Proceedings of the Ninth International Workshop on Targetry and Target Chemistry

Turku, Finland, May 23-25, 2002



Edited by Sven-Johan Heselius, Jan-Olof Lill and Johan Rajander

Turku PET Centre, Accelerator Laboratory, Åbo Akademi University, Porthansg. 3, FIN-20500 Turku, Finland

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The authors are responsible for the contents of the contributions submitted to these Proceedings. The contributions have been only slightly edited.

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Workshop organized by the Turku PET Centre

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Preface

The Ninth International Workshop on Targetry and Target Chemistry (WTTC9) was held at the Turku PET Centre, Turku, Finland, May 23-25, 2002, prior to the IX Turku PET Symposium. The Workshop was attended by 181 scientists and engineers representing 23 countries. Besides the traditional targetry workshop programme a Training Course for students and young scientists was introduced into the WTTC9. The members of the International Advisory Committee stimulated us to arrange this Training Course. The programme of the course was planned in co-operation with members of the Advisory Committee.

The Training Course was highly appreciated by the attendees. This is reflected in the feedback received. Especially younger scientists have informed me they learned a lot from the course. The cyclotron suppliers CTI, EBCO, GE and IBA are acknowledged for their open willingness to share their experiences with the targets and the radiochemistry units they brought to the Training Course.

I extend my thanks to the members of the Organizing Committee of the WTTC9 as well as to the members of the International Advisory Committee for excellent co-operation, and to all who helped in one way or another with the preparations for the Workshop and in the technical assistance during the Workshop. Special thanks go to the staff of the Congress Office of the University of Turku for their excellent work and for creating a stimulating atmosphere for the meeting. I also thank all the scientists and engineers who participated in the Workshop and the Training Course for their input and enthusiasm. The input of the attendees is always the source for the success of a meeting.

I am grateful to the session coordinators for participating in the organizing of the scientific programme of the Workshop and for moderating the sessions, and to the lecturers of the Training Course for well prepared and covering review lectures. The WTTC luminaries who guided the students of the Training Course are acknowledged for their enthusiasm showed to the students.

My co-editors, Mr. Jan-Olof Lill and Mr. Johan Rajander, deserve thanks for their timeconsuming work with these Proceedings.

Finally, I express my best wishes to Prof. Jerry Nickles and the Organizing Committee of the WTTC10 for success with the Tenth Workshop on Targetry and Target Chemistry, which will be arranged at the University of Wisconsin, Madison, August 13-15, 2004.

Sven-Johan Heselius Chairman of the WTTC9 Organizing Committee

NINTH INTERNATIONAL WORKSHOP ON TARGETRY AND TARGET CHEMISTRY Turku PET Centre, Turku, Finland, May 23-25, 2002

Targetry Workshop Venue: Educarium Building, University of Turku, Assistentinkatu 5

PROGRAMME

Thursday, May 23rd

Training Course in cyclotron targetry

08.30-09.15	Technology of cyclotrons for radionuclide production, Kenneth Buckley, TRIUMF.
09.15-10.00	Cyclotron targetry for radionuclide production, <i>David Schlyer</i> , Brookhaven National Laboratory.
10.00-10.20	Coffee Break
10.20-12.20	Practical Training . IBA Cyclone 3: Cyclotron service and production of ¹⁵ O-gases

- and ¹⁵O-water. **Note**: *This part of the Training Course takes place at the Turku PET Centre*. Coordinated by Hannu Sipilä, John Clark and Bruce Mackay.
- 12.20-13.20 Lunch
- 13.20-14.00 **Oral presentations by cyclotron suppliers** (CTI, EBCO, GE and IBA).
- 14.00-17.40 **Practical Training** (CTI, EBCO, GE and IBA). The trainees will be divided into 4 groups of approx. 8 persons. Each group will visit 4 venues according to the timetable below. The group will carry out their work under the supervision of representatives of the suppliers. The groups will also be accompanied by some of the following WTTC luminaries: Kenneth Buckley, John Clark, Lewis Carroll, Bob Dahl, Mikael Jensen, Jeanne Link, Didier Le Bars, Jerry Nickles, Bruce Mackay, Andy Roberts, David Schlyer and Tom Ruth together with the local team. This part of the Training Course takes place at the Educarium Building and is composed of:
 - Hands-on training in handling and mounting of different types of targets,
 - Training in cyclotron operation, and
 - Presentation of chemistry modules.

Group	CTI	EBCO	GE	IBA
А	14:00-14:50	14:50-15:40	16:00-16:50	16:50-17:40
В	14:50-15:40	14:00-14:50	16:50-17:40	16:00-16:50
С	16:00-16:50	16:50-17:40	14:00-14:50	14:50-15:40
D	16:50-17:40	16:00-16:50	14:50-15:40	14:00-14:50

15.40-16.00 Coffee Break

18.00-20.00 Welcome Reception at Educarium Building.

20.00-21.00 **Evening Lecture**: "Commissioning and Decommissioning of Cyclotrons" (45 minutes plus discussions), *Lewis Carroll*, Carroll Ramsey Associates.

Friday, May 24th

08.30-08.45	Opening of the Workshop <i>Sven-Johan Heselius</i> , Turku PET Centre		
08.45-10.15	Water targets and high beam currents - Specific radioactivity of F-18 Coordinators: Andrew D. Roberts, University of Wisconsin Olof Solin, Turku PET Centre		
10.15-10.45	Coffee Break		
10.45-12.15	High-power enriched gas targets Coordinators: Volker Bechtold, Karlsruhe Bruce Mackay, Hammersmith Hospital Thomas J. Ruth, TRIUMF		
12.15-13.30	Lunch		
13.30-15.00	Solid targets at low-energy irradiations. Transport of targets. Coordinators: <i>Ron D. Finn</i> , Sloan Kettering <i>Robert J. Nickles</i> , University of Wisconsin <i>Michael J. Welch</i> , Washington University		
15.00-15.30	Coffee Break		
15.30-17.00	High-energy irradiations of solid and gas targets Coordinators: <i>Syed M. Qaim,</i> Forschungszentrum Jülich GmbH, Germany <i>Nigel R. Stevenson</i> , Theragenics Corporation, USA		
18.30-18.45	Group Photo in front of the Aboa Vetus & Ars Nova Museums by the Aura river.		
19.00 - 22.00	Evening Party at the Aboa Vetus Museum, Address: Itäinen Rantakatu 4-6.		

