Direct Production of ^{99m}Tc via ^{100}Mo(p,2n) on Small Medical Cyclotrons

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1. Introduction

Technetium-99m (^{99m}Tc) continues to be the most widely used radioisotope in nuclear medical imaging today[1], with over 30,000 scans performed with this isotope in the United States each day and global consumption exceeding 40 million scans per year [2]. ^{99m}Tc is typically obtained from the in situ decay of ^{99}Mo on a ^{99}Mo/^{99m}Tc generator, which contains high specific activity ^{99}Mo embedded onto a small alumina column [3]. Daily extraction of [^{99m}Tc]TcO_4^- from generators has come to define community expectations of availability and workflow when dealing with ^{99m}Tc-based radiopharmaceuticals.

The parent isotope, ^{99}Mo is currently produced in nuclear reactors by the fission and recovery of ^{99}Mo from ^{235}U. However, the fragility of ^{99}Mo supply has recently come to light during recent shutdowns at two leading production sites [4]. These shutdowns were at times exacerbated by co-current shutdowns of both the NRU and HFR reactors in Canada and the Netherlands. Furthermore, the Canadian NRU reactor, which supplies 35%–40% of the global demand of ^{99}Mo, will terminate its isotope production service in 2016 [5]. Other reactors supplying ^{99}Mo are typically more than 40 years old and are at risk of prolonged or permanent shutdown in the near future, creating a risk for loss of a long-term, stable supply of ^{99}Mo for medical purposes [6].

By leveraging the existing infrastructure of legacy research reactors, the fission of enriched ^{235}U has long been a cost-effective approach to produce large quantities of high-specific-activity ^{99}Mo. However, the cost of building new nuclear reactors for isotope production is extremely high and when coupled to a requirement of full cost recovery on radioisotope production [7-,8,9], future prices of reactor-sourced ^{99}Mo are estimated to rise dramatically [8]. This price increase will be compounded by the effects of a shift from highly enriched uranium (HEU) to low enriched uranium (LEU) targets for ^{99}Mo production [7].

Aside from the adaptation of using LEU (i.e. ^{235}U content <20%) in existing reactors, the recent supply disruptions have prompted several governments to fund the development of alternative methods for the production of ^{99}Mo or the direct production of ^{99m}Tc itself. Fission-based alternatives include the Aqueous Homogenous Solution Reactor concept [10], and the Target Fuel Isotope Reactor concept [11]. Neutron activation methods include the irradiation of enriched ^{98}Mo targets in research [4,12], or power reactors [13]; while accelerator-based production methods [14] of both ^{99}Mo and ^{99m}Tc include ^{238}U photofission [15,16], phototransmutation of ^{100}Mo via the ^{100}Mo(γ,n)^{99}Mo channel [17,18] or the direct production of ^{99m}Tc via the ^{100}Mo(p,2n) transformation [19,20].

In 1971, Beaver and Hupf [19] first reported the direct production of ^{99m}Tc from both natural and enriched ^{100}Mo powder and foil targets. Yields were determined using low level irradiations on stacked Mo foils (13 disks, 0.003 in thick, 79 mg/cm^2) with 22 MeV protons over 0.0061 μA·hr and substantiated

with 97.42% enriched Al-encapsulated ^{100}Mo powder irradiations at 15.2, 20.2 and 21.4 MeV over $4.6x10^{-4}$ to $2.96x10^{-2}$ µA.hr. Extrapolating these results, the authors suggest a 400 µA, 25 MeV irradiation should produce 14 Ci/hr of ^{99m}Tc and 750 mCi/hr of ^{99}Mo. However, given the availability of ^{99}Mo, there was little motivation to explore this production option further, and much of the work done over the past 4 decades has been limited to several groups [21-,22,23,24,25,26] revisiting and refining the cross sectional probability of the ^{100}Mo(p,x) transformation, followed eventually by the development of practical [27] and large-scale cyclotron production methods [28] upon initiation by the Canadian federal government.

There are currently over 950 small medical cyclotrons manufactured by several companies (ACSI, GE, IBA, Siemens, Sumitomo, Best, etc.) installed around the world. Approximately 550 of these machines operate above 16 MeV and are capable of producing appreciable quantities of ^{99m}Tc. The distribution of these cyclotrons by manufacturers is shown in Figure 1.

