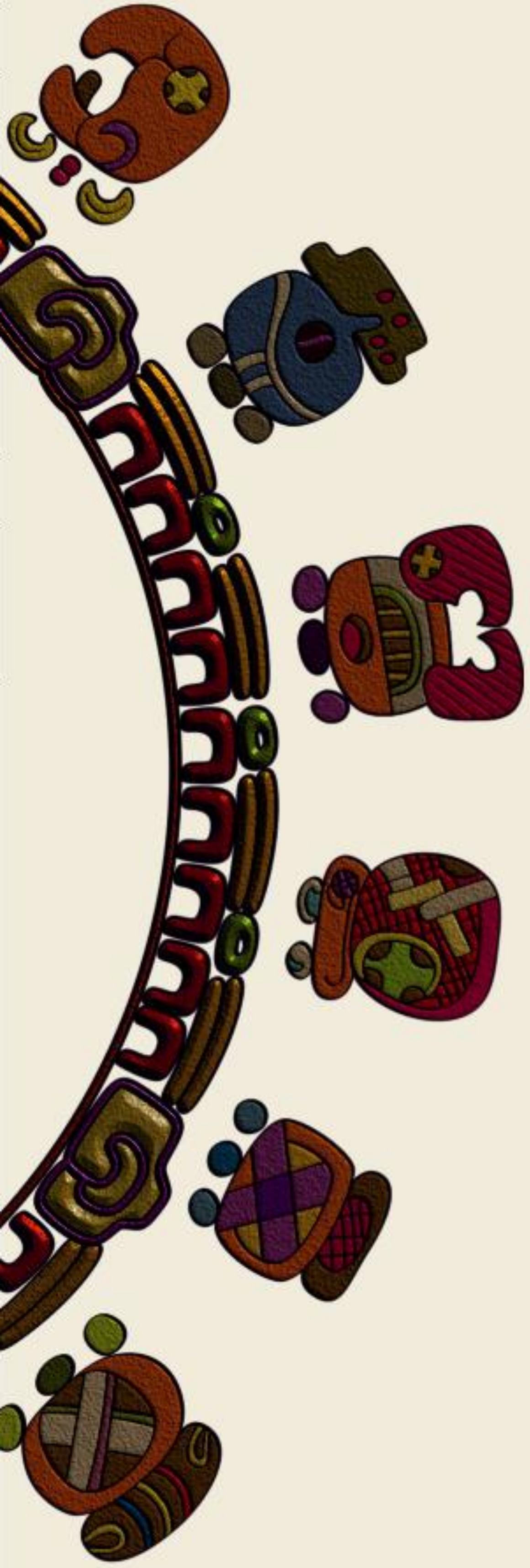
14th INTERNATIONAL WORKSHOP ON TARGETRY AND TARGET CHEMISTRY
(WTTC14)



Abstract Book

WTTC

2012

The *14th International Workshop on Targetry and Target Chemistry* (WTTC14) was held in Playa del Carmen, Mexico, August 26-29, 2012.

This series of workshops was initiated in 1985 with the purpose of exchanging information about the problems and solutions associated with the cyclotron-production of radioisotopes for biomedical applications. The Workshops are designed to bring experienced targetry scientists together with newcomers to the field, both from industry and academia, to discuss issues of targetry and target chemistry. In these workshops, experience, ideas and information are freely and openly shared; learning and collaborations are fostered, with active participation by all attendees.

For the first time in more than 25 years of Targetry Workshops, this workshop, critical for the dissemination of important information, is taking place in Latin America. The Faculty of Medicine of the National Autonomous University of Mexico (UNAM), through its PET Center, is honored to organize and coordinate the 14th WTTC in cooperation with the International Atomic Energy Agency (IAEA) and the support of the World Federation of Nuclear Medicine and Biology (WFNMB).

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Reports from Labs

ADVANCES AT ACSI: NEW TR24 CYCLOTRON CAPABILITIES AND OPERATIONAL EXPERIENCE

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Typical Biomedical cyclotrons have energy range from 11 MeV to 19 MeV, while commercial production SPECT cyclotrons typically have >30 MeV. In the recent years many research labs expressed interest in widening spectrum of their research capacity by complementing production of PET radioisotopes with a variety of SPECT isotopes. A number of regional radioisotope suppliers were also exploring business models which included production and supply of not only the traditional PET isotopes, F-18, C-11, O-15 and N-13, , but also of a variety of other isotopes, included, but not limited to I-123, Ge-68, In-111, Ga67.

In the last two years the nuclear medicine community also started researching alternatives to the existing reactor based supply of Tc-99m. In 2009 ACSI, in collaboration with a number of Canadian Universities and Research Centers started exploratory work directed at the development of commercially viable technology for the production of Tc-99m using a medium energy cyclotron. This coincided with the design completion of new medium energy, high current cyclotron. The TR24 cyclotron is based on the TR19 platform and utilizes main components and sub-systems of TR19 and TR30 cyclotrons. In 2010, the first TR24 was manufactured and 400 µAmp current were achieved during factory testing. There has been worldwide interest in this hybrid cyclotron, with 10 TR24 orders received in the last two years. In 2010, through the Non-reactor-based Isotope Supply Contribution Program (NISP), ACSI won a bid worth $11M to commercialize cyclotron production of Tc-99m using high current TR24 cyclotrons. The first high current TR24 cyclotron is now being commissioned at the Centre Hospitalier Universitaire de Sherbrooke (CHUS) and second machine coming to new Edmonton Radiopharmaceutical Center site at the University of Alberta.

Both cyclotrons have TR30 ion sources and 100 KW RF systems and potentially can achieve beam currents in excess of 1 mAmp. Our design target was 500 µAmp and during factory testing we have achieved 1 mAmp current at 1 MeV. Currently, as of end of April 2012, CHUS cyclotron is operated at 300 µAmp and the beam current is being gradually increased following CNSC (Canadian Nuclear Safety Commission) facility commissioning schedule. This cyclotron is equipped with two external beam lines and a high current, 500 uAmp, solid target station. Test results and first operational experiences will be reported.

TR24 Cyclotron specifications:

Extracted current:	>500 uAmp
Energy:	16- 24 MeV (variable)
Magnet orientation:	Horizontal
Extraction:	Dual, single or multiple extraction foils
Beam lines:	Up to 6 and/or 4-position target selectors mounted on the cyclotron
Targetry:	Full range of liquid, gas and solid targetry for PET and SPECT radioisotope production.

IN-HOUSE MAINTENANCE OF THE RDS-111 CYCLOTRON
REPAIR OF WATER COOLING LINES AND REPLACEMENT OF LOWER O-RING

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Introduction: Our experience at the University of Washington has demonstrated that many of the maintenance issues with the RDS-111 cyclotron can be effectively managed by our local staff of radiochemists and engineers, with consultation involving the experts in Knoxville. Perhaps the most challenging task that we have completed involved repair of a leak in cooling around the magnet. Four Cu cooling coils surround the electromagnet and are coupled together and to the outside by a manifold involving rubber hoses. They are not accessible without lifting the magnet and are located in close proximity to the ^{18}F target which produces a high flux of neutrons. After ~10 years of use, the cyclotron was leaking water at these rubber hose connections. This repair required lifting the vacuum chamber, electromagnet and water cooling lines out of the cyclotron body as a single unit. That procedure also implied that the large O-ring that isolates the vacuum chamber and the bottom tank be replaced. The cost estimate from CTI Siemens for this repair was only about $3,500 for replacement parts. However, because of the size constraints of our cyclotron vault, their estimate for labor was about $60,000, mostly for riggers. Thus, we undertook the project with our own staff.

Material and methods: The most pertinent engineering detail was that the vacuum chamber, electromagnet and cooling lines, which are an integrated unit, weighed ~2000 kg and would need to be raised about 50 cm. However, before the vacuum chamber/ magnet could be raised that high, the cyclotron tank top, 3700 kg, had to be raised higher to accomodate the unit for repairs. Our only option was to use vertical space and so we designed a frame consisting of triple Unistrut P1001A3 legs 150 cm long and resting on 1.27 cm thick steel plates. The legs were supported with cross bracing to anchor the frame to the concrete side shield and angle bracing to the edge of the cyclotron pit. Calculations suggested that this would support a vertical load of about 4 times the weight of the tank top.

For all lifting tasks we used the hydraulic jack system that is part of the RDS-111 for raising the tank top. This system provides 40 cm of vertical rise. To gain more vertical lift, we machined a steel bar (6.35 cm by 8.90 cm and 40 cm long) to screw on to the threads on top of the piston and that attached to tank's top ears.

The procedure was to fully retract the shields but otherwise leave them in place. We lifted the tank top 40 cm and inserted three safety cans, then removed the pins connecting the pistons to the tank, forced the piston down, added the extension and lifted the tank top an additional 40 cm. After inserting taller safety cans made from SCH80 structural Al 10 cm OD, this procedure was repeated with longer extensions to the pistons so that the tank top could be lifted about 1 meter, at which point we were restricted by light fixtures and HVAC. We inserted 4 cross pieces of P1001C41 close to the center of our frame and inserted new safety cans. The hydraulics could then be lowered enough to rest the tank top on the cross bars and safety cans. (Fig 1A)

The Cu assembly has tapped holes to which we attached a Unistrut bar and then used the hydraulics to lift the vacuum chamber and magnet. Full displacement of the piston was sufficient to expose the cooling coils for replacing the hoses and bottom O-ring. (Fig 1B)

The reverse procedure to re-assemble the cyclotron required considerable care to make certain that the vacuum chamber stayed perfectly vertical and that it was lowered without any rotation.

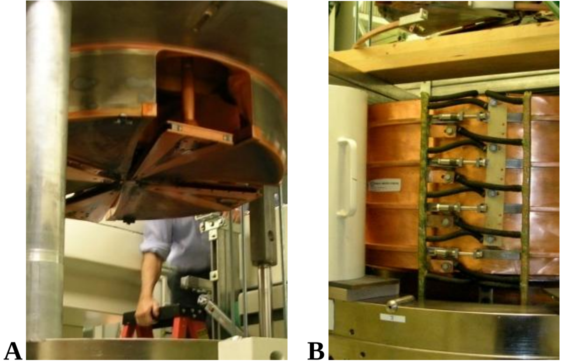

Figure 1. Photographs of raised tank top and of magnet.

Results and Conclusions: For sites that cannot afford full service contracts for major repairs, we have found that repair of the magnet cooling and vacuum chamber can be accomplished safely and at a minor cost and time delay. Our drawings are available to any group faced with the need to carry out such a repair without incurring a major cost or time delay waiting for skilled riggers.

Acknowledgments, disclosures and funding: The cyclotron was supported by an NIH High End Instrumentation grant, S10 RR17229, and overall research support was from P01 CA42045. We gratefully acknowledge the generous advice and cooperation of Glen Gimenez and colleagues at Siemens.

CONSIDERATIONS, MEASUREMENTS, AND LOGISTICS ASSOCIATED WITH LOW-ENERGY CYCLOTRON DECOMMISSIONING

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Introduction: There are currently approximately 150 active PET cyclotrons in the US. There are likely at least 3X that number, total, in the world. Despite the fact that the first wave of PET cyclotrons is in the decommissioning stage, there is still little information in the literature on the science, health physics, and regulatory framework surrounding the process. Here we present quantitative radioactive waste measurements associated with the University of Iowa's cyclotron decommissioning.

Material and methods: In the summer of 2011, the University of Iowa's 20-year-old 17 MeV Scandatronix cyclotron underwent decommissioning. In an effort to be both environmentally and economically responsible, we investigated the possibility of transferring ownership of our otherwise intact and functioning cyclotron. Although two potential recipients were identified, logistics precluded this most-optimal solution.

Since disposal of the cyclotron was, in our case, required, we were forced to run the regulatory gauntlet associated with the transport and disposal of more than 40 tons of low-level cyclotron related radioactive waste. Waste was classified into two categories: That associated with the cyclotron and targets, and that associated with the concrete vault wall that needed to be removed to remove the old cyclotron and bring in the new one. Multiple samples were taken from the concrete wall (via hammer drill with concrete dust collection) and analyzed with two independent High Purity Germanium detectors to assess concentration of neutron activation products. The first measurement was performed in-house, and the second was performed by an independent laboratory at the request of state safety officers. Results are in Table 1.

The cyclotron itself was stripped of useful spare parts, which were sent to sites with still-operating 17 MeV Scandatronix cyclotrons. Accumulated radioactive waste from 20 years of operation was bagged and placed in the cyclotron vacuum chamber. This included target foils which were first placed in lead containers to minimize gamma-shine from the cyclotron. The tank was then resealed for the last time. Assessment of the identity of the quantity of radionuclides associated with the cyclotron was required before cyclotron shipment to the waste disposal site in Clive, UT (Energy Solutions). This assessment was performed with the ISOCS (Canberra) nuclear spectroscopy/geometric modelling package. A simplified CAD drawing of the cyclotron, with its associated materials, was input into the modelling system, then collimated spectroscopic gamma measurements of the cyclotron were performed from several angles. Calculations, taking into account attenuation and geometry resulted in the data shown in Table 2.

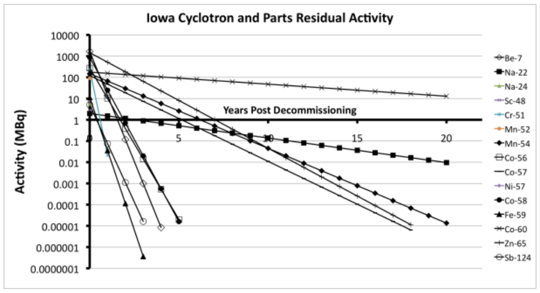
Results: **Table 1.** Measured concrete concentrations. All were below exempt concentrations, and so no special disposal of concrete was required.

	pCi/gm	±	Half-Life
Ce-141	0.043	0.019	32 days
Co-60	1.835	0.042	5.27 years
Cs-134	0.128	0.023	2.06 years
Eu-152	2.23	0.086	13.3 years
Eu-154	0.264	0.047	8.8 years
K-40	8.16	0.386	1.27e9 years
La-140	0.528	0.269	40.3 hours
Mn-54	0.436	0.036	312 days
Na-24	211.44	2.08	15 hours

Table 2. Measured cyclotron activities at disposal time

Nuclide	MBq	Half-Life
Be-7	1654.2	53 days
Na-22	2.0	2.6 years
Na-24	5.3	15 hours
Sc-48	2.9	44 hours
Cr-51	247.5	27 days
Mn-52	90.9	5.6 days
Mn-54	150.1	312 days
Co-56	273.1	77 days
Co-57	120.5	272 days
Ni-57	7.6	36 hours
Co-58	876.9	71 days
Fe-59	11.3	44 days
Co-60	176.1	5.3 years
Zn-65	1454.1	244 days
Sb-124	5.1	60 days

Figure 1. Radioactive waste quantities as a function of time during storage. After 15 years, all activities will fall below the 1 microCurie benchmark for all but Co-60.



Conclusion: A Non-commercial cyclotron operated at benign beam currents supporting typical PET research volumes over a 20 year period generates only modest quantities of waste with negligible environmental impact beyond 15 years.

DOWNWARD DOG: AN AFTER-MARKET, FIVE-PORT VERTICAL BEAMLINE EXTENSION FOR THE PETTRACE

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Introduction: The GEMS PETtrace is well-matched to serve clinical needs for conventional PET radionuclides: ^{11}C, ^{13}N, ^{15}O and ^{18}F. With 100 µA of 16 MeV protons and 80 µA of 8 MeV deuterons directed onto 6 beam ports, the needs for aqueous ^{18}F^{-}, ^{13}N-ammonia, ^{15}O-gases and ^{11}C–methylating agents are easily met. However, the UW PET research program calls for an expanded list, including ^{10}C, electrophilic ^{18}F and ^{34m}Cl, and the entire 3d-shell of transition metals. These synthons require highly specialized targets supporting corrosive and often molten target materials. To accommodate this breakout, a beam-line extension was designed and built by National Electrostatics Corporation (Middleton, WI) with 5 beam ports at 0°, ± 15°, and ± 30° oriented in the vertical plane. The critical specifications called for beam optics to focus the beam into a 5 mm FWHM beam strike, anticipating costly enriched isotopes. The downward-directed ports are intended for targets like ^{10}B$_2$O$_3$, elemental sulfur, calcium, gallium, zinc, selenium and strontium, with melting points that need gravity to confine the molten target substrates in a horizontal configuration.

Material and methods: In 2009, the PETtrace (#144) was bunkered in new space in the UW Institute of Medical Research. All targets are made in house. The cyclotron's raised placement and the service trench were designed to permit clear access all around, as well as 12 feet of clear run from the PETtrace beam ports for the future beam line. Specifications were sent out to three bidders, and the contract was let to NEC in 2010. Their careful beam optics calculations, starting from the emittance characteristics provided by GEMS for port 2 (upward directed by 2.5°), led to five elements:

- a ± 1° horizontal steerer, followed by
- a few degree vertical steerer to straighten out the beam, for entry into
- a quadrupole doublet, focusing the beam through
- a high-power quad slit and drift tube, leading to
- the 5-port, double-focusing switching magnet supporting the various targets.

The off-axis beam ports at ± 15° and ± 30° have co-linear ports at ± 165° and ± 150° suited for optical viewports for monitoring target conditions with IRtc and CCD TV telemetry.

Figs 1 and 2 show the schematic and photo of the constructed beam-line. Vacuum is mid-10^{-7} mm Hg, pumped by a Balzers-Pfeiffer TPU 240 turbopump. Installation was performed by the UW Cyclotron Gang, with alignment making use of a laser mounted on an overhead bridge crane. Irradiations employ the service laptop for cyclotron control, with manual control of the steerers, quads and switching magnet power supplies. Labview monitoring and logging of irradiation parameters is *en process*.

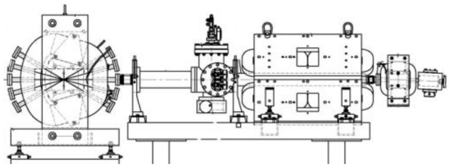

Fig 1. Beamline schematic.

Transmission from the PETtrace stripper to final target position is over 65%, with losses mainly at the molybdenum beam-defining aperture to the quad slit assembly. Until this transmission is improved, beam on the final target positions is limited to 25-30 µA, more than sufficient for our optical telemetry of molten targets.

Fig 2. The assembled beam-line on the UW PETtrace

Conclusions: Outfitting the modern cyclotron with with multiple beam ports has taken various pathways: magnetic beam switching, Gatling-gun turrets, linear slide arrays, wobbled flexible bellows and in-line series targets. The freedom afforded by our new construction, and the need to present a molten target to a downward-directed beam led us to this beam-line configuration. Our experience with a truly vertical beam line following a 90° switching magnet on our legacy RDS 112 has convinced us (1,2) that the gravitational containment of corrosive liquid targets is essential. The choice of vertically-angled beams permits even higher power irradiations while maintaining a horizontal surface.

Acknowledgements: The support of the NCI Training Grant T32 CA09206 and that of the staff at NEC are gratefully acknowledged.

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1. Nickles R.J. (1991). J Nucl Med **32**, 1091 (1991).
2. M. Jensen et al., (2002). WTTC 9,Turku, Finland.

FLEXIBLE, DURABLE PROTON ENERGY DEGRADERS FOR THE GE PETTRACE

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Introduction: Accelerator production of nonstandard radioisotopes for PET necessitates control of particle energy to limit formation of radioisotopic impurities. The General Electric (GE) PETtrace's 16.1 MeV beam in stock configuration offers scant control of entrance energies, inconveniencing users hoping to match irradiation energies to solid target production demands. We report a convenient method of energy degradation using foils of variable thickness. The design is tolerant of production beam currents and offers the possibility for parasitic production of useful isotopes in the degrader foil.

Materials and methods: The solution of the heat equation in generalized coordinates for a uniform beam incident on a thin foil with fixed boundary temperature is shown in Fig 1 below (1).

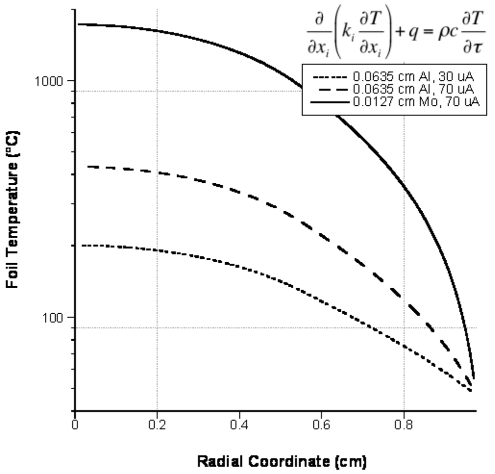

Fig 1. Temperature predictions for Al and Mo foils degrading PETtrace beam energy to 11 MeV at 40 μA. $m.p._{Al}$ = 660°C, $m.p._{Mo}$ = 2623°C.

A degrader was designed and built for routine production of ^{64}Cu, $^{66/68}$Ga, ^{44}Sc, ^{89}Zr, ^{45}Ti and others using homemade targets. The degrader accepts foils of variable thickness. An additional degrader with similar design but fixed thickness (445 μm) was machined from a single piece of Al. Foils are cooled by direct contact with an annular channel of 2 L/min water (Fig 2). Aluminum and molybdenum foils of 635 μm (Al) and 127 μm (Mo) thickness were tested in beam. Beam energies absent degraders and after the fixed degrader (445 μm thickness) were measured using a technique reported previously (2). Proton energies of 13.01 ± 0.01 MeV (mean±sd, n=2) were measured for the degraded beam, and an energy of 15.97 ± 0.06 MeV (n=3) was measured for the undegraded beam.

Fig. 2. Annular water channel and sealing o-rings in the variable thickness design.

Results: The 635 μm Al foil in the variable degrader housing withstands 75 μA irradiation currents with only minor discoloration and no failures in beam. These values are more than double the proton flux currently used to irradiate solid targets at the UW. The 127 μm Mo foil has proved similarly durable, tolerating beam currents up to 85 μA with the added benefit of parasitic ^{95m}Tc production for customers seeking long-lived analogs of the nuclear medicine isotope ^{99m}Tc. The 445 μm Al fixed degrader has proven reliable, tolerating 30 μA for routine production of several radionuclides and logging over 2400 uAhrs since first use with no visible wear or damage.

Conclusions: The benefits of limiting proton beams' interaction with target material to only the most energetically productive values have been reported (3). In the absence of variable extraction radii, these simple designs offer cyclotron operators access to cross section peaks and minimized target mass.

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2. K. Gagnon et al. (2011). Applied Radiation and Isotopes, 69, 247-253.
3. J.W. Engle et al., (2010). Proceedings of WTTC13, Roskilde, Denmark, 17.

Acknowledgments, disclosures and funding: We gratefully acknowledge the support of NIH Radiological Sciences Training Grant T32 CA009206.

PROTON IRRADIATION DAMAGE OF AN ANNEALED INCONEL BEAM WINDOW

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Introduction: Annealed Inconel 718 alloy was chosen for the beam window at the Los Alamos Neutron Science Center (LANSCE) Isotope Production Facility (IPF). The window was in use for 5 years and was recently replaced as part of preventive maintenance. The discarded window was used to characterize the effects of intense, long-term beam exposure on Inconel materials.

Material and methods: The beam window assemblies was shipped to a hot cell at the CMR facility and was cut from the beam pipe with a portable band saw (Fig 1).

Figure 1: Side (left) and front (right) views of the cut pipe containing the actual window (left).

GAFCHROMIC HD-810 dosimetry film was used to measure an activation profile of the excised beam window. The profile, exhibiting IPF's rastered beam shape, was used to create a plan for removal of additional small samples for addional characterization. Using this plan, tungsten bits were used to mill 3 mm OD samples from the window (Fig 2), which were polished and thinned on both sides to 0.254 mm thickness. We performed shear punch testing at 25°C on 21 samples to quantify shear yield, ultimate shear stress, and ductility as a function of dpa and irradiation temperature. MCNPX was used to predict the total average dpa from both protons and neutrons for each 3-mm OD sample and ANSYS to model the irradiation temperature distribution.The same shear punch tests were performed on 2 control samples of unirradiated, annealed Inconel 718 for comparison.

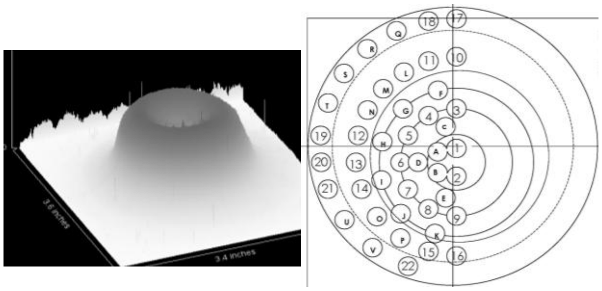

Fig 2: Measured beam profile and beam window cutting plan.

Results: Increases in shear yield and shear maximum stress with increasing dose were observed (22 and 28.8 dpa samples). Contrary to expectation, samples in the outer ring (0.4 dpa, 26°C) and outside beam collimator (5 dpa, 26°C), where radiation dose was expected to be relatively low, have a higher yield and ultimate shear stress than the control or high radiation dose (28.8 dpa, 109°C) samples (see Fig 3). Optical microscopy images of the fracture surfaces show no significant change in the fracture mode and reduction in ductility in the control and high radiation dose samples (Fig 4).

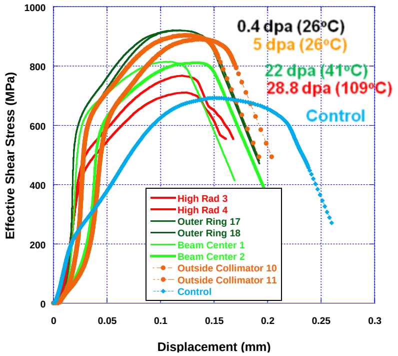

Fig 3: Shear stress measurements at 25°C of samples at various locations.

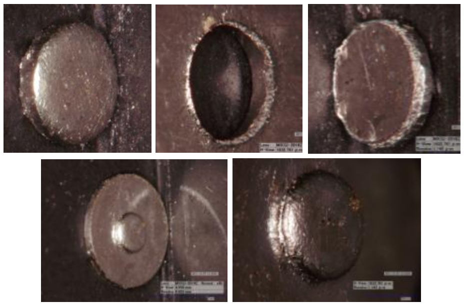

Fig 4: Optical images of control sample (top row) and high radiation dose sample #3 (bottom row).

Conclusions: The mechanical properties of annealed Inconel 718 alloy have been investigated after proton irradiation (up to 28 dpa, ~ 1mAh-yr). Despite evidence of radiation-induced hardening, the beam window retains useful ductility after 5 years of irradiation. The disagreement on the properties of the low dose and control samples warrant further studies on the initial and microstructure changes using Focus Ion Beam sample preparation and Transmission Electron Microscopy. This information will be used to establish more lenient preventative maintenance schedules for IPF, reducing worker exposure significantly.

THE NEW SOLID TARGET SYSTEM AT UNAM IN A SELF-SHIELDED 11 MeV CYCLOTRON

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Introduction: A dual beam line (BL) self-shielded RDS 111 cyclotron for radionuclide production was installed at the School of Medicine of the National Autonomous University of Mexico in 2001. One of the BL´s was upgraded to Eclipse HP in 2008 and the second BL was recently upgraded (June 2011) to the same version with the option for the irradiation of solid targets for the production of metallic radioisotopes.

Material and methods: Irradiation of solid targets was made possible by modifying the target carousel to accept a solid target mechanism that consists of a target holder, an insert, and a pneumatic cylinder machined in aluminum. The target holder contains cooling channels to route the cooling water onto the back of the solid target substrate through the insert.

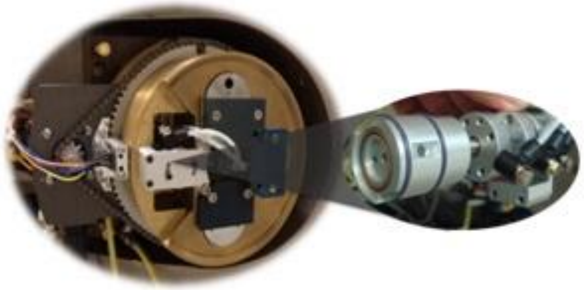


Figure 1: Target carrousel and detail of the insert.

A slot machined into the modified target carousel allows the target substrate to be dropped into and fall out of the target carrousel after irradiation (Fig. 2).

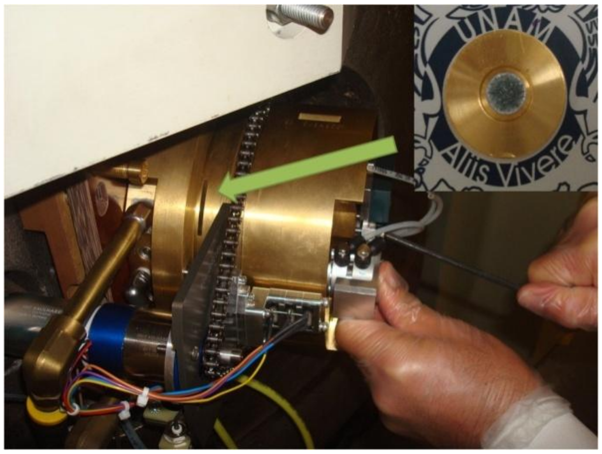
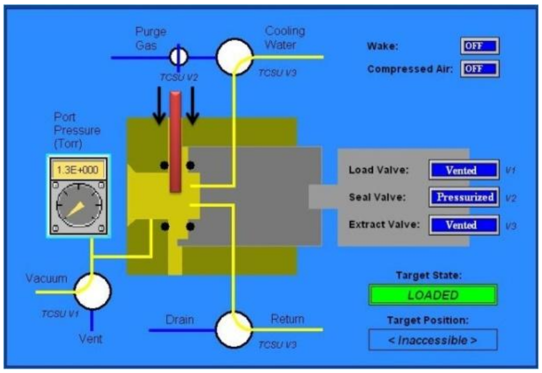


Figure 2: Slot machined to load the target substrate.

The target substrate is a gold disk (2.5 cm in diameter, 2 mm thick) with a central cavity for the electrodeposition of the target material to be irradiated. Automatic and manual operation of the solid target system is possible from the cyclotron control software and the graphical user interface (GUI) shows the status of all involved parameters (Fig. 3).



Wake: OFF
Compressed Air: OFF
Load Valve: Vented
Seal Valve: Pressurized
Extract Valve: Vented
Target State: LOADED
Target Position: < Inaccessible >

Figure 3: GUI of the solid target system.

Results: Acceptance test of the system was performed by irradiating the gold disk for 2h at 40μA without apparent signal of damage. The solid target system have been tested successfully producing Ga and Cu radioisotopes by irradiating electrodeposited targets of Zn and Ni, respectively. Nevertheless the success, some problems related to both the system and the target itself have arisen. Although not common, some times the gold disk does not drop out of the carousel when the insert is pneumatically retracted after the bombardment. In these cases, the insert need to be manually removed from the target holder in order to recuperate the irradiated target. The most common problem with the target is due to poor quality electrodeposition of the taget material that leads to the loss of mass during the bombardment.

Conclusions: A solid target system was fitted onto an existing self-shielded 11 MeV cyclotron. In our experience the system is capable to produce useful quantities of metallic PET radionuclides for preclinical applications, mainly limited by the manual removal of the target that increases radiation exposure to personnel.

Acknowledgments: We acknowledge the financial support of UNAM-DGAPA-PAPIIT TA200512 and International Atomic Energy Agency Grant RC16467.

HYDROGEN EMBRITTLEMENT IN PROTON IRRADIATED RADIOISOTOPE PRODUCTION TARGETS

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Introduction: The apparently random failure of Nb-encapsulated Ga targets in beam at the LANSCE IPF results in significant resource losses, increased dose to personnel, and an unreliable supply of critical Ge-68 to PET facilities nationwide. Between 2005 and 2011, 13 out of 96 (14%) irradiated Ga targets failed. We examine stress-induced hydride formation from the proton beam as a potential cause of these failures from a materials science perspective.

Material and methods: Ga targets are routinely irradiated with 230 μA of 100 MeV protons in the low energy slot of the target stack configuration shown below in Fig 1a. The predominant failure mode observed is the formation of cracks on the Nb rear window at the rim/window transition, the coldest location of the target (Fig 1b). MCNPX simulations were employed to characterize beam energy and current throughout the target stack. Assuming negligible H-diffusion out of the target, these simulations permit calculation of deposited H quantities within the target capsule during irradiation.