Saturday, May 25th

08.30-10.00	Poster session and Coffee
10.00-11.30	Oral presentations of selected poster Coordinators : Rich Ferrieri, Brookhaven National Laboratory Jeanne Link, University of Washington Thomas J. Ruth, TRIUMF
11.30-12.45	Lunch
12.45-14.45	Visit to facilities (2 groups, 15 visitors/group): - Accelerator Laboratory and Radiochemistry Laboratory, Gadolinia, Åbo Akademi University. - Turku PET Centre, Turku University Central Hospital.
14.45-15.15	Coffee Break
15.15-16.30	Reports from the laboratories Coordinators: <i>Didier Le Bars</i> , University of Lyon <i>Steve McQuarrie</i> , University of Alberta
16.30-17.00	Summary of the Workshop and Closing Remarks <i>Thomas J. Ruth</i> , TRIUMF
17.00-17.10	Closing of the Workshop Sven-Johan Heselius, Turku PET Centre
18.00-20.00	WTTC9 Farewell Party /Turku PET Symposium, Get-together Party, Educarium Building

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Water Targets and High Beam Currents. Specific Radioactivity of F-18

Coordinators: Andrew D. Roberts, University of Wisconsin Olof Solin, Turku PET Centre

Operational Experience with a Niobium Target Body for the Irradiation of O-18-H $_2$ O

K.R. Buckley¹, J. Wilson², S. Jivan¹, M.J. Adam¹, P. Piccioni¹, E.T Hurtado¹ and T.J. Ruth¹

¹UBC/TRIUMF PET Program, 4004 Wesbrook Mall, Vancouver, BC, Canada ²Cross Cancer Centre, University of Alberta, Edmonton, AB

Aim

To assess the performance of a water target constructed of niobium metal.

Methods

We have operated a niobium bodied water target for the production of F-18-fluoride for approximately 1 year. During this time we have observed the operational characteristics of this target and had occasion to compare the synthesis of F-18-FDG made from this F-18-fluoride with that made from F-18-fluoride produced in a silver bodied water target.

Results

Typically the saturation yield for a 2-hour irradiation at 15-25 microAmperes is 130 mCi/microAmpere.

Conclusions

We will present the operational parameters, trends in yield data, and synthesis yields.

Production Test Results from the Pulsar Linac Targets

*Robert W. Hamm¹ and G. D. Robinson, Jr.*²

¹AccSys Technology, Inc., 1177A Quarry Lane, Pleasanton, CA 94566, USA ²Sandia National Laboratory, Livermore, CA 94550, USA

Introduction

Several types of linear accelerators (linacs) have been built and tested during the past decade for the production of PET radionuclides^{1,2,3,4} but these systems are not yet in general use. To achieve wide acceptance for this application, the targets for any linac must perform reliably with radionuclide yields comparable to compact cyclotron targets. The purpose of the present study was to demonstrate that the targets developed for use on the AccSys PULSARTM proton linac system⁵ can produce the quantities of F-18 and C-11 required by PET users currently employing compact cyclotrons. These tests were also completed to obtain initial data for the development of linac targets to produce O-15 and N-13. Initial results with this target at lower beam currents have been previously presented.⁶

The 7 MeV proton beam from the PULSARTM Model PL-7 linac has a pulsed peak current variable from 5 to 15 mA at a duty factor up to 1.3 % with a repetition rate of 100 Hz. This linac accelerates either H⁺ or H⁻, is 4.2 m long, weighs 1200 kg, and requires 25 kW of AC power. The Model PL-7 PET radionuclide production targets are similar to cyclotron targets, but incorporate grid supported foil windows that allow use of a thinner window, provide more cooling and provide an expanded irradiation area⁷.

Target description

This patented target^{*}, developed by Brookhaven National Laboratory in a collaboration with AccSys, produces fluorine-18 via the ¹⁸O(p,n)¹⁸F reaction. The target body, either silver or niobium, is held in an aluminum holder for cooling and support. A 55 % transparent grid of copper and stainless steel supports a 25-mm diameter, 25 micron thick titanium foil in front of a 0.3 mm thick O-18 water target volume. The volume of O-18 water in the target is 0.3 ml. The prototype target used to conduct the ¹⁸F production tests presented in this paper is shown in figure 1.

The entrance foil and O-18 water thickness were selected to degrade the proton energy to less than 3.5 MeV as the beam enters the back of the target. A finite element thermal analysis was conducted for the target and the results of this analysis are shown in figure 2. The key to the performance of this target is that the temperature of the target water is independent of the beam size and only depends on the beam current density in a single aperture of the target not exceeding a limit of 35 μ A/cm². Hence, the expected output of this target has been calculated as a function of the beam irradiation diameter and is shown in figure 3.

*U.S. Patent No. 5,915,874



Fig. 1. Prototype water target for production of ^{18}F .



Fig. 2. Thermal analysis results for gridded target.



Fig. 3. Calculated yield for gridded target.

Experimental results

The F-18 target designed for the PULSARTM linac was irradiated under argon overpressure of 300 psig with beam currents in the range of 7-35 μ A and irradiation times from 15 to 120 minutes. The grid-supported foil window was tested with both silver and niobium bodied O-18 water targets in more than 50 test runs. Low enrichments of O-18 water were used to reduce the activity being handled during this testing. The data from all runs are summarized in figure 4, normalized to the equivalent F-18 production per hour with 95 % enriched O-18 water. The theoretical data plotted for comparison were calculated using the saturated yields for F-18 recently published by Hess et. al⁸.

These tests demonstrated that the supported foil target configuration is robust enough to be used for F-18 production with a proton beam current density up to $35 \,\mu\text{A/cm}^2$ at a pressure of 300 psig. F-18 production yields varied from 60 to 95 % of theoretical, with the lowest yields always achieved on the first run with a "fresh" target. Extended runs have shown that the yield from the target is 1000 mCi/hr for a target current of less than 60 μ A. In addition, the yields from the niobium target were found to be statistically identical to the yields from the silver target.



Fig. 4. Experimental results for gridded water target.

The C-11 gas production target, which can also be used to produce O-15 from N-15, is made of aluminum with a 100 mm long tapered bore (25 to 38 mm) and uses the same foil support system as the F-18 target. The $^{14}N(p,\alpha)^{11}C$ reaction was used for carbon-11 production. The C-11 target performed as expected during 10 minute irradiations at beam currents of 6-12 μ A. Production of large quantities of C-11 were demonstrated. The pressure rise ratio (PRR) method was used to optimize the target fill pressure during these limited test runs. These results are summarized in figure 5. For both F-18 and C-11, target

yields were measured in a calibrated ionization chamber and radionuclidic purity was estimated from the measured decay curves.



Fig. 5. Experimental results for gridded gas target.