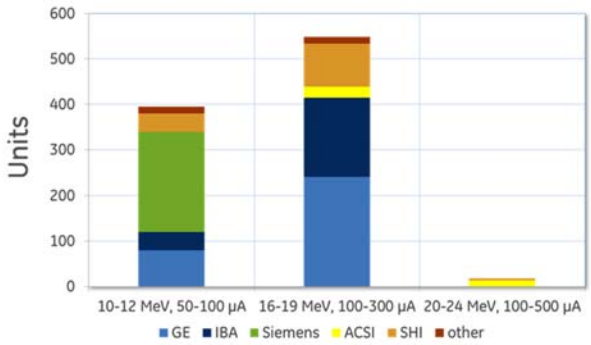

Figure 1 - Estimated PET cyclotron numbers by manufacturers (with data from ACSI, GE, IBA and Siemens, Sumitomo data estimated)

GE is presently the market leader in small medical PET cyclotrons with an installed base of more than 320 cyclotrons worldwide as seen in Figure 2. GE offers the PETtrace 800 (Figure 3) and MINItrace (PETtrace 700) series of machines, with a new, smaller unit under development, the PETtrace 600. About 250 of these installed machines are PETtrace 800 series cyclotrons operating at 16.5 MeV protons. Here we report our results in implementing a complete solution for the direct production of ^{99m}Tc on the GE PETtrace cyclotron. For the purpose of the present work, we will discuss technology developed only for those machines with a final proton energy greater than 16.5 MeV. For the PETtrace 800, the maximum accelerated beam intensity of up to 130 µA.

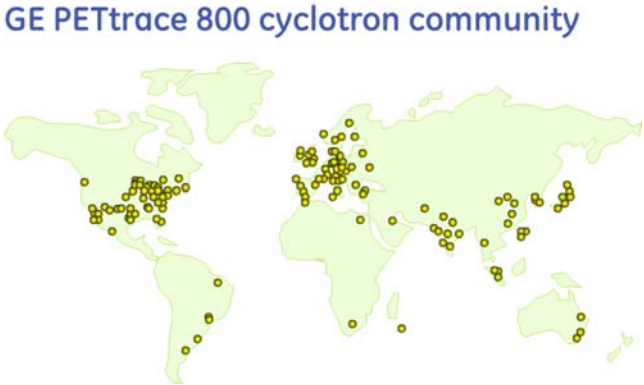

Figure 2 - GE PETtrace 800 series cyclotrons worldwide distribution

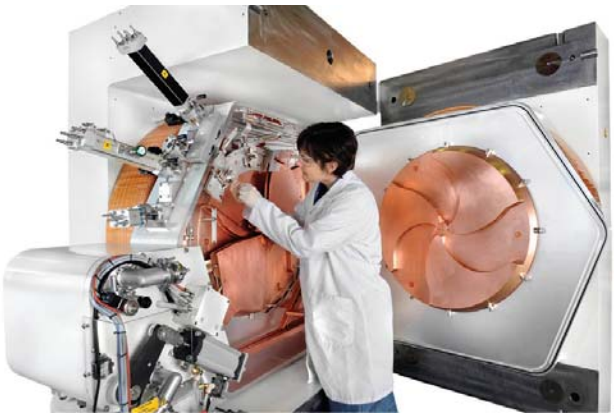

Figure 3 - GE PETtrace 800 cyclotron

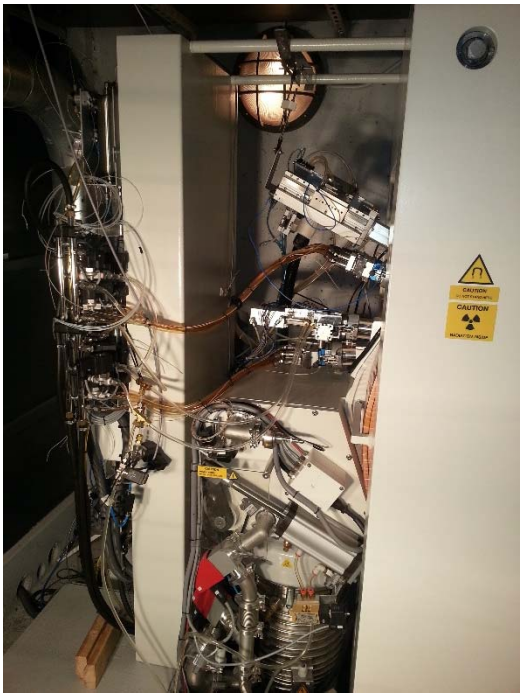

Figure 4 – ^{100}Mo target assembly as installed on beam port 2 of a GE PETtrace cyclotron. Services panel is shown to the left of the cyclotron beam ports.