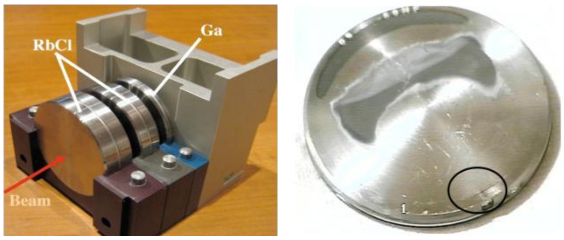

Figure 1a (left) and b (right). RbCl-RbCl-Ga target stack and crack at the rim/window transition of the Nb rear window of target #80. Failure location is outside of the beam path.

Results: In the IPF target irradiation design, most of the beam energy is utilized in the production target. Specifically, the beam protons lose their energy within the Ga target and stop inside the Nb capsule within 0.5 mm of the rear window. About 90% of incident protons make it through the two RbCl targets and into the Ga target. Thanks to materials' increased proton stopping power at lower energies, the Ga target must endure the most intense volumetric heating of any target in the stack (Fig 2). Deposition of protons also potentially creates potentially destuctive H_2 partial pressures in the Ga target.

Calculations indicate that at 230 μA, internal H_2 pressure (pp H_2) inside the Nb capsule volume approaches 1 MPa, and H/Nb ratios between 0.05 and 0.1 are achievable (Table 1). These pressures are potentially destructive, and could explain the location of target failure outside the beam where thermal stresses are expected to dominate consideration.

Table 1. Estimated hydrogen pressure inside the entire volume of Nb capsule as function of beam charge.

Sample ID	**Beam Charge (μA-hr)**	**H_2 (moles)**	**Pressure @ 573K (MPa)**
23	1.5E+05	2.45E-03	1.15
80	9.0E+04	1.47E-03	0.69
27	6.0E+04	9.81E-04	0.46
31	5.0E+04	8.17E-04	0.38
2004	5.0E+04	8.17E-04	0.19

Stress from increasing local pp H_2 increases with integrated beam current. Ductile fracture of Nb has been observed at 130-300°C with a H/Nb ratio of 0.261 [1]. Cleavage fracture of Nb is reported at temperatures less than 27°C with H/Nb ratios as low as 0.0008 when coupled with Nb-β-hydride formation [2].

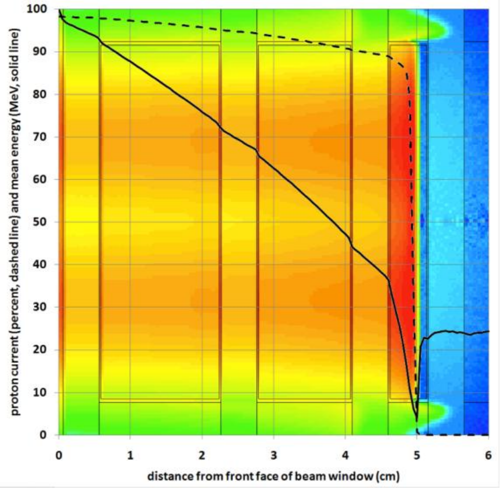

Figure 2: MCNPX calculations show qualitative temperature variation and proton energy/current changes in the target stack configuration.

Conclusions: The failure of Nb-encapsulated Ga targets is most likely caused by a combined action of hydride formation and beam-related thermal stresses. Further studies on fracture morphology and the presence of hydrides will give us more insight into the failure mechanism and enable us to optimize a more robust capsule design.

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PROMPT RADIATION DETECTORS TO MONITOR TARGET CONDITIONS *IN SHOOTERO*

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Introduction: Unanticipated target conditions can result in undesireable results during cyclotron irradiations, e.g., low water, insufficient over-pressure, or electroplated target material flaked off by beam heating. These and a host of other issues are revealed immediately by a change of signature gamma and neutron flux within the irradiation vault, visible with careful selection of detectors for *in-shootero* irradiation monitoring. We present a selection of methods for obtaining this useful diagnostic information.

Material and methods: An $^{18}O(p,n)$ irradiation that will ultimately produce 10 Ci of ^{18}F at end of saturated bombardment produces 3.7e11 fast neutrons per second immediately. These are accompanied by several times more gammas, direct and secondary, from neutron absorption in the cramped accelerator vault. Peta-Hz event rates demand detectors operating either in the current mode, or with miniscule (10^{-8} pulses/event) sensitivity. A high degree of intrinsic n/γ discrimination is also needed to tease apart the two characteristic signatures. Various techniques, such as pulse-shape discrimination in organic scintillators, provide this separation at 10 kHz count rates but fail at PET tracer irradiation levels. Furthermore, the detector must not become activated, and the support electronics must be "hard" in the high neutron flux. *A. Gammas.* Scintillators provide a light output proportional to the energy deposited in their interior. In the pulse mode, each pulse can be shaped and interrogated to discriminate whose full energy ("photopeak") events characterize a "successful" nuclear reaction. In the case of proton irradiation of ^{18}O, the gamma spectrum is actually dominated by the 5.25 MeV γ from $^{18}O(p,\alpha_1)^{15}N$ and the 1.98 MeV γ from inelastic scattering in $^{18}O(p,p')^{18}O$. While these γ's are not characteristic of ^{18}F production, they are the signatures that the beam is on the right target material. This reassuring spectroscopy, provided by a highly collimated $LaBr_3$ detector at sub-microamp irradiations at 11 MeV, becomes hopelessly overwhelmed at tens of µA during a realistic production run. A simpler and more robust detector is simply a 1 cm^2 patch of $CaWO_4$ scrap from a discarded X-ray image intensifier screen mounted onto a 931A photomultiplier tube, with its nA-µA anode current read out by a Keithley 610 electrometer. *B. Neutrons.* A variety of neutron detectors are described in the literature, varying over ten decades in neutron sensitivity S and n/γ discrimination D. Five detector types stand out in Table 1 below. The support electronics for the scintillators (D,E) utilize Ametek Acemates, providing high voltage, pre-amp, amplifier and single channel analyzer to drive Labview data loggers. The others (A,B,C) need a charge-sensitive pre-amp and research-grade NIM-based amps and SCA's for low-noise operation and good n/γ discrimination.

	Detector	Mechanism	S	D
A	^{235}U-fission	proportional	-6 to -9	excellent
B	p-recoil	H(n,p)	-6 to -9	good @ E> 1 MeV
C	$^{10}BF_3$	proportional	-5 to -7	excellent @ E>1MeV
D	Eljen 410	H(n.p) scint	-6 to -7	excellent @ E>1MeV
E	Eljen 426	$^6Li(n,\gamma)$scint	-6 to -9	excellent @ E>1MeV

Table 1. Summary of neutron detector options, S = $\log_{10}$ sensitivity, D = n/γ discrimination.

While the ^{235}U-fission proportional counter's small size is well-suited for placement directly on the cyclotron target, its high cost, limited (≈ 1 year) lifetime and high security profile due to its µgram of HEU make it less than favorable. Based on cost and n/γ discrimination, the Eljen 426 ($^{10}B(n,\alpha)$; ZnS) scintillator and the LND $^{10}BF_3$ proportional counter, each surrounded by ≈ 10 cm of hydrogenous moderator win out for reproducibility, low cost and ruggedness. The actual utility of independent data logging of n/γ count rates hinges on systematic recording as target materials vary from natural to high enrichment. At 11 MeV proton energy, these two rates, and their quotient, are very characteristic of the target conditions. The neutron rate serves as the input signal R for a "leaky integrator" (1),

$$\frac{dN}{dt} = R - \lambda N$$

integrating the first-order differential equation predicting the end-of-bombardment activity.

Conclusions: As E_p rises from 11 MeV (Siemens RDS/Eclipse) to 16 MeV (GE PETtrace) the distinction between natural and enriched targets revealed by the n/γ flux diminishes but still suffices to alert the operator of mishaps that would otherwise go unnoticed by telemetry of the usual beam current, pressure and temperature parameters. Finally, using the n/γ signature to reflect the target conditions is predicated on the assumption that reactions at the target dominate. Modern negative ion cyclotrons with their excellent beam transmission, and a careful attention to the materials used in neutral beam baffles, help ensure this. Similarly, the location of the detector in close proximity to the target, minding the effects of fringe fields, make the systematic logging of these characteristic radiations a welcome diagnostic aid to PET tracer production.

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SIMPLE BEAM PROFILE MONITOR

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Introduction: An inexpensive beam profile monitor is based on the well proven rotating wire method. The monitor can display beam position and shape in real time for particle beams of most energies and beam currents up to 200μA. Beam shape, position cross-section and other parameters are displayed on a computer screen.

Material and methods: The monitor was designed especially for isotope production accelerators but it is equally useful in any application where particle beam shape and position information is required. The helical wire scans the beam in vertical and horizontal plane and is parked outside the beam path when at rest. Each scan takes approximately 200ms. The scans can be single, continuous or at any desired interval.

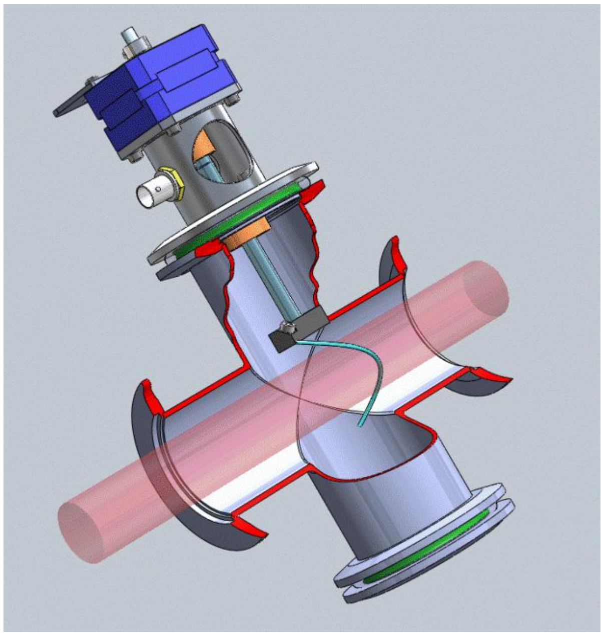

Figure 1: Beam monitor on beam line

The monitor is mounted on a cross, usually in front of a target. Standard mounting is KF40 flange, but other fittings can be supplied on request. In the standard configuration the wire can scan beams up to 30mm in diameter. Larger scan-wires are available; up to 60mm diameter beams.

A small control box operates the device. It connects to the scanner drive via 7 pin connector and a coaxial connector for the beam information. USB interface to the computer.

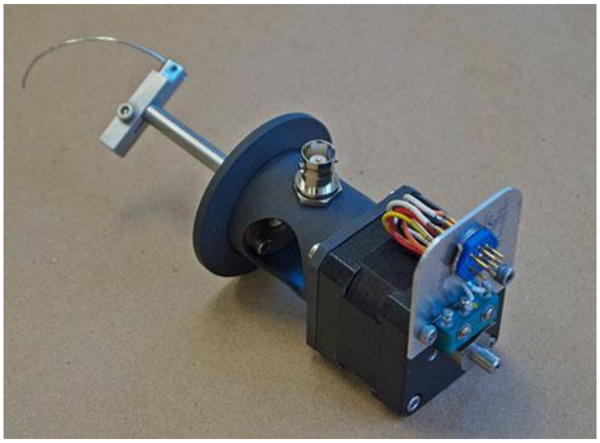

Figure 2: Beam monitor

Results: Beam information is displayed on a computer monitor. The user can choose among many parameters and display formats. Beam scans can be shown as plots or cress-sections. Each scan information can be stored and replayed as an image of animation. The operating software is written in Java.

Despite its simple construction, the beam monitor is a rugged device. The use of ball-bearings, Vespel seals and pure silver for the scanning wire ensures long operating life.

Conclusion: While not new in its basic concept, the design and construction aim was to minimize cost and to provide a simple, inexpensive and reliable device for beam monitoring.

WIRE SCANNER FOR BEAM PROFILE OF HIGH CURRENT PARTICLE ACCELERATOR BEAMS

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Introduction: Accelerator beam profile scanners are used to determine particle beam dimensions and intensity distributions. The goal is in many cases to achieve uniformity of the beam for radionuclide production. The maximum proton beam current for a wire scanner is typically low, a few tens of µA, limited by the beam-induced heating destroying scanning wires. For some applications higher beam currents are needed. Our goal was to develop a beam profile scanner that can be used at currents beyond 100 µA.

Material and methods: The experiments were carried out at the TPC CC18/9 cyclotron using proton beams of 18 MeV. A U-shaped wire holder was used to support a 1 mm diameter wire or 0.8 -0.38 mm diameter tubes. For wires, cooling was achieved by heat conduction from the wire material to the wire holder for current measurement and by thermal radiation. For the tubes an HPLC pump were used to force cooling water through the tube and thereby make the cooling more effective. Various materials were tested; tungsten, tantalum, stainless steel (316L) and copper. The wire or tube was moved through the beam at a speed of 2 mm/s by a stepper motor driven mechanism. Industrial Ethernet modules connected to a computer were used for the analog measurements and to control the stepper motor. Only vertical scans were performed at this stage. Target-, collimator-, and wire currents, water temperatures and pressure were monitored. The scanner unit was mounted on the 40 mm diameter beam line at 15 cm from a target. The beam was collimated to a diameter of 10 mm, and the beam current target/collimator ratio was 70/30 %.

Results: For the 1 mm solid wires, tungsten with the highest melting point melted and broke when the total beam current exceeded 60 µA, tantalum broke at 40 µA and stainless steel and copper at about 20 µA. Table 1 shows the melting and breaking points for different water cooled tubes.

Table 1: Dimensions and breaking points of water cooled metal tubes used in wire scans.

Material	Outer diam.	Wall	Breaking point
	[mm]	[mm]	[µA]
Tantalum	0.80	0.15	**85**
Stainless Steel	0.80	0.31	**55**
Stainless Steel	0.80	0.28	**40**
Copper	0.75	0.26	**90**
Copper OFHC	0.38	0.08	**>120***

*maximum current tested to date

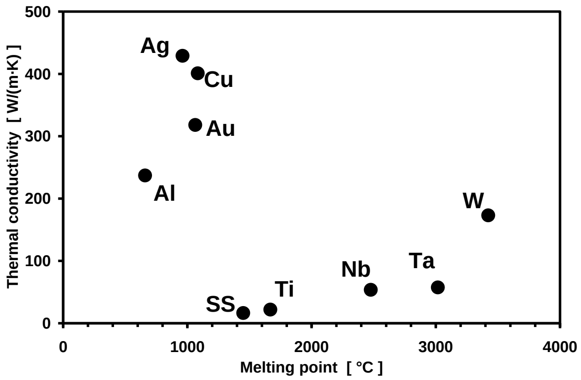

Figure 1: Heat transfer coefficients as function of melting points for various metals.

Conclusions: Water cooling enhances the resistance of the tube against breakage. High thermal conductivity is more important than a high melting point. Obviously, the thinner the tube the better as less thermal power is deposited in the tube. Thus, the thin-walled copper tube was the best of the materials studied to date when looking for high beam current resistance.

A REAL-TIME BEAM-PROFILE MONITOR FOR A PET CYCLTRON

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Introduction: The beam profile of a PET cyclotron is typically measured by an autoradiography technique or even by a scintillator that can be viewed in real time [1,2]. Another method is to use collimators in front of the target to assess the beam centering [2]. All these methods have potential drawbacks including an inability to monitor the beam in real time, exhibiting a non-linear correlation in signal response to the power deposited, or not providing a 2-dimensional beam profile. Our goal was to design a beam-profile monitor that is able to withstand the high absorbed power of a PET cyclotron and monitor the deposited energy linearly and in real time.

Material and methods: The beam-profile monitor is designed for the TR13, a 13MeV negative hydrogen-ion cyclotron at TRIUMF. The design follows that of a ‘harp’ monitor, widely used at TRIUMF for tuning proton and radioactive ion beams, and is not separated by a foil from the tank. The TR13 monitor is designed to withstand a 13MeV proton beam up to a beam current of 25µA, has an active area of 10 by 10mm and does not affect the 10^{-7}torr tank vacuum. It consists of a water-cooled Faraday cup made out of aluminium for low activation and two orthogonal rows of eight tungsten electrodes mounted on a water-cooled support frame and spaced 1mm apart from each other, see Figure 1.

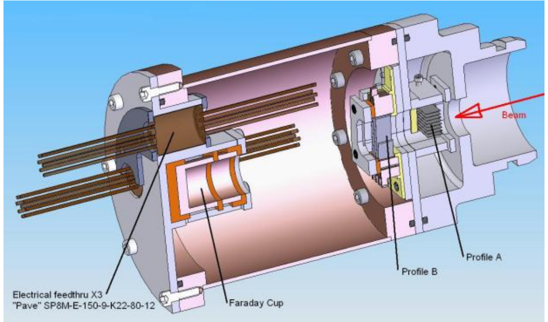

Figure 1: Design drawing of beam-profile monitor.

The electrodes are electrically isolated from each other and each has a current pick-up soldered to it. The material and the shape of the electrodes are optimized to withstand the deposited power of the proton beam. A voltage of -88V is applied to the electrodes to repel secondary electrons and prevent cross-talk between neighbouring electrodes. The electrode current is amplified using a custom current amplifier, and read by an ADC. From there, the current data is displayed on a PC. This allows one to see changes of the beam profile in ‘real time’. The electronics are designed to read out all sixteen channels in parallel, or, if only a limited number of ADC channels are available, to cycle through the different channels. In our current setup all sixteen channels are read out simultaneously.

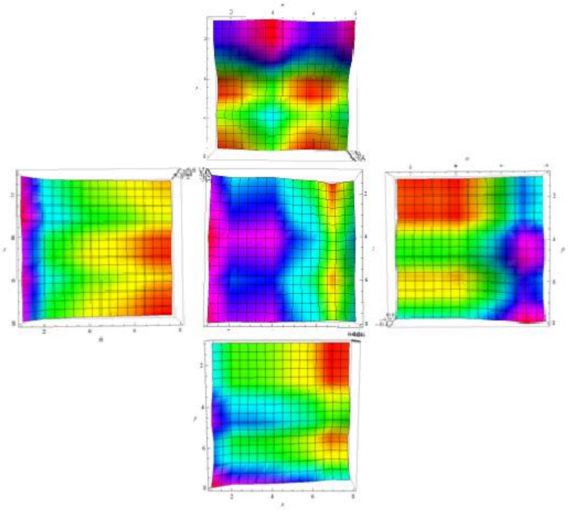

Figure 2: Monitor read-out for different beam positions. The currents from the eight horizontal and vertical electrodes are displayed in a 2D representation. In the center panel, the beam is centered on the monitor. The four other panels demonstrate corresponding beam shifts to the top, right, bottom and left of the monitor (clockwise from top panel). Magenta is high bam current, red is low beam current.

Results: Our initial data clearly shows a positive correlation of the beam monitor to the beam movement (see Figure 2). Future studies are planned in order to understand the structure seen on the monitor. Apparent inconsistencies could be due to some unresolved issue of cross-talk problems. Plans are in place to further reduce this by having some of the electrodes grounded.

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CHARACTERIZATION OF THE PROTON BEAM FROM AN IBA CYCLONE 18/9 WITH RADIOCHROMIC FILM EBT2

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Introduction: The characterization of a cyclotron beam is very important to optimize targets or to develop a new one. The two most important factors are the beam energy and the beam profile. The measurement of the beam profile can be used for the correct alignment of the targets or to know the state of the foils and also the deposited energy distribution may be included in simulations codes, as Monte Carlo (MC) or heating and cooling codes. The use of radiochromic films EBT2 is an easy and inexpensive method to measure the beam profile and also could be used to measure the beam energy.

Material and methods: Two different experiments were carried out with the radiochromic films EBT2: the measurement of the beam profile and the measurement of the beam energy of an IBA cyclone 18/9. For the measurement of the beam profile various aluminum foils, with different thickness, were irradiated and then radiochromic films were placed over them. The use of foils with different thickness allows the study of the influence of this parameter in the beam size.

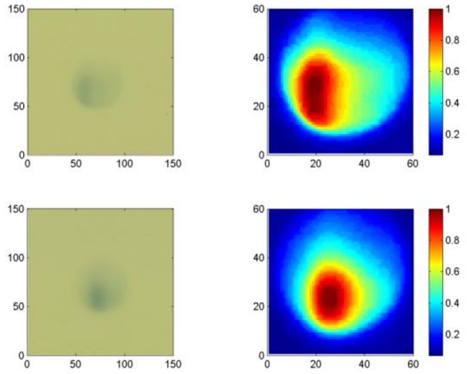

Figure1: Beam profile during initial measurements (top) and after stripper replacement (bottom).

To measure the beam energy the radiochromic films EBT2 were placed inside a ^{11}C gas target, perpendicular to the beam, and the projected range were studied. The MC code GAMOS [1], a Geant4 based code, was used to model the beam shape and energy to reproduce the experimental curve obtained with the films. In the MC simulations the titanium foil, the aluminum foil and the helium cavity of the ^{11}C target were included.

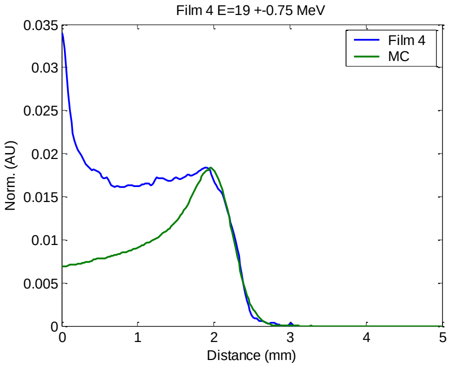

Figure 2: Projected range and Bragg peak measured radiochromic film EBT2(Film 4) and calculated with MC (MC).

Results: The beam profile and beam size obtained with the radiochromic films EBT2 has been constant for the different foils, with different thickness, used. Furthermore, the beam shape was very similar to the one obtained by Avila-Rodriguez [2], in which a damaged stripper was suggested. After its replacement, the beam shape was measured again, see Fig.1, and the beam was much focused, confirming the damage to the stripper. The radiochromic film EBT2 irradiated inside the 11C target suffered an overexposure and the Bragg peak cannot be seen clearly, but the fall of the peak and the projected range can be distinguished with sufficient resolution for the proton incident directly on the film only, see Fig 2. The MC simulations that reproduced the film curves indicate an initial Gaussian proton beam with a FWHM=1.76 MeV, and mean energy of 18.5, 18.75 or 19 MeV depending of the film studied.

Conclusions: The use of radiochromic film EBT2 is an easy and inexpensive method to measure the beam profile. And the thickness of the foil used, between 0.5-1.5 mm, has a negligible influence. The measurement of the beam energy with radiochromic film EBT2 could be a useful method in the future but differences obtained indicate that it still pedroneeds to be improved, for example, reducing the beam intensity or ensuring the perpendicularity of the beam inside the target. Acknowledgement to CDTI funded project (CENIT CIN/1559/2009), AMIT project.

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PRODUCING CARBON STRIPPER FOILS CONTAINING BORON

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Introduction: Parameters being actively tested by the accelerator community for the purpose of extending carbon stripper foil lifetimes in fast ion beams include methods of deposition, parting agents, mounting techniques, support (fork) materials, and inclusion of alloying elements, particularly boron. The latter requires specialized production apparatus, for both sequential deposition and co-deposition of boron in carbon foils. A dual-use vacuum evaporator for arc evaporation of carbon and electron-beam evaporation of boron and other materials has been built for such tests, and to extend our conventional production capabilities. Production has begun and improvements are in progress.

Materials and Methods:

Figure 1: Dual-use vacuum evaporator.

Key components of the evaporator are a high-speed diffusion pump, gate valve and cold trap, a small reliable electron-gun source, a high-conductance carbon arc (not shown), and updated electronics permitting the arbitrary choice of electrical parameters for the arc. The electron gun was chosen for its flexibility of use and ease of mounting and dismounting it.

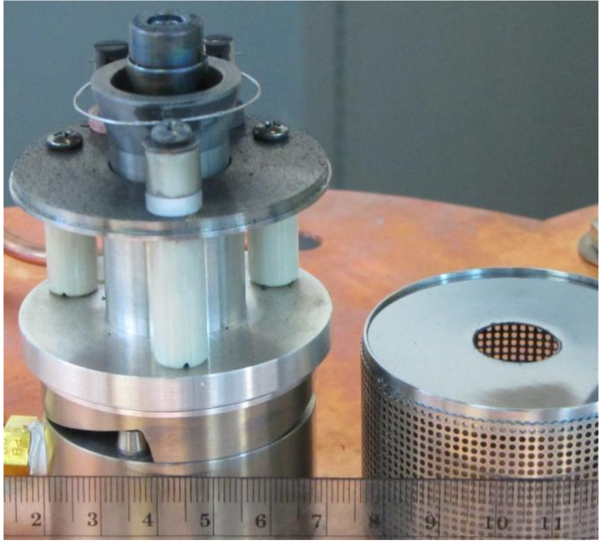

Figure 2: Electron gun for evaporating boron coatings onto carbon stripper foils. Boron in the water-cooled crucible is shown at the top left**.** The electrostatic shield on the right side is placed over the crucible and filament for operation.

Results and Conclusions:

The capability of this system to evaporate boron onto carbon foils, either pre-mounted or on substrates, has been demonstrated. Testing of the arc system and combining it with the e-beam system are in progress.

Figure 3: Unsupported 100 µg/sq.cm Boron-10 on 60 µg/sq.cmCarbon-12.

SOLUTION TARGETS – AN APPROACH TO RADIONUCLIDE PRODUCTION

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Introduction: There is a list of radionuclides which are produced by irradiation of solid targets. Handling and processing of those targets have several disadvantages. There is an interesting alternative to this approach, namely irradiation of a liquid target filled with aqueous solution of target nuclei[1,2,3,4,5]. It makes the target processing significantly easier and allows for automation of the process. This work summarizes some practical aspects of this process.

Material and methods: Enriched isotopes were purchased from JV Isoflex, Moscow. Trace select ultra grade HNO_3, HCl were purchased from Sigma-Aldrich. Puratronic grade $(NH_4)_2CO_3$ was purchased from AlfaAesar. High purity de-ionized water was used (specific resistance 18.2 MΩ/cm).

The main part of target assembly was water cooled chamber (volume 2.4 ml) made out of pure Nb with Ti or Nb (in the case of chlorides) entrance foil. Target chamber is connected to the automated filling and handling system. It is a closed system filled with helium. The concentration of irradiated solution was between 35 – 50 % (w/w). After irradiation, the solution was transferred to the vial, target was washed with 0,1M nitric or hydrochloric acid and water. All wetted path were then washed with water and helium.

Radionuclidic purity and activity of produced radionuclides was measured with γ-ray spectrometry (HPGe detector GMX45, Ortec).

After irradiation and separation all solution potentially contain enriched material were collected together. The volume of the solution was reduced by evaporation on heated magnetic stirrer and if necessary filtered. Recovery of enriched material was done as usual.

Results: With our system we have prepared ^{86}Y, ^{68}Ga, ^{61,64}Cu. The yield of irradiation corresponds well to the published data and given content of target nuclei in the target matrix. Radionuclide purity was excellent and given, by isotopic composition of enriched material and irradiation condition as by solid target irradiation.

Conclusions: During irradiation there is significant pressure increase. To avoid exceed maximum operating pressure of the system few steps must be done. Irradiated solution must be degassed and system must be filled with helium. This work presents a compact, fully automated system for production of some interesting radionuclides in activity and quality suitable for radiopharmaceutical production. Transport of irradiated target matrix via a capillary to a separation unit minimizes problematic handling of radioactive material and losses of expensive enriched material. It also reduces significantly personnel radiation burden.

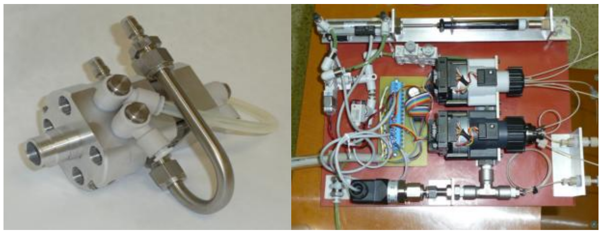

Figure 1: Target body and filling system

This work shows that this system is capable to prepare radionuclides repetitively.

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PRODUCING RADIO-METALS IN LIQUID TARGETS: PROOF OF FEASIBILITY WITH ^{94m}Tc

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Introduction: Widespread acceptance of new and promising radioisotopes can be challenging due to their limited availability. This is typified by many radio-metals that have demonstrated promise as molecular imaging probes, or are of interest based on their known emission properties; yet their production is difficult to execute in a hospital-based medical cyclotron facility. To produce these isotopes most facilities would require the purchase of an isotope generator (if available) or invest substantially in installing a solid-target infrastructure – two expensive options, especially if preliminary biological studies are required in order to justify further investment.

The approach described here provides a facile method for most medical cyclotron facilities to produce clinically useful quantities of radio-metals by adapting liquid targets already in place for the production of other PET isotopes, such as ^{18}F. This allows for the production of ^{94m}Tc without a significant investment in a solid-target station and transfer system. This liquid-target production method can be easily extended toward other metal radioisotopes and could facilitate a quick turnaround for the investigation of these isotopes as alternatives for a specific study. Liquid targets have already been successfully used for the production of ^{89}Zr, ^{68}Ga, ^{86}Y, ^{123}I, and ^{77}Br [1].

Material and methods: The isotope ^{94m}Tc has a half-life of 52.0 minutes, a large positron branching ratio of 72%, and a medium positron end-point energy of 2.47 MeV. This makes it a suitable candidate for PET. Its main appeal is in its chemical exchangeability with ^{99m}Tc, the most common radioisotope for imaging in nuclear medicine, widely used in SPECT. A range of radiopharmaceuticals are currently available for technetium and ^{94m}Tc can therefore be used as a possible PET alternative to the established SPECT tracer. This provides a possibly unique solution to future shortages of ^{99m}Tc. For our preliminary studies, we used Mo of natural abundance, either as MoO_3 or as $(NH_4)_6Mo_7O_{24}$ dissolved in water, H_2O_2, and NH_4OH. The metal-salt solution was loaded into a modified liquid-target system on the TR13, a 13MeV negative hydrogen-ion cyclotron at TRIUMF. All runs were performed with a beam current of 5 µA for a maximum of 60 minutes. The irradiated solution containing the desired ^{94m}Tc was then transferred to a purification system utilizing solid phase extraction as a means to separate the ^{94m}Tc from the target solution [2].

Table 1: The different solutions that were used.

	$(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ (g)	**H_2O_2 (ml)**	**H_2O (ml)**	**NH_4OH (ml)**
A	6.5	1	16	-
B	13.0	1	14	-
C	19.9	1.2	12	-
	MoO_3 (g)			
D	6	4	10	4
E	12	4	10	6
F	6	1	10	4

Irradiation results varied widely when using different concentrations of Mo (Table 1). After an initial rise due to the proton-beam strike within the target solution, the pressure continues to rise. With the maximum safety threshold of target pressure being 450 psi, not all solutions were able to run for a full 60-minute irradiation (see Figure 1).

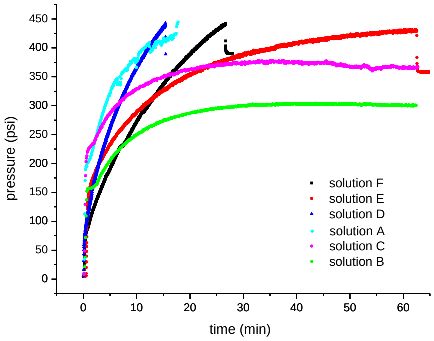

Figure 1: Pressure rise during irradiation of different solutions.

Results: Quantities large enough for pre-clinical studies were achieved. The maximum yield after a 60-minute run at EOB was 120±30MBq (solution C, Table 1). Future studies will examine the production metrics for other isotopes (^{89}Zr, ^{68}Ga, ^{86}Y [1]).