Conclusion

These experimental measurements have proven that the linac targets using a grid supported window are robust and reliable for F-18 or C-11 production with the 7 MeV PULSARTM linac. Target performance was predicted through thermal analysis to be dependent on incident beam current density, not total current, and experimental measurements have proven this to be the case. F-18 production was routinely demonstrated at an average of 80 % of theoretical yield over a beam current range of 7 to 35 μ A. The performance of the PULSARTM 7 using the grid supported F-18 target meets its current production specification of 1 Ci /hour. The goal is to soon demonstrate routine production of 2 Ci /hour of F-18 by operating the linac at a higher output current with a larger beam spot on the target. The grid supported window has also been experimentally proven for use with the PULSARTM gas target. In addition, gas target performance has been shown to not be affected by the pulsed linac beam.

The experimental results reported are being used to guide fabrication of the production targets for the PULSARTM to be shipped to Japan in 2003. The gas target for C-11 and O-15 production will also be completed and tested on that system. Development of the N-13 production target for the PULSARTM is now in the early design stages.

Acknowledgement

The authors gratefully acknowledge the assistance of Dr. David Schlyer of Brookhaven National Laboratory and Dr. Henry Van Brocklin of Lawrence Berkeley National

Laboratory in the experimental measurements described in this paper. In addition, the dedicated staff at AccSys is acknowledged for their support during these tests.

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F-18-Fluoride Production in Recirculating O-18 Target

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Aims

To investigate the possibility of recirculating O-18 water through the cyclotron target during irradiation which allows extraction and delivery of F-18 fluoride without interrupting irradiation and/or emptying the target.

Methods

Approximately 10 ml of O-18 water was loaded in an apparatus containing a 5 ml storage vessel, pump, 1.8 or 2.0 ml silver target attached to 16.5 or 18 MeV cyclotron, 10 micron filter, backpressure regulator, conductivity meter, several valves and ion exchange cartridges. The water was continuously pumped through the target during proton bombardment at a rate 5 ml/min. Every 1-2 hour the water flow was directed through an ion exchange cartridge to remove accumulated F-18 fluoride. The later was recovered by rinsing the cartridge with bicarbonate solution and delivered to the remote hot cell. Target material was also passed through deionising cartridges to reduce electrical conductivity. Water pressure, conductivity and radioactivity levels in the storage vessel and ion exchange cartridge were continuously monitored by a computer.

Results

7 hour continuous irradiation with beam current ranging from 30 to 40 μ A (total integrated beam current was 219 μ Ah), resulted in total of 486 GBq of F-18 delivered in 6 portions averaging 2.2 GBq/ μ Ah. Total of 2 ml of O-18 water was lost, presumably due to evaporative loses and leaks, averaging over 200 GBq of F-18 per ml of consumed water. Conductivity of target material at the end of the last production cycle was lower than at the beginning of the first irradiation. It was also shown that the ion exchange cartridges could be reused for over 20 production cycles allowing for weekly maintenance schedule suitable for a production facility.

Conclusion

The results indicate that recirculating of the target water can significantly increase production of F-18 in relation to consumed O-18 water material. It can also increase productivity by eliminating unnecessary idle periods for re-filling the target. A backpressure regulator can reliably control target pressure. This method also allows for continuous monitoring of the target material conductivity and accumulated radioactivity as well as target pressure improving system reliability and predictability of production results.

Production of F-18-Fluoride in the Nuclear Interface Titanium Target on a MC-17 Cyclotron

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Aims

All the MC-17 cyclotrons (Scanditronix AB) were installed with a water target for F-18 production that was made from silver with a Havar entrance foil. The silver target has been used for more than seven years and produced sufficient amounts of fluoride (26 GBq after 1 hour irradiation). The beam intensity put on this target was limited to 12 μ A to have a reliable daily production. Under these conditions no cleaning or other corrective maintenance was required. The preventive maintenance includes drying of the targets and the teflon lines with helium after each production for at least 30 minutes and changing the teflon lines every year. In order to increase the production capacity to 60 GBq after a 1 hour irradiation (25 μ A), we developed an interface for the Nuclear Interface high pressure titanium water target to make the target suitable for the MC-17 cyclotron.

Methods

Window for entrance of beam and water cooling is a 50 μ m titanium foil, 950 μ l target volume. The entrance of 19 mm of the collimator results in a beam transmission of 50 % calculated from the Faraday cup, due the fact that the MC-17 is installed without external beam line and focusing optics. Based on the excitation function and the power dissipated energy (GBq/W), the optimal beam energy (from 17 MeV to 14.5 MeV) was obtained by inserting a 0.5 mm thick alumina entrance foil. This also decreased the problem of activation of the titanium target leading to the production of V-48 (production rate in irradiated water: < 1.5 kBq/ μ Ah). During the use of the first version of the target the main problem was that the maximal allowable beam current was 15 μ A. Higher currents resulted in an unacceptable target pressure (>2700 kPa). Therefore we tested the following parameters: enhanced helium cooling, water cooling on both the collimator and the target, water cooling flow, external either internal expansion volume (100 and 200 μ l), different thicknesses of the titanium entrance or back foil (25-75 μ m).

Results

In all these cases there was no significant improvement. Increasing the beam current to its maximal allowable pressure lead to malfunctioning due to a pinhole exactly on the borderline of the electronic welded foil in the insert, mostly on the water cooling side of the target. For the daily production we used a beam current of 15 μ A corresponding to a target pressure of 1430 +/- 430 kPa. The target has been used for nearly three years for

daily routine production. When the target beam current is limited to 15 μ A, the mean life time of the titanium insert is about 1500 uAh. The saturation yield of the the total 796 runs is 7.8+/- 2.4 GBq/ μ A. To increase the life time of the insert work is in process to develop an insert with a front foil of 75 μ m and the back foil of 300 μ m.

Conclusions

The target has consistenly been able to produce yields of fluoride up to 40 GBq after 1 hour irradiation giving high radiochemical yields of products made with this fluoride (FDG: 50-70 % EOB) and made the system useful for the routine production of [18F]compounds.

Recirculating Low-Pressure Target for F-18 and N-13 Production

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AIMS: The increasing clinical demand for F-18 Fludeoxyglucose requires a greater yield of F-18 fluoride along with conservation of the highly enriched O-18 target water. Research PET facilities also need to maintain N-13 capabilities. We describe a simple redesign of the low-pressure silver-body water target of the RDS-112 cyclotron that meets all three requirements.

METHODS: By providing 3-way valves at both the load and unload ports, the target was easily re-configured for O-18 water recirculation and F-18 production, as well as for bolus loading of O-16 water for the occasional N-13 production. In-target pressure was controlled either by the flow rate of an HPLC pump during O-18 water circulation, or regulated by adjustable pressure relief valves during N-13 production. Continuous inert gas purging of the target chamber and common valves between production runs helped minimize cross-contamination and dilution of the enriched O-18 target water.