2. Experimental

a. Cyclotron System – PETtrace 880

All irradiations were performed using either a self-shielded (Lawson Health Research Institute, London, ON) or a vaulted (Centre for Probe Development and Commercialization, Hamilton, ON) GE PETtrace cyclotron, both of which had been upgraded to enable 130 µA beam current onto a single target. Each machine has 6 beam ports, capable of simultaneous irradiation (with a sum total of 130 µA) to 2 target stations. A self-shielded machine maintains a configuration of shielding units that can be moved to enable access to the cyclotron system itself. A vaulted machine maintains an identical core

cyclotron configuration including target stations and services but is housed and shielded in a concrete vault.

b. Target System Design

A combination of the proximity of the target services panel (see **Figure 4**), the convoluted transfer path and the limited target cave capacity in the self-shielded machine mandated a solid target system that minimized the size of all components [29]. A target of minimum length was designed with an aluminum target holder, capable of accommodating a ø 28 mm target plate which had mounted to it a ø 17 mm enriched ^{100}Mo disk brazed to the backing as described elsewhere (Figure 5, [30]). Prior to irradiation, the capsule and target disk were assembled manually and placed in a holder designed into the mechanical target transfer drive [31]. The capsule was then delivered through the transfer line to the target station at the cyclotron. After irradiation, the targets were retracted with the same tape drive to the hotcell for dissolution and purification.

Figure 5 - Pressed-Sintered and Brazed Mo-Cu Target Disc for GE PETtrace Cyclotron

c. Target Disk Preparation

As we report elsewhere [30], enriched ^{100}Mo targets were prepared following conventional press & sinter methodology. ^{100}Mo powder was obtained commercially from Isoflex (San Francisco, USA) in various enrichments. A green pellet was produced by compacting approximately 1.5 g of this powder using a cylindrical tool of 20 mm diameter and hydraulic press (Across International, Livingston, USA). A pressure between 25 kN/cm^2 and 250 kN/cm^2 was applied for 0.5 min after which the green pellet was sintered in a reducing atmosphere (Ar/2% H_2) at 1,700 ^{o}C for five hours. The resulting ^{100}Mo plates have 90-95% of the bulk density of molybdenum. The ^{100}Mo plate was then furnace brazed at 750 ^{o}C onto a backing manufactured from a dispersion strengthened copper composite (e.g. Glidcop AL-15) using a high temperature silver-copper brazing filler (Johnson Matthey, Royston UK). This process yields a unique, mechanically and thermally robust target system for high beam power irradiation.

d. Target Irradiations

Targets were irradiated at 100 μA for 15 minutes and 130 μA for 30 minutes and visually inspected after each irradiation. Subsequent irradiations were performed at 130 μA for 2 hours and 6 hours. Beam current was brought up over a few minutes. In all cases irradiations proceeded uneventfully with no vacuum changes or cyclotron instabilities.

e. Target Dissolution and Purification Process

^{99m}Tc was isolated from irradiated targets, while mounted in the target capsule, by placing the capsule on a custom aluminum dissolution chamber in a hot cell (Comecer). Co-dissolution of the ^{100}Mo/^{99m}Tc mixture was accomplished using 40 mL of 30% H_2O_2 pumped through the dissolution chamber at ~1 ml/min while the chamber was heated to ~95°C. The dissolved target solution was then transferred to a vessel containing 8 g of NaOH in 10 mL of distilled, deionized H_2O and thoroughly mixed prior to transfer to the automated purification module (Trasis MiniAiO, Ans, Belgium). Na$^{99m}TcO_4$ was isolated using a solid-phase extraction procedure previously published by our group [28,32]. Briefly, a 4 M NaOH solution containing $^{99m}TcO_4$ and $^{100}MoO_4$ was transferred at a rate of 2 mL/min through a cartridge containing 500 mg of Chemmatrix resin (PCAS Biomatrix, PQ, Canada). The Tc radioactivity was immobilized on the resin while ^{100}Mo and other non-Tc radionuclidic impurities were diverted to a waste-recovery vessel for future recycling. After loading, the resin was washed using 10 mL of 4 M NaOH which was added to the same waste-recovery vessel. The resin was readily eluted with water (2 mL/min) through a Dionex On-Guard II H cartridge (Sunnyvale, USA) and onto a second-stage basic alumina

(Waters) column. A purification efficiency of 78 ± 8 % (n=3) was determined by comparing the radioactivity in the product vial to the inventory of radioactivity in the waste vials and remaining on the cartridges and filters.