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ELECTROLYSIS DURING ZIRCONIUM-89 PRODUCTIONS IN A SOLUTION TARGET CONTAINING YTTRIUM SALTS

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Introduction: Solution target methods for production of radiometals have recently been investigated for ^{86}Y,[1] ^{68}Ga,[2] and ^{89}Zr.[3] Although production yields are lower than achievable with solid targets, the solution target approach is readily implemented on self-shielded PET cyclotrons. This study employed yttrium nitrate and yttrium chloride salts to further clarify the mechanism of gas evolution from solution targets toward optimizing the conditions for radiometal production.

Material and methods: A Bruce Tech. TS-1650 target was used (3 mL Nb insert, 0.11 mm Ta window foil) within a PETtrace cyclotron. Incident proton energy to the solutions was ~14MeV. Aqueous solutions of $Y(NO_3)_3$ or YCl_3 and other solutes were loaded into the target as listed in Table 1. For mechanistic study, beam current was 25 µA and irradiation time 5 min. A backpressure regulator limited target pressure to <60 psi[3]. Evolved target gas volume was measured using a volumetric syringe and gases were quantitatively analyzed for oxygen content (YSI Instruments) and qualitatively analyzed for H_2 (SRI) and Cl_2 (EMD). Post-irradiation target solutions were analyzed for turbidity and pH. Effluent target water vapor was condensed in a trap and the pH was measured. Cl_2 was scrubbed by a NaOH trap before gas efflux was measured.

Results: All effluent gases contained 33.3±0.4% oxygen, with hydrogen also qualitatively present. The effluent from YCl_3 and NaCl solutions (**D-H**) was found to contain Cl_2 gas. Inclusion of 0.25-1N HNO_3 resulted in 38-45% reductions in gas efflux and increased acidity of the target solution and the trapped water vapor (Table 2). In case of YCl_3 solutions containing EtOH (**F**) or NaCl (**G**), preci-pitates were observed in the target dumps. ^{89}Zr production yields were 3.54-3.63 MBq/µA per h for the $Y(NO_3)_3$ solutions and were similar for YCl_3.

Conclusions: The use of nitrate rather than chloride salt decreases water electrolysis by 87-90% as reflected in gas efflux rate. Addition of HNO_3 further decreased gas efflux rate. The profound effects of counteranion and nitric acid supplementation in the presence of similar radiolysis environments argue that the dominant mechanism for H_2, O_2 and Cl_2 production is electrolysis as opposed to radiolysis. Although longer irradiation times will be required, the results support the feasibility of ^{89}Zr productions using a solution target.

Table 1: Experimental conditions

Condition	Target Solutes
A	1.7mM $Y(NO_3)_3$
B	1.7mM $Y(NO_3)_3$ + 1N HNO_3
C	1.7mM $Y(NO_3)_3$ + 50mM EtOH
D	1.7mM YCl_3
E	1.7mM YCl_3 + 0.25N HNO_3
F	1.7mM YCl_3 + 50mM EtOH
G	1.7mM YCl_3 + 1M NaCl
H	1.7 mM NaCl

Table 2: Experimental results

Condi-tion	^{89}Zr Yield (MBq/ µA h)	Target pH	Target Ppt*	Gas Efflux (L/h)	Gas Trap pH
A	3.54	6.0	-	0.312	3.3
B	3.55	<2	-	0.171	<2
C	3.63	6.5	-	0.229	4.4
D	2.41	6.5	-	2.46	4
E	2.96	<2	-	1.53	<2
F	3.89	6.5	+	2.46	4
G	3.44	5.3	+	2.49	3.3
H	Na	3.9	-	0.924	3.9

* ppt = precipitate

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SOURCES OF CARRIER F-19 IN F-18 FLUORIDE

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Introduction: One of the challenges to nanochemistry for ^{18}F is the added carrier in ^{18}F for synthesis. Theoretical specific activity for ^{18}F is 6.33 x 10^4 GBq/micromol or 0.58 nmoles per 37 GBq, but most reported syntheses have 10 to 1000 fold lower specific activities. We evaluated sources of carrier fluoride and other anions in materials and reagents used in ^{18}F synthesis.

Material and methods: ^{18}F was made by the $^{18}O(p,n)^{18}F$ reaction using a Siemen's Eclipse cyclotron with a tantalum target. Fluoride and other anions were measured using a Dionex AS12A anion exchange column 2 mm ID X 200 mm with suppressed-conductivity detection. A mixed carbonate (2.7 mM sodium carbonate and 0.3 mM sodium bicarbonate) mobile phase was used.

Various materials and solutions were tested. Tubings were obtained from Upchurch Scientific or from Alltech Associates. Reagents were from ABX or Sigma Aldrich except for ^{18}O water which was obtained from multiple suppliers. For tubing, first 1 m lengths of the tubing were rinsed with deionized water and then had 200 mCi of ^{18}F target water in each tube for 1.5 min after which the target water was pushed out of the tube. Anion concentrations were measured from 2.4 mL of deionized water rinses of the irradiated tubes. Solvents were tested by evaporation under argon in a polypropylene tube and rinsing the dried tubes with deionized water. Potassium carbonate overwhelmed the detector and was measured after dilution with deionized water.

Results: The conductivity response was linear with concentration over the range of measures down to a detection limit of 50 microliters of 16 ng / mL, 2 nmoles of F^- for a 2.4 mL target volume.

When tubing was tested, fluoride was not detected except from the chlorofluorocarbon tubes. Surprisingly, the greatest fluoride concentration was found in Halar tubing, the most radiation resistant chlorofluorocarbon tested. (Table 1).

For reagents (^{18}O-water and reagents of Figure 1), fluoride was below the detection limit except for 0.04 M potassium carbonate that had almost 0.5 microgram per mL of fluoride.

Chloride was high in many samples. After irradiation of the ^{18}O-water, nitrate levels were almost 1 microgram / mL. Our silver target had more ions than our tantalum target. All reactions had large amounts of nitrate in solution, presumably as a result of in-vial radiolysis. Sulfate was found in all of the solvents except acetone and in the potassium carbonate.

Table 1: Measured Fluoride from different tubings and fittings, ND is below detection.

Tubing type	Nanograms Per mL	Nanomoles Per 2.4 mL
PEEK fitting	<16	<2
Teflon (PFA)	up to 11	<2
Teflon (FEP)	up to 83	<2 to 5.6
Halar	44	10.5
PEEK	<16	<2
Stainless Steel	<16	<2

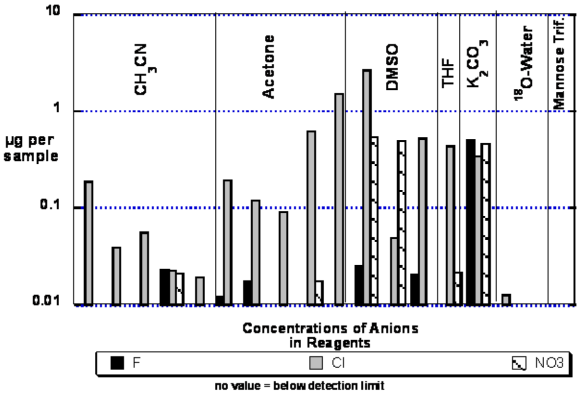

Figure 1: Amount of anions found in solvents, reagents and ^{18}O water

Conclusions: Our measures show that commercial ^{18}O-water has very low levels of anions. Simple methods can be used to avoid measurable amounts of fluoride carrier if potassium carbonate is not used. The bigger challenge to nanochemistry will be removal of the chloride and nitrate.

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ROUTINE $^{18}F^{-}$ PRODUCTION WITH >160 μA TARGET BEAM CURRENT ON A GE PETTRACE 800 CYCLOTRON

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Introduction: The GE PETtrace 800 is currently specified at a maximum total target current of 130 μA (dual 65 μA) for $^{18}F^{-}$ production. We recently reported the feasibility of operating at target currents up to 160 μA (1). We have extended this work by exploring: i) the requirements and results of routine $^{18}F^{-}$ productions at >160 μA and ii) the potential for service dose reduction, which is an important imperative at high production rates, using a prototype self-shielded target.

Material and methods: High current operation was achieved through the following upgrades and enhancements: upgrades to cyclotron and RF control systems, Liquid Target Fillers (LTF) and the ion source anode; Ag targets replaced with larger volume Nb targets; tantalum collimators replaced with graphite collimators and Al extraction foil carousels replaced with graphite units. All these components are now standard on new GE PETtrace 800 cyclotrons.

RF and ion source parameters were adjusted to provide the optimal compromise between load on RF system and ion source current. Ion source wear was reduced by flushing the ion source with a low flow of H_2 gas overnight while the cyclotron is off.

The prototype self-shielded target replaced the standard Al housing of the $^{18}F^{-}$ target with a W-Cu alloy to shield the Havar foils and the target contents. The new target design was evaluated with dual target irradiation of one standard and one self-shielded target (same accumulated charge per target) for direct comparison.

Results: The $^{18}F^{-}$ saturation yields for 36 μA to 90 μA target currents are given in Table 1. No systematic decrease in yields with increasing target current was observed and yields were in line with the 8399 MBq/μA measured at acceptance of the cyclotron in 2002.

Table 1: $^{18}F^{-}$ Saturation Yields

Beam Current / target (μA)	Yield (MBq/μA)	n
36	8299±159	4
65	8221 ± 52	4
70	8377±211	21
80	8510±318	6
90	8223±248	4

The [^{18}F]FDG yields from productions using the TRACERlab Mx module are plotted in Figure 1. No decrease in yield is observed with increasing beam current.

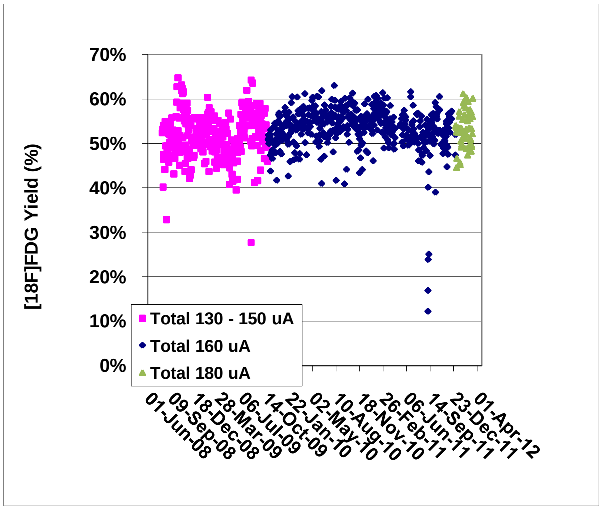

Figure 1: FDG yields as a function of total beam current for dual target irradiations. The lower yields in September 2011 were due to contaminants in the LTF.

Routine $^{18}F^{-}$ production with 180 μA beams has been implemented. Test beams up to 200 μA have been performed without adverse effects. The self-shielded target reduced the dose from the Havar foils, a main service dose contributor, by a factor of 8-10. Reliability was not adversely affected by high current operation.

Conclusions: After upgrades and optimization to our GE PETtrace cyclotron, beam currents for routine production of $^{18}F^{-}$ were successfully increased from 75 μA (original) to 180 μA, which is well in excess of the current 130 μA specification**.** No adverse effects on yields and reliability were observed at the higher currents. The self-shielded target promises to reduce the radiation dose during cyclotron maintenance.

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150 µA ^{18}F$^-$ TARGET AND BEAM PORT UPGRADE FOR THE IBA 18/9 CYCLOTRON

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Introduction: A high power (~3 kW) target platform has been developed for the 18/9 cyclotron. New designs for the airlock, collimator and target subsystems have been fabricated and deployed. The primary project goal is reliable commercial production of 18F- at 150 µA or greater, while secondary goals include improving serviceability and extending service intervals relative to OEM systems.

Material and methods: The target airlock and collimator sections are designed as an integral assembly. The construction is primarily hard anodized aluminum (6061-T6), with a limited amount of PEEK used for insulators and bushings. The ring collimator material is low porosity graphite housed in a water cooled cavity. An "off the shelf" VAT vacuum valve is used for airlock isolation. Compatibility with the OEM roughing valve and airlock control scheme was maintained. The collimator and target port section has vertical adjustment for beam alignment, and it can be removed for service without venting the main vacuum chamber.

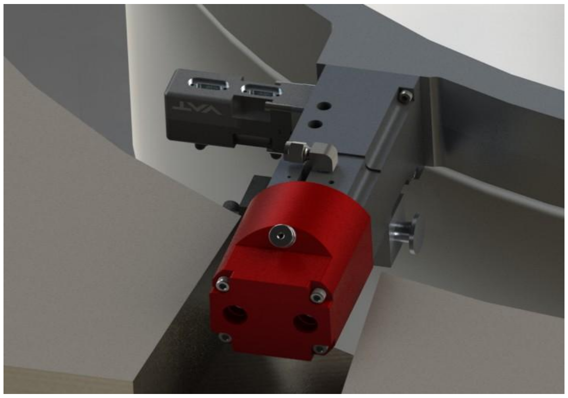

Figure 1: Prototype target port and target.

Three water target prototypes have been employed. All targets have similar construction consistent with U.S. Pat. Application 12/434,002. Target materials include niobium (chambers), 6061 aluminum (bodies) and 316 stainless steel (process connections). A single 37 µm or 50 µm thick Havar window (no helium cooling or support grid) is used in all prototypes.

The initial prototype, a TS-1650P[1] (commercially available PETtrace target), was selected for initial evaluaton of the new airlock and collimator design during routine production. The thermal limit of this design is approximately 1.7 kW, or roughly 95 µA at 18 MeV.

The second prototype is a modification of the 1650P, in which both the wall thickness of the chamber and the diameter of the axial cooling channels were reduced to 0.5 mm (0.020"). This was selected to determine the sensitivity of these geometry parameters, and for validation and refinement of the computational models [2]. The model predicted increase in total heat transfer is 10-15%.

The third prototype is designed for a thermal limit of 3 kW, or 165 µA at 18 MeV. This is accomplished primarily via increased heat transfer area by lengthening the chamber vertically. Chamber depth was also increased from 15 to 20 mm. Critical seals were moved out from the hottest sections of the target insert in an effort to lengthen seal life.

Results: The airlock, collimator and first prototype were operated almost exclusively in routine commercial production at a beam current of 90 µA for 6 months. Testing of the second protoype has been underway for 3 months at 100 µA. Testing of the third prototype will be underway by WTTC 14.

Table 1: Summary of prototypes.

Prototype	Volume (mL)	Material	Current (µA)	Months in Production
1	3.2	Nb	90	6
2	3.2	Nb	100	3
3	4.0	Nb	-	-
Prototype	Sat. Yield (mCi/µA)	Yield - 2 hr (mCi)	Yield - 3 hr (mCi)	Rebuild Interval (µA-hr)
1	239	11400	14600	16000
2	246	13000	16700	18000
3	-	-	-	-

Conclusions: The prototype airlock, collimator and targets have met expectations thus far. Pending results from the third prototype, a commercialized design, will be implemented later in the year.

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VISUAL OBSERVATION OF BOILING IN A HIGH POWER LIQUID TARGET

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Introduction: Batch-style water targets for F-18 production operate under boiling conditions in the target irradiation chamber, but the distribution of vapor in the chamber under steady-state operating conditions is unknown. Prior experiments have been performed using a vertical sight tube to provide visual observation and recording of displaced liquid volume from the target during steady-state operation due to density change associated with boiling. These experiments only provided information about the total average void in the target, with no indication of void distribution or behavior. Thermal performance of batch targets was found to be directly correlated to average void, and performance models were developed [1].

Current Bruce Technologies batch targets operate at 28 bar (400 psi) with heat inputs of 1 to 3 kW and fill volumes of 2 to 4 mL. Prior publications by other researchers on visualization targets were restricted to significantly lower power levels and used fill volumes either significantly smaller or significantly larger than typical production targets [2, 3].

Material and methods: A batch-style water target with transparent viewing windows has been developed to perform visualization tests at realistic operating beam powers and chamber pressures. The test target has an aluminum body with an integral aluminum window and features two viewing windows made of optically clear sapphire (Al_2O_3). Due to the excellent physical and thermal properties of the sapphire viewing windows and the use of well-optimized water cooling, the target can be operated at typical production beam powers and operating pressures with a realistic chamber volume. The total chamber volume is 3.15 mL, but the target may be operated with smaller fill volumes. The use of an integral window allows for a direct view of any nucleate boiling off the window.

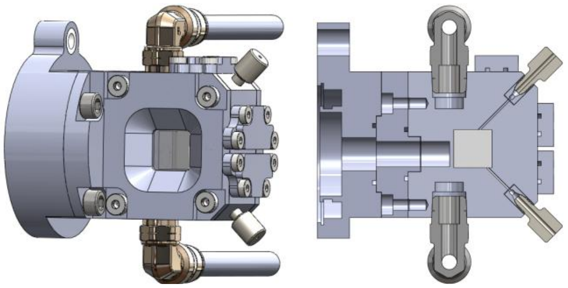

Figure 1: Isometric view and vertical cross-section.

The target can be used to determine the size and distribution of bubbles, the location where they collapse, and the position of the Bragg peak. It can be used to determine the effects of fill volume, overpressure gas, and pressure level on target dynamics. The target can also be used to examine beam collimation effects and to study critical heat flux.

During irradiation, the proton beam will excite the water molecules, producing visible blue light emissions during de-excitation. These light emissions can be recorded using a video camera in dark ambient conditions and used to determine if the position of the Bragg peak shifts during steady-state operation. With good ambient lighting, it will also be possible to see and record bubble formation and transport in the chamber.

Results: Initial modeling indicates the target should operate with a coolant mass flow rate of 4 L/min and have a thermal capacity of roughly 1.5 kW. Initial experiments will be conducted on an 18/9 cyclotron in May of 2012, and the results will be presented.

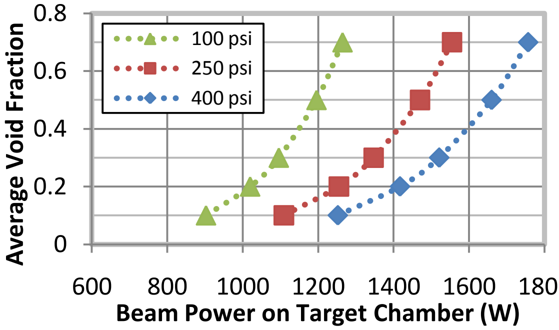

Figure 2: Beam power vs. predicted average void.

Conclusions: A batch-style water target with transparent viewing windows has been developed to perform visualization tests at up to 1.5 kW and 400 psi chamber pressure.

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IMPROVED COMPOSIT TARGETS FOR SMALL SCALE ^{64}Cu PRODUCTION COMPARING Au- AND Pt -FOILS AS ^{64}Ni BACKING

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Introduction: Advantages of a stacked assembly of target support components for ^{64}Cu production via ^{64}Ni(p,n)^{64}Cu reaction were reported recently.[1] The present work shows the applicability of these composit targets for beam currents up to 22 µA. Gold and platinum foils were evaluated as ^{64}Ni backing. The effective specific activity (ESA) and specific activity (SA) were determined by TETA titration at room temperature and at 80 °C and compared with additional copper quantification results via stripping voltammetric trace analysis (VA).

Material and methods: The irradiations were performed with a Cyclone 18/9 (IBA, Louvain la Neuve, Belgium) cyclotron equipped with a solid target holder for perpendicular irradiation mounted on a beam-line. The beam-line was sealed with a 1 mm Al vacuum foil (99.999%) from Goodfellow (Huntingdon, England). ^{64}Ni with 99.60% isotopic enrichment (Isoflex, San Francisco, USA) was the target material. Gold foils (12.5 × 12.5 mm, 0.25 mm thickness, 99.999%, 1 ppm Cu) and platinum foils (15 mm diameter, 0.1 mm thickness, 99.99+%, <1 ppm Cu) were used as ^{64}Ni support. An aluminum disk (22 mm diameter, 1 mm thickness, 99.0%, hard) with rubber O-ring (16 mm diameter) and an aluminum lid (23 mm diameter, 10 mm hole, 99.0%, hard) were purchased from Goodfellow (Huntingdon, England). VA for Cu and Ni quantification were performed with a 797 VA Computrace (Metrohm AG, Herisau, Switzerland). As helium pump was used N1200 AVE.(KNF Neuberger Gmbh, Germany).

Results: Higher helium pressure in front of the O-ring sealed targets leads to a better contact between Al disk and Au or Pt foils and therefore to a higher cooling efficiency throughout irradiation. Beam currents of 22 µA were applied for 120 min without visible overheating, melting or substantial change of the composit targets. ESA values close to and SA values higher than 1 TBq/µmol were determined for both backing materials gold and platinum. Beside the well-proven Au foils the applicability of Pt foils were studied due to its higher mechanical strength and better resistance to hydrochloric acid.

Significant differences were observed in terms of Ni target layer dissolution after irradiation. Using similar conditions (40 min, 90 ° C) for both Au and Pt foils only 30% of the produced ^{64}Cu was separated in case of the Pt foil. Only prolongation of dissolution time or twofold repetition of the dissolution process yields in the isolation of the complete ^{64}Cu-fraction.

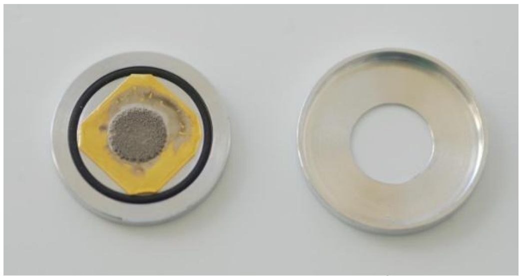

Figure 1: Al disk with O-ring and ^{64}Ni on Au foil, right: Al lid with 10 mm hole.

Figure 2: Opened target left: Al disk with O-ring, ^{64}Ni on Pt foil, right: Al lid with 10 mm hole.

Conclusions: The beneficial usage of composit targets for ^{64}Cu production could be shown for beam currents of 22 µA. Advantages that accrued by use of Au foils as Ni backing exceed clearly that of Pt foils. Especially the dissolution of Ni and Cu from Pt foils is challenging and needs special conditions.

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Acknowledgments: We thank Norman Dohn for excellent conduction of target part manufacturing and Diana Hampe (VKTA) for realization of stripping voltammetric trace analysis.

ROUTINE PRODUCTION OF COPPER-64 ON 18 MeV CYCLOTRON: TARGET FABRICATION, TARGET PURIFICATION AND QUALITY CONTROL FOR 'PROOF OF CONCEPT' MICRO-PET/CT

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Introduction: Copper-64 has ideal physical characteristics for PET imaging with a number of target agents (eg. Peptides, proteins and nanomaterials) ($T_{1/2}$ = 12.7 hours, β^+_{avg}= 278keV, β^+_{max}= 652.9keV, 17.87%). The aim of this work is to develop a cost-effective and reproducible process for the production of high purity ^{64}Cu, at sufficient quantities for research purposes and ultimately clinical use.

Material and methods: Enriched ^{64}Ni (95%) was electroplated onto an Au foil (as $^{64}NiSO_4$ solution, with $(NH_4)_2SO_4$ added as a pH buffer, using single- or multi-foil electroplating device). The ^{64}Ni target was placed in a custom-built solid target assembly, positioned external to the cyclotron. The target was bombarded with 11.6MeV protons (degraded using a custom built graphite degrader) at a current ranging from 15-40µA, for up to 120 minutes. A novel anion exchange separation process using organic solvent mixtures and AG1-X8 resin was developed to separate ^{64}Cu from the target material and contaminating radionuclides (eg. ^{55}Co and ^{57}Co). The ^{64}Cu product was assayed for radionuclidic and chemical purity using gamma spectroscopy and ICP-AES/MS respectively. The specific activity of of the ^{64}Cu determined by ICP-MS was compared with that obtained by titrating with varying concentrations of DiamSar and analyzing ^{64}Cu complexed by TLC. ICP-MS requires the ^{64}Cu sample decay prior to analysis, while the latter method can be conducted directly after production, providing 'real-time' specific activity data. Current research applications involve development of ^{64}Cu-SarAr-labelled and nanoparticles for application in future pre-clinical PET/CT imaging.

Results: Nineteen targets (with 13.89 – 29.35mg ^{64}Ni) were irradiated between July 2011 to March 2012. Up to 1.2GBq of ^{64}Cu was successfully purified from each target using an anion exchange resin. The ^{64}Cu batches (at approx. 10000GBq/mL) had a specific activity ranging from 25 to 57TBq/µmol. The radionuclidic and chemical purity were high (>98%) with <20ppm of contaminating metal ions (i.e. Al, Fe and Pb) in each batch. The production yield varied between 5.5 to 21.3 MBq/uA.hr. The ^{64}Ni was recycled (up to three times) and re-irradiated, with no evidence of change in metals contaminates nor in ^{64}Cu production yield.

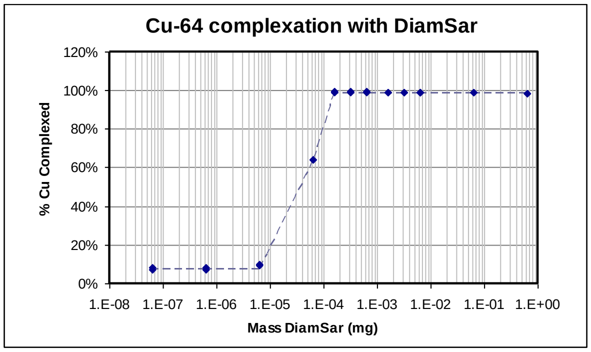

Figure 1: Per cent of ^{64}Cu complexed with DiamSar (using fixed volumes of ^{64}Cu and DiamSar, with varying concentrations of DiamSar in solution), to calculate the specific activity of ^{64}Cu)

Conclusions: The radiopharmaceutical production team at SCGH has in place a reliable and cost-effective process for the production and transport of ^{64}Cu. Up to 1GBq can be isolated after irradiation of an enriched ^{64}Ni target at 40µA for 70 minutes. The specific activity of the ^{64}Cu ranged from 25 to 57TBq/µmol.

Acknowledgments, disclosures and funding: An Australian Institute of Nuclear Science and Engineering grant was awarded in 2010. The Australian Nuclear Science and Technology Organisation have provided funding for equipment to support solid target research at Sir Charles Gairdner Hospital. Funding for travel has been obtained from SCGH and the University of Western Australia.

CYCLOTRON PRODUCTION OF ^{61}Cu USING AN ENRICHED ^{64}Zn TARGET

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Introduction: Copper-61 (^{61}Cu; $T_{1/2}$ = 3.4h; β^{+}_{mean} range = 0.242 - 0.527MeV) is suitable for radiolabeling diacetyl-bis(N^4-methylthiosemicarbazone) [^{61}Cu-ATSM], for imaging of hypoxic tissue (1). ^{61}Cu can be produced using a number of nuclear reactions, including ^{61}Ni(p,n)^{61}Cu, ^{62}Ni(p,2n)^{61}Cu and ^{64}Zn(p,α)^{61}Cu (2,3). Given the significant natural abundance of ^{64}Zn (48.6%), making it a cheaper target source than Ni isotopes, we explored production of ^{61}Cu from natural and enriched ^{64}Zn targets using an energy-degraded proton beam from an 18MeV cyclotron. A challenge is the development of a rapid and efficient separation process to isolate the desired ^{61}Cu, removing gallium radioisotopes co-produced during bombardment.

Materials & Methods: Natural Zn foils (d=15mm; thickness=50μm; 99.99% purity) were purchased (Goodfellow). Enriched ^{64}Zn (99.8%; Isoflex) was electroplated onto an Al disc cleaned with 0.05M HCl. These Zn targets were irradiated for up to 60min using 11.7MeV protons at 30μA. At end of bombardment, the irradiated target was transferred to a hot-cell and dissolved in a minimal (500μL) volume of 10M HCl at room temperature. The digest was quantitatively transferred to a cation exchange column (200-400 H^+; Bio Rad AG 50W-X8). Cu & Zn isotopes were eluted with 25mL of 10M HCl; gallium isotopes were retained on the column. Eluted fractions were combined and transferred onto an anion exchange column (200-400 Cl^-; Bio Rad AG1-X8) and the ^{61}Cu was finally eluted with 20mL of 2M HCl. The fractions containing ^{61}Cu were combined and evaporated to dryness, and then dissolved in 0.05M HCl. The Zn was eluted using 30ml of 0.05M HCl and the fractions evaporated to dryness. The resultant residue was digested with 2mL of 6M H_2SO_4, evaporated to dryness, and then dissolved in MilliQ water (10mL), ready for re-use in electroplating.

Results: SEM shows the electroplated Zn had an acceptably smooth surface (see fig.) The separation of ^{61}Cu using two columns was complete within 120min. The final product had >98% radionuclidic purity and a yield within 5% of the theoretical calculation.Recovery of the enriched zinc target material was >95%.

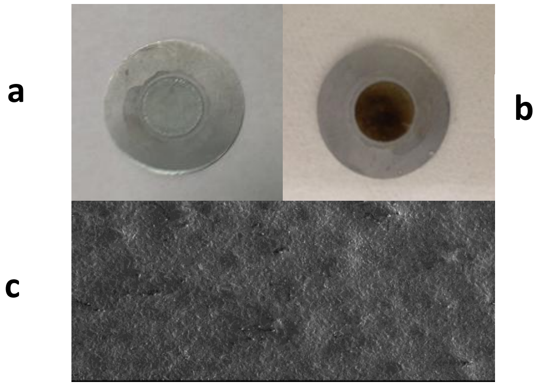

Figure 1. Images of ^{64}Zn electroplated on Al backing plate; (a) before irradiation; (b) after irradiation with 11.7MeV protons and total irradiation of 30□A.hr; (c) SEM of target surface before irradiation (100x magnification).

Conclusions: A rapid and efficient separation process for ^{61}Cu from Zn (primarily enriched ^{64}Zn) targets has been developed. A process for recycling electroplated enriched ^{64}Zn yielded a high purity product for re-use.

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PRODUCTION AND SEPARATION OF ^{55}Co VIA THE ^{58}Ni(p,α)^{55}Co REACTION

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Introduction: ^{55}Co is a positron emitting isotope that is of interest to the nuclear medicine community to be used in PET tracer compounds. It has a maximum beta energy of 1.5MeV and a half-life of 17.5hrs. The daughter decays by isomeric transition to the ground state of ^{55}Fe giving off several gamma rays, the most abundant being 931keV (75%), 477keV (20%), and 1.409MeV (16.9%). It can be made on a medical cyclotron by the reaction ^{58}Ni(p,α)^{55}Co.

Material and methods: ^{58}Ni, obtained from Isoflex (99.48% isotopic enrichment), was plated onto a gold disk by an electrodeposition method described by McCarthy[1] et al. To electroplate, 55mg of ^{58}Ni was dissolved in a 50% solution of HNO_3 and stirred on medium heat until all the liquid was evaporated and a green film remained. Then 10-20 drops of concentrated H_2SO_4 was added to the film followed by the slow addition of 10mL milli-Q water. The solution was then mixed on low heat until a seafoam colored film remained. Approximately 4-5mL of milli-Q water was added to the film and mixed until the solution became a clear green color. Concentrated NH_4OH was added dropwise until the solution was a deep royal blue and then 0.1g NH_4SO_4 was added to the solution and mixed until dissolved. The solution was then placed in an electroplating cell and a voltage of 2.5V was applied for 12hrs. The target was then irradiated with 15MeV protons at 10μA for one hour. Two hours after end of bombardment the target was submerged in 10mL of heated 6M HCl with reflux to dissolve the nickel from the gold disk. Subsequent separation of ^{55}Co from the ^{58}Ni material was performed by an anion exchange column with 2.5g AG1-X8 ion exchange resin. The nickel elutes with 6M HCl and the cobalt elutes with 0.5M HCl. All solutions and chemicals used were very high purity trace metal grade. One milliliter fractions were collected and analyzed by an HPGe gamma spectrometer.

Results: ^{58}Ni was electroplated onto a gold disk with an average plating efficiency of 93% and thickness of 315μm. A small amount of ^{57}Ni (35.6hr) was produced by the decay of ^{57}Cu (196ms) made by the ^{58}Ni(p,2n)^{57}Cu reaction. Due to the presence of the ^{57}Ni we were able to visualize the separation of ^{55}Co from the original ^{58}Ni material by analyzing the 1mL fractions on an HPGe gamma spectrometer. Good separation was achievable and is shown in Figure 1. At EOB 2.1mCi of ^{55}Co was produced which was in agreement with yields calculated from cross-sections detemined by Kaufman[2].