RESULTS: Our conventional low-pressure F-18 target (170 kPa) typically produced only 2.83 GBq/ μ A when irradiated for 90 min with 22 μ A of ~10.2 MeV protons. When operated in the new recirculation mode at only 4 mL/min and 690 kPa, a 30 μ A run for 90 min on 10 % O-18 water yielded 0.43 GBq/ μ A of recovered F-18 fluoride ion. At 95 % enrichment, such yield would reach 4.04 GBq/ μ A. Furthermore, under constant flow conditions of 4-5 mL/min, the redesigned target has tolerated 45 μ A irradiations while producing an F-18 yield only 10 % lower than that obtained at 30 μ A. When hi-purity O-16 water was irradiated under no-flow conditions and 275 kPa pressure, N-13 production reached 0.27 GBq/ μ A with a 10 μ A beam. However, at 20 μ A, the yield dropped to 0.22 GBq/ μ A and at 30 μ A, to only 0.17 GBq/ μ A. While slightly lower than that obtained with the high-pressure RDS-112 N-13 target, especially at higher beam currents, the N-13 yield from this dual-purpose target was more than sufficient to produce unit doses of N-13 ammonia for cardiac perfusion PET-imaging.

Following irradiation, the O-18 target water flow was diverted through a small anion exchange column (~20 mg MP-1:HCO₃⁻ form) to collect the F-18 fluoride ions. Dry nitrogen gas was then routed through the collection resin to sweep away and recover the trapped O-18 water, prior to fluoride elution with 2 mg K₂CO₃. The mass of enriched O-18 water loss per irradiation and recovery was periodically measured and found to be <100 mg.

CONCLUSIONS: With minor plumbing changes, and the mere implementation of continuous target water recirculation during irradiation, we have more than doubled the F-18 fluoride output of a low-pressure silver target. The chemical reactivity of the recovered fluoride for FDG production has not been adversely affected by this modification. Automatic loading and unloading routines have been developed to facilitate rapid changeover whenever N-13 production is required.

Production of Multi Curie [¹⁸F]Fluoride using a Niobium Target Chamber at Small PET Cyclotrons

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Irradiation of ¹⁸O-enriched water is the mostly used method to produce [¹⁸F]Fluoride on a multi curie scale. Based on a target chamber design optimised in respect of experimental thick target yields the performance and reliability of a target system is mainly determined by selection of foils, seals and target chamber cooling.

In particular the target chamber materials have to be carefully chosen. Material properties to be taken into account are (see Table 1):

- chemical resistance;
- thermal conductivity;
- activation of the target chamber;
- reactivity of the [¹⁸F]Fluoride produced;
- contaminants in the [¹⁸F]Fluoride produced.

Until now Silver and Titanium have found to be the most favourable target chamber materials.^{1,2,3,4} Recently, Zeisler *et al.* described the successful use of Niobium as target material⁵. Their results as such are very promising. However, the construction of the target chamber, based on two Niobium hemispheres drawn from circular Niobium foils, is unsuited for application on a low energy cyclotron, because energy loss in the cooling water in front of the entrance foil is unacceptable when 10 or 18 MeV cyclotrons are used. For this reason, based on our experience with Silver and Titanium target chambers, a Niobium insert is designed and machined that fits in a standard IBA target support (Figure 1). The Niobium target was tested both at an IBA 10/5 and an IBA 18/9 PET cyclotron. In a standard target system the inner cavity is completely closed and self pressurised under bombardment. The target window system consists of 25 μ m and 50 μ m Havar foils for respectively the IBA 10/5 and IBA 18/9 PET cyclotron. The target windows are cooled with a stream of Helium and the target chamber is cooled with water.

It is demonstrated that a Niobium insert can be successfully used for the production of multi Curie amounts of [¹⁸F]Fluoride using a standard system. Therefore the results obtained by the Niobium insert could directly be compared to results obtained by target inserts constructed from Silver and Titanium. The results are summarised in Table 2 and 3. The drawback of Silver (in particular the formation of colloids leading to a decrease of yield of [¹⁸F]Fluoride and to obstruction of tubings and valves) and Titanium (the high

activation of the target chamber) can be avoided by using Niobium as target chamber material.

As could be expected there is no significant difference in experimental thick target yields for the different materials by the same effective volume of the insert. The amount of produced [¹⁸F]Fluoride is directly related to the maximum operational beam current. It is demonstrated that the beam intensity influences the internal pressure of the target. The cooling efficiency of the target chamber is determined by the thermal conductivity of the insert material and the insert wall thickness.

It is demonstrated that, related to differences in thermal conductivity, higher beam currents can be used in target chambers constructed of Niobium instead of Titanium, leading to higher amounts of produced [¹⁸F]Fluoride.

We could not detect any radionuclidic impurities originated from nuclear reactions on Niobium, in the resulting [¹⁸F]Fluoride solution. The only detected radionuclidic impurities were identified as nuclides formed under proton irradiation of Havar. Therefore in future research the possibility of exchanging Havar foils for Niobium foils will be investigated.



Fig. 1. Front and back view of the target chamber.

Material properties	Ag	Ti	Nb
(+ = high; 0 = average; - = low)			
chemical resistance	-	+	+
thermal conductivity	+	-	0
radiation safety of target chamber ¹	+	_2	+3
reactivity of ¹⁸ F produced	0	+	+
contaminants in ¹⁸ F produced	-	-	+
target pressure	+	-	0^4

Table 1. Properties of target chamber materials.

¹ Plus sign means relatively low activation of the target body.
² see Figure 4
³ see Figure 3
⁴ see Figure 2

Table 2. Yields obtained with IBA 10/5 after 120 minutes of 10 MeV proton irradiation.

Target insert material	Beam intensity (µA)	¹⁸ F Yield @ EOB (Ci)	Thick target yield @ sat (mCi/µA)
Ag	70	$4.2 \pm 0.5 (n=23)$	116
Ti	55	3.1 ± 0.3 (n=63)	106
Nb	65*	3.5*	111*

*extrapolated value

Target insert material	Beam intensity (µA)	¹⁸ F Yield @ EOB (Ci)	Thick target yield @ sat (mCi/µA)
Ag	40	5.1 ± 0.7 (n=95)	237
Ti	30	$3.9 \pm 0.3 (n=51)$	245
Nb	35	$4.4 \pm 0.4 (n=95)$	237

Table 3. Yields obtained with IBA 18/9 after 120 minutes of 18 MeV proton irradiation.



Fig. 2. Evolution of the pressure v.s. beam intensity.



Fig. 3. Evolution of the dose rate at 30 cm from the Nb target set up on a Cyclone-18/9.



Fig. 4. Evolution of the dose rate at 30 cm from the Ti target set up on a Cyclone 18/9.

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Effect of the Beam Profile on the F-18-Fluoride Target Saturation Yield.