3. Results and Discussion

The GE PETtrace cyclotron represents the largest installed cyclotron base in the world today (Figure 1). With an on-target proton energy of ~16.5 MeV, we hypothesized that this machine could produce an appreciable quantity of ^{99m}Tc with the proper configuration. One critical requirement is the development of high current (130 μA) solid target hardware, also capable of withstanding high power density (< 1.2 kW/cm^2 average) over an extended period of time. Our team has overcome several challenges en route to establishing a simple, reliable production route for Ci-quantity production of ^{99m}Tc. Such an approach amounts to decentralized production in which a number of cyclotron centres would work together to provide ^{99m}Tc as part of a network of distribution sites. This model has precedence in how ^{18}F is produced and distributed to various PET centres today. Such as paradigm could form an appreciable component of the future ^{99m}Tc isotope production landscape, especially in light of the upcoming cessation of ^{99}Mo production at the Chalk River reactor in 2016 [15].

a. Target plate preparation

One of our key challenges was to develop a high power density target, capable of withstanding multi-hour, high current irradiations at the kW power level. Mo metal has a high melting temperature (>2600°C), but without adequate heat transfer and cooling, this temperature could easily be achieved during irradiation, potentiating premature activity mobilization, or worse, catastrophic target failure. In addition, such a high melting temperature, when coupled to the reactivity with oxygen at relatively low temperatures (~440°C), lead to a formidable challenge in target manufacture. We explored electroplating [33] and sugar-composite [34] (ref.), and more recently electrophoretic deposition (EPD) [28], while others have looked at thermocompression bonding to aluminum [35]. Our past success with EPD enabled 240 μA irradiations at 18 MeV albeit with an average power density of 0.3 kW/cm^2, achieved by having the target oriented at 10° relative to the incident beam. When we attempted EPD deposited targets for the GE PETtrace, we discovered that despite the lower power (16.5 MeV, 130 μA), the orthogonal orientation and higher power density caused the thicker, porous Mo layer to fail, as was evident within minutes of irradiation at beam currents as low as 40-60 μA (Figure 6). To mitigate this issue, we developed the novel pressed, sintered, and brazed (PSB) target system reported here.

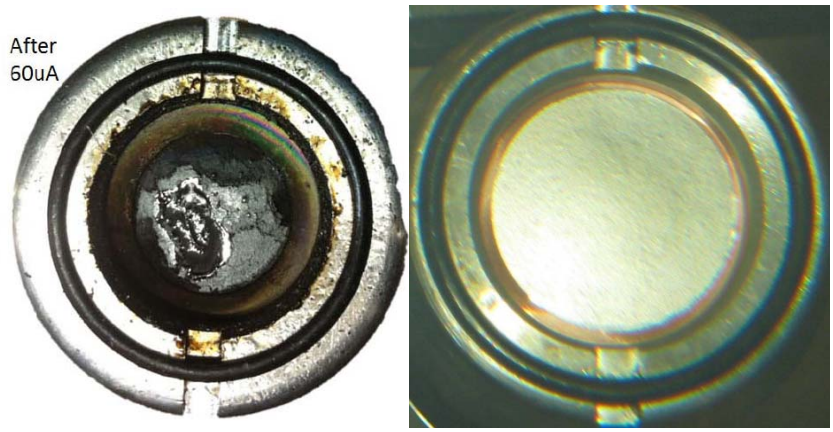

Figure 6 - Targets manufactured using EPD (left) and PSB (right) methods. The target on the left was irradiated for less than 1 hour at 60 uA while the target on the right at maximum current (130uA).

b. Target Irradiations

Up to 4.7 Ci of ^{99m}Tc have been produced on the GE PETtrace to date. The saturated production yield (2.7 GBq/μA), was consistent with calculated yields at 16.5 MeV and remained constant between 2 hour and 6 hour irradiations [24,36].