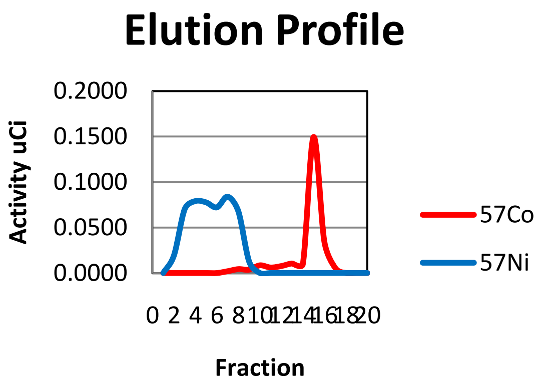

Figure 1: Elution profile. Shows the separation of Co from Ni using ^{57}Ni and ^{57}Co produced from the secondary reaction ^{58}Ni(p,2n)^{57}Cu.

Conclusions: ^{55}Co was able to be produced and separated from the original target material with an average recovery of 72.5%. At EOB an average of 2.1mCi of ^{55}Co was produced and after separation an average of 1.5mCi was available for use. The only identified radioactive impurity in the final sample was ^{57}Co (1.65μCi 0.11%). Measurements of specific activity are in progress. Future experiments will be performed to conjugate ^{55}Co to PET tracer compounds for cell and animal studies.

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STANDARIZED PROCEDURE FOR THE PRODUCTION AND PURIFICATION OF ^{89}Zr AT MEMORIAL SLOAN KETTERING CANCER CENTER

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Introduction: ^{89}Zr is an attractive medical isotope for a variety of reasons. Its target is 100% naturally abundant, can be made on a small cyclotron, has a positron emission of 22% and is ideal for the labeling of proteins and antibodies as well as smaller fragments, such as small peptides due to its half life of 78.41 hours.These are very favorable characteristics when considering the circulation time required by larger molecules such as monoclonal anitbodies [1]. In this work, we report standardized methods for the routine production and isolation of high-purity and high-specific-activity ^{89}Zr using a small cyclotron.

Material and methods: ^{89}Zr was produced with a high current cyclotron via the ^{89}Y(p,n)^{89}Zr nuclear reaction at a current of 15 μA with a proton beam energy of 15 MeV with a solid target set-up that was coupled to a watercooled backing. The target is available as a small, thin metal plate with dimensions measuring 48×16×0.1 mm. After proton beam irradiation, the ^{89}Zr target is dissolved in 2 mL of 6M chelex HCl in a metal-ion free PTFE tube. Chelex water is added to bring the HCl normality to 2M. Radiochemical separation of ^{89}Zr from the Y target solution is performed by passing the solution through a resin bed that has been treated with acetonitrile, saline, and 2M HCl, all of which were treated with chelex resin. The resin bed was prepared by functionalizing the carboxylate groups of the silica-based Waters Accell Plus CM weak cation exchange resin with hydroxamates [2].The insoluble Y impurities sit at the top of the resin bed. The soluble Y impurities pass through the column and are washed away with 2M HCl and chelex water. The ^{89}Zr is washed off of the column with 1M oxalic acid [1].

Results: Conditions reveal high average yields of 1.52±0.11 mCi/μA·h at a proton beam energy of 15 MeV and current of 15 μA using a solid, commercially available ^{89}Y-foil target (0.1 mm, 100% natural abundance). ^{89}Zr was isolated in high radionuclidic and radiochemical purity (99.99%) as [^{89}Zr]Zr-oxalate by using a solid-phase hydroxamate resin with 99.5% recovery of the radioactivity. The effective specific-activity of ^{89}Zr was found to be in the range 5.28–13.43 mCi/μg (470–1195 Ci/mmol) of zirconium. Table 1summarizes production for ^{89}Zr for 3 consecutive runs using the optimized conditions established by us. Figure 1 displays the decay scheme and mode for ^{89}Zr [3]. Since 2009, there has been an average of 4 irradiations per month, with each irradiation producing 60 mCi on average with a mean recovery of 90% of ^{89}Zr at the end of the targetry chemistry per run.

Table 1: Energy parameters and activity produced.

Target	Proton Energy/Current	Irradiation time	^{89}Zr activity
^{89}Y	15 MeV/15 μA	2 hours	40 mCi
^{89}Y	15 MeV/15 μA	2 hours	43 mCi
^{89}Y	15 MeV/15 μA	2 hours	41 mCi

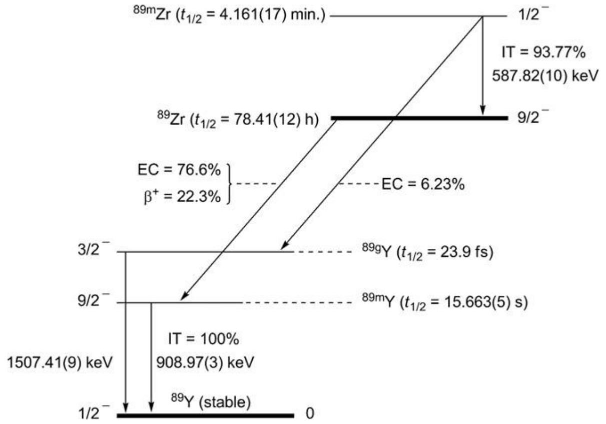

Fig. 1. Nuclear decay scheme showing the main pathways for the decay of ^{89}Zr and ^{89m}Zr to ^{89}Y.

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ESTABLISHING RELIABLE PRODUCTION OF THE PET ISOTOPE ^{89}Zr FOR RESEARCH USE: FROM TARGET FABRICATION TO PRECLINICAL IMAGING

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Introduction: ^{89}Zr, with its long half-life (78hr, β^{+}_{mean}=0.4MeV; 23%) is a candidate for immuno-PET imaging, particularly when extended monoclonal-antibody (mAb) circulation time facilitates tumour penetration. Challenges in purification of ^{89}Zr and its labelling of mAb have restricted its use. Introduction of an isothiocyanate group to the desferrioxamine (DFO)-based conjugation of mAb (1), plus improvements in ^{89}Zr targetry will expand applications of ^{89}Zr.

Materials and methods: A semi-automated in-house devised external beamline, delivering >40μA at 11.7MeV (degraded from 18MeV to suppress ^{88}Y & ^{88}Zr radionuclidic contaminants) produced ^{89}Zr from ^{89}Y(p,n)^{89}Zr. Graphite degrader is integrated with a graphite water-cooled collimator. Target comprised of 2 stacked pure (99.9%) yttrium foils, each (mean) 127μm thick & 15mm in diameter, helium-cooled on the beam face and cradled in an Al backing plate (Fig. 1). When pressed against a Viton O-ring seal this plate is cooled on its back by a water jet. (Water contamination of discs must be avoided). Beam is aligned using thermocouples embedded in a dummy target disc. Irradiated target was then dissolved in 6M HCl, then diluted with pure water, followed by elution through an hydroxamate ion-exchange column, then washes through column of HCl (2M), then water. Zr then eluted with 1M oxalic acid (2). Recovery was 95%, radionuclidic purity >98% & chemical purity <0.2ppm Zr (n=5 runs, ICP-AES/MS). ^{89}Zr as oxalate (or Cl^{-}) was used to label DFO following (2). Specific activity was measured using chelator titration plus ITLC to determine chelated vs. free ^{89}Zr, following (1), with modifications including using Varian papers heated to >90°C, plus 0.5M citric acid for mobile phase. For mAb conjugation we followed (1), using the bifunctional chelator *p*-isothiocyanatobenzyl-DFO B to premodify the mAb. Chelate:mAb ratio was determined by labeling the immunoconjugate with a known excess of Zr (Zr spiked with ^{89}Zr). Generally following (1), DFO-mAb was labelled with ^{89}Zr at 24°C for 1hr, purified by size-exclusion chromatography; then analysed by ITLC (as described above) and HPLC. 'Proof-of-concept' μPET imaging was performed on a Balb/c nude mouse xenograft colorectal tumour model (LS174T HER2-expressing), comparing free ^{89}Zr (chloride) vs. ^{89}Zr-DFO-trastuzumab tumour uptake.

Results: EOB activity (by HPGe γ-spectr.) of ^{89}Zr in target discs, derived from multiple runs, was 80-90% of theory. Specific activity of purified ^{89}Zr was 426 MBq/μg, comparable to published data (196-496; [2]). Figure 2 shows that purified ^{89}Zr does not bind non-specifically to mAb and 100% binding of ^{89}Zr-DFO to mAb is achievable. μPET imaging demonstrated marked tumour-specific uptake of labelled trastuzumab, but nil free ^{89}Zr (as chloride) tumour uptake.

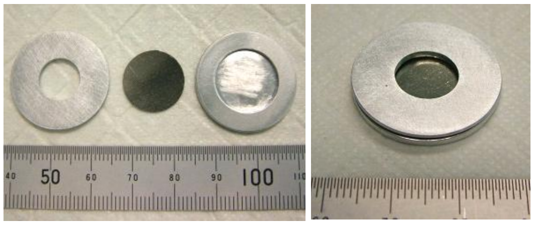

Figure 1: Assembly of yttrium stacked-discs target. Following slotting into external beamline, pneumatic compression permits He cooling on front (between Havar vacuum 'window' and target surface) and water cooling on back.

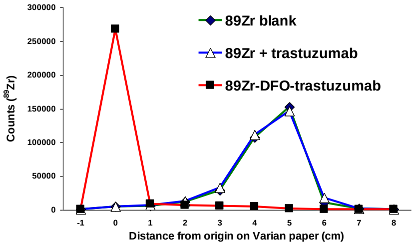

Figure 2: ITLC separation of free and mAb-bound ^{89}Zr.

Conclusions: This study has achieved a capability for reliable (research) production of radionuclidically and chemically pure ^{89}Zr of acceptable specific activity – from targetry design & construction through to validating product use in preclinical tumour imaging.

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Acknowledgments and funding: The Australian Nuclear Science & Technology Organisation generously funded equipment. RKS received an AINSE Scholarship.

CYCLOTRON PRODUCTION FOR RADIOMETAL OF ZIRCONIUM-89 IN PETIC WITH AN IBA CYCLONE 18/9 AND COSTIS STS

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Introduction: The development of biological targeting agents such as proteins, peptides, antibodies and nanoparticles with a range of biological half-lives demands the production of new radionuclides with half-lives complementary to these biological properties[1]. As a result, methods of producing the radiometals Zr, Y, Cu and Pt have been investigated. Zirconium-89 is the most promising radionuclide for development of new immuno-PET agents (in vivo imaging of cancerous tumours and radioimmunotherapy planning). Besides the convenient half-life of 78.4 h, Zr-89 has a β^+ emission rate of 23% and a low maximum energy of 0.9 MeV delivering a short range in tissue (≈1mm) and a good spatial resolution as a consequence. The daughter radionuclide is Yttrium-89 (stable). Zr-89 has only one significant γ-line of 909 keV emitted during decay.

Material and methods: There are three nuclear reactions that have been explored for the production of Zr-89 (tab 1). As PETIC is unable to perform α bombardment, the $^{nat}Sr(\alpha,xn)^{89}Zr$ reaction is not an option. Effective deuteron bombardment of Y-89 is also not possible because 9 MeV maximum energy is deemed to be too low.

Table 1: Nuclear reactions for Zr-89 production.

$^{89}Y(p,n)^{89}Zr$
$^{89}Y(d,2n)^{89}Zr$
$^{nat}Sr(\alpha,xn)^{89}Zr$

Since Yttrium has only one stable isotope and the product can be made relatively pure at low energy (10-11 MeV)[2], as an ideal reaction for production of Zr-89 the $^{89}Y(p,n)^{89}Zr$ was chosen. The target material Y-89 (100% natural abundance) is used in form of the 150 μm thick foil 99.9 % pure provided by Goodfellow Cambridge Ltd. To simplify pre and post processing of the solid target a well known[3] holder construction was used (fig 1).

The proton beam of Cyclone 18/9 cyclotron has been degraded from 18 MeV to 10-11 MeV by the 0.5 mm thick Niobium window foil installed in the COSTIS Solid Target System (STS) equipped with the FlexLink conveyor belt (safe solid targets transportation outside the vault).

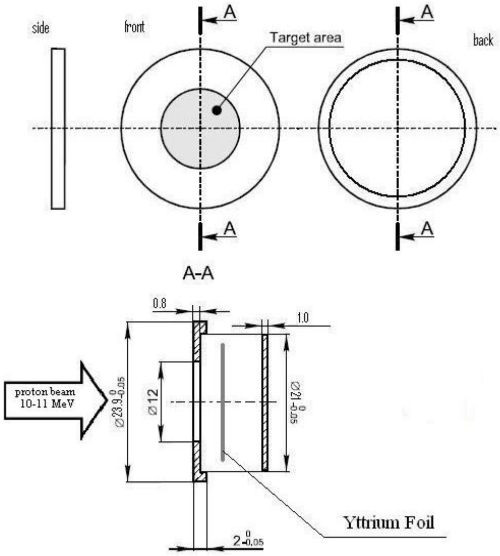

Figure 1: Solid target material holder.

Several irradiated Y-89 foils with different beam parameters have been checked for radionuclidic purity by MCA spectrometry.

Results: Degradation of energy by means of 0.5 mm thick Nb foil was simple and did not suffer from overheating problems associated with long irradiation times. The lower proton energy has been demonstrated to produce radionuclidically pure ^{89}Zr.

Conclusions: Zr-89 production by means of Cyclone 18/9 and COSTIS STS was achieved.

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AUTOMATED PRODUCTION OF ^{124}I AND ^{64}Cu USING IBA TERIMO PROCESSING AND PINCTADA METAL ELECTROPLATING AND PROCESSING MODULES

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Introduction: With the installation of our new IBA (Belgium) 18/9 cyclotron in 2008, the desire and need to produce solid target isotopes at the Austin P.E.T. Centre has significantly increased. This has led to the recent installation and commissioning of a new lab dedicated to fully automated solid target isotope production.

Material and methods: An IBA 18/9 cyclotron with a 2-meter external beam line is coupled to a Nirta Solid Compact (COSTIS) target. The irradiated target disks are transported by a custom designed Tema Sinergie (Italy) pneumatic Solid Target Transfer System (STTS) to Tema hotcells. The IBA Terimo module is used to process the ^{124}I ($T_{½}$=4.18 days) targets while IBA Pinctada Metal modules are used to electroplate and process the ^{64}Cu ($T_{½}$=12.7 hours) targets.

^{124}I target disks were prepared by melting at 780°C, 300mg of ^{124}TeO$_2$ + 6% AlO$_2$ onto a platinum disk using the Terimo furnace. After irradiation (14.9MeV beam), the target disk was left to decay to reduce the ratio of ^{123}I/^{124}I. Radioiodine separation by the Terimo was carried out at 782°C for 15min followed by 650°C for 2 hours with a 50mL/min flow into a 1mL alkaline (0.01M NaOH) solution to trap the iodine.

^{64}Cu target disks were produced by direct electroplating ^{64}Ni onto an Ag target disk. Disks were first prepared by fine sanding, followed by electro etching the plating face in 1M nitric acid (50mA for 5min) and then rinsing with D.I. water and acetone. ^{64}Ni was dissolved in 12M HCl and refluxed for 2 hours. The Pinctada electroplating module's bath was filled with the desired ^{64}Ni solution topped up to 55mL with ammonium hydroxide. Electroplating was carried out at 5.0mA using a chopped saw tooth current for approx. 10 hours (dependant on desired plating thickness).

After irradiation (14.9MeV beam), the target disk was transferred to the Pinctada dissolution module to dissolve the ^{64}Ni plating in 3mL 12M HCl at 70°C, and purified using an AG 1-X8 anion exchange cartridge, eluting the ^{64}Cu with water.

Results: The following table and graphs show the results of the ^{124}I and ^{64}Cu productions to date:

Table 1: ^{124}I & ^{64}Cu production results.

Isotope	Irradiation Parameters	Yield EOS MBq(mCi)	DC to EOB MBq(mCi)	% Theore.
^{124}I #1	10µA, 3hrs	168 (4.5)	274 (7.4)	46
^{124}I #2	12µA, 3.5hrs	455 (12.3)	601 (16.2)	72
^{64}Cu #1	42µm plating 25µA, 6.3hrs	800 (20.6)	6290 (170)	88
^{64}Cu #2	9.8µm plating 20µA, 5.5hrs	157 (4.2)	508 (13.7)	44

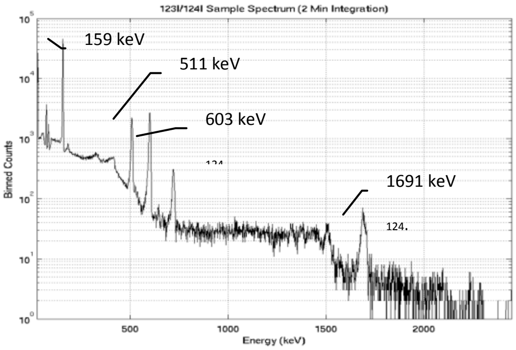

Figure1: γ spectrum of the ^{124}I product at EOS.

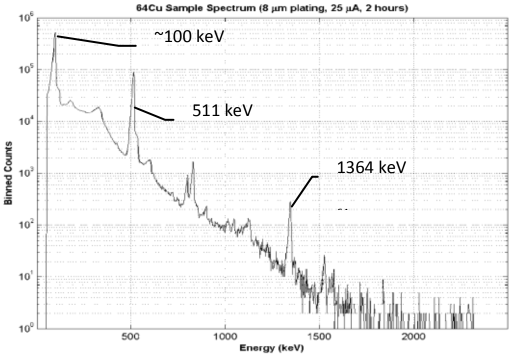

Figure 2: γ spectrum of irradiated ^{64}Ni target disk.

Conclusions: We have successfully implemented fully automated ^{124}I and ^{64}Cu production at the Austin P.E.T. Centre which has increased the suite of isotopes we can provide for in-house research as well as use throughout Australian research facilities.

Acknowledgments, disclosures and funding: This research was undertaken using the "Solid Target Laboratory, an ANSTO-Austin-LICR Partnership".

OVERVIEW OF ^{99m}Tc PRODUCTION AT THE UNIVERSITY OF ALBERTA

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Introduction: The recent shortages in reactor produced ^{99}Mo/^{99m}Tc, along with the pressure to move towards non-HEU ^{99}Mo/^{99m}Tc production strategies has induced a growing interest in recent years in the large-scale cyclotron production of ^{99m}Tc via the ^{100}Mo(p,2n)^{99m}Tc reaction. We presented preliminary cross section measurements for the ^{100}Mo(p,2n)^{99m}Tc reaction along with thermal modelling simulations used to predict the thermal performance of a molybdenum target at WTTC13 (Denmark 2010). We have since made substantial progress in the scale-up of cyclotron production of ^{99m}Tc and an overview of the progress to date is described.

Materials and methods: Studies to date have used the existing TR19/9 cyclotron infrastructure at the Edmonton PET Centre and have been limited to beam currents below 100 μA. Several target designs were considered and tested including thick Mo foil, melting of Mo powder into a Ta plate, pressing of Mo powder into a support plate, and sintering of Mo powder (under H_2 @ 1600 ºC) to form a solid Mo pellet followed by bonding the pellet into an aluminum support plate. Each strategy has its limitations, however, we found that the sintering method led to structurally stable targets capable of tolerating >1.4 kW of beam power. Material losses during target preparation via sintering were typically <2% and many targets could be prepared at once.

To extract the ^{99m}Tc from the irradiated target, we made use of ABEC^{TM} resin. Since this method requires a high ionic strength of biphase promoting anions, we strategically selected to dissolve our molybdenum targets with hydrogen peroxide followed by addition of 3M $(NH_4)_2CO_3$. This not only allowed for extraction of ^{99m}Tc using ABEC, but also allowed for easy isolation of ammonium molybdate by sublimation of the volatile salts and water. The isolated ammonium molybdate was reduced back to the metal and reconverted into additional sintered targets for subsequent irradiation and processing.

After manual small scale optimization of the extraction method, we adapted a Bioscan Reform Plus unit for automated extraction using the ABEC column and Curie-size batches of ^{99m}Tc were processed with this unit.

Results: Extensive QA/QC of the extracted [^{99m}Tc]TcO_4^- demonstrated that the product complied with all relevant USP specifications (e.g. pH, RCP, endotoxin content, sterility, etc.) and had low levels of chemical Mo (<5 μg/mL) and H_2O_2 (<1 μg/mL). Radionuclidic purity was also evaluated, but this has yet to be defined in the USP for the cyclotron produced ^{99m}Tc. While we did not assess the ^{99g}Tc content for each batch, experimental evaluations of the ^{99g}Tc cross sections in the 8–18 MeV range allowed this contribution to be calculated as a function of the irradiation conditions. Labelling studies were also performed along with biodistribution studies in mice and/or rabbits using [^{99m}Tc]MDP, [^{99m}Tc]disofenin, and [^{99m}Tc]pertechnetate. This extensive quality data was compiled as part of a Phase I Clinical Trial application.

Conclusion: Significant progress has been made at the University of Alberta with regards to the scale-up of cyclotron produced ^{99m}Tc. This progress includes: experimental ^{100}Mo(p,2n)^{99g}Tc excitation function measurements [1], development of a metallic target system capable of handling >1.4 kW of beam current, efficient isolation and recycling of metallic ^{100}Mo [2], development of an automated system which demonstrates reliable Curie quantity extraction of ^{99m}Tc, and completion of pre-clinical studies with [^{99m}Tc]MDP, [^{99m}Tc]disofenin, and [^{99m}Tc]pertechnetate using cyclotron produced ^{99m}Tc with comparable biodistributions to generator-based ^{99m}Tc noted. With this data, a Phase I Clinical Trial application was approved by Health Canada Sept 2011, and completed earlier this year. Data analysis is currently underway.

Despite these successes, several challenges remain with the TR24 (June 2012 installation) cyclotron capable of irradiation currents of 500 μA up to 24 MeV. Studies are therefore currently underway to adapt the target design to withstand even higher beam currents.

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SOLID TARGETS FOR ^{99m}Tc PRODUCTION ON MEDICAL CYCLOTRONS

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Introduction: Solid ^{100}Mo metal targets for the production of ^{99m}Tc on medical cyclotrons via the ^{100}Mo(p,2n)^{99m}Tc reaction have been developed. The isotopically enriched ^{100}Mo target material is electrodeposited on a tantalum backing and then sintered. The targets thus produced have been irradiated at power densities of up to 1.1 kW/cm^2.

Material and Methods: Our method for manufacturing high current solid targets for the production of commercial quantities of technetium-99 is based on the electrophoretic deposition (EPD) of ^{100}Mo from a suspension of fine molybdenum powder in an organic polar solvent following the procedure described by Gutierrez et al. [1]. The deposited layer is then sintered in a tube furnace at 1,700 °C under inert gas atmosphere (Fig. 1).

^{100}Mo powder obtained from various suppliers exhibited a highly non-uniform grain size distribution, which resulted in substantial variability in the target manufacturing process. To mitigate this risk, commercial ^{100}Mo powders were oxidized by dissolution in peroxide followed by reducing the dried trioxide back to molybdenum metal with hydrogen under carefully controlled conditions [2]. Uniform deposits were achieved by using re-processed molybdenum powder of <10µm grain size (Fig. 2).

SEM/EDX was used to characterize the powder both when obtained from the commercial supplier as well as after reprocessing.

Targets were irradiated at the GE PETtrace cyclotron at the Lawson Health Research Institute with 16.5 MeV protons and beam currents of up to 80 µA (power density 1.1 kW/cm^2).

The enriched target material was recovered after irradiation and ^{99m}Tc extraction. Recovery was afforded by separating ^{100}Mo-molybdate from impurities via ion exchange. The molybdate was then thermally decomposed to MoO$_3$, which was then reduced back to molybdenum metal with hydrogen [3,4].

Results: The targets showed excellent stability under the above irradiation conditions. After bombardment, the Mo deposit could be completely dissolved in peroxide within a few minutes. -- Recovery of the ^{100}Mo powder was achieved with ~90% efficiency.

Figure 1: ^{100}Mo-targets prepared by EPD / sintering

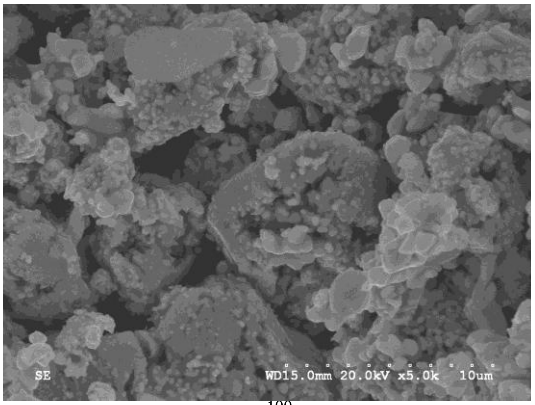

Figure 2: Pre-processed ^{100}Mo powder

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Acknowledgments:

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THE USE OF NEUTRONS FROM A SMALL CYCLOTRON FOR MAKING Mo-99 / Tc-99M GENERATORS FOR TEACHING

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Introduction: Authorized user and board training for nuclear medicine residents requires practical experience with radionuclide generators. In the past most nuclear medicine clinics had a technetium generator on site. Now central nuclear pharmacies make it impractical for many clinics to have generators. We describe the use of neutrons from our cyclotron reactions to make ^{99}Mo/ ^{99m}Tc generators for teaching purposes.

Material and methods: Approximately 1 g each of molybdate ammonium salt ($(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$) (Sigma Aldrich Co) was placed in polyethylene vials and surrounded by ~5 cm of polyethylene to thermalize the neutrons from cyclotron target reactions. The polyethylene / molybdate vials were placed on the top of our Siemens Eclipse magnet in line with the targets, within the radiation shield, and left there during ~ 0.5 hour of 30 microamperes on a ^{16}O (p,□) ^{13}N water target.

Gamma spectra were taken of the irradiated "target". After >24 hrs, the irradiated solid was dissolved in >10 mL of water, heated at 90°C until dissolved, cooled and passed through aluminium oxide lite Sep-Pak cartridges (Waters Corp). The alumina Sep-Paks were rinsed with at least 3 bed volumes of isotonic saline and the liquid that passed through the cartridges was counted after elution and after more than 2 half-lives of ^{99m}Tc to determine ^{99}Mo breakthrough as a function of mass loaded on the cartridges. The Sep-Paks were re-eluted after ingrowth and counted.

For comparison, a direct irradiation was done in a 20 X 20 cm field of fast neutrons from a Be target on a Scanditronix MC50 cyclotron beam line with a yield of ~2 to 3 X 10^8 thermal neutrons s^{-1} cm^{-2} for 485 seconds with 5 cm of polyethylene moderation.

Results: After irradiation, NaI(Tl) gamma spectrometry, 75% efficiency for ^{99m}Tc, showed multiple gamma photopeaks. After 24 hours, the molybdate spectra showed only the 141 keV photopeak for ^{99m}Tc (Figure 1).

Loading of the Sep-Pak at >1 mL/minute had breakthrough of over 90% of ^{99}Mo from 0.7 g of molybdate solution. With a low loading rate of 0.25 mL/ min, breakthrough was much lower and ~90% of the molybdate was retained on the Sep-Pak **(~0.6** g of ammonium molybdate loaded)

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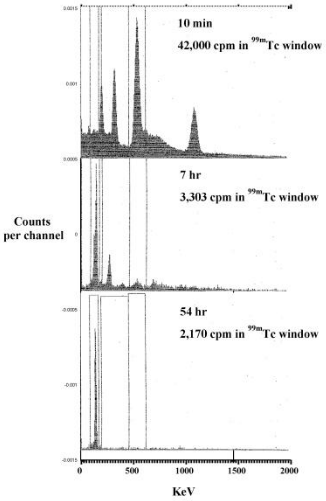

Figure 1: Serial gamma spectra post Mo irradiation.

Irradiation gave a yield of 2 X 10^4 atoms of ^{99}Mo per gram of ammonium molybdate per 10^8 thermal neutrons giving a count rate of ^{99m}Tc at 54 hours post bombardment of ~2,000 counts per minute. From placing vials on the top of the cyclotron for 30 minutes of irradiation we obtained a ^{99m}Tc ingrowth count-rate of ~200 cpm per 0.5 g of ammonium molybdate or 700 cpm from ~ 1 gram of molybdenum metal 78 hours post bombardment.

Greater than 98% of the ingrown ^{99m}Tc eluted from the Sep-Pak in 3.0 mL of normal saline for injection. Residents were given molybdate solutions to load on Sep-Paks then eluted the cartridges as specific times post loading and measured ^{99m}Tc recovery and compared it with theoretical yield for sequential decay.

Conclusions: Cyclotrons produce sufficient neutrons to make ^{99}Mo for teaching purposes and aluminum oxide Sep-Paks make adequate sorbents for the ^{99}Mo. More irradiation and using (p,n) reactions should produce higher yields.

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IMPACT OF SUBSEQUENT IRRADIATION ON THE COMPOSITION OF RECYCLED HIGHLY ENRICHED ^{100}Mo TARGET MATERIAL

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Introduction: Technetium-99m is the most widely used medical radioisotope. In the recent years shortage of ^{99}Mo has induced a research work to develop new technology to produce ^{99m}Tc, which does not depend on nuclear reactors. One obvious route is to develop an accelerator based alternative to the conventional ^{99}Mo/^{99m}Tc generator. Among the charged particle induced reactions the (p,2n) reaction provides the highest yield. To guarantee high specific activity ^{99m}Tc highly enriched ^{100}Mo target should be used. The expensive target material should be recycled and subsequently used for ^{99m}Tc production.

Material and methods: As in practice 100 per cent enrichment cannot be produced, the ^{100}Mo target material always contains minor amount of lower mass number molybdenum isotopes too. The amount of these different stable Mo isotopes should be kept as low as possible since at any bombarding energies selected for production of ^{99m}Tc through the (p,2n) reaction on ^{100}Mo target also unwanted radionuclides will be produced on the lower mass Mo isotopes present in the target material. Irradiating highly enriched ^{100}Mo target besides the ^{99}Mo and ^{99m}Tc different other radionuclides are formed on ^{100}Mo as well as on lower mass Mo target isotopes. Some of the produced radionuclides decay back to stable Mo isotopes. In that process the composition of the original target material is slightly changed. Recovering the irradiated target material and use it again and irradiate it again subsequently can gradually change the composition of the original enriched Mo target. The tendency is that the subsequent irradiation partly transforms the higher mass stable Mo isotopes to lower mass stable Mo isotopes. The amount and activity of the unwanted technetium and other radionuclides can be estimated by calculation using cross section data of the involved nuclear reactions. This way the change of quality of the original target material can be predicted.

Results: We have calculated the amount of different unwanted radionuclides using both experimental cross section data and theoretical ones in those cases, when no or not acceptable quality experimental data were available for a real target material that can be purchased on the market. The calculations were performed at different bombarding energies to estimate the possible change in the target composition after one irradiation.

Table1: The number of produced radionuclei at different bombarding energies on highly enriched ^{100}Mo target for 6 h, 100□A irradiation at EOB.

Energy MeV	**^{99m}Tc**	**^{99}Mo**	**other**
17	4.2E+14	6.3E+13	2.3E+15
24	8.0E+14	4.1E+14	5.8E+15
26	8.4E+14	5.7E+14	6.9E+15
32	9.3E+14	1.1E+15	1.0E+16

Composition of the target used in the calculation: ^{100}Mo 99.54%, ^{98}Mo 0.41%, ^{97}Mo 0.0016%, ^{96}Mo 0.0012%, ^{95}Mo 0.0076%, ^{94}Mo 0.0051%, ^{92}Mo 0.006%

The tendency is obvious, using higher bombarding energy larger amount of unwanted radionuclides are produced since more reaction channels are open and generally the cross sections are higher for higher bombarding energies. The number of produced radioisotopes are several order of magnitude lower than the number of ^{100}Mo in the target therefore only small change can be expected in each irradiation cycle. The scale of the change in the ratio of different stable Mo isotopes in the target depends on the irradiation parameters. The change is small but it is growing gradually by recycling and reuse of the target material.

Conclusions: We give an estimation about the rate of “contamination” of the target material due to subsequent activation and decay processes. We also estimate the accumulation of stable and long-lived niobium radionuclides.

