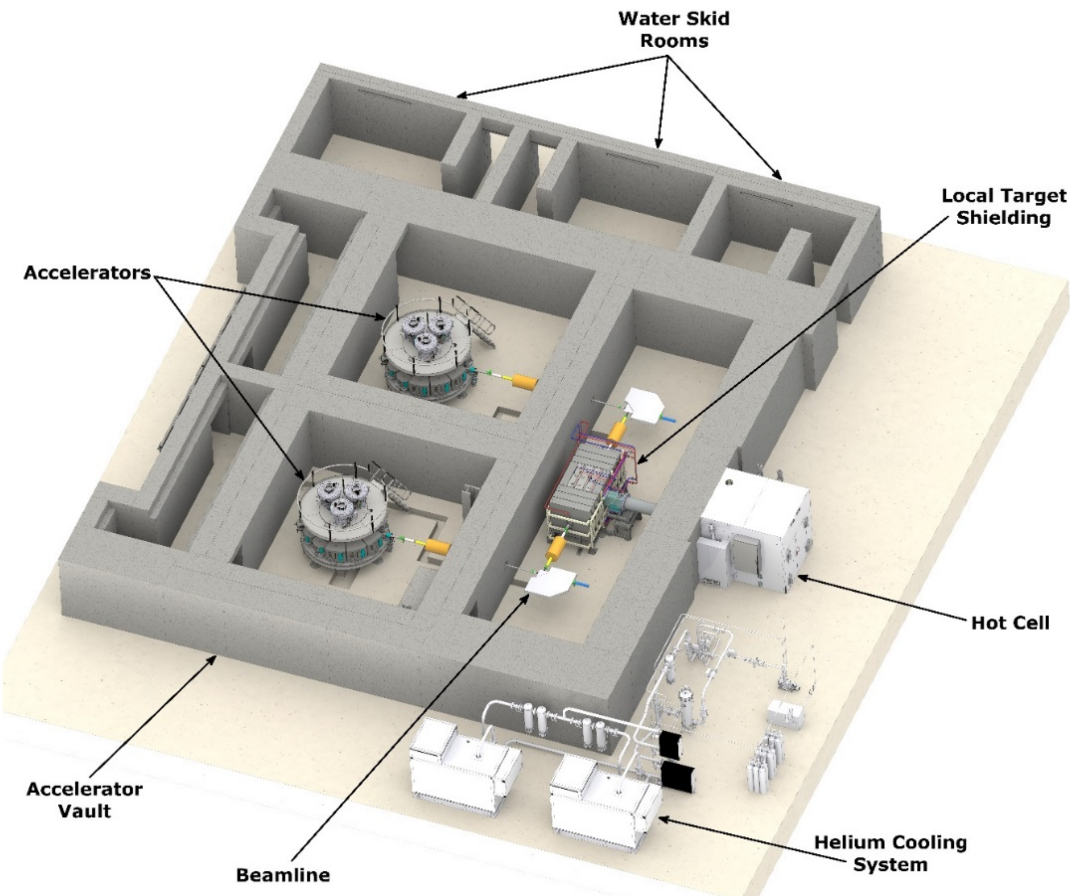

Figure 1: Rendering of the process space of NMR's irradiation facility that will use accelerators to produce Mo-99.

Table 1: Accelerator Specifications

Manufacturer	IBA Industrial
Accelerator Type	Rhodotron
Model	TT300-HE
Energy	40 MeV
Power	125 kW average (each)
Duty Factor	12.5%
Pulse Frequency	50 Hz

Figure 2: Rendering of IBA's TT-300HE Rhodotron electron accelerator.

Radiation Safety

NMR designed the radiation shielding of the production process to ensure maximum reliability and availability of its Mo-99 supply to radiopharmacies. As shown in Fig. 1, each accelerator is located within its own vault, and both of these vaults are separated from the target vault. This separation allows for the maintenance of one accelerator to occur during the operation of the other accelerator. Each vault also has its own separate area, known as a water skid room, which is used to house the needed cooling water. This water will be activated during operation, and as with the larger main vaults, this room separation allows for smoother maintenance operations. These vaults are all constructed with high-density concrete blocks.