c. Target Dissolution

The dissolution rate of the molybdenum is controlled by the flow rate of peroxide over the face of the plate and by the temperature of the apparatus. By minimizing the volume of the apparatus the volume of peroxide in contact with the molybdenum is also minimized thus preventing the exothermic reaction from getting out of control. In our initial tests we recirculated the peroxide but found this process to be unstable as the molybdenum content in the peroxide reservoir occasionally caused the reservoir to overheat and expel material. In addition the peroxide concentration declined as the process continued so the dissolution rate of the molybdenum declined during the process. Withdrawing fresh peroxide from one reservoir and depositing the effluent of the dissolution chamber in a second reservoir resolved both of these issues.

The mass of molybdenum on the target plate is sufficient to stop the entire proton beam before it enters the copper backing in order to prevent the co-production of zinc isotopes. As such the complete dissolution of the molybdenum is not necessary to recover all the Tc radioactivity. We have found that it is advantageous to halt the dissolution process when approximately 25 mL of peroxide have been pumped through the dissolution chamber as this is sufficient to extract the Tc but minimizes the amount of copper that is dissolved from the target plate. We presently measure 1.06 ± 0.12 g (N=4) of material dissolved from the target plate. Excessive copper was seen to plug filters specifically added to the apparatus to prevent the copper from possibly plugging the downstream cartridges of the purification apparatus. Experiments with modifying the dissolution process to minimize the co-dissolution of the copper are currently underway and appear promising. A later processing step will likely be implemented to recover the remaining ^{100}Mo for recycling.

d. Pertechnetate Purification

The ^{99}Mo/^{99m}Tc generator contains high specific activity ^{99}Mo embedded onto an alumina column [3]. Daily extraction of [^{99m}Tc]TcO_4 is accomplished in a hospital and/or radiopharmacy setting by exploiting

the mobility differences between the $^{99}MoO_4^{2-}$ and $^{99m}TcO_4^-$ ions on alumina in isotonic saline. Selective chromatography defines the radionuclide generator concept and also largely defines the expectations of the nuclear medicine community when dealing with ^{99m}Tc-based radiopharmaceuticals. For this reason, we sought to tailor any alternative production and purification method of ^{99m}Tc to US Pharmacopeia (USP) standards for chemical, radiochemical and radionuclidic purity. But we also wanted enable access to ^{99m}Tc without requiring substantial infrastructure changes within the healthcare community. Alternative ^{99m}Tc purification methods have recently been reviewed [37].

We have tested several methods applicable to recovering ^{99m}Tc from a bulk level of Mo, most of which exploit the favorable free energy of hydration of TcO_4^- over other components of the target mixture [38]. Various resins are commercially available, including ABEC-2000™, AnaLig™ and more recently, Chemmatrix™ resins [39]. Using an automated column purification method, we were able to establish a high-efficiency, reliable separation with Chemmatrix as the first stage and an in-line SCX-basic alumina SepPak series as the second stage.

The entire pertechnetate purification process is readily amenable to meet good manufacturing practice (GMP) compliant production. This purification process is applicable for separation of Ci-quantities of sodium pertechnetate (Na[$^{99m}TcO_4$]) from any solution containing excess molybdate (MoO_4^{2-}) ions.

e. Radionuclidic Purity Analysis

Cyclotron production of ^{99m}Tc will result in the concomitant production of minor Tc radioimpurities depending on the isotopic composition of the target material, proton beam energy and irradiation time [36]. Preliminary gamma spectroscopy experiments suggest that the technetium radionuclide content at end of bombardment is over 99.5% relative to all other technetium radioisotopes produced. In recognizing the importance of technetium impurities to Na$^{99m}TcO_4$ shelf-life and downstream kit formulation as well as patient dose, a thorough, quantitative radionuclidic anaylsis is currently underway and will be reported under separate cover.