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HIGHLY REACTIVE $^{66/68}$Ga FROM RECYCLED ZINC TARGETS FOR PET

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Introduction: We report production of very high specific activity $^{66/68}$Ga from ^{nat}Zn(p,xn) and ^{66}Zn(p,n), with emphasis on ^{66}Ga for use with common bifunctional chelates. Principle radiometallic impurities are ^{65}Zn and ^{67}Ga. Separation of $^{66/68}$Ga from target material is with cation exchange chromatography in HCl media. Zn target material is easily recycled using electrodeposition from zinc chloride. The reactivity of ^{66}Ga for common bifunctional chelates, decay corrected to the end of irradiation, is 740 GBq/μmol using natural zinc as a target material. Recycling ^{66}Zn targets increased the reactivity of ^{66}Ga for DOTA and NOTA.

Material and methods: ^{nat}Zn foils (0.25 mm thick) and ^{nat}ZnCl$_2$ (both 99.999%) were from Sigma Aldrich. Optima grade HCl was from VWR or Fisher. Isotopically enriched ^{66}Zn (98.58%) was from Isoflex (San Francisco). Enriched zinc contained 0.76% ^{64}Zn, 0.6% ^{67}Zn, 0.055% ^{68}Zn, and 0.005% ^{70}Zn. Cation exchange resin (AG50W-X4, 100-200 mesh) was from Biorad.

Electrodeposition (6 V, 30-60 mA) using a platinum wire anode deposited 91 ± 3% (n=6) of target zinc from 0.05 N HCl onto gold discs. Targets were irradiated with up to 40 μA of protons on a GE PETtrace (13 MeV, Al degrader) or Siemens Eclipse HP (11 MeV) cyclotron without losing mass. Irradiated targets of ^{nat}Zn were left on the cyclotron overnight (13-16 hrs) so that short-lived products decayed, and 2.5 ml 10 N HCl dissolved the targets after removal. The solution was loaded onto a column containing 7 g strong cation exchange resin preconditioned with 10 N HCl, as reported previously (1). The column was washed with 20 ml of 10 N HCl to remove unwanted metals. An additional washing step was added to previously reported cation exchange methods, using 20 ml 7 N HCl to remove additional contaminant metal before eluting the ^{66}Ga fraction in 4 N HCl. The 4 N HCl fraction was evaporated, and ^{66}Ga was recovered in 0.1 N HCl for labeling. Zinc target stock was efficiently recovered from combined 10 N HCl column wash and residual electroplating solution with a single addition and evaporation of 0.05 N HCl.

Results: Radio-TLC-measured reactivity of produced $^{66/68}$Ga for DOTA or NOTA using 0.25 mm ^{nat}Zn foil targets does not exceed 370 MBq/μmol at end of bombardment (EoB). With electroplated targets, reactivities of 200-400 GBq/μmol (max 740 GBq/μmol) for DOTA or NOTA, decay corrected to EoB, are routinely achieved. Radioisotopic purity is summarized in Table 1.

Table 1: Radioisotope product ratios of ^{68}Ga, ^{67}Ga, and ^{66}Ga from 1 hour irradiations at various energies.

Product/ $t_{1/2}$	**Reaction(s)**	**Ratio to ^{66}Ga 14 h post-EoB @ 11 MeV***	**Ratio to ^{66}Ga 16 h post-EoB @ 13 MeV**
^{65}Zn / 244 d	^{66}Zn(p,2n+β) ^{66}Zn(p,pn)	Not detectable	Not detectable
^{66}Ga / 9.5 h	^{66}Zn(p,n); ^{67}Zn(p,2n)	1.0	1.0
^{67}Ga / 3.3 d	^{67}Zn(p,n); ^{68}Zn(p,2n)	6.7x10^{-2}	7.0x10^{-2}
^{68}Ga / 68 m	^{68}Zn(p,n)	6.0x10^{-3}	3.3x10^{-3}

* Thin target (11 → 6 MeV)

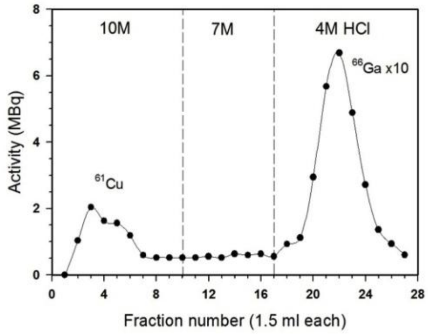

Figure 1: AG50W-X4 elution profile of Zn-Cu-Ga (7 g, 1.5 cm ϕ column). Zinc co-elutes with ^{61}Cu.

Conclusions: $^{66/68}$Ga has been produced in very high specific activities (<2 ppb cold gallium) from zinc targets. Reactivities for common bifunctional chelates are 6% of carrier free specific activity. Radionuclidic purity of the product is >95% between 2 and 5 half lives of ^{66}Ga following irradiation and exceeds 99.9% when the ^{66}Zn target is used. The separation is simple and the principle cost incurred, even with enriched targets, results from the use of ultra-pure reagents.

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^{44g}Sc FROM METAL CALCIUM TARGETS FOR PET

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Introduction: ^{44}Sc is garnering interest due to its availablility from ^{44}Ti generators. However, in order to justify the expense and maintenance of a generator the viability of ^{44}Sc as a PET-nuclide must first be proven pre-clinically. Therefore, cyclotron production and subsequent target chemistry of ^{44}Sc is worthy of developement. For this study we produced ^{44g}Sc by irradiating natural metallic Ca. We developed a chemical separation method on a small column of hydroxamate functionalized silica gel resin. The efficacy of separation was tested by chelation of the isolated radioscandium with DOTA.

Materials and methods: 99.99% calcium dendritic chunks were obtained from Sigma Aldrich. Aristar Ultra grade HCl was from VWR. Hydroxamate functionalized resin was created from Waters CM resin following the procedure of Holland *et al* [1]. Also a series of CM light sep-paks were activated with the same recipe using cyclicly flowing reagents. Sodium acetate was from Sigma Aldrich, dissolved and diluted to 0.25 M with Millipore water, and stored over Chelex resin (5 g/L). Thick calcium targets (300-600 mg) were pressed with a mechanical lever press into an aluminum holder and irradiated with protons at 16 MeV (extraction energy) and 13 MeV (degraded by aluminum) at 20 μA with a GE PETtrace. Irradiated targets were dissolved in 11 ml 2N HCl, and the pH was adjusted to 3-4 with 0.25 M sodium acetate. The solution was loaded onto a column containing 50 mg hydroxamate resin, preconditioned with 5ml 0.1M HCl followed by 5ml 0.25M sodium acetate. The loaded column was washed with 5 ml pH 4.5 0.2M sodium acetate (adj. with HCl), and 2ml 0.01M HCl. Activity was eluted from the column in 1ml 0.1 M HCl.

In order to test the reactivity of the purified radioscandium, the eluted fraction was added to pre-heated (95 °C) sodium acetate buffer (pH 4), and dispensed into 10 vials containing buffered and pre-heated DOTA solutions of known concentrations from 1 to 1000 nM. The vials were incubated for 1 hour at 95 °C and then spotted onto Al-backed silica gel ITLC plates (EMD, New Jersey). The solvent was 0.75 M NH_4OH (Optima, Fisher).

Validation of the hydroxamate resin was performed by taking a single pH adjusted irradiated Ca sample and splitting it into four fractions. One was separated on hydroxamate resin, another on un-reacted CM resin, a third on silica gel, and the final on polyethylene frits. The trap and release of radioscandium was compared between the methods, as well as the reactivity with DOTA.

Results: After 1 hour of irradiation at 16 MeV, the radionuclidic purity of ^{44g}Sc was greater than 95%, with saturation production over 200 MBq/μA. ^{43}Sc, ^{48}Sc, ^{44m}Sc, and ^{47}Sc comprised the radio-impurities.

Overall, the hydroxamate resin trapped 87±10% of the Sc activity. 72±11% of this retained activity was recovered in 1 ml 0.1M HCl. Radio-TLC-measured reactivity of produced ^{44g}Sc for DOTA was roughly 100 GBq/μmol, decay corrected to EoB. The separation procedure concluded about 30 minutes post-EoB.

The comparison of different substrates for the separation showed that the hydroxamate and carboxylate resins behaved similarly for trap and release, but the reactivity of the hydroxamate-purified scandium was higher by a factor of two. The silica gel and polyethylene frits retained activity, though not as well as the other two resins. Therefore the hydroxamate resin was selected for further study.

Fig. 1: Pressed Ca Target

Conclusions: With the procedure described above, accelerator-produced ^{44g}Sc is of sufficient purity and scale for pre-clinical PET studies. This comes with neither investment in enriched ^{44}Ca, nor concerns over procurement, handling, and storage of a long-lived ^{44}Ti generator.

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Acknowledgments: This project was funded by the NIH Radiological Sciences Grant T32 CA009206, and NIH/NCI P30 CA014520.

^{211}At PRODUCTION USING AN EXTERNAL TARGET SYSTEM

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Introduction: Capable of accelerating α-particles (E_α = 27.0–47.3 MeV) with currents up to 70 µA, the positive-ion Scanditronix MC-50 cyclotron at the University of Washington Medical Center (UWMC) has ideal characteristics for the large scale production of ^{211}At via the ^{209}Bi(α,2n)^{211}At reaction. This cyclotron's primary application is, however, for fast neutron therapy. As such, in developing a target system for production of ^{211}At, an external target system was deemed necessary to allow for target design modifications and troubleshooting without interfering with the busy fast neutron therapy schedule.

Although ^{211}At saturation yields on the order of 200–400 MBq/µA have been reported using an internal target system in the energy range of ~28–29.5 MeV [1, 2, 3], reduced yields (e.g. ~50–100 MBq/µA) have been noted for external target systems [2, 3].

This work reports on the development of an external slanted ^{209}Bi target for production of ^{211}At along with an extensive summary (N>100) of test irradiations performed over a 5 year period with this target.

Materials and methods: A 10 degree slanted target design was implemented for these studies. Aluminium was used as a backing plate and consisted of a depression on one side (12 cm x 1.8 cm x 0.3 mm) in which the bismuth was deposited and a 4 mm water-cooling cavity with 2 mm deep fins on the other side.

Targets were prepared by melting an excess of polycrystalline bismuth pellets (99.999% metal basis, Alfa Aesar) at ~330 ºC into the aluminium depression. To minimize the formation of air bubbles and obtain better adherence, the aluminum surface beneath the molten bismuth was constantly scratched with a porcelain spatula during heating. Upon cooling, the resulting bismuth surface was machined to achieve a uniform bismuth thickness of approximately 170 mg/cm^2.

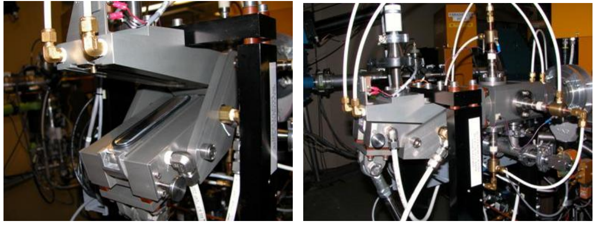

Figure 1: Pneumatic target system with Al/Bi plate in lower jaw in the open (left) and closed (right) position. The bismuth is open to vacuum during irradiation.

Figure 1 shows the pneumatic target station used for these studies (Applied Technology Group, TRIUMF, Canada). Initial irradiation studies were performed with a nominal E_α of 28.0 MeV. Energy optimization studies revealed, however, a 30% increase in ^{211}At production yields at 29.0 MeV with no detectable co-production of ^{210}At. All subsequent studies have therefore employed a nominal E_α of 29.0 MeV.

Results: A summary of the measured saturated yields and corresponding irradiation conditions is given in Table 1. The reported yields are comparable with those which can be achieved using an internal target system, and are improved over previous external target systems. When examining the yield as a function of the irradiation current, consistent yields are noted as the current is increased (Figure 2).

Table 1: ^{211}At saturation yields

Nominal E_α (MeV)	N	Yield (MBq/µA)	Average current (µA)
28.0	34	181 ± 16	46 ± 9
29.0	83	241 ± 17	43 ± 8

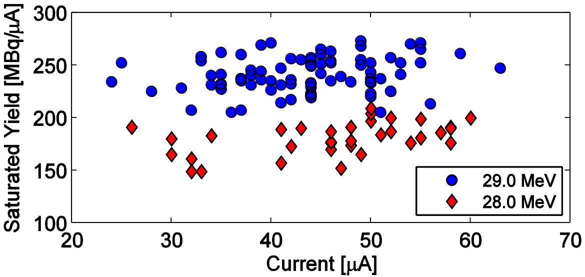

Figure 2: ^{211}At yield as a function of beam current.

Conclusion: The external target at the UWMC has been extensively irradiated for ^{211}At production since 2007. Consistent saturation yields are reported independent of irradiation current. Production of 2.1 GBq ^{211}At for a 2 hour irradiation at an average current of 55 µA has been recently demonstrated with this target.

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PRODUCTION OF ^{211}At USING THE JSW BC3015 AT THE UNIVERSITY OF PENNSYLVANIA CYCLOTRON FACILITY

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Introduction: Using ^{211}At for targeted radiotherapy has been discussed since the mid-1980s. Availability of cyclotrons with appropriate α-particle energies is limited to a few machines in North America and Europe. We describe the production of ^{211}At using 30 MeV α-particle beams accelerated with the Japan Steel Works, BC3015 cyclotron at the University of Pennsylvania with the goal of ^{211}At-MABG production.

Target manufacturing and cooling is discussed. Active beam monitoring using a beam-profile monitor insures a uniform particle profile across the target. A head-on irradiation geometry is used. Cross calibrations with a germanium detector and known sources determined dose calibrator settings and thick target yields. Extracted amounts of ^{211}At from the target, and limits to the production of ^{210}At will be discussed. We will also discuss our MABG labeling results and yields.

Material and methods: The JSW BC3015 is a four particle (p, d, ^{3}He, α) and three energy (nominal E_p = 15, 22, 30 MeV) positive ion machine. We have used our -15° beam line with a solid target station to perform Astatine production via the ^{209}Bi(α,2n)^{211}At reaction. Irradiation is in a head-on configuration with a water cooled cold finger. Target thicknesses are typically 230-250 µm thick on a 2 mm aluminium backing.

The nominal α-particle energy at the highest acceleration frequency is 31.5 MeV. To suppress the production of ^{210}At (and ^{210}Po) via the (α,3n) reaction, we use a 0.076 mm (0.003") aluminium degrader foil to lower the energy to ≈ 28.4 MeV thus remaining below the ^{210}At threshold production energy of ≈ 29 MeV. To date, our irradiations have been done at a maximum of 5 µA. Production currents of 10 – 15 µA will be needed for MABG production in clinical amounts. However, we have run the accelerator at beam currents as high as 22 µA on the Faraday cup in front of the target. We will report on results at higher projectile currents.

To insure uniform irradiation of the Bi target and avoid target melting, the beam profile is actively monitored using a Danfysik System 5100 x-y beam-profile monitor. The system is dynamically read out and we have developed real-time two-dimensional monitoring software for the two dimensional profiles. Temperature of the cooling finger is monitored using a probe in the cooling water stream that is in contact with the back of the target.

Distillation of the ^{211}At from the target was performed in a quartz tube furnace running at 700° C for 30 minutes using a set-up similar to Zalutsky.

Results: Initial experiments were designed to determine the optimal degrader foil to minimize the production of ^{210}At as much as possible. Foil thicknesses of 0.025, 0.076, and 0.127 mm (0.001", 0.003", and 0.005" respectively) were used to produce effective α-beam energies of 30.5, 28.4, and 25.8 MeV. Using a surface barrier detector and an α-spectrometer it was determined that production of ^{210}At did not exceed 1:2 x 10^3 at 30.5 MeV and 1: 2 x 10^7 at 28.4 MeV.

We performed cross calibrations using a calibrated ^{22}Na source and a HPGe detector. Calibrations confirmed a dose calibrator setting of 044[1] or a setting of 2.2 • (the value measured at the setting of ^{133}Xe).[2]

At 28.4 MeV we have measured a thick target yield of 11.1 MBq/µA-hr (300 mCi/µA-h) in good agreement with other head-on target configurations reported in the literature. Care must be exercised in measuring the activity due to the absorption of the x-rays by the aluminium target backing.

The first distillation experiment extracted approximately 20% of the available ^{211}At. The degrader foil was removed prior to distillation. The distillation second experiment with the degrader foil and with careful rinsing of the distillation recovered 30%.

Conclusions: By using a single thin aluminium foil, we have shown that straggling is minimized and we are able to produce ^{211}At virtually free of ^{210}At using a water-cooled, head-on target configuration. Active x-y beam-monitoring and 2D software has been developed to aide in producing uniform target irradiation. We have verified dose calibrator settings and have measured thick target yields from our experiments and found them to be in agreement with the bulk of published data. Distillation of the ^{211}At with the degrader target foil in place has yielded a 30% recovery rate. We believe this can be further improved. Increased beam current results will be shown. Labeling methodology. experiments, and results of ^{211}At MABG production including chemical yields will be reported.

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PRODUCTION AND CHEMICAL ISOLATION OF POSITRON-EMITTING ISOTOPES OF ARSENIC FOR ENVIRONMENTAL AND MEDICAL APPLICATIONS

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Introduction: Arsenic has long been important in the fields of environmental science and toxicology. More recently, there has been interest in taking advantage of the unique benefits of positron-emitting isotopes arsenic-72 ($t_{1/2}$ = 26.0 h) and arsenic-74 ($t_{1/2}$ = 17.8 d) in the investigation of slow physiological processes such as the biodistribution of monoclonal antibodies[1]. These benefits include the nuclides' long half-lives and arsenic's unique chemistry allowing for its covalent bonding to thiol groups. The present work focuses on the development of cyclotron targetry and radioseparation chemistry for the production of radioarsenic PET tracers for both environmental and medical applications.

Materials and methods: Megabecquerel quantities of ^{72,74}As were produced by irradiating natural germanium dioxide powder with 2 µA of 16.5 MeV protons from a GE PETtrace cyclotron. Targets of 100 – 200 milligrams of GeO_2 were pressed into a stainless steel beamstop and covered with an aluminium containment foil. After irradiation, a PTFE dissolution apparatus was fitted directly onto the beamstop, allowing for the dissolution of the target with minimal spread of irradiated GeO_2 powder.

A lead-shielded chemistry apparatus capable of multi-step procedures involving precipitation, distillation, evaporation and column chromatography was fabricated inside a radiochemical fumehood. Two CsI(Tl) radiation detectors monitor the transport of radioactive solutions. The reaction vial is heated using a temperature-controlled aluminium heating block, allowing fine control of the vial temperature.

After irradiation, the GeO_2 target material was dissolved in 4 M NaOH. The Ge/As solution was transferred to a precipitation column and the GeO_2 was reprecipitated by neutralization with the addition of a minimal volume of concentrated HCl, allowing for a bulk separation of arsenic and germanium. The arsenic filtrate was then carefully evaporated and reconstituted in an appropriate medium for anion exchange (AX) chromatography for the removal of the remaining germanium. Several AX procedures were experimentally investigated utilizing As/Ge solutions in 10 M HCl[2] or 9 : 1 :: glacial acetic acid: 9M HCl loaded onto an BioRad AG1x8 AX resin column.

The activity of ^{70,71,72,73,74,76}As, ^{67}Ga, and ^{69}Ge were monitored by taking small samples at various points along the separation procedure. These samples were analyzed by high purity germanium gamma ray spectroscopy. Thin-layer chromatography (TLC) was also performed on these samples using a 3 : 1 :: 0.01 M sodium tartrate : methanol solution as mobile phase. This TLC procedure allowed for the determination of the arsenic oxidation state (As(III) vs. As(V)) at important points in the separation procedure[4].

Results: Observed production yields of ^{72,74}As were consistently ~50% those predicted from calculations utilizing $^{nat}Ge(p,xn)^{72,74}As$ cross section data[5]. The initial precipitation step of the radioseparation procedure effectively removed 80% or greater of the GeO_2. Between 20% and 50% of As activity has been observed to remain with the GeO_2, though this is minimized by repeated washing of the precipitate. While both tested AX procedures effectively isolated radioarsenic from germanium, the procedure utilizing the acetic / hydrochloric acid mixture loading solution was advantageous in that the AX resin traps and releases arsenic, allowing for minimal resin masses and the use of water or buffer for the elution of the arsenic fraction. Current decay-corrected arsenic yields of the entire 2 – 3 hour separation procedure are ~20%.

Conclusions: The constructed chemistry apparatus offers safety and flexibility in the handling and separation of radioarsenic and germanium solutions. Separation procedures involving precipitation and anion exchange chromatography effectively isolate tracer-scale ^{72,74}As from bulk germanium. Continuing research will investigate the use of ^{72,74}As in radiolabelling biologically relevant molecules and in imaging plants to assess their potential role in the bioremediation of toxic waste sites.

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SOLID TARGET IRRADIATION AND TRANSFER SYSTEM

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A Compact, fully automated solid target irradiation, handling and transfer system was developed for the production of ^{99m}Tc, however it can be used for any solid target material. The system is using small copper or silver targets (figure 1).

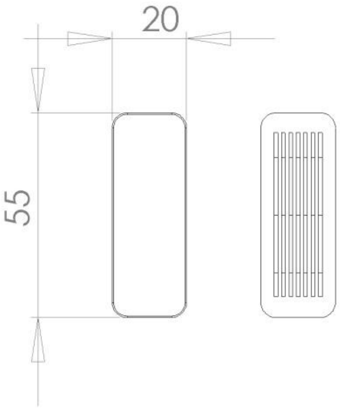

Figure 1: Target, front and back

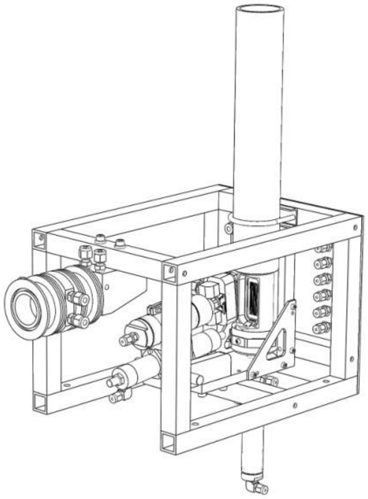

Figure 2: Target irradiating station

All the target handling is fully automated. The target is pneumatically transferred to the irradiation station where is removed from the carrier, placed in the irradiation chamber and the cooling water connected.

At the end of irradiation the target is returned to the carrier and transfer to the processing hot-cell.

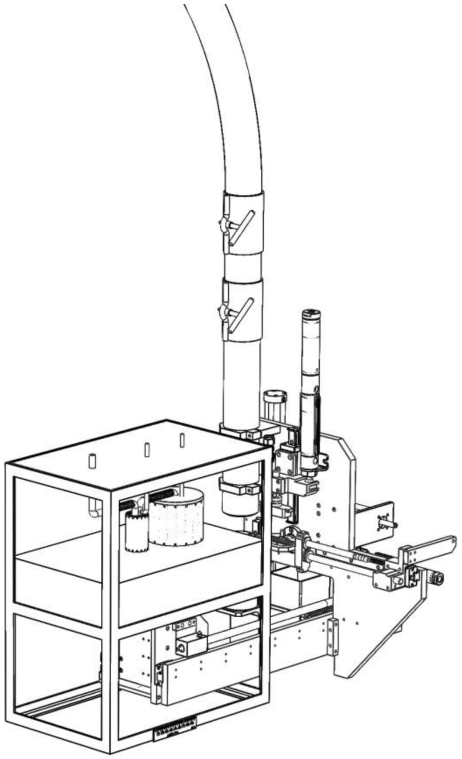

Figure 3: Target processing unit and loader

All the stages of removing the target from the carrier and placing it in the reaction chamber are done automatically. The processed targets are transferred to a storage container and a new target placed in the carrier and sent for irradiation.

The transfer line is 2” (50mm) PVC pipe. The small diameter of the pipe simplifies the installation of the transfer line. The pneumatic transfer is using vacuum to move the carrier. The progress of the carrier along the line is monitored by magnetic sensors.

The target is designed to handle 5KW with surface temperature of 350°C. It is placed at 15° to the beam. A collimator in front of the target collimates the 13mm diameter beam to 10mm diameter. The irradiated area on the target face is a 10x38 mm ellipse.

Four sector silver mask in front of the conical collimator allows accurate centering of the beam.

A NEW TRANSFER SYSTEM FOR SOLID TARGETS

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Introduction: As part of a collaborative research project funded by Natural Resources Canada TRIUMF has designed and manufactured target and processing systems for the production of technetium-99m with cyclotrons.
Generally, it is desirable to perform the transfer of the target to and from the cyclotron remotely. In summary,
a target needs to be prepared and placed into a hot cell. From there it is transferred remotely to the cyclotron. After bombardment the target is returned to the hot cell for processing.
Customized systems have been manufactured for the BCCA TR19 and the GE PETtrace cyclotrons at LHRI and CPDC.

Material and methods: A schematic of the tape drive and the receive station is shown in Figure 1. The principle mechanism for moving the target capsule to and from the target station is based on a motorized spring steel tape drive (plumber's tape). The system employs a piston controlled roller - clutch assembly to drive the tape. A corrugated polymer tube is used to connect the receive station to the target station on the cyclotron. When loading the target for irradiation, the target capsule is pushed forward inside the transfer tube by the tape drive until it reaches the target station. A mechanical locking mechanism is used to retrieve the target capsule after irradiation (Figure 2). It releases the target capsule upon arrival in the hot cell.

Results: So far two target transfer systems have been installed and commissioned successfully (LHRI, CPDC). Minor improvements to the tape drive mechanism are in progress.

Acknowledgments: This project was funded by Natural Resources Canada under NRCan-NISP.

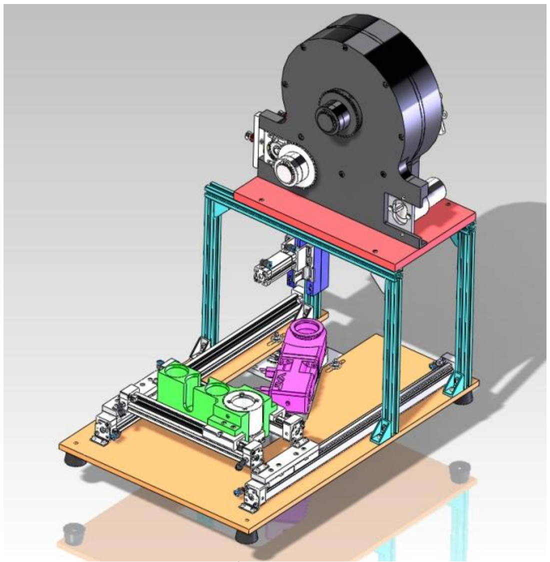

Figure 1: SolidWorks® 3D-drawing of tape drive with receive cell remote handling system.

Figure 2: SolidWorks® 3D-drawing of locking mechanism for target pick-up.

A FEASIBILITY STUDY FOR ROUTINE PRODUCTION OF ^{124}I BY (α,xn) REACTIONS ON ^{nat}Sb AND ^{121}Sb AT THE IEN's CV-28 CYCLOTRON: CURRENT STATUS

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Introduction: According the experimental available data[1], the production of ^{124}I, via (α,n) reaction in Antimony, has relatively low yield. In order to have an economically viable production, with satisfactory level, it is required beam current of about 30 μA, for long irradiation periods.

Considering that these requirements can be achieved in our laboratory, we are proposing this alternative way to produce ^{124}I, in a regular basis. Our first purpose was to measure the thick target yields for the ^{nat}Sb(α,n)^{124}I and ^{121}Sb(α,n)^{124}I reactions, in the energy range 19 to 12 MeV, with our experimental setup.

Initially, we have focused efforts in two main systems. The first one was a dedicated beam line, at the IEN's cyclotron CV-28, that will not be discussed here. The second one was the development of a special target-holder[2] that will be our main subject.

Material and methods: A new customized target-holder system - In the conception of that target-holder, the main concern was the capability to withstand high power. Also, we have considered following points as critical:

- Inclination of the target with respect to the beam direction in order to increase the irradiation area;
- Cooling of the target backing/support, with a special geometry for a good heat exchange of the whole target-holder;
- Cooling capacity, also directly on to the target´s “face”, with a laminar flow of cold water, protected by a thin Al window, so that both combined can act as an adjustable energy degrader;
- Independent system for cooling the Al window, using He gas;
- A convenient way to disassemble, with a system-fit without screws, minimizing radiation exposure;
- Compatibility with the existing output flanges at the IEN’s CV-28 cyclotron.

The target is accomplished[3], and the testing phase is still going on. The first used Al window was ~120 μm thick, which degrades the energy of α-particles from 28 to 22 MeV. In turn, the laminar flow of water was ~110 μm, and degrades the energy from 22 to 19 MeV.

Samples of ^{nat}Sb oxides and electroplated Sb in Cu were bombarded with α-particles.

The characteristic activity of the ^{124}I was counted with a large volume HP-Ge detector, in close geometry, to maximize the detection efficiency.

Preliminary Results: Considering that this is a phase test, the irradiations were conducted with limited conditions of cooling. From the first results, we obtained a thick target yield of ~3 μCi/μAh.

Our plans for more conclusive tests are scheduled for the end of this year.

Conclusion: Despite that the initial results could not be deeply considered in the feasibility analysis; it can be regarded as a checkup on the operation of the system as a whole.

From our initial study and some available experimental results[4,5], we may conclude that the production of pure ^{124}I, via reaction (α,n), and for practical purposes, is feasible only when using the ^{121}Sb, with enrichment above 99%. This will be the guide line for the rest of the planned work.

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RADIONUCLIDE PRODUCTION AT THE SOLID TARGET STATION OF THE NEW IBA CYCLONE® 30XP: ^{73}Se FOR PET

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Introduction: The increasing demand on novel positron emitting radionuclides for various applications demands the customisation of new flexible target systems. The radionuclide ^{73}Se is a promising tracer for PET studies and shall be produced in high yield at a new solid target station in Juelich. To allow automation of the radiochemical processes an ion-chromatographic separation procedure has been developed to retrieve ^{73}Se in radiochemical pure, n.c.a. form. This procedure shall replace the current dry-distillation method.

Material and methods: The most efficient way of producing ^{73}Se is given via the ^{75}As(p,3n)^{73}Se reaction. For the preparation of an As target suitable for high-current irradiations a Cu-As alloy has proved useful [1]. A radiochemical isolation method of ^{73}Se from the target bulk using ion-chromatography was investigated. Distribution coefficients were measured using different ion-exchange resins and solvents.

In near future ^{73}Se shall be produced at the recently installed cyclotron *Cyclone 30XP* from IBA. This accelerator prototype is able to deliver a 15 to 30 MeV proton beam up to 350 µA as well as 7 to 15 MeV deuteron and 30 MeV alpha particle beams. In addition to fixed target stations for the production of standard PET radionuclides, the cyclotron will be equipped with two additional beam lines for research and the production of non-standard radionuclides using an *IBA Mark II Solid Target System*. Due to the laboratory situation a specific target handling system had to be designed. (Fig. 1) Using a transport shuttle which is mounted onto an aluminium tube the irradiated target can be automatically transferred to the reception station, from which it is brought to the chemistry site.

Results: Aim of this work was the provision of a reliable ^{73}Se production method having the potential to provide n.c.a. radiotracers for extensive radiopharmaceutical applications. A radiochemical isolation method of n.c.a. ^{73}Se was developed combining cation- and anion-exchange processes. Firstly Cu and contaminations of radioactive Zn isotopes were removed using a DOWEX 50x8 cation-exchange column and 0.1 M HCl as eluent. The final product was eluted from a DOWEX 1x2 anion-exchange column with 1 M NaOH after removing remaining As with concentrated HCl.

The optimum proton energy range found by Mushtaq et al. [2] cannot be covered with the *Cyclone 30XP*. Thus, the possible production yield in the energy range of 30 to 26 MeV is calculated to amount only to about 280 MBq/µAh. However, the combination of the commercially available *Mark II Solid Target System* and the specifically designed automatic transport system will allow for high-current irradiations of Cu_3As targets, leading to the possible production of ^{73}Se in amounts of more than 30 GBq.