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AIMS: Beam quality parameters play an increasing role in terms of efficacy of target irradiation at PET cyclotrons. In order to quantify the effect of the quality of the beam, namely the particle beam density and the shape of the beam, on the productivity of certain targets we performed a series of measurements. Two different approaches were used to influence on the beam parameters. Increasing the distance between the beam exit and the target makes use of beam natural divergence, this is achieved by installation of a spacer tube before the vacuum target foil (called "beam line " by the manufacturer). Installation of additional metal foils (called "degrader") on the way of the beam degrades the particle energy and adds dispersion of the beam.

METHODS: Irradiations by 18-16 MeV proton beams of 5-30 μ A intensities were performed on CYCLON 18/9, IBA cyclotron. Beam line was produced by IBA and represented a spacer tube of aluminium with the length of 30 cm installed before the vacuum foil of the target. Degrader was placed prior to the vacuum foil of the target at the end of the beam line and consisted of the stack of 20 Al foils having thickness of 0.02 mm each. The beam spot geometry was assayed by autoradiography of the target foil using Cyclone Storage Phosphor Screen (Packard) or the Linear Analyzer (Berthold). Efficiency of the irradiation was estimated by measuring the saturation yield of F-18-fluoride from the standard IBA small volume silver target (Ag body, 0.6 ml cavity for O-18-enriched water).

RESULTS: Installation of the beam-line enlarged the beam spot only by 10 %. Nonetheless 15 % increase of the F-18-fluoride saturation yield was obtained. Installation of degrader had a major influence on the homogeneity of the beam profile. The "hot spot" measured as a Full Width at Half Maximum of the radioactivity profile on the irradiated target foil (FWHM) was increased by 62 %. Installation of the degrader induced a loss of energy of the proton beam which caused significant decrease of the F-18-fluoride saturation yield at 15 μ A (measured 5.7 GBq/ μ A for combination of degrader with the beam-line vs 6.7 GBq/ μ A for beam-line alone). However, the energy loss could be compensated by the better homogeneity of the beam profile, as visualised by autoradiography. This allowed to run the F-18-fluoride target at higher currents (at 20 μ A saturation yields were 4.9 vs 4.0 GBq/ μ A correspondingly).

CONCLUSIONS: The quality of the beam profile is important for the reliable operation of the targets at higher intensities. The distance between the stripper and the target has a lower influence on the beam homogeneity than beam dispersion on the metal degrader foils. Installation of the 30 cm beam line between the stripper and the target in combination with the degrader allowed to improve significantly the homogeneity of the beam. This fact is important for irradiation of sensitive solid materials as for instance Te-124-tellurium oxide for I-124-iodide production.

A Convenient Method for the Purification of O-18 Water

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Aims

During the purification of O-18-water by conventional distillation certain contaminations, like acetonitrile will not be removed entirely because they form an azeotropic mixture. Moreover the enrichement of O-18-oxygen is reduced by an exchange with O-16-oxygen from e.g. MnO_4^- . The extremely small amounts of O-18-water used per batch, force the user to collect several batches to receive sufficient material for the distillation process. A satisfying yield of F-18-fluoride from the irradiation of O-18-water, however, can only be achieved if there are no organic contaminations and if the isotopic enrichement is sufficient.

Methods

Used O-18-water is cleaved into its constituents O-18-oxygen and hydrogen by electrolysis, thereafter the gases are carried via different tubes into a fuel cell where it is catalytically oxydized back into water. Since electrolysis proceeds quite slowly, the supply of incoming water is regulated by a remote controlled module. Automation of the process provides continual operation of the system.

Results

Used O-18-water can continually be purified in a simple manner from contamination originating from the separation of F-18-fluoride. The volume of the electrolyte chamber can be kept quite low at 4 to 6 ml. Over 99,9 % of the contamination could be removed in a single pass.

Conclusion

Electrolysis combined with fuel cell technology is suggested as a convenient alternative for O-18-water purification.

Self-Regulating Thermosyphon Water Target for Production of F-18-Fluoride at Proton Beam Power of One kW and Beyond

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Aims

PET cyclotrons can deliver proton beam currents above the limit tolerated by current generation enriched O-18-water targets producing F-18-fluoride ion. We seek to demonstrate that much more of this beam power can be utilized by implementing bottom-pressured thermosyphon targets, which more effectively optimize the evaporation/ condensation mode of heat transfer than top-vented or top-pressured reflux targets.

Methods

Thermosyphon geometry appropriate for enriched water targets uses the beam strike as the boiler section and a volume above it as a condenser section. The device is completely filled with water, closed off at the top, and high pressure helium is applied on a liquid-filled exit port at the bottom. Beam heating causes thermal expansion to force water out of the target bottom until boiling begins, and then additional liquid is moved out due to beam strike bubbles and condenser vapor volume, where bubbles leave the liquid surface and condense at the top to run back down the sides. This condenser vapor volume increases as necessary to provide an evaporation/condensation space adequate to remove increasing beam heat, and decreases if beam power is reduced. This self-regulation results in a full liquid fill again if all beam power is removed. Transport of pure water vapor is thus not impeded by the presence of foreign gas molecules. Experiments at 22 MeV and 30 atm were conducted on three prototype targets (TS-1, TS-2, TS-3), all with a 10 mm diameter by 10 mm deep boiler volume, and with condenser volumes of 0.3, 0.5, and 1.0 times the boiler volume. Calorimetry on side and back wall cooling partitioned heat removal at about 4 to 1 respectively, and detected no beam reaching the back. Pressure is monitored with a Kulite transducer in the target base. Natural water exeriments used a vertical glass sight tube (3 mm ID) with water extending continuously from inside the target up into the tube. Dynamic movements of the water in and out of the targets as a function of beam current were observed via TV by watching the tube level. LabVIEW control software coupled to field point modules loaded and delivered target water via valves and pumps, and displayed and recorded pressures and temperature differentials on line.

Results

TS-1 and -2 reached heat transfer limits at 22 and 28 microamps (464 and 616 watts) respectively, when vapor began intruding the beam strike. TS-3 operated comfortably to 46 microamps (1012 watts), at which point the cyclotron's preseptum sustained damage. The TS-3 data extrapolate to 60-70 microamps, but experimental measurement requires a

negative ion cyclotron with a safe extracted beam power of at least 1500 watts. One hour runs on enriched water with TS-2 below its power limit produced F-18 saturation yields of 12.2 GBq per microamp, in good agreement with data obtained from E. Hess and S. Qaim. TS-3 yields at 40 microamps are planned at both a bottom and a top pressure configuration for comparison.

Conclusion

Our data indicate a self-regulating bottom-pressured thermosyphon target may offer a way to significantly increase yields of F-18 at existing and future PET cyclotron facilities. We plan to pursue beta testing at appropriate cyclotron sites to establish performance limits, reliability, and ability to synthesize FDG.