4. Planned efforts to increase the accelerated beam intensity

The negative ions are generated in two internal cold cathode PIG type ion sources, as shown in Figure 7, and are accelerated to the final energy by RF high voltage. Extraction is performed using carbon stripper foils. As we saw in the previous section, to produce efficiently ^{99m}Tc directly by proton bombardment of solid ^{100}Mo metal target, we would need high intensity beams, preferably in the 16-19 MeV range. In order to increase the beam intensity, we would need more ions extracted from the ion source. This would require higher gas flow to the ion source. Because the ion sources are sitting in the center of the cyclotron vacuum tank, the gas introduced in the ion source will flood the vacuum tank and contribute to the collisional stripping of the negative ions. The extra electron on the H^- ion is bound only with 0.75 eV and it is easily lost in collisions with residual gas along the accelerating path. As soon as an electron is stripped in a collision, that particle becomes a neutral atom and the magnetic and electric fields will not act on it, effectively losing it to the vacuum vessel walls. This puts a limit in increasing the gas flow to the ion source; there is an optimum gas flow to maximize the accelerated beam intensity.

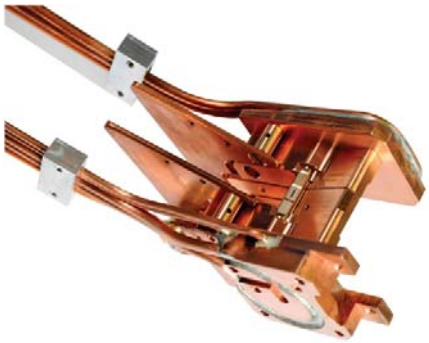

Figure 7 - Present dual PIG ion source of PETtrace 800 cyclotron for H- and D-.

One way to increase the accelerated beam intensity with an internal PIG ion source is to increase the usage efficiency of the ions extracted from the ion source. Our simulation studies [44] done for benchmarking the existing design in preparation for a more radical change described in the next section, showed that the present Central Region is far from being fully optimized. There is considerable loss on different CR components during the first accelerating turn. We anticipate that by giving up the dual beam capability and replacing the present larger twin PIG source with a H^- only source, similar to the one used in the MINItrace cyclotrons, as seen in Figure 8, will allow more room for the first turn, which – together with some other component redesign – will decrease greatly the first turn losses.

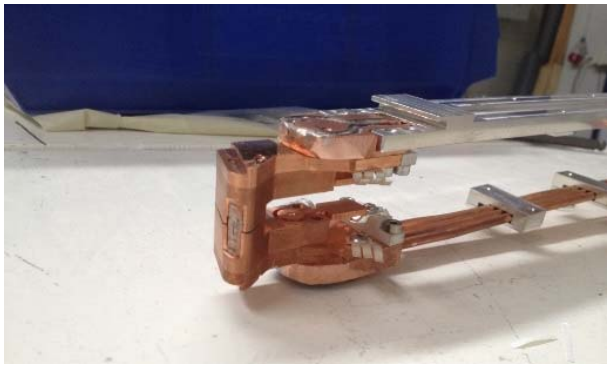

Figure 8 - MINItrace H- PIG ion source.

The other method to use the available ions from the PIG source more efficiently is to improve the ion extraction. Presently the extraction is done with an electrode which is at the variable dee electrode potential. This means that the sinusoidal changing extraction voltage [-38 kV to +38 kV] will extract H^- ions only half or the period, the negative voltages will extract protons from the plasma of the ion source. These protons are bent in the opposite direction and will not get accelerated by the dee electrodes. In the space charge limit, the extracted ion beam intensity is proportional with the extraction voltage at 3/2 power (Child-Langmuir law). Our simulations showed that only ions extracted ~+/-20 degrees around the maximum RF voltage value will make all the way to the extraction, as seen in Figure 9. If we can somehow enlarge this angular acceptance window, we can accelerate more ions extracted from the same plasma, in this way we can increase the accelerated beam intensity without increasing the gas fed in the PIG source. Alternatively, it would be possible to reduce the gas flow in the ion source and with more efficient use of the available extracted ions, still maintain the same final accelerated intensity at a lower background pressure. This would decrease the collisional stripping and the resulting activation of the cyclotron vacuum vessel.

Hudson et al. [40] invented an extraction system for the Oak Ridge National Laboratory ORIC cyclotron which accomplished exactly this goal. They placed an electrode biased at a DC high voltage (typically around 20 kV) between the PIG source exit slit and the RF puller electrode as seen in Figure 10. An added benefit of the DC biased intermediate electrode would be the creation of a potential hill for the extracted protons in the negative half of the RF voltage. In this way the back acceleration and bombardment of the exit slit of the PIG source chimney would be greatly diminished, contributing to the extension of the lifetime of the ion source.