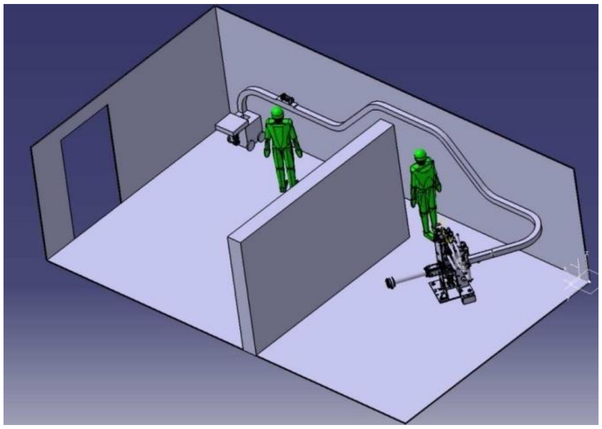

Figure 1: Design of dedicated target handling system in Jülich. (Image: IBA)

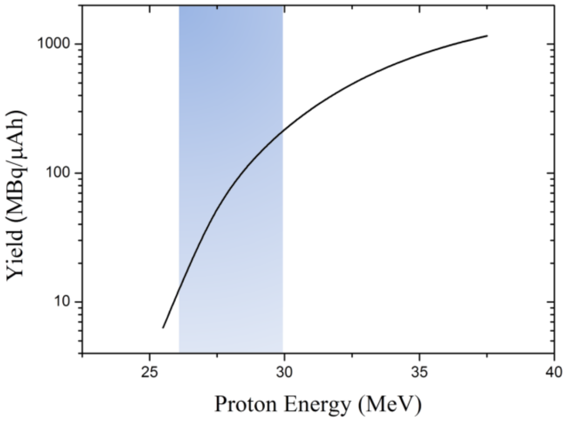

Figure 2: Integral yield of the ^{75}As(p,3n)^{73}Se reaction calculated from the excitation function.

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CROSS SECTIONS FOR PROTON INDUCED REACTIONS ON TERBIUM AT 200 MeV

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Introduction: The Los Alamos Neutron Science Center (LANSCE) has the capability to make nuclear physics measurements using protons below 800 MeV. Several uncharacterized nuclear reactions might be used to produce radioisotopes from Tb targets in this energy range. In particular, ^{153}Gd (240.4 d, 100% EC) emits several photons with energies below 100 keV, has been identified as a line source for medical imaging experiments, and is needed for off-stability astrophysics experiments at LANL (1,2).

Material and methods: The proton-induced cross sections for production of several radioisotopes including ^{153}Ga, ^{153}Tb (2.34 d, 100% EC) were measured with an incident energy of 197.1 ± 0.4 MeV in the Target 2 area (Blue Room) of the LANSCE Weapons Neutron Research (WNR) facility (2). Al foil (99.999%, Goodfellow) was used for beam current monitoring via the ^{27}Al(p,x)^{22}Na reaction, and SS foil was used for beam profile monitoring using Gafchromic films. Each foil was encapsulated by Kapton tape (25 µm thick) on both sides to prevent cross contaimination between different stack elements. Targets were irradiated for 1 hour.

After the irradiation, foils were individually packaged and transferred to the Chemistry-Nuclear Research (C-NR) Division's counting facility for gamma spectroscopy where they were assayed for a period of 75 days at predetermined intervals. Analysis of collected spectra was performed using the in-house code SPECANL to integrate photopeaks characteristic of target isotopes and Kaleidagraph (Synergy Software, UAE) to apply linear regressions to integrated photopeaks tracked over time. Error in parameters generated by this method was calculated as the standard error of mean values. Cross sections are reported as total cross sections unless otherwise indicated, implicitly considering the contribution of co-produced parent isotopes to daughters' quantities through decay.

Results: Several isotopes presumably produced (e.g., ^{154}Dy, ^{157}Tb) are impossible to identify without the use of potentially destructive α- or x-ray spectroscopy, which will be undertaken in future experiments. Still other isotopes possess half lives or hide beneath gamma interferences which make them nearly impossible to report with confidence, even given only hours-long separations between end of bombardment and the start of counting. The quantity of data generated by long counting terms and high proton energies creates a time-consuming analysis challenge; almost 20 radioisotopes have been identified in spectroscopic data at 200 MeV. Table 1 below summarizes results achieved to date.

Table 1: Measured cross sections for proton-induced production of identified radioisotopes at 200 MeV.

Isotope	**σ (mb)**	**± (mb)**	**γ (keV)**
Eu-145	25.5	2.3	894, 1658
*Eu-146	16.1	1.2	634, 747, 1058
Eu-147	56.7	4.9	121, 197
Eu-148	13.0	5.3	550, 572, 630
Eu-149	45.5	29.5	93
Gd-146	41.1	20.1	114, 155 155
Gd-147	41.8	3.2	370, 396, 625, 929
Gd-149	76.9	6.0	150, 299, 789
Gd-151	88.9	6.7	115, 243 243
Gd-153	113.5	8.8	103
Tb-151	58.6	5.1	287, 426 479, 616
Tb-152	93.9	7.0	1109
Tb-153	92.1	6.9	109, 170 212, 250
Tb-154	20.1	2.9	1123, 1274
Tb-155	87.0	6.5	86, 180
Tb-156	90.6	51.4	1222, 1421
Dy-155	21.7	1.7	226
Dy-157	11.8	1.9	326

*Direct Production Cross Section

Conclusions: Cross section values for proton-induced reactions on Tb at 200 MeV have been measured; work will continue in an attempt to fully describe these reactions over a wider energy window. These data will be used to design thick targets for eventual production irradiations at LANSCE and to determine the scope of future efforts using the Isotope Production Facility's 40, 100, and 800 MeV irradiation capacities.

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Acknowledgments, disclosures and funding: We are grateful for technical assistance from LANL C-NR, C-IIAC, AOT-OPS, and LANSCE-WNR groups' staff.

COPPER-67 PRODUCTION ON ELECTRON LINACS—PHOTONUCLEAR TECHNOLOGY DEVELOPMENT

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Introduction: Despite modest photonuclear cross sections, such as for the $^{68}\text{Zn}(\gamma,p)^{67}\text{Cu}$ reaction, electron linac technology appears to be a commercially promising option for production of valuable isotopes. Electron accelerators—sources of Bremsstrahlung gamma radiation—are presently available and under-utilized and may offer an affordable route to an expanded supply of ^{67}Cu and other isotopes. Two key developments have been demonstrated for ^{67}Cu production: large (100g) solid metal targets; and rapid (1-d) separation of trace amounts of product from the target mass.

Methods and materials: Development of methods has been conducted on linacs at Argonne National Lab, RPI (Troy, NY), and KIPT (Kharkiv, Ukraine).

We chose to maximize isotope yield by designing solid metallic Zn targets (maximum atom density), with large volume (optimized dimensions for 20- to 28-cm^3 cylinders) and high linac beam power (~ 10kW). Rapid handling and target processing is achieved by several innovations. The irradiating electron beam passes through air to the target station, and at EOB the linac is turned off and the target is quickly moved to a transport container. In the processing facility the target's screw-on cap is easily removed to expose the bare Zn ingot, and the open target capsule is placed in a ceramic tube for sublimation removal of the Zn from the residual ^{67}Cu.

Besides speed, sublimation processing offers two additional benefits. First, dry separation eliminates the use of large volumes of reagents (a potential source of chemical impurities) and restricts wet chemistry to small-volume ion exchange purification operations. Second, recycle of enriched ^{68}Zn should result in very high specific activity ^{67}Cu, since cold Cu traces are further reduced with each sublimation procedure.

Materials issues posed a major challenge since Zn liquid and vapor reacts with metals and glass, causing corrosion and/or apparatus failure, as well as contaminating the final ^{67}Cu product. A variety of ceramics have proven to be successful for fabricating target capsules and sublimation tubes.

Results: Gamma photons (~35-45MeV) are attractive because their power deposition is over a large volume (~3cm deep into the metal), which facilitates heat removal. Our targets have operated without failure with:

- long runs (10h)
- high beam power (10kW)
- yields in accord with MCNPX [>120 MBq (3mCi) for 100µA-h fluence with 100g of natural Zn]
- demonstrated low-activation structural materials (for ease of handling).

With successive campaigns our target processing has improved in handling speed and quality of the final product. Sublimation progress is documented with a NaI detector that monitors zinc (Zn65) deposition in the top of the tube. The figure shows 100g of Zn sublimation in 90 minutes at 650C.

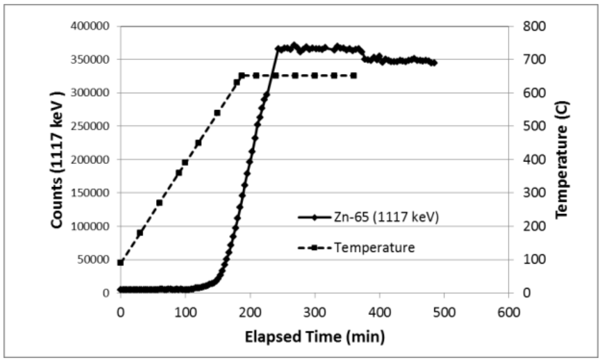

Figure 1: Sublimation temperature and mass transfer vs. time.

Several issues remain prior to commercialization:

- finish upgrade of linac operations to ~24kW
- transition processing to hot cell operations
- quantify final product's expected high purity and high specific activity
- straightforward changeover to enriched ^{68}Zn

Conclusions: Up to this point batch production has been limited to ~120 MBq (3mCi), by radiochemical operations in a hood. A successful completion of our development work should permit batch production of ~70 GBq (2000mCi) with a 48-h linac run.

Acknowledgments: We have benefited from our work with R. Dronov, M. Ayzatskiy, and S. Uvarov (KIPT); and we gratefully acknowledge the assistance of R. Block and P. Brand (RPI). This work was partially supported by the U.S. Dept. of Energy, Off. of Science; Argonne National Laboratory; and by Iotron Medical, Inc. This technology is protected under a pending patent; see Pub. No.: US 2010/0028234A1.

LITHIUM TARGET FOR ACCELERATOR BASED BNCT NEUTRON SOURCE INFLUENCE BY THE PROTON IRRADIATION ON LITHIUM

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Introduction: Boron neutron capture therapy (BNCT) is a new concept therapy with different to existing radiation therapy, and it is expected to be a new cancer therapy for future.

Neutron source for BNCT depended on the reactor until now. By changing a neutron source from a nuclear reactor to accelerator, it can install this accelerator-based BNCT system into medical facility. And medical facility does not need to have a nuclear fuel, and safe.

We chose 7Li (p,n)7Be reaction as a neutron source based on accelerator.It is said that lithium thickness will become thin by irradiation of proton beam.

Therefore, we examined how lithium would be influenced by irradiating proton beam to vapor-deposited lithium actually.

Material and methods: Lithium was deposited by vacuum deposition with a thickness of 20 ~ 50µm in diameter of about 40mm on circular copper plate (130mm in diameter) of 8mm thick.

Irradiation test with proton beam was performed in an facility of NASBEE of NIRS.

Lithium thickness measurement was performed comparatively and quantitatively by using Laser thickness measurement device (accuracy: 0.1µm).

The accelerator and target side were divided with 6µm harvar foil as not having any influence to the accelerator even if lithium would be scattered by proton beam irradiation.

Collimator with 5mm radius was installed in irradiation chamber of the Lithium target and then we examined the Lithium change at boundary while placing i right above the Lithium target and defining the borderline between irradiation area and non-irradiation area.

Proton energy and density of the beam were 2.5MeV and 60~126µA/cm2 respectively.

The target was cooled down by water with 18 degrees.

The lithium target was made by vacuum deposition in advance and was kept with blanking cover under argon gas conditions.

Lithium target was set to irradiation chamber after confirming the beam profile and its location by quartz in advance. The proton beam irradiation was conducted for three hours continuously with the condition of cooling the havar foil by cooled helium gas.

Results: In three hours continuous irradiation by proton beam, trace of beam irradiation was found.

But the difference of lithium thickness between irradiation area and non irradiation area was not demonstrated. The amount of neutrons production gradually decreased over time, and after 3 hours it was reduced by approximately 10%. And it had no relevancy between helium cooling and non cooling.

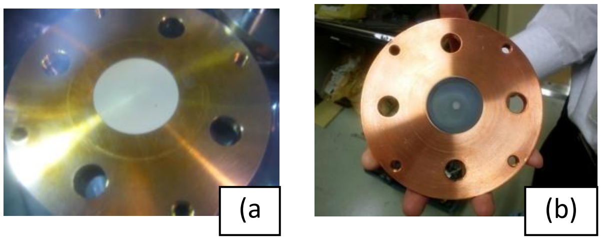

Figure 1: Test sample of lithium coated copper plate.
(a) before irradiation
(b) after irradiation.

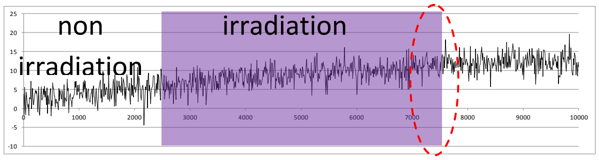

Figure 2: profile of lithium surface
Measuring the amount of change in edge

Conclusions: It was said that lithium would have a low melting point and weakness against proton beam irradiation. But it was suggested in this experiment that lithium demonstrate sufficiently resistance to continuous long time irradiation without lithium decomposition.

For the gradual reduction of neutron, it was considered that the reduction did not occur by lithium consumption but occurred by denaturalization of lithium nitridization.

PRELIMINARY INVESTIGATION OF PARASITIC RADIOISOTOPE PRODUCTION USING THE LANL IPF SECONDARY NEUTRON FLUX

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Introduction: The Isotope Production Facility (IPF) at Los Alamos National Laboratory produces ^{82}Sr, ^{68}Ge, ^{72}Se, and other isotopes using 100 MeV protons. The IPF's high beam current and lengthy irradiations produce a secondary neutron flux with a utilitarian scale that is beyond the reach of medical cyclotrons and energetically distinct from reactor neutron fluxes. This neutron field will likely broaden the portfolio of radioisotopes sourced from and studied at Los Alamos facilities. Current simultaneous production of ^{82}Sr and ^{68}Ge results in the emission of 10^{17} neutrons in a single run (4π), or ~10^{12} n/s/cm^2, values comparable to fluxes produced in medium research reactors.

Material and methods: The current IPF target stack situates 3 encapsulated target pucks in the path of a 230 μA proton beam, which enters the front face of the first target at approximately 93 MeV. This geometry has been reproduced in Monte Carlo Neutral Particle-eXtended (MCNPX/CINDER90) simulations. Spatial mesh-tally binned neutron fluxes from these simulations have identified locations in the target carrier which maximize exposure to the neutron fluence and are facile to repurpose as carriers of target materials (Fig. 1). MCNPX simulations also describe the energy dependence of the neutron spectrum, which is relatively constant throughout the target geometry. MCNPX was also used to model the ^{184}W(n,α)^{181}Hf reaction during experiemental production of ^{186}Re with a 25 g $^{nat}WO_3$ target for comparison with measured values after chemical separation. To confirm the results of these simulations, a threshold activation experiment will be used to unfold neutron fluence energy distributions from known cross sections and yield measurements of irradiated foils. The SAND-II nuclear code will be used to simplify computation (1). Monoisotopic foil materials with smoothly varying σ(E) for neutron activations and a selection of reaction threshold energies are being prepared for resumption of IPF beam in July 2012: ^{27}Al(n,α)^{24}Na, ^{64}Zn(n,p)^{64}Cu, ^{58}Ni(n,p)^{58}Co, ^{62}Ni(n,α)^{59}Fe, ^{197}Au(n,2n-4n)$^{194\text{-}196}$Au, ^{209}Bi(n,2n-5n)$^{205\text{-}208}$Bi, and ^{89}Y(n,p)^{89}Sr.

Results: MCNP predicts a total (4π) average flux of 10^{14} n/s/cm^2 around the target carrier (Fig 1). This neutron energy distribution is graphically shown in Fig 2. For the ^{nat}WO3 irradiation, MCNPX/CINDER90 predicted a yield of 0.05 ± 0.02 μCi, in reasonable agreement with HPGE γ-spectroscopy's measured values of 0.02 μCi after separation chemistry.

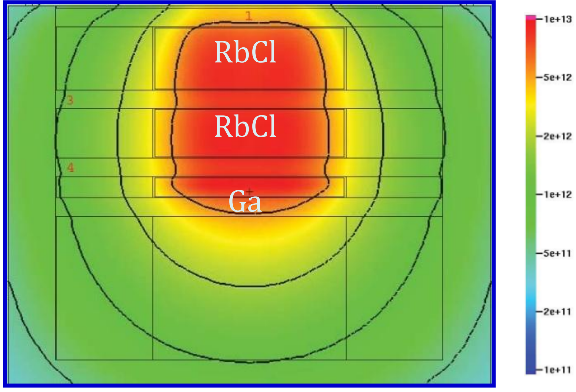

Fig. 1. MCNPX mesh tallies of secondary neutron flux during a 200 μA irradiation (fluxes are in n/s/cm^2 and are independent of energy distribution).

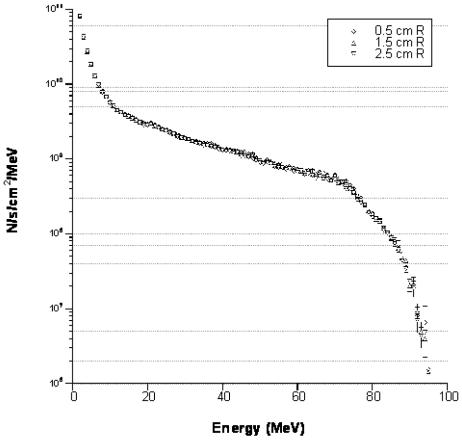

Fig 2. Ring detector tallies for r ≤ 0.5 – 2.5 cm behind Ga target at 200 μA.

Conclusions: The neutron flux, once characterized, can be used as a tool for materials science development and for the production of radioisotopes in the service of the larger scientific community. The possibilities include small amounts of ^{67}Cu, ^{225}Rn, ^{103}Pd, ^{142}Pr, ^{125}Sb, ^{153}Sm, and others.

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Acknowledgments, disclosures and funding: We are grateful to the DOE Office of Science for their financial support.

TARGET CHAMBER BODY TEMPERATURE AND HYDROGEN CONTENT IN $[^{11}C]CH_4$ PRODUCTION

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Introduction. $[^{11}C]CH_4$ is preferred over $[^{11}C]CO_2$ as an in-target produced precursor when striving for high specific radioactivity of ^{11}C-labelled radiopharmaceuticals. However, difficulty in $[^{11}C]CH_4$ production is experienced widely in the scientific community [1, 2]. The $[^{11}C]CH_4$ yields are even at best far from theoretical amounts, as calculated from the nuclear cross section for the $^{14}N(p,\alpha)^{11}C$ nuclear reaction[3]. A systematic investigation on N_2-H_2 target performance is presented in terms of saturation yields (A_{sat} [GBq/µA]) as a function of target body temperature, hydrogen content and irradiation current.

Materials and methods. Two aluminium bodied chambers were used for $[^{11}C]CH_4$ production with N_2-H_2 gas targets. A conical chamber (**Target 1**) measured 11.2 x 90.0 x 19.4 mm (front I.D. x length x back I.D.) and had a volume of 16.9 cm^3. The second chamber (**Target 2**) was obtained by boring a 20.0 x 77.1 mm (I.D. x length) cylinder in the back end of the **Target 1** cone resulting in a volume of 25.6 cm^3. In both cases the inlet foil was supported by a metallic grid having a transparency of ~ 76 %. In all irradiations the chambers were loaded at 20 °C to a pressure of 35 bar, for **Target 1** or 41 bar, for **Target 2**, (thick target) and irradiated for 20 minutes. Varied parameters were a) the target body temperature (10, 40, 70 °C), regulated with a cooling fluid circuit and a heat exchanger, b) the irradiation current (10, 20, 30, 40 µA) and c) total hydrogen content (volumes for **Target 1** and **Target 2**, and gas compositions 5 and 10 % H_2). All irradiations were carried out in duplicate. The proton beam was from a fixed energy (17 MeV) negative ion cyclotron (CC 18/9, D.V. Efremov Institute, NIIEFA, St. Petersburg, Russia). The irradiation product was measured as reported elsewhere[4].

Results. The general behaviour was a decrease in the $[^{11}C]CH_4$ saturation yield [GBq/µA] as a function of irradiation current and an increase as a function of chamber body temperature, see figure. From **Target 1** with 5 % H_2 content in the target gas a linear decrease for saturation yield is observed as a function of increasing beam current and an increase as the temperature of the target body is increased. Using the same 5 % H_2 target gas, but larger volume chamber **Target 2**, the saturation activity remains at a 5-6 GBq/µA as the current increases and then decreases at around 15 µA. The high current data points remains at higher level than in the **Target 1**-5 H_2 % case. Figure 1 demonstrates the behaviour at even higher H_2 content: the large volume chamber (**Target 2**) and 10 % H_2 in the target gas. The graph decreases slowly as a function of current, where the $Y_{sat(11CH4)}$ at high currents is at remarkably higher level compared to both **Target 1**-5 % H_2 and **Target 2**-5 % H_2.

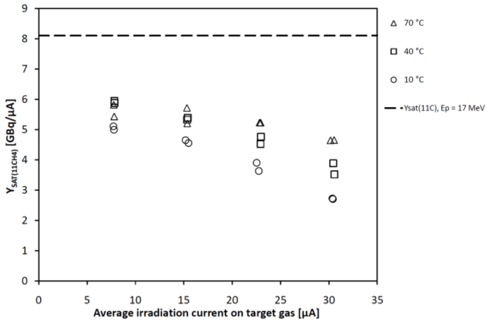

Figure 1. **Target 2** and 10 % H_2. $[^{11}C]CH_4$ saturation yield as a function of irradiation current at 10 – 70 °C. The dashed line is the theoretical limit.

It is noteworthy, that it was possible to maintain the $[^{11}C]CH_4$ saturation yield at the same approx. 5 GBq/µA level throughout the investigated current range by compensating the current dependent decrease with heating the target chamber body.

Conclusions. An irradiation current intensity effect was observed in saturation yield of $[^{11}C]CH_4$ from N_2-H_2 targets, having a detrimental effect on the yield with increasing current. The saturation yield of $[^{11}C]CH_4$ was increased by elevating the chamber body temperature, increasing H_2 partial pressure and H_2 total content.

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OPTIMISATION OF [^{11}C]CH$_4$ YIELDS FROM A HIGH PRESSURE GAS TARGET

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Introduction: We have previously developed a high pressure gas target for production of [^{11}C]-labelled carbon dioxide and methane via the ^{14}N(p,α)^{11}C reaction[1]. Whilst [^{11}C]CO$_2$ can be produced and recovered with close to theoretical yields, [^{11}C]methane recovery decreases with both increasing beam current and irradiation times. This effect seems to be increasingly exaggerated with decreasing target size and is thought to be due mainly to target wall interactions. We found that a quartz liner in the target significantly improved recoverable [^{11}C]methane yields, but this effect could be due to either the chemical inertness or the thermal conductivity of the quartz liner. Helin et al[2] have presented data which showed that [^{11}C]methane yields increase proportionally with target temperature (data up to 70 ºC). We wished to further explore this phenomenon with our target system using even higher temperatures.

Material and methods: The target is aluminium with a 25 mm diameter cylindrical bore (volume 98 cm^3). The irradiation is provided by 16 Mev protons using a Scanditronix MC32 cyclotron. The target is water cooled with a flow rate of 2.8 L/min as standard. In order to increase the target temperature during irradiation, we experimented with reduced water cooling and air cooling using cooling fins mounted on each side of the target. Target temperature was recorded with a thermocouple placed at the end of the target. All irradiations were performed at a current of 25 µA with an initial fill pressure of 26 bar (target gas: 10% hydrogen in nitrogen). Irradiations were performed for 20 or 40 minutes followed by a simple venting of the target (down to 1 bar) into a liquid nitrogen cooled Carbosphere™ trap (ca. 2 g) placed in a dose calibrator. Trapped activity was noted at 40 minutes post-irradiation, in order to allow decay of any co-trapped [^{13}N]nitrogen, and corrected to yield in GBq at end of bombardment (EOB).

Results: With standard water cooling the target temperature increased up to 34 ºC after a few minutes and then remained stable for the duration of the irradiation. With reduced cooling flow the target temperature continued to increase reaching ca. 80 ºC after 40 minutes. With cooling fins attached to the target the temperature increased more rapidly, reaching ca. 120 ºC after 40 minutes (Figure 1).

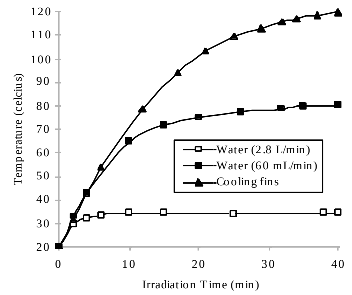

Figure 1: Effect of type of cooling on target temperatures

The effect of target temperature on recoverable yields of methane can be clearly shown in Figure 2. For a 40 minute irradiation at 25 µA the yield of recoverable [^{11}C]methane increased by 23% with only air cooling compared with standard water cooling, reaching 86% of the theoretical value.

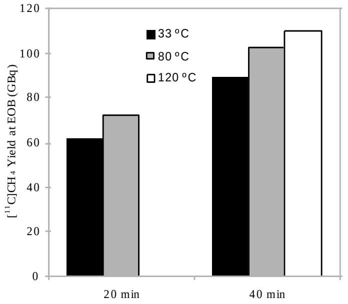

Figure 2: Yield of [^{11}C]CH$_4$ at different target temperatures

Conclusions: Based on our initial results there is a clear increase in recoverable [^{11}C]methane yields at higher target temperatures and the best yields are close to that expected for the production of [^{11}C]CO$_2$ in the same target. Work is in progress to build a system to keep the target at a constant temperature in order to conduct more controlled experiments.

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THE HAVAR FOIL IN FRONT OF NITROGEN GAS TARGETS: A SOURCE OF COLD CARBON IN C-11 PRODUCTION

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Introduction: Modern cyclotrons and state-of-the art gas targets are easily capable of producing C-11 in Curie amounts EOB. Decay losses during synthesis, purification and QC decrease the activity available for injection by factors 10 - 50. In order to achieve specific activities more than a few hundred MBq/µmol, care is needed to avoid all sources of non-radioactive ("cold") carbon in the target. We have studied the role of the target foils made of Havar as a potential source of such cold carbon. Obviously, the undamaged metal foil itself at room temperature does not leak carbon compounds into the target gas. It can however be speculated that the sum of heat and radiation damage could enhance carbon mobility through the foil.

Material and methods: Most cyclotron manufacturers prefer the high strength Havar alloy[1] (Hammilton Precision Metals , Lancaster, PA, USA) as target foil in thicknesses between 25 and 50 µmeters. The nominal composition of Havar is shown in table 1. To our knowledge most targets have a free target foil diameter span in the order of 20 mm, This thickness and size leads to a typical initial carbon content of 10 micromole in the foil.

The importance of this carbon content for the emerging specific activity is analyzed on the basis of the mobility, release and replenishment of the carbon reservoir in the foil. Although the mobility of carbon in steel and the exchange with gas phase environment is one of the best studied metal-gas interactions [2], this theoretical and practical knowledge is not easily extended to alloys with high cobalt content and with inherent high degree of radiation damage. No experimental data has been found on the diffusion on carbon in Havar, with or without radiation damage. For this reason, the transport of Carbon through the foil is here studied on the basis of the semi-empirical formalism of Miedema [3] describing both the diffusion and the solid gas exchange on the basis of formation enthalpies. The formalism allows the calculation of a temperature dependent diffusion coefficient in the foil. Using Ficks law, the transport of Carbon can then be found. However it should be remembered that in this most general case it is not the concentration but the local chemical potential of Carbon that drives the transport.

The enthalpy of the interstitial migration is taken from the extended metallurgical literature on binary compounds[4, 5].

Table 1: Havar Composition:

	Weight-%		**Weight-%**
Fe	19.1%	**W**	2.7 %
Co	42.0 %	**Mo**	2.2 %
Cr	19.5 %	**Mn**	1.6 %
Ni	12.7 %	**C**	0.2 %

Results: The theoretical calculations predict that Carbon in the foil can be regarded as completely stationary below foil temperatures of 350 Deg C. Extended heating above this temperature will migrate Carbon to the area of lowest chemical potential, in this case the nitrogen gas contents. For many irradiations this will confound specific activity. The initial inventory will however deplete, restoring specific activity. Most importantly, however, is the possible uptake of Carbon from cracked oil deposition from cyclotron or Helium cooler side of foil and its transport through the foil. This is both thermodynamically and kinetically possible. The presented results are conservative, as they ignore radiation damage that in general increases impurity element diffusion

Conclusions: Proper control of beam spot size and front foil cooling can be important parameters for obtaining ultimate specific activity in C-11 production. Equally important is the requirement for keeping Carbon deposition on front side of target window very low. Experimental verification of these findings would be very valuable, but we have not been able to design a safe yet clear tracer experiment (^{14}C) to test the findings.

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IMPROVING PRODUCTION OF ^{11}C TO ACHIEVE HIGH SPECIFIC LABELLED RADIOPHARMACEUTICALS

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Introduction: Molecular imaging is usually based on the recognition by the radiopharmaceuticals of specific sites which are present in limited number or density in the cells or biological tissues. Thus is of high importance to label the radiopharmaceuticals with high specific activity to be able to achieve a high target to non target ratio ratio. The presence of carbon dioxde (CO_2) from the air containing 98,88% of ^{12}C and 1,12% ^{13}C compete with $^{11}CO_2$ produced at the cyclotron. Our aim was to minimise the presence of these isotopes along the process of irradiation, transferring and synthesis of radiopharmaceuticals labelled with ^{11}C.

Material and methods: Carbon dioxide labelled with ^{11}C was produced by $^{14}N(p,\alpha)^{11}C$ reaction in a PET-Trace 10 cyclotron. Activity produced ranged from 37 GBq to 111 GBq, with irradiation times from 12 to 55 min and intensity of beam from 40 to 50 uA. Target gas was N_2 (6.0) spiked with 1% O_2 (5.0). Previous to the irradiation the target was 3-4 times flushed with He (5.7) as a cold cleaning, followed by a similar conditioning of the line, from the target up to the module, and finally. A hot cleaning in order to desorb $^{12}CO_2$ and $^{13}CO_2$ was performed by irradiation during 1 min at 5 uA (3 times). In addition, with the aim of improving quality of gas target a water tramp (Agilent) was incorporated in the inlet line of the target.

Even using the gas quality recommended by the cyclotron and module manufacturer, and with that widely reported in the literature, this was detected as a critical parameter. So gas purificators for Hellium and Hydrogen (Agilent) were also installed in the gas inlet of the module used for the ^{11}C-radiopharmaceuticals synthesis (FX-CPro Module, GE)

This process was applied for the production of ^{11}C-2-(4-N-[11C]methylaminophenyl)-6-hydroxybenzothiazole (^{11}C-PIB), ^{11}C-methionine and ^{11}C-choline. Specific activity was calculated by quantification of the amount of the respective labelled compound by HPLC, as well as radiochemical purity. Radionuclide purity and identity was analysed by gamma spectrometry and by determination of half-life. Besides, residual solvents by gas chromatography and biological controls were also done.

Results: The radiopharmaceuticals were produced with a yield (non decay corrected) from 18 to 27% for ^{11}C-methionine, 12 to 25% for ^{11}C- choline and 0,5 to 11,9% for ^{11}C-PIB.

Quality control performed to the radiopharmaceuticals were in agreement to USP or EP requirements and specifications stablished by CUDIM according to literature.

^{11}C-PIB was the critical product in terms of the need of high specific activity (more than 100 GBq/umol), in order to obtain suitable image quality and data analysis from the patient. Starting with an initial specific activity less than 10 GBq/umol, before applying the described improvements, it with was possible to reach a range between 200 – 400 GBq/umol. In the case of ^{11}C-methionine and ^{11}C-choline no significative difference was observed.

Conclusions: Target conditioning process (cold and hot flushings) as well as line cleaning and desorption of unlabelled CO_2, in addition to increasing gas purity, both in the target and in the modules were critical parameters that enable to achieve ^{11}C-radiopharamaceuticals with high specific activity.

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EVALUATION OF THE HP C-11 TARGET ON THE GE PETTRACE CYCLOTRON.