In addition to the main vaults, the production system also utilizes shielding precisely placed around the target. This Local Target Shielding (LTS) serves as a primary radiation barrier for the target, which allows for reduced thickness of the target vault walls and prolongs the lifetime of equipment within the target vault be reducing dose rates. The LTS (shown as part of Fig. 3), is a modular design, to again ease maintenance. Two types of modules are used, with one type composed of steel plates separated by concrete, with the other type composed of a mix of steel balls and water. Both of these designs serves as effective shields of neutrons and x-rays, and the steel/water mix modules also remove heat from the LTS.

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Target Manipulation

For simplicity and ease of maintenance, NMR inserts the target into the irradiation zone using a push/pull chain, which is housed in a hot cell on the far side of target vault wall. All moving parts of the chain are easily accessible from the hot cell. The chain is removed from the target during irradiation, and plugs are inserted between the target and hot cell to shield radiation. The spatial relationship between the hot cell, target vault wall, and LTS is shown in Fig. 3.

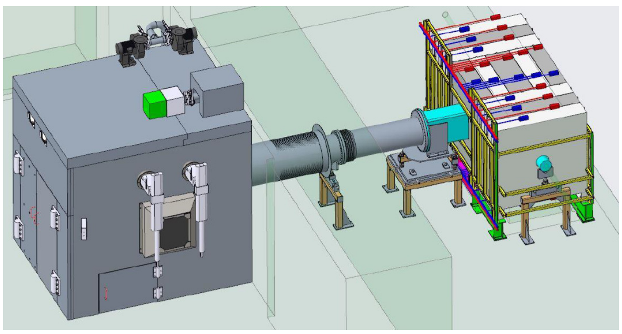

Figure 3: Rendering of NMR's target manipulation system, showing the hot cell joining with the (LTS).

FACILITIES

Accelerator Irradiation

NMR's accelerator irradiation facility was designed around the production process, with an emphasis on ensuring the stability of NMR's Mo-99 supply. The facility is located in close proximity to a power substation, and has access to redundant power utilities. In addition, all HVAC, chilled water, and other secondary utilities were also designed with redundancies.

Isotope Processing

While NMR's accelerator Mo-99 is created within the irradiation facility, before being transferred to its Isotope Processing Facility. In this facility, the solid Mo target disks are processed in hot cells, via steps such as dissolution and filling of the source vessels. After the disks are processed, NMR fills source vessels [5] which are then shipped to radiopharmacies for use on the *RadioGenix System*.

PROJECT STATUS

Production Process

The construction of the accelerator and target vaults, as well as the water skid rooms, have been completed.

The accelerators successfully passed initial testing at IBA's factory before they were shipped to NMR's facility. Both accelerators have been rigged into their respective vaults, and the first accelerator (shown in Fig. 4) is currently being installed.

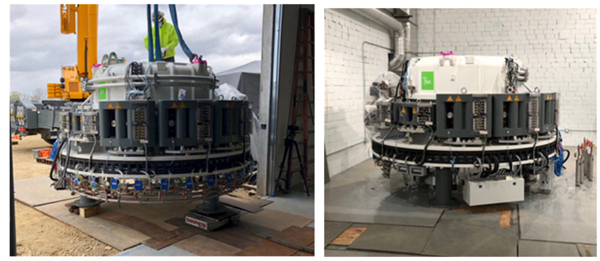

Figure 4: The first accelerator during (left) and after (right) rigging into its vault.

The hot cell and LTS are in final design, and fabrication is in progress. In addition, the design of the helium cooling system was completed and the system is being installed in the irradiation facility.

Accelerator Irradiation Facility

As shown in Fig. 5, the construction of the Irradiation facility is almost complete. The facility has obtained occupancy, and has begun commissioning process utilities.

Figure 5: NMR's Accelerator Irradiation Facility.

CONCLUSION

NorthStar continues to successfully drive towards its goal of supplying accelerator produced Mo-99 to U.S. radiopharmacies. Using support from the NNSA, IBA, and other vendors, NorthStar has nearly finished all process design, and is currently on schedule to supply Mo-99 by the end of 2022.

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