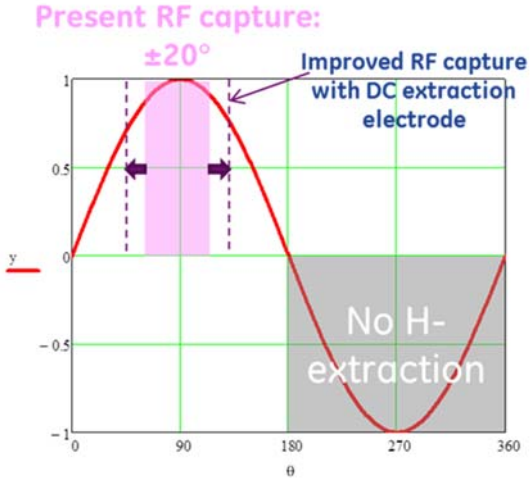

Figure 9 - Present and improved RF capture domain.

Besides the stripper foil wear, the ion source wear is the most common failure of an H^- cyclotron, which of course, can be prevented with well scheduled maintenance. However, increasing the period between maintenance shutdowns would be an important improvement for most of the PET cyclotron operators, reducing also the dose received by the service personnel. Engineering an extra electrode biased to +20 kV is not a trivial task; it will require detailed simulation work and possible redesign of the whole Central Region CR. By eliminating the D- ion source and associated deuterium gas line, it will be possible to use the freed gas feedthrough place on the cyclotron vacuum tank to use a HV feedthrough instead and bring in high voltage in a place where there is very little room for any added hardware.

It is anticipated that these hardware modifications will be part of an upgrade kit which can be installed in the cyclotrons already in service. This will allow the current GE cyclotron operators to increase their cyclotron output intensity to ~200 – 250 µA. We believe that this relatively small modification of the CR of the existing installed base cyclotrons will be a very attractive avenue for most of our users.

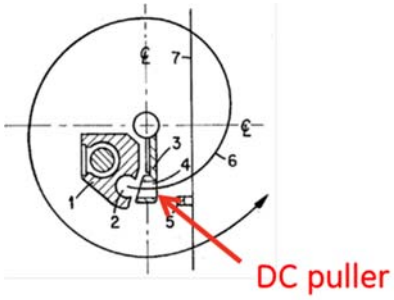

Figure 10 - Internal PIG ion source with DC biased puller electrode [40].

A much more radical approach is to remove the ion source from the cyclotron and to use an external H^- source with an associated Low Energy Beam Transport line and a spiral inflector. Such configurations are already offered by some of the commercial manufacturers, e.g., the TR19 and TR24 cyclotrons made by ACSI [41]. The external ion source is more common on larger cyclotrons, as the TR30 by ACSI, or Cyclone 70 by IBA [42] etc. which are used primarily for SPECT isotope production. The vast majority of the cyclotrons used for research are also equipped with external ion sources. Presently, the only PET cyclotrons in regular service equipped with external ion sources are made by ACSI and they are rated 300 µA [41]. Best Cyclotrons are advertising a 14 MeV PET cyclotron equipped with external ion source capable accelerating 400 µA [43], but to the authors' best knowledge, there are no such cyclotrons yet in service.

Our preliminary feasibility study based on charged particle trajectory simulations with the SNOP code developed in the Joint Institute for Nuclear Research, Dubnashowed et al. [44] calculate that it is possible to accelerate ~500 µA H^- beam in a modified version of the PETtrace 800 cyclotron using an external H^- ion source capable delivering 10 mA H^- beam at ~25-30 kV extraction voltage. The conceptual layout of the PETtrace 900 cyclotron is shown in Figure 11.

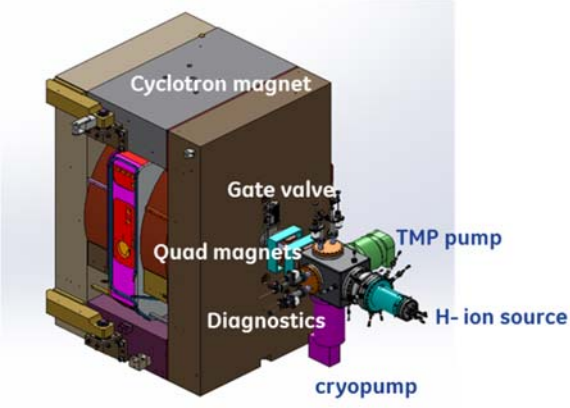

Figure 11 - Conceptual layout of the PETtrace 900 cyclotron equipped with an external H- ion source.