Regenerative Turbine Pump Recirculating Water Target for Producing F-18-Fluoride Ion with Several kW Proton Beams

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Aims

Some PET cyclotrons can deliver proton beam current at power levels above 1.5 kW. We are not aware of demonstrated or previously published proposed O-18(p,n)F-18 target systems capable of dissipating this level of power while maintaining yield-thick water in the beam strike. We are pursuing the goal of designing and building a system which will operate reliably at several kW. This can be done if target water can be passed through the beam strike with a transit time so short that the boiling point will not be reached, or that a minimum amount of Bragg peak vapor bubbles will be produced and those surviving will be quickly swept away and condensed. The target must also recirculate the enriched target material through heat exchangers capable of removing the beam heat. The cost of the recirculating water inventory must also be held to an acceptable value. The key to the success of such a system is a minature pump that will operate cleanly and reliably at high flow rate and high pressure. After considerable study, we have selected the regenerative turbine as the pump of choice. This pump has the added advantage of tolerating pumped fluid containing entrained vapor without sustaining cavitation damage.

Methods

Our recirculating target system is being designed as an integrated interconnected assembly, with all surfaces contacting target water actively cooled except the turbine rotor (pump housing, intercoolers, and target body). The initial emphasis has been on sizing the preliminary pump design by characterizing the flow characteristics with mechanical prototypes. Following this, details of the intercoolers and target body can be developed, as well as pump seals and bearings appropriate for extensive beam testing. A magnetically-coupled motor drive is under consideration.

Results

A 0.86 ml prototype pump with 2 mm thick 25 mm diameter rotor has been tested from 1500-3500 rpm up to 1 atm pressure differential and up 0-30 atm overpressure. Flow varied from 1.3-2.7 liters/min at maximum and minimum pressures respectively. This pump has been modified to a 2.41 ml prototype with 3 mm thick 28 mm diameter rotor, and is being prepared for testing with a larger drive motor.

Conclusions

Feasibility of acceptable performance and operating cost has been studied for a high power recirculating water target system based on a minature regenerative turbine pump. This system has the potential to operate at proton beam currents of several kW. The first pump prototype test has been successful. Preliminary design of the intercoolers and target body for an integrated system is in process. These will be tailored to the pump geometry developed from ongoing mechanical testing. We hope to fabricate an integrated system suitable for beam testing by late 2002, to allow the start of beam testing at 1 kW on the Duke CS-30 cyclotron by the end of the year. We speculate that considerable evolution of the target body configuration will occur during thorough 1 kW beam testing, as well as significant modification of the pump and intercoolers. Beta testing at an accelerator site that can provide several kW of proton beam power is anticipated following successful completion of Duke beam testing.

High Power Enriched Gas Targets

Coordinators: Volker Bechtold, Karlsruhe Bruce Mackay, Hammersmith Hospital Thomas J. Ruth, TRIUMF
Target Foil Grid Supports for PET Isotope Production

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Introduction

Proton cyclotrons remain the accelerator of choice for production of radioisotopes for PET applications; however, alternative approaches have been explored over the years. One such alternative was a linear RFQ device that accelerated helium-3 [1]. The particle choice, energy and accelerated beam dimensions presented formidable challenges to targetry development. The peak power densities of pulsed rf beams are normally handled by the use of high aspect ratio beam strike geometries in the targets. The downside of the approach is the loss in target foil rupture pressure. The problem is exacerbated with He-3 due to the particle's high rate of energy loss in materials, thus demanding the use of very thin windows. Others have encountered similar target design difficulties [2, 3].

The use of mechanically supported target foils has been previously reported [4]; however, to address some of the issues at hand, a novel target foil grid support was conceived: the foil would be 1) supported by an array of hexagonally-shaped holes separated by a thin septum, 2) fabricated from a high thermal conductivity metal(aluminum or copper) and 3) water-cooled via channels machined into the structure's perimeter. A honeycomb pattern affords a greater fraction of beam transmission than round holes and efficient heat removal can result from high water coolant velocities. The grid support's potential was extended by further suggesting that a second, upstream grid could be used as a heat shield or "sacrificial" structure.

Before fabrication of any such supports was initiated, the merits of the design concept were tested via Computational Fluid Dynamics/Finite Element Analysis(CFD/FEA) modeling. This analysis helped to identify the key parameters that would most likely affect the grid's performance in the anticipated environment of the He-3 RFQ. Analyses were extended to include the structure's utility for dc proton accelerator targetry.

Results presented herein for this grid support concept include:

- CFD/FEA analyses for beams of 12 MeV protons and 10.5 MeV helium-3;
- Experimental failure pressures for several typical target foil materials supported by a hexagonal grid. Some failure pressures are compared to those generated in the presence of a 11 MeV proton beam;
- Calorimetry measurements intended to evaluate the grid's heat removal capabilities under proton irradiation.

Materials and methods

Grid supports were fabricated from 6061-T6 aluminum or OFHC copper and comprised an array of 3.175 mm hex holes within a 10 mm diameter, separated by septa of varying dimensions(0.254-0.381 mm) plus integral coolant channels at the structure's perimeter. Physically bonded and non-bonded foil/grid combinations were used in this investigation. Several common target foil materials were pressure tested using the hex hole grid support and compared to unsupported foils of the same diameter. Foils were placed in a special rupture fixture with pressure supplied by either regulated helium gas or an hydrostatic pump.

Selected grid-supported and unsupported foils were hydrostatically ruptured under proton irradiation conditions using the Duke CS-30 cyclotron. The target and associated apparatus are diagrammed below. The test target was aluminum, 10 mm ID, and variable depth. Water cooled grids were either aluminum or Hycon 3 Cu/Be. A 9 mm water-cooled collimator/degrader dropped the proton energy to 11MeV.



Calorimetry experiments were performed via 1) 18 MeV H⁺ irradiation of a modified CTI RDS112 ammonia target fitted with an edge-cooled aluminum grid connected to a closed loop cooling system decoupled from the accelerator cooling and 2) 22 MeV H⁺ irradiation of a test target fitted with an upstream aluminum collimator/degrader/sacrificial grid assembly followed by an aluminum target body support grid. Conventional accelerator system cooling was used. Grid, collimator/degrader and target body inlet/outlet water temperatures were monitored via T- or K-type thermocouples.

Results

CFD/FEA Analyses

To minimize initial computational complexities, the following design parameters and operating conditions were assumed:

- the structure would be a copper disc with 3.175 mm cell size honeycomb holes and 0.508 mm septum to which is soldered a 0.00635 mm Havar foil. A heat shield would be ignored at first;
- edge cooling would be provided by 13°C water, 80 psig pressure drop, through three 0.508 wide by 2.54 mm deep channels;
- uniformly distributed dc beams of 12 MeV x 75 μ A protons (1 cm diam) and 10.5 MeV x 100 μ A helium-3 (1 cm diam and 2 x 10 cm) were assumed;
- two water target scenarios were investigated: i) submerged forced-jet cooling of the Havar and ii) a 350 psig pressurized natural convection target. A separate CFD analysis was required to determine a heat transfer coefficient for the natural convection case.