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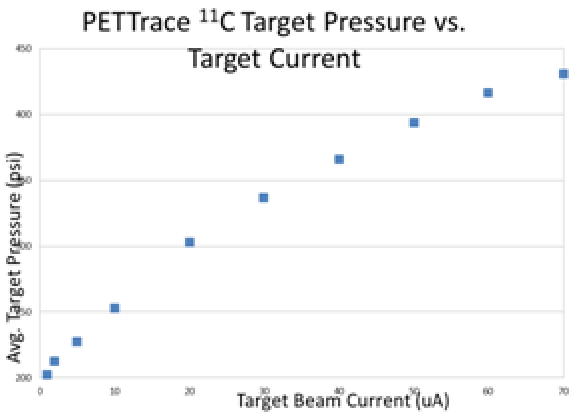
INTRODUCTION: We recently installed a GE PETtrace cyclotron to replace our 22 year old MC17 machine. The PETtrace was delivered with an “HP” C-11 target which can run at higher pressures and higher beam currents than that on the MC17. However the initial production of $^{11}CO_2$ from the HP target was disappointing. It produced about half as much $^{11}CO_2$ at about 15% of the specific activity that we achieving with the MC17. We decided to measure the target characteristics to evaluate the source of the problem.

METHODS: The change in gas pressure as a function of beam current was measured , from 10 to 70 microamps. The yield of $^{11}CO_2$ and ^{11}CO were measured by directly emptying the target through an ascarite and cuprous chloride/charcoal trap(1) each of which was in a dose calibrator. Bombardments where performed from 10 to 70 microamps at 30 minutes each. The yield of the $^{11}CO_2$ was converted to an S\` value and expressed as mCi’s/microamphr. Yield calculations, particularly at low currents, are complicated on the PETtrace as the operating system performs an optimization, called an isochronous hunt, which essentially bombards the target at 13 microamps for 3 minutes before the formal bombardment begins. Specific activity was measured by synthesizing PIB and measuring the product specific activity. After the initial runs were completed the incident angle of the beam on the target was changed by adjusting the internal collimators and stripper foil and mechanically raising the end of the target. This attempts to correct for the effects of the fringing magnet field on the beam in the target.



$$S' = \frac{A_{EOB}}{I_{Beam}\left[1-\left(\frac{1}{2}\right)^{\left[t_{Beam}/t_{1/2}\right]}\right]}$$

RESULTS: The pressure/current plot indicated that the target was thick at high currents. The initial S\` values were ~96 mCi’s/microamphr and independent of current. After adjustment for the effects of the fringing field the S’ value was raised to ~108. This compares to 140 mCi’s/microamphr from the MC17. The $^{11}CO_2/^{11}CO$ ratio was independent of current. The specific activity was initially ~1.2 Ci/micromole at 32 minutes EOB. After ~100 runs on the target the specific activity improved to ~5 Ci/micromole. This compares to ~7Ci/micromole form theMC17..

CONCLUSION: As the target is still thick even at the highest beamcurrents and the S\` values are independant of beam current then the lower performance of the PETtrace versus the MC17 must be because beam is striking the target walls before the energy drops below the threshold for the $^{14}N(p,\alpha)^{11}C$ reaction. The target has in internal ID of ~2cm. This could lead to to a significant percentage of beam loss because of small angle scatter of the beam striking the target walls. Alternatively the beam could be curved within the target because of the fringing magnetic field.

We would urge the use of S\` rather than S to describe the target performance. Although both terms use the same equation and give the result in the same units they are describing different phenomena. The S value is an absolute value and describes how well a nuclear reaction produces a particular product radionuclide, assuming that all the incident particles only interact with the target material. S\` describes the **target** performance, how well the target keeps all the target material in the beam strike zone through the energy range of interest.

INDIRECT MEASUREMENT OF SPECIFIC ACTIVITY OF [^{11}C]CO$_2$ AND THE EFFECS OF TARGET VOLUME FRACTIONATION

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Introduction: Achieving high specific activity of [^{11}C]carbon dioxide remains a challenging task in PET tracer production. Apart from carrier carbon introduced during labelling synthesis and that already present in the reactants, arguably the major part of isotopic dilution stems from the target gas. Hypothesising that the concentration of cold carbon in the target contents and the delivery lines may not be equally distributed after target irradiation, we attempted fractionation of the gas delivered to our ^{11}C synthesis module.

Material and methods: The [^{11}C]carbon dioxide was produced via the ^{14}N(p,α)^{11}C reaction. This was done on an IBA Cyclone 18 MeV cyclotron and an IBA NIRTA 40ml gas target. The target gas was 99.5% nitrogen and 0.5% oxygen, both were of grade 6.0. Irradiation time was 90 seconds at 20μA. In the absence of equipment capable of performing direct measurement of carbon dioxide, the specific activity was determined by the carboxylation of trityllithium and subsequent detection by HPLC-UV[1]. The trityllithium was prepared in a glovebox from triphenylmethane and butyllithium. All chemicals was aquired from Sigma-Aldrich. The HPLC system used was a Shimadzu Prominence equipped with a diode array UV detector.

Results: The deep red color of trityllithium solution was convenient to determine if the reactant was still fresh. Another andvantage is that labelled acid elutes before the triphenylmethane from RP columns.

On the downside the UV absorption of triphenylacetic acid was not sufficient for producing adequate signal for quantification using our HPLC detector. Furthermore, trityllithium appers to be reactive not only to [^{11}C]carbon dioxide, but also to other compounds that can be present in the target gas, such as nitrogen oxides. As a result [1-^{11}C]triphenylacetic acid constituted less than 30% of the radioactivity in the reaction mixture. Analytical chromatograms of the reaction mixture showed significant amounts of UV-absorbing species, in a range of retention times close to that of triphenylacetic acid.

Conclusions: High unspecific reactivity of trityllithium and insufficient UV absorbance of triphenylacetic acid turned out to be a hindrance for adopting this reaction for determining specific radioactivity of [^{11}C]carbon dioxide. This prompted us to search for a more specific and less reactive [^{11}C]CO$_2$ trapping reagent. Work is in progress and we hope to have more results to come.

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HIGH PRESSURE GAS TARGET WITH AUTOMATED WINDOW CHANGER

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A novel high pressure gas target design features hydrostatically formed windows, efficient cooling system and a provision for an easy, in-situ window change.

The unique feature of this target is the domed-shaped window. The Havar alloy window is electron beam welded to a metal ring, thus forming one, interchangeable assembly. The window assembly is sealed by knife-edges locked by a pneumatic toggle.

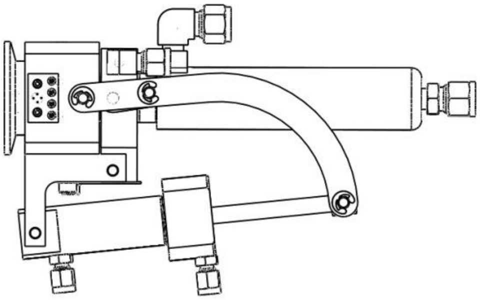

Figure 1: Closed

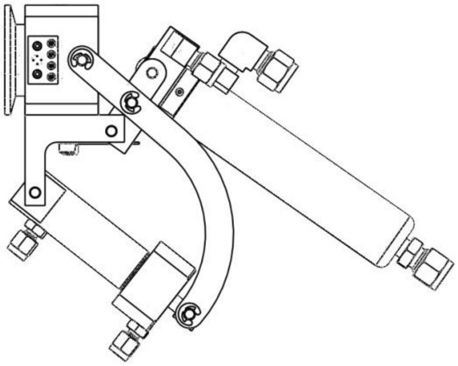

Figure 2: Open

The change of the window is initiated by applying air pressure to the pneumatic actuator (constructed out of aluminium and graphite) of the toggle mechanism. This opens the target exposing the window assembly. The old window can be easily removed with a long grabber and a new window dropped in its place. The operation takes less than a minute.

In the present configuration the target chamber is 10.5mm diameter x150mm long. Impending water cooling is employed at the beam stop and the target body is water cooled via spiral channels surrounding the gas chamber.

The over-the-centre toggle locks positively thus providing a full closure without the need for continuous air pressure in the pneumatic actuator.

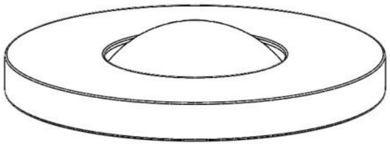

Figure 3: Window assembly

The target is designed to operate at a pressure of 80 bar. The semi-spherical geometry of the window combined with full temper of the Havar following the forming operation, greatly increases the window strength. Window cooling is by the target gas thus eliminating the complicated and expensive double-window helium cooling. The front of the target consist of an integral collimator and a four sector silver mask for accurate beam cantering. The target can be mounted directly on the beamlina by the KF40 flange terminating the target assembly. The total length of the target assembly is only 220mm.

The target body is made out of high purity aluminium and all the materials used are radiation hard. No elastomers are employed in the construction. Consequently the target needs no maintenance except a schedule window change every 100 A-hour of beam.

The target is designed for 14MeV, 300µA beam. A 13mm diameter beam is collimated to 10mm diameter.

With small changes in the construction the same design can be used for different beam energies, currents and sizes.

HIGH CURRENT GAS TARGET ASSEMBLY FOR PRODUCTION OF ^{123}I

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Introduction: The design and control of high current gas target systems well adapted for making effective use of modern cyclotrons beam performance is an essential technical challenge. The Target assembly and materials not only have to withstand beam currents well above 100µA for maximizing the production capacity, it too needs to be controlled continuously over extended irradiation periods for a safe, reliable and economic routine production. Improved target body and target window issues, process control devices and requirements to beam transport into and through the target are exemplified by our isotope production system KIPROS (**K**arlsruhe **I**sotope **Pro**duction **S**ystem) for large scale ^{123}I production. The method is based on the well known nuclear reaction of protons with highly enriched ^{124}Xe.

Target System: The technical characteristics of our standard KIPROS target system are designed to operate at 100 to 200 µA at 30 MeV delivering a bulk yield of 350 MBq/µAh of ^{123}I (at EOB+6h) as [^{123}I]NaI at high isotopic and radiochemical purity. The production unit is fully automated and allows continuous in-process control of each operation: target preparation, ^{124}Xe transfer, irradiation, ^{124}Xe recovery, ^{123}I recovery and target qualification for the next batch. All operations are monitored and archived, and are retraceable. In-process controls are displayed on the control screen.

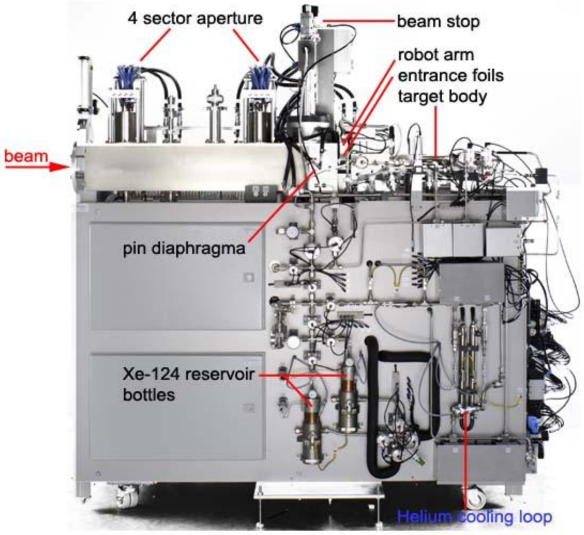

Fig 1: Outline of KIPROS for routine ^{123}I production

The KIPROS system is being employed in routine operation at various facilities worldwide. The target assembly consists of:

- A diagnostic unit for beam adjustment and control during the irradiation process. One pair of four sector collimators and one ring collimator ensure a parallel or slightly convergent proton beam at the target entry. Currents on the collimators (each sector) and the target body are monitored separately, recorded, and may be followed online allowing a reliable and narrow beam control during the irradiation.
- An improved aluminum target body with a nickel plated inner surface ensuring consistently goodproduct purity. The target body is equipped with pressure and temperature sensors for online recording the proton beam situation in the target gas. Especially the gas pressure is highly sensitive to the accurate beam alignment.
- A remote target window exchange mechanism for replacement of the Helium cooled target window at minimum radiation exposure. The Helium cooling loop is controlled by a temperature and pressure monitoring system for the early tracing of a beginning foil insufficiency or leakage.
- A gas storage vessel for ^{124}Xe located close to the target body with a short gas transfer line, minimizing ^{124}Xe losses from batch to batch and allowing a close balancing of the Xe inventory as part of the in-process controls. The gas transfer part is separated from the “wet” radioactivity wash-out part.

Development: A further refinement of our KIPROS high current gas target system is still ongoing and will be described. It is directed to the improvement of the target body and the double foil window configuration, and the respective cooling efficiency for a safe, repeated and long period use at 200 µA. Additionally its adaption to 24 MeV cyclotrons is envisaged which could deliver reasonable yields of ^{123}I at high current operation. A test target set-up has been used to derive data about the temperature and pressure profile in the target and in the target window up to 250 µA. Helium flow profiles and its heat removal efficiencies have been simulated and compared to the measured data. First results will be presented for discussion.

DESIGN AND DEVELOPMENT OF A SEMI-AUTOMATED MODULE FOR THE PREPARATION OF METALLIC PET RADIONUCLIDES

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Introduction: In the last few years there has been a growing interest in the use of PET ligands labeled with radiometals, particularly isotopes of copper, gallium and zirconium. Future clinical applications of these tracers will require them to be produced reliably and efficiently without increasing radiation exposure to personnel. The method for the production of metallic radionuclides has been widely reported [1], and most of them share a common ion chromatography purification technique. The aim of this work is to design and develop a semi-automated remotely controlled module for the purification of metallic PET radionuclides via cation exchange chromatography.

Material and methods: The design of the module features 14 electrovalves and a peristaltic pump resistant to agresive acidic fluids and operating at 24 VDC. A liquid chromatography column is packed with cation exchange resin. The system is equipped with miniature radiation detectors and two hot-blocks, one for dissolution of the target material and other housing a v-vial to evaporate to dryness the eluted fraction containing the radioactivity. For remote control a microcontroller ATmeg1280 is used and all the electronics for data adquisition and control devices is designed.

Results: The electronics required for electrovalves, motor control and temperature data acquisition has been completed and it has been tested for its correct function (Fig. 1).

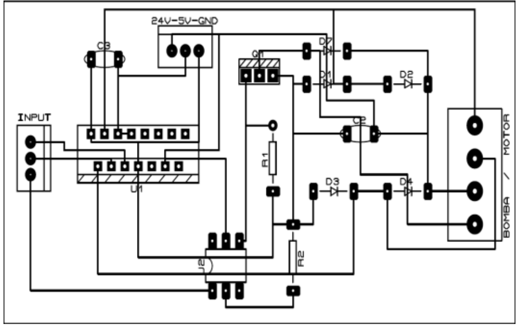

Figure 1: Electronic card for motor control.

The ATmeg1280 microcontroler has been programed using LabVIEW and a view of the graphical user interface (GUI) to control the system is shown in figure 2. The GUI allows a friendly individual control of electrovalves, heaters and other devices as well as the visualization of temperature and radiation values at different points of interest. The system has been successfully tested for transfer of fluids (efficiency and sealing).

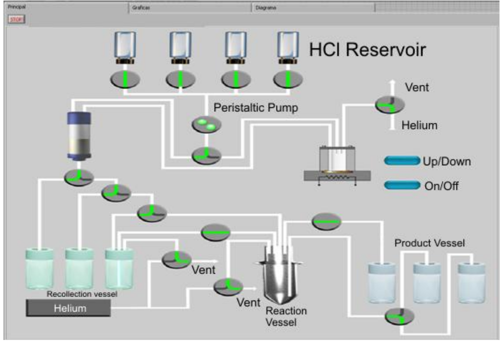

Figure 2: GUI for remote control of the system.

The developed module has the desired characteristics of a semi-automated, safe, robust and remotely controlled system for the separiton of metallic positron emitters from the target material electroplated on a solid target substrate. The dissolution block consist of a Teflon insert with a central aperture exposing to the acid bath only the electroplated area of the target substrate, which limit metallic impurities to the lowest level allowing high specific activities of the activated products.

Conclusions: A custom made flexible module for the reliable purification of metallic PET radionuclides was developed using commercially available components. The remote operation of the system decreases significantly the radiation exposure to personnel.

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DEVELOPMENT OF AN AUTOMATED SYSTEM FOR LARGE-SCALE PRODUCTION OF ZIRCONIUM-89 RADIOISOTOPE

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Introduction: Zirconium-89 (^{89}Zr) is a useful metallic radioisotope for radioimmunological positron emission tomography (PET) imaging.[1] This isotope enhances PET image resolution because its decay includes a positron (β^+) emission with a relatively low energy (0.90 MeV).[1] Additionally, ^{89}Zr has a half-life ($t_{1/2}$) that is long enough ($t_{1/2}$=3.27 d) to provide time for sample preparation (purification, chelation, immunolabeling) and adequate circulation time in a patient for immunotargetting to occur.[1] However, in addition to being a β^+-emitter, ^{89}Zr emits five gamma (γ) rays, one of which has both a significant branching fraction and a high energy (909.1 keV) compared to γ-rays from other metallic PET radioisotopes. This γ-ray contributes substantially to the dose received by radiation workers, making production of ^{89}Zr by hand a potential radiation safety risk. Here, we present an automated system that can be used to safely purify in a hot cell relatively high levels of ^{89}Zr activity for potential extramural distribution.

Material and methods: Our approach was to create a system that would automate the chemical purification of ^{89}Zr that was first introduced by Meijs *et al.*[2] and subsequently improved by Holland *et al.*[1] Since our system is still in the developmental phase, it has only been tested with a low level of activity so far. A circular disc (~1 cm diameter) was cut from yttrium (Y) foil and secured in a niobium (Nb) target holder. This assembly (“target assembly”) was placed in a cyclotron with a fixed beam energy of 15 MeV, where it was bombarded with protons (15 min., 5 μA) for a low-level test run of the automated system. Immediately prior to purification, the target assembly was transferred into a Teflon dissolution vessel mounted on the automated system. The lid to this vessel was closed and actively held shut for the entirety of the purification by a pneumatically actuated arm. The hot cell containing the automated system was sealed, and the entire purification process was completed without reopening the hot cell. The automated system consisted of: the target dissolution vessel, a hydroxamate resin column, a dessicator, a vacuum trap, a Venturi pump, and an advanced digital mass flow controller (MFC) that was connected to a compressed air supply via a regulator. The MFC had a large dynamic range (0.2-10 mL/min) and was capable of slowly moving liquids through the system, which was necessary for this purification. The electric components of the system were controlled by a computer outside of the hot cell running a custom program created in-house using the LabVIEW software platform. This custom program featured a graphical user interface (GUI) that included a live digital video feed that monitored liquid in the column, as well as four real-time radiation detectors that monitored the movement of radioactive material within the system.

Results: The automated system effectively purified ^{89}Zr from the ^{89}Y target foil. This foil appeared to have been completely dissolved in the dissolution vessel, and the Nb target holder showed no evidence of chemical etching. Based on gamma spectroscopy for the low-level test run, the system yielded 338 μCi of ^{89}Zr in the product and 6 μCi in the target holder, indicating a recovery rate of approximately 98%. Furthermore, the only radioisotope other than ^{89}Zr to be identified in the product was ^{88}Zr at only an estimated 112 nCi, indicating a product purity above 99.9%. Measurements using a dose calibrator ~3 h after purification revealed only 1, 14, and 34 μCi of activity remained in the waste vial, the column, and the empty dissolution vessel, respectively, after the low-level test run. The level of activity tested was increased as the system was improved.

Conclusions: We have designed, built, and tested a new automated system that will safely purify high levels of ^{89}Zr activity inside a hot cell. This system demonstrated high recovery rate and product purity, and it was optimized for mass production of ^{89}Zr for distribution to other research centers.

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AUTOMATED PRODUCTION OF ^{64}Cu AT TURKU PET CENTRE

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Introduction: In Turku, quantities of up to 40 GBq of ^{64}Cu have been routinely produced. Only radiation hygiene is the constraining factor to produce more, because at present the target for ^{64}Cu-production is often handled with only glove-protected hands. Therefore, if and when larger amounts of radioactivity will be produced, an automated target-handling system is needed.

Material and methods: In Turku ^{64}Cu is produced by bombarding a solid ^{64}Ni-target (electroplated on a gold disc) with protons. So far, the target has been taken away from the irradiation station by hand and carried in a lead shield to the radiochemistry laboratory. There the separation of ^{64}Cu from the target material is done inside a hot cell with a dedicated, semi-automatic purification module. The target removal from the irradiation station and handling inside the hot cell are now being automated. The automation consists of a system which transfers the target disc into a lead shield, and also handles the disc inside the hot cell.

Results: A module for moving the target from the irradiation position into a lead shield has been built and installed. The module was fully designed and built in house.

For handling the target inside the hot cell a robotic arm, model IRB120 from ABB (Asea Brown Boveri) has been bought and installed with custom-made tools. The equipment in the hot cell had to be modified for a more functional interface with the robot.

Conclusions: Final user tests and modifications are at the moment being done to the target-removal module and to the automation inside the hot cell. The work is well under way and should considerably improve the radiation hygiene of the workers with ^{64}Cu. Automatic transport of the lead shield (or only the gold disc) from the irradiation station to the hot cell will be left for future.

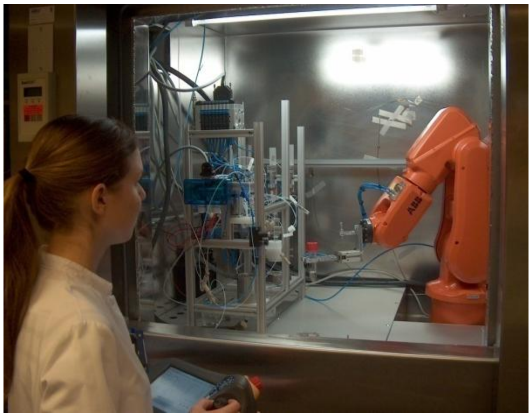

Figure 1: Target handling inside the hot cell using ABB IRB120 robotic arm.

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A PERISTALTIC PUMP DRIVEN ^{89}Zr SEPARATION MODULE

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Introduction: In order to facilitate the separation of ^{89}Zr activity from natural yttrium target material and to decrease the dose burden to personnel a computer aided separation module was designed and assembled.

Material and methods: The module consists of a peristaltic pump (Welco, 6-12 VDC) and 6 two way pinch valves (Takasago, 12 VDC) which are mounted on an alumina plate (fig 1). On the upper side of the pinch valves, syringes and hydroxamate resin[1,2] were connected with Luer Lock tips to a Pharmed BPT tube (1 mm i.d and 3 mm o.d). On the lower side of the pinch valves the tubes were connected to a common line with 3 port valves. Before separation, 100 mg hydroxamate resin was manually activated[2] and connected to the module. Also water and HCl-syringes were connected to the module before an irradiated yttrium foil was placed in the dissolving vial. Pinch valves and pump was controlled with an 8 channel USB relay card. To perform separations a valve/pump control-sequence was programmed with Labview. The peristaltic pump is placed so that liquids on the right side of the pump can go to vials on the left side of the pump and vice versa by reversing the direction of the pump rotation. This setting was used to perform the separation similar to Holland et al.[2] (because of larger target masses in this work, water and HCl volumes were increased proportionally). Foils were dissolved in several steps by pumping, 1 ml, 6 M HCl from syringe 6 (fig 1) to the dissolving vial and wait 75 sec before next addition (total of ~18 ml). During the dissolving step the exhaust was active by circulating water through a water jet vacuum pump. ^{89}Zr was normally produced in ~50x20x0.64 mm^3, ~3 g, yttrium foils with 45 µA, 12.8 MeV protons[3] (1h irradiation results in 2110 ± 240 MBq). Elution can be done in many different ways. To decide an elution distribution profile the resin was eluted with ten manually, 200 µl-1 M oxalic acid injections into the module (fig 2). The separated activity was used to label[4] trastuzumab-Fab and tested against HER2 expressing SKOV-3 cells.

Results: Dissolving, loading and collecting of ten ^{89}Zr fractions took less than 90 min. More than 85% of activity measured in foil, (or 95% of transferred to resin) was collected in total of 2 ml oxalic acid. Approximately 10% of foil activity was trapped in the dissolving vial. The overall labeling yield of ^{89}Zr-Df-trastuzumab-Fab was over 99%. The radioconjugate was stable in PBS for at least 1 week and retained its binding specificity to HER2 receptors *in vitro*.

Conclusions: We have designed a simple and cheap automated separation module which reduces personnel doses. This is helpful for sites with the aim to distribute large amounts of ^{89}Zr activity. All syringes, three port valves and tubes in contact with liquids and foil are disposables and can be changed before a new separation.

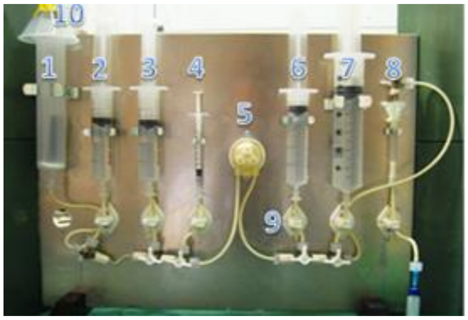

Figure 1: 1:Dissolving vial, 2:2 M HCl, 3:H_2O, 4:1 M Oxalic Acid, 5:Peristaltic Pump, 6:6M HCl, 7:H_2O, 8:Hydroxamate Resin, 9:Pinch Valv, 10:Exhaust

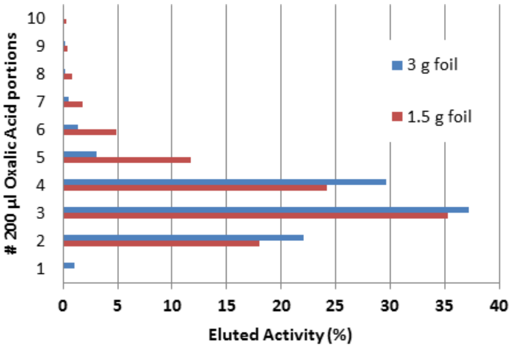

Figure 2: Typical elution distributions of activity passing the resin.

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^{45}Ti EXTRACTION USING HYDROXAMATE RESIN

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Introduction: With a β^+ branching ratio of 84.8% and the negligible emission of other non-511 keV photons, ^{45}Ti ($t_{½}$=184.8 minutes) has decay properties that are well-suited for positron emission tomography. Furthermore, ^{45}Ti is attractive as it can be made in high radionuclidic purity using natural abundance monoisotopic ^{45}Sc as a target material. While several publications have reported the production and extraction of ^{45}Ti [1–3], these methods rely on large ion exchange columns or solvent extraction techniques, both of which result in large final elution volumes.

For this study, we produced ^{45}Ti by irradiating Sc foil and have developed a chemical separation method that uses a small column of hydroxamate functionalized silica gel resin. Reactivity of the extracted ^{45}Ti product was assessed via chelation with desferal.

Materials and methods: Scandium foils (99.9%, 100-120 mg, 0.25 mm, Alfa Aesar) were irradiated on a GE PETtrace with 13 MeV protons using a degraded target system and irradiation currents up to 20 µA. The irradiated targets were removed and dissolved in 3 mL 6 N HCl (Aristar Ultra grade).

Hydroxamate functionalized resin was prepared from Waters CM resin following the procedure of Holland *et al* [4]. Prior to loading of the resin into a 3 mL Grace column, the resin was washed with 1 mL 1 M oxalic acid and 1 mL 18 MΩ H_2O. The resin was loaded into the column and then conditioned with 10 mL 18 MΩ H_2O, 10 mL MeCN, 10 mL 18 MΩ H_2O, and 2.5 mL HCl.

Optimization studies were performed with 6 M, 2 M, 1 M, and 0.5 M HCl to evaluate the optimal column conditioning and activity loading conditions. For validation purposes, comparison to unreacted CM resin was also performed (CM conditioned at 2 M HCl). Loaded columns (~110mg) were washed with 2.5 mL HCl (respective concentration) and 2.5 mL 18 MΩ H_2O prior to elution with 1 M oxalic acid (3 @ 200 µL fractions). Loading efficiencies and overall decay-corrected recoveries were recorded (Capintec # 395).

Following this initial optimization study, N=4 irradiations were performed, with ~150 mg hydroxamate resin, 2 M HCl, and 4 @ 300 µL 1 M oxalic acid elution fractions. Reactivity was assessed by adjusting the eluted activity to pH 8.0 with 0.25 M HEPES buffer, reacting with desferal (0.1 ng–1 µg) for 1 hr at 25 °C, and performing radio-TLC with Al-backed silica gel plates and 0.05M DTPA as a mobile phase.

Results: Figure 1 reports the results of the initial optimization studies to evaluate the loading and overall decay-corrected recovery of the ^{45}Ti activity as a function of HCl concentration. For comparison, the loading efficiency on unreacted CM resin is also reported.

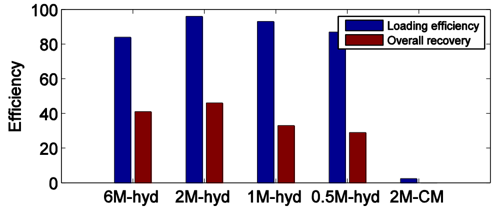

Figure 1: Loading and recovery efficiencies as a function of HCl concentration on hydroxamate resin.

With 2M selected as an optimal HCl concentration, four additional irradiations/extractions were performed as described above. An average trapping efficiency of 74 ± 4% and an average overall decay corrected ^{45}Ti recovery of 56 ± 6% are reported. The maximum activity reported for a single 300 µL fraction was 2.66 GBq (8.36 GBq loaded), or 32% (36% decay-corrected) of the total activity. When comparing these loading results to the values noted in Figure 1, reduced efficiencies are attributed to the increase in scandium mass loaded on the column (each sample in Figure 1 was only a small fraction of a single irradiated foil).

Overall, the entire ^{45}Ti separation procedure was concluded approximately 1 hour post-EOB. Effective specific activity of the extracted ^{45}Ti ranged from 5 to 38 GBq/µmol when reacted with desferal.

Conclusion: The procedure described above resulted in extraction of ^{45}Ti using a small hydroxamate resin with >50% recovery in ~1 mL of 1 M oxalic acid. With the ability of chelating ^{45}Ti to desferal, this radionuclide may prove to be an interesting alternative to ^{89}Zr when the evaluation of shorter kinetic processes is desired. Further optimization studies (e.g. resin volumes, flow rates, etc.) are required.

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SEPARATION METHODS FOR HIGH SPECIFIC ACTIVITY RADIOARSENIC

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Introduction: Two radioisotopes of arsenic have potential utility in PET imaging and radiotherapy, namely As-72 and As-77. Arsenic-72 is a 26 h half-life positron emitter that is potentially available from a Se-72/As-72 generator system. Selenium-72 has an 8.5 day half-life and decays by electron capture to As-72. The efficient separation of arsenic from selenium is feasible via anion exchange systems that take advantage of the differences in the chemistries of arsenic and selenium, in particular the oxyanions of arsenic and selenium in their maximum oxidation states, AsO_4^{3-} and SeO_4^{2}. At low pH the arsenate ion is fully protonated while the selenate ion retains a negative charge. Arsenic-77 is available from neutron irradiation of an enriched Ge-76 target followed by beta decay. Arsenic-77 has a 38.8 h half-life and emits a beta particle with a maximum energy of 0.683 MeV along with a 239 keV gamma ray.

Material and methods: Natural sodium bromide targets were proton irradiated at Los Alamos National Laboratory and shipped to MURR, following removal of bromine, and evaluated by anion exchange chromatography for separation of As-72 from the Se-72 produced. Germanium-76 targets (GeO_2) were neutron irradiated at MURR to generate high specific activity As-77; extraction methods were evaluate to isolate As-77 from the Ge target material.