There are several types of external H^- ion sources examined for our purpose. The most mature design is the filament based volume cusp H^- ion source developed in TRIUMF many years ago by Kuo et al. [45]. This type of H^- ion source or some version of it is in use on the ACSI, IBA or Best Cyclotrons made machines, as well as the cyclotrons designed in CIAE in Beijing, China [46]. This ion source is commercially available from a Canadian accelerator company D-Pace [47]. GE designed such a filament based ion source, shown in Figure 12. The only drawback of this type of ion source is the limited lifetime of the filament (300 to 500 hours, depending on the ion source output). The LEBT being equipped with a gate valve between the ion source and the rest of the system, it is relatively straightforward operation to replace the filament, without venting the whole LEBT and cyclotron. The downtime associated with the filament replacement is estimated only to couple of hours needed to physically replace the back plate of the ion source with the fresh filament and to pump down the ion source volume.

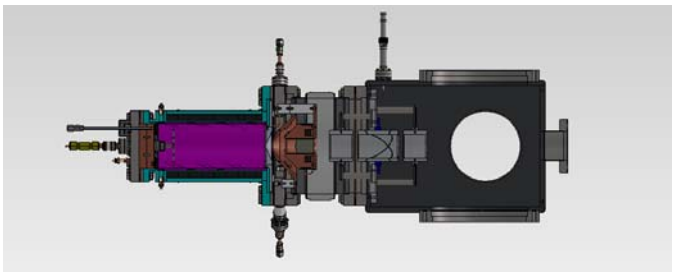

Figure 12 - Conceptual design of the GE filament based H- ion source and extraction electrode system.

Another attractive solution would be a microwave ECR H^- ion source, as described by Jayamanna et al. [48]. The source has been tested for H^- and achieved 2.1 mA at 0.25π mm mrad normalized emittance for 500 W of input power at a frequency of 2.45 GHz. The main advantage of this type of ion source is the lack of any consumable part, which theoretically makes this ion source infinite lifetime. With some further development work it seems reasonable to attain 5-10 mA intensity from such type of ion source, more than enough for a small medical cyclotron to accelerate ~500 μA beam.

The results of the LEBT beam transport simulation, spiral inflector design, CR modification, magnetic field optimization and beam orbit simulation inside the cyclotron will be presented elsewhere [49].

5. Conclusions

We have engineered and demonstrated the production of large quantities of ^{99m}Tc on GE PETtrace cyclotrons. These results demonstrate the feasibility of supplying a medium to large population base from a single cyclotron and that a network of such machines could provide a decentralized and redundant supply of Na[$^{99m}TcO_4$]. With some modifications of existing cyclotron infrastructure, this approach could be used to implement a highly decentralized medical isotope production model, eliminating the requirement for enriched uranium and radioactive waste associated with nuclear fission.

With improvements to the existing ion source, RF capture, etc. we anticipate yields of 7.3-9.1 Ci (270-337 GBq) per 6 hr run at 200-250 μA. By redesigning the PETtrace platform to support an external ion source and thus increasing current output to 500 μA, we anticipate single-run production quantities of up to 675 GBq (18.2 Ci) of ^{99m}Tc can be produced in 6 h. These yields would surpass production on a TR19 operated at 300 μA at 18 MeV [28]. Our target dissolution and ^{99m}Tc purification process was completed in approximately 75 min with average purification yields of 84%. Further optimization is possible to reduce the processing time and improve yields.

GE is committed to pursue the intensity upgrade of the PETtrace cyclotrons in the above mentioned two step approach. In this way it will enable its large installed base to upgrade their cyclotrons and be prepared for the direct production of ^{99m}Tc, as well as a new cyclotron with external ion source will be the first choice for an ultimate intensity PET cyclotron, capable also to produce ~20 Ci ^{99m}Tc in a 6 hours run with a 500 μA beam intensity. Increasing the ^{18}F production capability is also a strong motivator for many of our present and future customers, anticipating an increased demand for an ever increasing variety of different molecular imaging agents labelled with ^{18}F. Even at the present demand, reducing the necessary irradiation time with available increased intensity can change several operating business models, to the benefit of the customer and ultimately making the PET imaging modality more accessible to a larger segment of the population.

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