The most important results derived from these initial calculations included:

- Havar temperature profile is predominately due to target water cooling heat transfer coefficient vs heat conduction to the copper structure;
- for a 1 cm beam diameter, forced jet cooling is required in the case of helium-3;
- the heat shield may not be necessary.

Additional calculations were suggested by making obvious changes in some parameters, to include beam dimensions, target foil and target plus heat transfer scenarios. The results of these calculations and the various scenarios are summarized in Figure 1. What was learned from these additional calculations included:

- thermal conductivity of the foil material makes a profound difference in the foil's calculated beam strike temperature;
- for uniform beam heating of an edge-cooled window, the maximum temperature of the foil is <u>independent</u> of the foil thickness. This result is of more value to a pulsed proton beam than helium-3;
- with the larger beam dimension, a natural convection target appears workable with a dc beam.

Foil failure tests

Results of rupture test for various grid supported and unsupported foil materials in the presence and absence of a proton beam are summarized in Tables 1 and 2.

Calorimetry: Closed-loop experiments

All experiments were done at 250 psig with water flowing through the beam strike at 1 cc/min. Assuming the water enters the target at 20°C and leaves at 208°C (boiling point at 250 psig), 13.1 watts are removed through this path. Initial scouting experiments determined optimum grid coolant volume and general behavior of the system, especially any other heat loss. The slope of the temperature drop of the reservoir after beam is turned off gives a heat loss from the warm grid coolant to the colder cyclotron coolant of about 55 watts.

Irradiations were performed at 20, 30 and 40 μ A (20 min) for the grid only cooled via the 3 liter water supply. The power that goes with the temperature rise rate observed was

calculated, then the 55 watt loss was added to get the actual heat removed. In all cases, this was greater than the heat expected to be dissipated solely in the foil and grid. The cooling scheme was reversed, running the 3 liter supply through the target cooling path, and putting regular cyclotron chilled water across the grid. The loss in conduction between the two stages was expected to be the same but in the opposite direction, so in the last two calculations, 55 watts is still added. Additionally, 13.1 watts lost from the temperature rise of the beam strike water is added. Nevertheless, we cannot account for as much heat from the target body as one would expect from the beam that makes it through the foil and grid. In all cases there is an apparent, and not insignificant, cooling of the target water by the grid/foil combination.



Fig. 1. Parametric variation of Havar foil temperature for proton and helium-3 DC beam environments (HS = heat shield; NTC = no target cooling).

Foil, thickness(mm)	Proton current(μA)	Rupture(psig)
Cu/2 % Be, 0.0508	20	740
Cu/2 % Be, 0.0508	20	880
Cu/2 % Be, 0.0508	30	880
Cu/2 % Be, 0.0508	40	820
Havar, 0.0127	20	880
Havar, 0.0127	30	880
Havar, 0.0127	40	840

Table 1. Beam-on foil rupture data.

¶ Havar was grid supported, Cu/Be was not.

<u>Calorimetry</u>: Thermosyphon target experiments

A target configuration based on a self-regulating thermosyphon operating principle has proved invaluable in demonstrating the heat removal benefits of an edge-cooled grid up to nearly a kW of beam power. The target components that include combinations of upstream sacrificial and target body grids plus a sight tube for beam strike target water expansion measurements have allowed for careful heat balance and partition measurements among the components used.

The reader is directed to these Proceedings' paper by B. Wieland et al. on "Self-Regulating Thermosyphon Water Targets for Production of F-18-Fluoride at Proton Beam Powers of One kW and Beyond" for results and discussion of grid performance at relatively high beam powers.

Foil	Thickness (mm)	Vendor	10 mm diam rupture(psig)	3.175 mm hex/ 0.254 mm septum rupture(psig)	Hex/Thru	Temper tested
Al	0.0254	unknown	140	370/430	2.86	unknown
Au	0.0254	Reactor Expts.	30/25	150	5.45	unknown
Arnavar	0.00762	Arnold	105	635/615	5.95	unknown
Havar	0.00635	Hamilton	145	520/500	3.52	cold rolled
Havar	0.01016	Hamilton	275	800	2.91	cold rolled
Havar	0.0254	Hamilton	1000	n/a	n/a	unknown
Havar	0.03048	Hamilton	1200	2800/2900-3000	2.4	cold rolled
Havar	0.03048	Hamilton	1700	4500	2.65	annealed
Та	0.0254	Alfa Aesar	440	1200	2.73	unannealed
Та	0.0508	Goodfellow	975	n/a	n/a	annealed
Cu/2 % Be	0.008255	Hamilton	90	320	3.56	hard
<i>Cu/2 % Be</i>	0.0254	Goodfellow	200	750-800	3.75-4.00	as rolled
Cu/2 % Be	0.0508	Goodfellow	925	2700	2.92	half hard
Ti	0.0254	unknown	860	>1600	>1.86	unknown

Table 2. Static rupture pressures of various foils.

Data in italic are hydrostatic rupture pressures.

Table 3. Heat balance data	from BRF.

				Observed power	Apparent heat
	Watts into		Total power in	(corrected for heat	removed from
μA x time	grid (<i>target</i>)	Watts into foil	(calculated)	loss)	target water
20 x 20	73.8	12.1	85.9	119.8	33.9
30 x 20	111	18.1	129.1	162.7	33.6
40 x 20	148	24.2	172.2	198.3	26.1
20 x 20	274		274	183.2	91
30 x 20	411		411	261.6	146.4

Summary

Resource constraints during the ³He RFQ project demanded that minimal time be devoted to accelerator cleanup resulting from target foil failures. This requirement was nicely satisfied by the high aspect ratio hexagonal pattern foil grid support. Edge cooling of the device provides the other primary feature, the benefits of which are being exploited in the ongoing development of high power, high pressure proton targetry for F-18-fluoride ion production. Grids have been easily fabricated from high thermal conductivity materials (e.g., aluminum, copper, copper/beryllium and graphite) via conventional CNC and wire EDM technologies. The pressure integrity, heat removal and high transmission of the hex grids allow for single foil target operation, eliminating the need for helium window cooling.

Our computational and experimental results reported herein lead us to the following conclusions regarding the foil grid support:

- grid supported foil rupture pressures were found to be 2.5 to 6 times greater than unsupported foil pressures. The ability to operate water targets at higher boiling points allows higher temperature differentials at the internal surfaces of the target;
- thermal contact between foil and support is adequately provided by the target internal pressure without having to resort to bonding agents;
- thermal conductivity of the target foil profoundly impacts its beam strike temperature;
- when backed by target water, foil supported and unsupported beam-on failure pressures dropped insignificantly or not at all up to 40 μA of 11 Mev protons;
- we estimate that 10-25 % of the heat deposited in a proton-irradiated water target is actually removed by the foil/grid composite.