Results: Bio-Rad Dowex 1x8 (100-200 mesh) anion resin demonstrated the best separation of As-72 from Se-72, with the acid, acid concentration, and pH optimized. Additionally, conditions to convert the selenium present to selenate prior to anion exchange were determined; initially both selenate and selenite were present. Peroxide oxidation of selenium solutions converted the selenium present to selenate. Nitric acid elution was found to give the best separation and recovery of arsenate. Germanium oxide targets were dissolved in KOH, acidified with HCl and solid KI was added to generate As(III), which was extracted into cyclohexane as AsI_3. More than 90 % of the ^{77}As was obtained in three extractions with cyclohexane, with less than 1 % of the germanium extracted. The isotope ratio of As:Ge improves by nearly 10^3. The As(III) can be back extracted from the cyclohexane in an aqueous solution with 0.1 to 0.2% H_2O_2 solution as arsenate, which is not retained in cyclohexane. Thin layer chromatographic (TLC) methods were developed to determine the arsenite/arsenate ratios.

Conclusions: Methods to obtain high specific activity As-72 and As-77 from proton irradiated NaBr targets and neutron irradiated GeO_2 targets, respectively, are being developed and will be reported.

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RECOVERY AND IRRADIATION OF ISOTOPICALLY PURE Zn-68 AND Sr-86 AT BROOKHAVEN LINAC ISOTOPE PRODUCER

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Introduction: Higher irradiation yield, better specific activity and superior radionuclidic purity are among the reasons why isotopically enriched targets are often used in production of radionuclides. However, ceased activities on the electromagnetic isotope separation resulted in extremely high costs and limited supply of the enriched isotopes. Hence researches have been facing with the necessity to engineer production schemes and methods where the target material is recovered and reused.

A positron emitter ^{86}Y and radiotherapeutic beta emitter ^{67}Cu are two of the many radionuclides whose production benefits from the use of the enriched isotopes. While the irradiation of monoisotopic ^{86}Sr is conducive to production of ^{86}Y with the lowest level of $Y^{87/87m}$ impurities the proton bombardment of ^{68}Zn results in 4-5 times improvement ^{in} ^{67}Cu yield compared to the natural Zn. In this paper we describe our experience with recovery and consequent irradiation of the ^{86}Sr and ^{68}Zn targets

Material and methods: ^{68}ZnO was received from Oak Ridge National Laboratory. Electroplated ^{68}Zn disks (1-3 g) were sealed aluminum capsule and proton-irradiated at Brookhaven Linac Isotope Producer for 24-66 hours at the beam currents ranging from 40 to 80 µA (Table1). Target disks for the experiments 1-3 was made of fresh ^{68}Zn, 3-11 – with recovered ^{68}Zn. The experiments are arranged chronologically.

Table 1: Irradiation conditions of ^{68}Zn disks.

Exp.	Energy, MeV	Time in beam, h	Mass of target, g	µA-h
1	105	45.0	2.13	1892.8
2	128	24.0	3.58	1072.2
3	92	24.0	0.74	1110.3
4	128	24.0	2.34	1612.8
5	92	24.0	1.51	1443.4
6	92	24.0	1.80	1431.4
7	92	24.0	1.11	1286.4
8	105	70.6	2.55	3962.3
9	105	66.7	1.28	3982.0
10	105	66.3	1.38	5066.8

After irradiation ^{67}Cuwas chemically separated using procedure reported previously. Solution of irradiated ^{68}Zn in 0.5 M acetate buffer was collected and its volume reduced to 40 ml by evaporation. Re-plating of ^{68}Zn was carried out on Ti disk at initial pH above 1.5 for 6-7 hours at 160 mA

Electroplating cell was set up in a lead shielded hot box. Upon completion of electroplating, the obtained disk was rinsed, dried, weighed and sealed in to the aluminum capsule for irradiation. The remaining solution was saved for additional ^{68}Zn recovery.

In a typical ^{86}Sr recovery experiment solution of ^{86}SrCl$_2$ in 2.5 N HCl as it comes out of the processing was removed from the hot box and evaporated to dryness. The obtained powder was hand-packed into the target and irradiated for 1 h at beam currents 60-80 µA at 14.5 MeV to produce ^{86}Y

Results: The irradiation yield of ^{67}Cu ranged from 0.6 to 1.2 MBq/µA-h×g ^{68}Zn (15-33 µCi/µA-h×g). The yield decreased from experiment to experiment as ^{68}Zn was put through recovery cycles (Figure 1). Before the electroplating, pH of the solution has to be adjusted up to about 3 with NaOH. Hence, accumulation of the sodium salts in the solution resulted in contamination of replated Zn disk. While it did not adulterate the radiopurity of the product, effective concentration of ^{68}Zn atoms decreased resulting in lower ^{67}Cu yield.

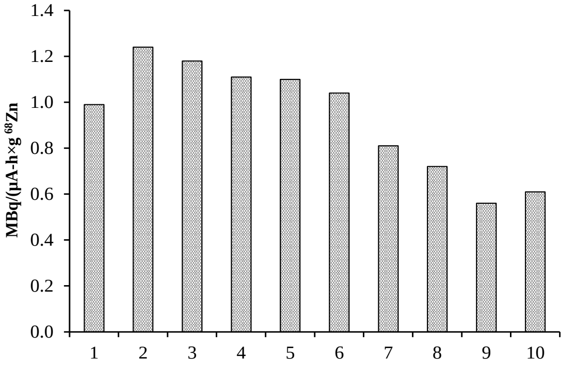

Figure 1: Irradiation yield of ^{67}Cu

Irradiation yield of ^{86}Y 18.5-74 MBq/(µA-h×g^{86}SrCl$_2$) which is about 2 times lower than data obtained in the small “medical” cyclotrons. However, higher beam current capability allows production of up to 50 mCi of ^{86}Y in 2 hours irradiation. The recovery of ^{86}SrCl$_2$ is much less complicated since dose rates are low enough to assemble the target outside the hotbox.

Conclusions: While recovery and re-irradiation of ^{86}SrCl$_2$ is straightforward, ^{68}Zn may require additional purification before electoroplating both from sodium salts and co-produced radioimpurities to reduce dose rate.

NOVEL, SIMPLE AND FAST AUTOMATED SYNTHESIS OF ^{18}F-CHOLINE IN A SINGLE MODULE SYNTHERA

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Introduction: The ^{18}F-Fluorcholine has demonstrated to be an important molecule as a radiotracer for brain, lung or prostate tumors. Taking into account that ^{18}F-Fluorcholine has been recently approved for its use in humans by countries like Germany and France, we undertook the task to supply this important radiopharmaceutical to the argentine nuclear medicine community. Until now the synthesis of this important radiopharmaceutical has been carried out with different modules. The published synthesis to obtain this molecule with the Synthera module requires the utilization of two modules connected in series(1,2). In the present work we utilize a totally automatic synthesis using only one module.

Material and methods:

I. Reagents and columns:

We used the commercial kits supplied by ABX for the synthesis of ^{18}F-Choline. The used reagents are: Kryptofix solution, dibromomethane in dry acetonitrile (DBM), dimethylaminoethanol (DMAE), NaCl 0,9%, ethanol and water for injection. The columns used are: Sep-Pak Light Accell Plus QMA, Sep-Pak Plus Silica cartridge, Oasis HLB Plus Sep-Pak Cartridge and Sep-Pak Plus Accell Plus CM cartridge.

The Integrated fluidic processor (IFP) was also supplied by ABX. We used an IFP for FDG synthesis with some modifications (Figure 1).

The enriched water was supplied by Nukem, Gmbh, Germany

II. Labeling protocol and system description

The ^{18}F was produced by the $^{18}O(p,n)^{18}F$ nuclear reaction with an IBA Cyclone 18/9 cyclotron. The fluoride is passed through a QMA column and eluted afterwards with the Kryptofix solution. Subsequently an azeotropic evaporation until dryness is carried out. The DBM solution is added and it is made to react in the closed vial at 110 ºC during 5 minutes. In this step the ^{18}F-fluoride assisted by Kryptofix attacks the molecule of dibromomethane and an intermediate reaction product of fluorbromomethane is obtained, which is subsequently distilled at 60 ºC during 20 minutes using nitrogen pulses. The product is passed through the silica columns and reacts with the DMAE on the surface of the HLB column, on which the DMAE was previously charged. Afterwards the column was eluted with ethanol. The obtained ^{18}F-choline passes from the HLB to the CM column where it is retained and washed with 9 mL of water. Finally the solution is eluted with 3 mL of NaCl 0.9%. The duration of the synthesis was 55 minutes.

The quantitative determination of residual solvents was carried out by gas chromatography at the School of Pharmacy and Biochemistry, University of Buenos Aires.

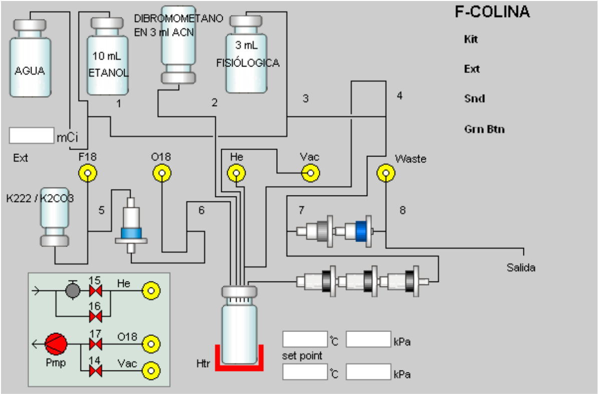

Figure 1: Scheme of the IFP connections.

Results:

After five syntheses we got a decay corrected radiochemical yield of (16 ± 5) %. The residual solvent content was below the limits established by USP 34th Ed.

Conclusions:

This development allows carrying out the synthesis maintaining a high yield and reproducibility as well as a decrease of the duration and cost of the synthesis. This allows easing its implementation for routine production.

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AN AUTOMATED SYSTEM FOR THE CENTRALIZED CONTAINMENT OF RADIOACTIVE WASTE GAS

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Introduction: The method for containment of radioactive gases resulting from radiopharmaceutical synthesis has historically been improvised, often with a singular purpose and tailored to the specific synthesis module. These methods have included 1) plastic capture bag or balloon, 2) long-tube delay line, 3) large volume flow-through diffusion tank and 4) compressed gas storage tank.

Because of the unique waste gas output requirements for each synthesis module (very high or low flow rates, tolerance to backpressure or vacuum, total volume of waste gas release and half-life of radionuclide), none of these systems can provide a combined solution for all synthesis applications.

The system developed here is an automated, interactive, reliable and centralized system to capture, and store and radioactive waste.

Material and methods: Our system was based on the compressed waste gas cylinder storage model (*fig 1, purple*). This model is easier to leak test and less likely to develop leaks over time. The following items were then added to adapt it to its centralized waste gas management role.

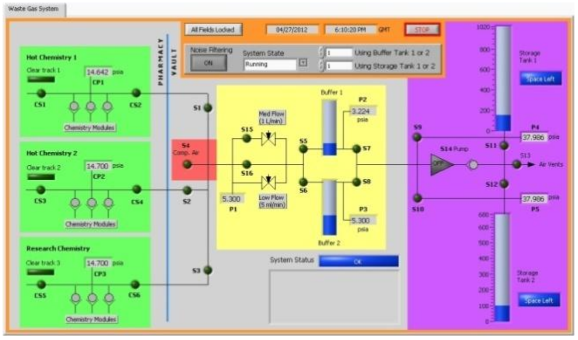

Figure 1: Highlighted areas referenced in the text.

Rugged, Web-Access Micro-PLC Controller: (fig 1, *orange*) A Compact FieldPoint device (National Instruments) provides the base for the system: a simple-to-program platform with numerous plug-in modules for analog, digital and control signal i/o and a user-friendly, network-accessible web interface. This interface allows the user to control the parameters of automated operation as well as change to manual control of the pump and all valves.

Multi-Input Distributed Manifold Panels: (*fig 1, green*) Generally placed, one behind each group of hot cells, these panels receive the waste gas from each synthesis module while adding scalability to the system. A check valve to vent on each panel prevents the system from drawing a vacuum.

Buffer Tanks with Proportional Flow Paths: (*fig 1, yellow*) These tanks, pumped down to $^{1}/_{3}$ atm, act to draw the waste gas from the manifolds. As the vacuum is depleted in one tank, the other takes over, then the first is rapidly pumped to the storage tanks. This provides continuous draw even when there is a relatively high-flow waste gas supply. Also the flow from the manifolds can be controlled by diverting though one of three flow-regulated paths.

Compressed Air Supply For Leak Checking: (*fig 1, red*) The automated system performs a routine weekly pressure and leak check after purging the decayed waste gas from the storage tanks. Also, failure modes during normal operation are monitored for conditions indicating a leak.

Results: The vacuum pump used for multiple purposes is capable of drawing down one of the buffer tanks in a very short period of time. The system has a storage tank capacity of 1,350 litres, and will operate continuously at flows approaching 1L/min; or higher flows for short periods of time.

The design is limited to simple components: solenoid valves, pressure transducers, needle valves, check valves, standard 50-litre gas cylinders, a vacuum pump and a dedicated PLC controller. Though numerous, all of the parts were selected for ruggedness. The total cost for all components was less than 12,000 USD.

Conclusions: This waste gas system, operational in daily use for 4 years has proven itself to be an effective mechanism for the containment of radioactive waste gases produced by our radio-pharmaceutical synthesis modules. The benefits of this system over existing commercial and ad hoc containment systems are: Reliability, Scalability, Continuous Function, Automated Leak Checking, Scheduled Automated Release Capability, Simplicity of Design & Implementation, and Adaptability to Synthesis Requirements.

SEPARATION OF MOLYBDENUM AND TECHNETIUM

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Introduction: A critical aspect in the production of ^{99m}Tc via the ^{100}Mo(p,2n)^{99m}Tc reaction is the requirement to separate ^{99m}Tc from bulk ^{100}Mo. There are two challenges with this compared to commonly used generator systems; (i) the large amount of molybdenum that needs to be separated from the technetium; and (ii) to produce ^{99m}Tc of high radionuclidic purity on a medical cyclotron, highly enriched ^{100}Mo must be used. The natural abundance of ^{100}Mo is 9.63% and there are high costs associated with the isotopic separation of ^{100}Mo from natural molybdenum. Therefore it is attractive to have a separation method which enables easy and quantitative recycling of the ^{100}Mo. There are previous reports of the recycling of enriched molybdenum in the context of ^{94m}Tc production[1]. However, to the best of our knowledge, these reports are limited to oxide targets, while for our application metallic Mo targets will be employed due to better thermal conductivity which enables the use of higher beam currents. Recently, two reports on the recycling of metallic molybdenum have been published using aqueous biphasic extraction chromatography as well as ion extraction chromatography for the separation of technetium and molybdenum, both showing efficient separation[2,3]. This study presents a thorough theoretical review as well as experimental investigations of techniques that can be used for the separation of molybdenum and technetium, with a focus on methods deemed practical for the full process automation of ^{99m}Tc production using medical cyclotrons.

Material and methods: “Wet” methods to separate pertechnetate (TcO_4^-) and molybdate (MoO_4^{2-}) are evaluated, including liquid – liquid extraction, ion exchange chromatography, aqueous biphasic extraction chromatography, as well as electrochemistry. To determine the quality of separation, the activity of generator ^{99m}Tc and ^{99}Mo are measured. The activity measurements are performed using a high purity germanium gamma ray detector. “Dry” methods, such as thermochromatography are deemed unpractical for automation purpuses and are not included in this study.

Results: This paper presents work in progress. Several of the “wet” methods have been investigated to date. Initial tests using the Analig Tc-02 resin from IBC Advanced Technologies have indicated only partial success at separating technetium and molybdenum. However alternative procedures and reagents may improve the efficiency of separation. Efficient recycling (87%) of enriched metallic ^{100}Mo targets has been shown following extraction with aqueous biphasic extraction chromatography, ABEC^{TM}, resin[2].

Conlusions: Even though promising results have been shown using the ABEC^{TM} resin, a thorough comparison of the various separation techniques needs to be made. In addition, potential licensing restrictions regarding the ABEC^{TM} has prompted the acceleration of this ongoing investigation.

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EVALUATION OF A SIMPLE SPECTROPHOTOMETER TO QUANTIFY FLUORINE GAS FROM A CYCLOTRON TARGET

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Introduction: There are a growing number of compounds that are only accessible through electrophilic radiofluorination starting from $[^{18}F]F_2$ gas and key intermediates, namely acetyl hypofluorite, fluoroperchlorate, pyridyl fluorides and xenon difluoride. Fluroine-18 is created by the $^{18}O(p,n)^{18}F$ nuclear reaction using the "two shoot" process, which involves the irradiation of $^{18}O_2$ followed by a second irradiation with $^{19}F_2$ carrier gas to recover the ^{18}F as fluorine gas[1]. In order to provide for efficient exchange of the ^{18}F from the target wall, the target must undergo a series of target irradiations (passivation) with an $^{19}F_2$/argon gas mixture until a consistent amount of F_2 is released during each unload[2]. Thus after each irradiation, the target is unloaded into a trap containing aqueous potassium iodide. The resulting reaction yields iodine: $F_2 + KI \rightarrow KF + I_2$. Titration with standardized sodium thiosulfate using a starch indicator quantifies the mass of iodine and thus the mass of $^{19}F_2$ released[3]. For radiochemistry purposes, it is also important to know the amount of carrier $^{19}F_2$ that is released from the target with the labeled $[^{18}F]F_2$ gas.

Titrations are time consuming in both reagent preparation and execution, and require either radioactive decay of the solutions or titration on the hot material. Alternatively, the spectrophotometric absorbance of I_2 is well known and can be measured without the above complexities. We recently reported our modification[4] of a spectrophotometric system for measuring I_2 vapour during the gas phase production of $^{11}CH_3I$[5]. Expanding upon this work we report here a similar device for the absorbance measurement of I_2 in solution phase.

Material and methods: A simple spectrophotometer consisting of a Blue LED (470nm), a 13mm test tube sample cell and a photodiode (PD) was fabricated to measure the light transmitted through the different KI/ I_2 solutions. The unamplified current output of the PD was sampled as the voltage drop across a 1MOhm resistor and read out with National Instuments Fieldpoint hardware. LabVIEW software was used for data collection and the development of a calibrated readout.

Titration: 5 iodine standards (3.75mM-8.0mM) were titrated against sodium thiosulfate using a starch idicator. Spectroscopy: Nine iodine standards (0-10mM) were measured and the solution absorbance was calculated using Beer-Lambert law $[A=\log_{10}(I/I_o)]$.

Figure 1: Simple spectrophotometer based on an LED light source and Photodiode.

Results: Titration: Measurements from the titration of the iodine solutions (3.75mM to 8.0mM) showed a linear relationship with $R^2 > 0.999$. Spectroscopy: Data measured using standard iodine concentrations (3.75mM to 8.0mM) resulted in a linear relationship with $R^2 > 0.981$.

Conclusions: Titration and spectroscopic methods for quantification of F_2 were examined, both methods were suitable and showed a linear relationship spanning the range of concentrations used. The simple spectrophotometer was capable of measuring the $^{19}F_2$ content of the cyclotron target in a more rapid and hands free manner.

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CONVERSION OF A COMMERCIAL UV DETECTOR FOR IN HOT CELL USE

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Introduction: In a research lab hot cell, reliable chemical instrumentation is necessary, but space is often at a premium, so instruments with readout electronics located outside the hot cell and with small-footprint/low volume detectors can be of great value. As HPLC UV detectors are traditionally designed for benchtop applications, readout electronics, flow cell, and detector are housed together and therefore are poorly suited for use in a hot cell but yet UV absorbance traces on preparatory separations can be useful along with radioactive signal traces.

The BioRad EM-1 EconoUV fixed-wavelength detector has a control/readout module decoupled from the optics module, making it better suited for a hot cell application. However, the supplied interconnect cable (90cm) is not long enough to run from the optics module inside a hot cell to the control module outside the hot cell. We have improved upon the design of the EM-1, building an extension cable and adding USB data communications for PC readout and control of the instrument. PC control allows for software control of lamp power, zeroing of signal, and elimination of preset absorbance ranges.

Material and methods: The BioRad EconoUV EM-1 consists of two parts, an optics module and a control unit[1]. The optics module consists of a mercury vapor lamp, a manually selectable 254/280 nm filter and two photo diodes (flow cell path and reference). The flow cell has a 80µl volume and 2mm path length. The control module consists of a lamp power supply (20KHz, 140VAC, 20 mA), switch board, and analog-to-digital converters (ADCs) on a logic board. Control box outputs include scaled and unscaled analog outputs and chart recorder controls. A 90cm cable connects the optics unit to the control unit.

A 1.8m extension cable has been built using two cables running in parallel. Photodiode voltage signals are transmitted via a 24G 4-conductor cable with braided shielding while lamp power is transmitted through a USB 2.0 cable (28G, braided shielding). The cable is terminated with Viking Thorkom 12 pin circular connectors, matching the unit’s original connectors.

USB readout and control is realized through the use of a National Instruments USB-6008 multifunction data acquisition device (DAQ). The DAQ hardware is mounted in the space inside the cover of the EM-1 with only minor modifications to its housing (Fig. 1). The EM-1’s on-board ADC and signal processing is bypassed as voltages on both photodiodes (reference & flow-cell) are sampled directly at test points on the EM-1’s logic board, and read by two channels of 12-bit ADCs on the DAQ. Absorbance calculations and associated ‘zeroing’ are performed in software. Remote control of lamp ON-OFF function via the DAQ is via a TTL output driving a transistor-mechanical relay circuit powered by the +5V USB bus power. When activated, the relay shorts the power button on the control unit, just as depressing the button would do. Lamp power status is determined by reading the LED indicator supply voltage directly wired from the indicator panel to a digital input line.

The EM-1 was originally equipped with female Luer-lock fittings connected to 1/16” PEEK tubing, but we replaced the fittings with 10-32 male fittings for better compatibility with our current plumbing setup.

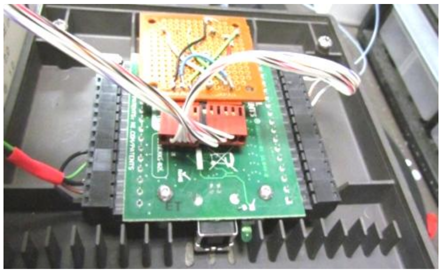

Fig. 1: Photo of DAQ hardware mounted under EM-1’s cover. Relay driver circuit is under brown proto-board.

Results: Designing the cable extension was a particular challenge, but in running the lamp power cable in a separate shield and using fine-gauge cable, we were able to overcome the power loses associated with high frequency lamp power transmission. The USB remote control and monitoring system works reliably with high sensitivity.

Conclusions: With the described modifications, the BioRad EconoUV EM-1 proves to be a valuable tool for UV monitoring of preparatory HPLC separations with a small optics unit inside the hot cell.

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A SIMPLE LOW-COST PHOTODIODE RADIATION DETECTOR FOR MONITORING IN PROCESS PET RADIOCHEMISTRY

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Introduction: We have found that placing radiation detectors throughout our radiochemistry synthesis rigs is advantageous for determining the progress of radioisotopes through the system, delineating thresholds and triggering steps in a sequence, monitoring radiochromatographic separations, providing process feedback and adjustment, and determining maintenance needs, in addition to troubleshooting. In our carbon-11 synthesis module we monitor no less than 9 radiation detectors during a typical synthesis[1]. Often we find that the more points of feedback we have the better we are able to maintain high and consistent yields and overall system reliability.

Standard photodiodes are routinely used as inexpensive and compact radiation detectors for work in radiochemistry[2,3]. However, they can introduce additional issues if the detectors are not simple to use and easily wired up for low-noise operation. In addition, it is important that detectors are insensitive to temperature fluctuations, given their nearness to chemical reaction vessels.

Material and methods: We herein report a compact, low-noise, detector design based on off-the-self amplifier and two-wire 4-20 mA transmitter chips that can easily be connected to standard analogue input electronics with only a single twisted pair of wires. The photodiode and all electronics fit into a small epoxy-sealed package shaped as a 12 mm diameter cylinder that is 37 mm long, allowing the detector to be placed within a few centimeters of the source.

Results: Placed at 5 cm from a radiation source, approximately 3 pA of current is seen in the detector per 37 MBq (1 mCi) of Carbon-11 (using a Hamamatsu S6967 PIN Photodiode; active area 5.5x4.8 mm). This is amplified and converted into an output signal of about 7.5 □A. Noise is dominated by the statistical variation of the incoming gamma rays reacting with the photodiode, rather than by the electronics. Temperature sensitivity is low: for typical temperature fluctutions, changes in the current output are less than or equivalent to the current derived from 37 MBq (1 mCi) of Carbon-11.

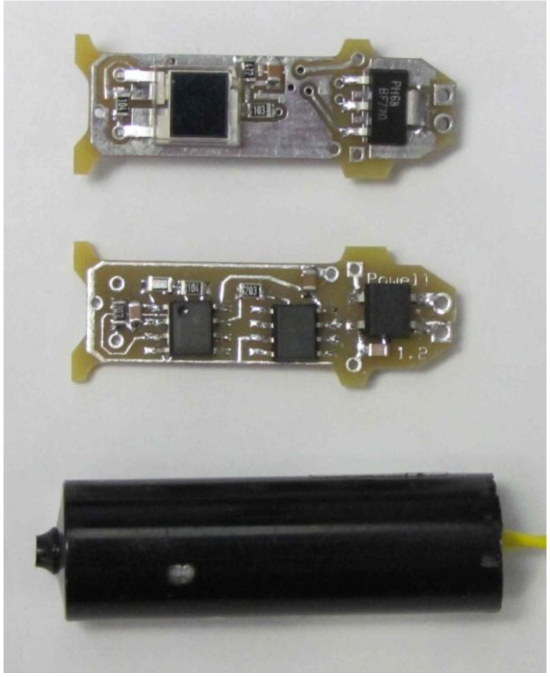

Figure 1: Photograph of detector board and epoxy incased detector module.

Conclusions: The radiation detectors described herein are low-cost, easy to construct, and reliable. We are able to incorporate a large number into our radiosynthetic processes due to these favorable properties. Their relative insensitivity to temperature allows for placement near cryogenic traps or high temperature ovens.

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ELEVEN YEARS OF PET APPLICATIONS AT THE NATIONAL AUTONOMOUS UNIVERSITY OF MEXICO

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The Positron Emission Tomography (PET) Center of the National Autonomous University of Mexico (UNAM) is a core facility offering state-of-the-art molecular imaging studies and radiopharmaceuticals for the community of the Valley of Mexico. It was the first PET Center in Mexico and nowadays it continues at the forefront in PET technology in the country. The facility, inaugurated in 2001, is located in the University´s Campus and belongs to the School of Medicine.

Major equipment and areas of operation includes an accelerator laboratory for radionuclide production, a fully equipped laboratory for radiopharmaceutical production, a preclinical imaging laboratory for small animals (Concorde Microsystems, microPET Focus 120) and a PET/CT scanner for clinical studies. The original RDS 111 cyclotron was upgraded to Eclipse HP. In 2007 the ECAT EXACT HR+ dedicated PET scanner was replaced by a Biograph 64 PET/CT, while the Chemistry Module CPCU for FDG production was replaced by a Explora FDG4.

Main clinical applications of PET in Mexico are in oncology with more than 90% of the studies performed in this area. There are currently 4 cyclotrons for radioisotope production (two in Mexico City, one in Monterrey and one in Guadalajara), 16 PET/CT hybrid cameras, one dedicated PET scanner, and 3 dual head coincidence cameras in the country, most of them centralized in Mexico City. Several other hospitals are in the process of acquiring PET/CT scanners. Another cyclotron will enter into operations this year in Mexico City and in 2013 one more cyclotron will be installed in Guanajuato. However, the cyclotron at the UNAM PET Center is the only one in a public institution and provides with radiopharmaceuticals to 14 of the 16 centers that perform PET studies in Mexico City. More than 10k unidoses of radiopharmaceuticals were produced in this Center in 2011.

For several years after the UNAM PET Center entered into operation FDG was the only radiopharmaceutical available for clinical applications. Currently, the production of non-FDG tracers has increased to the point where 10 tracers are now available for applications in oncology, cardiology and neurology: [^{18}F]FDG, [^{18}F]FLT, [^{18}F]NaF, [^{18}F]FMISO, [^{18}F]FES, [^{18}F]F-L-DOPA, [^{11}C]Acetate, [^{11}C]Raclopride, [^{11}C]DTBZ and [^{13}N]Ammonia.

The growing capacity to produce target-specific radiopharmaceuticals was recently enhanced with the acquisition of three automated synthesis devices for [^{11}C]carboxylation/methilation (TracerLab FX-C Pro), and [^{18}F]fluorination by nucleophilic (TracerLab FX-FN) and electrophilic (TracerLab FX-FE) substitution, respectively. In addition, one of the beam lines of the cyclotron was recently upgraded with the option for the irradiation of solid targets for the production of metallic radioisotopes.

Figure 1: Chemistry modules at UNAM PET Center.

The achievements of the UNAM PET Center are mainly due to its academic setting, the recognized prestige of the institution, the collegial relationship with the users, and its initiative to satisfy the demand of high quality PET molecular imaging and target specific radiopharmaceuticals maintaining after more than ten years the forefront of innovation in the field in Mexico and Latin America.

Acknowledgments: We acknowledge the financial support of UNAM-DGAPA-PAPIIT TA200512 and International Atomic Energy Agency Grant RC16467.

IMPLEMENTATION OF A SOLID TARGET PRODUCTION FACILITY

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Introduction: Following the commissioning in 2008 of a new IBA (Belgium) 18/9 cyclotron along with a 2-meter external beam line, we were able in 2011 to implement a fully automated solid targetry facility for the production of ^{124}I, ^{64}Cu, ^{89}Zr and ^{86}Y. Our aim was the implementation of a safe and cost effective system utilizing commercial equipment from manufacturers who were able to demonstrate convincing data for the production of the intended radionuclides.

Choosing the right equipment: Two commercial solid target systems were readily available to plug onto our external beam line: Comecer ALCEO Solid Target and IBA NIRTA Solid Target. Although the IBA system was significantly dearer, it appeared more versatile with production results available for all 4 proposed radionuclides.

Several hotcell manufacturers responded to our tender; however TEMA Sinergie (Italy) was the only one who proposed a customized design fitting precisely our requirements, especially in terms of functionality for operating the processing modules to be enclosed.

No appropriate Solid Target Transfer System (STTS) for transferring the irradiated target disk up to the dedicated hotcell was available on the market. Fortunately, after discussing our requirements with both manufacturers (IBA and TEMA), TEMA Sinergie agreed to design and build such a system.

A few radiochemistry processing modules exist on the market, but again only IBA provided strong data supporting the successful processing of ^{124}I (TERIMO system) as well as the evidence of the design of a versatile module (Pinctada Metal system) compatible for the dissolution/purification of a variety of metallic targets.

Results: The IBA NIRTA Solid Target allows the loading of up to 3 target disks into a charger for sequential irradiation, without re-entering the vault between irradiations. Although the installation of the NIRTA Solid Target was straight forward and took a few hours only, optimization of the beam shape with homogeneous distribution onto the target disk required significantly more work, including the physical re-alignment of the 2 meter beam line already installed.

The three TEMA hotcells were installed side by side separated at the back from the target vault by an 800mm technical corridor. The hotcell dedicated to ^{124}I is shielded with 100mm of lead and equipped with two telemanipulators as well as a shielded drawer for insertion/extraction of items or lead pot. The adjacent 2 hotcells dedicated to ^{64}Cu, ^{89}Zr and ^{86}Y are 75mm thick and equipped with one manual teletong and a shielded drawer for insertion/extraction of small items as well as a drop-vial with independent lead pot extractor. All hotcells feature a touch screen display for control and sensor monitoring, providing air tightness to Class II and GMP Class C environment.

Solid target processing hotcells (Tema Sinergie, Italy).

The STTS is operated from a touch screen display conveniently located on the front of one of the hotcells. Loading of the target disk into the shuttle as well as pneumatic transfer from the irradiating station to either one of the two receiving hotcells is fully automated.

The TERIMO module is a closed system with an integrated charcoal filter. The system allows for the baking of $^{124}TeO_2$ powder into the target disk recess, as well as distillation at 780°C for recovery of ^{124}I into an alkaline solution post irradiation.

The Pinctada Metal module is a closed system allowing the clamping of the target disk and acidic etching as well as ion exchange separation/purification of the radionuclides.

Conclusions: A fully automated solid target facility was successfully installed at Austin Health. Batch productions of ^{124}I & ^{64}Cu have shown results in accordance with theoretical calculations.

Acknowledgments, disclosures and funding: This research was undertaken using the “Solid Target Laboratory, an ANSTO-Austin-LICR Partnership.

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