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Further Progress on Targetry for the Production of Ultra-High Quantities of F-18-Fluoride

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Aims

To build a target capable of producing multi-curie quantities of F-18-fluoride while being able to recycle the target material.

Methods:

We have reported our work on a gas target system to produce ultra-high quantities of F-18fluoride at the 8th Workshop on Targetry and Target Chemistry and in the literature[1] using a SS target body. While these results demonstrated proof-of-principle concepts there were improvements to be made around the efficiency of F-18 extraction from the target walls and the chemical reactivity of the F-18-fluoride. Since that time we have designed another gas/liquid handling system and other target bodies.

Results

We will report on the performance of the modified system with respect to yields and chemical reactivity of the obtained F-18-fluoride.

Conclusions

A gas target for producing F-18-fluoride has been demonstrated to operate at 50 microAmperes with the possibility of even higher beam currents which would result in extremely high production rates.

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Development of Target System for [F-18] Fluorine Production via the O-18(p,n)F-18 Nuclear Reaction

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AIMS: The number of PET scanners installed in Korea has been sharply increasing for a few years. F-18-fluorine has been gaining increasing importance in various F-18 radiopharmaceuticals production because its electrophilic reaction can afford many versatile pathways in F-18 compounds synthesis.[1] We have experience of success in making the enriched O-18 water target for ourselves for the routine F-18-FDG production with nucleophilic substitution reaction. In order to produce new F-18 compounds, promising agents in oncology study, we decided to make the enriched O2-18 gas target system to produce F-18 fluorine.

METHODS: Our target system for F-18 fluorine production consisted of target chamber, enriched O_2 -18 gas loading/cryogenic recovery system, collimator/energy degrader[2], gas and vacuum control system. Conical shaped target chambers were fabricated of aluminum and the target chambers were mounted on the multi-target irradiation station made by ourselves. Also, 4 sectors carbon collimator (dia.=1.5 mm) was installed to control the proton beam on the target. All valves in the gas and vacuum control system were the VCR type of Swagelok product to maintain high pressure and vacuum.

RESULTS: Two-step irradiation [3] protocol was adopted to recover the F-18 produced with the first irradiation on the enriched O-18 gas and sticked into the chamber wall. 15 bar of the O-18 gas was intoduced to the chamber for the first irradiation and the beam current could be increased up to 40 μ A. In the second irradiation, after crygenic recovery of O-18 gas, Ar/1 % F2 mixture was introduced and a short proton irradiation was done for recovery of the F-18 fluorine from the target chamber.

CONCLUSION: Our target system is very useful for routine production of F-18 fluorine in saturation yields of 59 mCi/ μ A at EOB. The loss of O-18 gas after production has been lower than 1 % in 12 runs without any problem .

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Production of an Intense O-15 Radioactive Ion Beam using Low Energy Protons

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The production of adequate quantities of ¹⁵O for astrophysical applications has been a source of concern at TRIUMF and ISAC for some time. The production of a ¹⁵O beam is needed for two experiments ($^{15}O(\alpha,\gamma)^{19}Ne$) and $^{15}O(^{6}Li,d)^{19}Ne$) at ISAC. Difficulties arise due to the fact that oxygen is very reactive chemically and thus is difficult to extract from a thick spallation target. The beam flux required for these experiments is extremely high, between 109 and 1011 ¹⁵O/s for the (α,γ) reaction) and thus high efficiencies at all steps in the process will be required.

These studies involve increasing our understanding of the process of elemental synthesis in stars, and the mechanism of the cataclysmic events of stars such as novae, x-ray bursts and supernovae, which lead to the release of these elements into the universe. A series of fast (seconds) network of nuclear reactions occur in explosive events involving short-lived radioactive nuclei. Observations of gamma rays using observational telescopes confirm our general understanding of these events, but further research is needed to truly understand them. A key reaction in the ignition of novae, x-ray bursts and possibly supernovae is the reaction of the isotope, ¹⁵O with helium nuclei in the very hot stellar environment. The rate of this reaction at stellar temperatures is presently unknown. At TRIUMF with the new radioactive beam facility, ISAC, combined with the new DRAGON reaction measurement facility, the rate of this reaction could be measured and shed light on these ignition processes. Unfortunately, oxygen is a very reactive element and it is difficult to produce an intense beam of the radioisotope, ¹⁵O, (half-life = 122.2 sec).

The possibility of using one of the small cyclotrons on site (TR13, CP42 or TR30) for the production of this isotope (¹⁵O) has been discussed. This new production approach will involve the use of low energy protons to interact with a nitrogen gas target via the ¹⁵N(p,n)¹⁵O reaction, which is accessible with attainable particle energies using these cyclotrons. The BEARS project in Berkeley has had considerable success (1.0 x 108 particles/sec) with producing ¹⁴O beams with a similar method. Preliminary results using the ¹⁴N(p,n)¹⁴O reaction as a model for the ¹⁵N(p,n)¹⁵O reaction have been obtained and will be presented, describing the appropriate on-line chemistry to separate, trap, purify, and transfer the ¹⁵O. The preferred chemical form of ¹⁵O, (C¹⁵O) would be available for introduction into an RF type of ion source for the production of the high intensity ¹⁵O ion beam at ISAC.

Solid Targets at Low-Energy Irradiations. Transport of Targets

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The Electron Beam Test Facility for Cyclotron Isotope Targets Examination

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Abstract

Aims: Use of internal cyclotron beam for radioisotopes production requires reliable solid targets, stable under high power radiation and heat flows. The main goal of the present work was to design and construct experimental equipment allowing to generate the heat flow with the same or higher power density than under cyclotron irradiation.

Methods: Electron gun was selected as a heater. Electron beam test facility equipped with solenoid lens and electromagnetic beam scanning system allows to form homogeneous irradiation area of different size. The target system used for tests is exactly the same as for radioisotopes production at the cyclotron.

Results: Electron beam stand with maximal energy of electrons of 25 keV and beam current up to 200 mA was designed and constructed. A number of experiments with different targets was performed. The results of electron beam tests with high and known beam-power density was used for calculation of maximal cyclotron beam current for specific target materials. The technology of Zn and Tl high current target preparation was successfully developed.

Conclusion: The electron beam test facility is routinely used for cyclotron targets examination before radioisotope production. Such quality control gives a reliable guarantee of safety of cyclotron irradiation. This technique also provides wide possibilities for research and development of new target construction and target preparation technologies.

Introduction

In the Institute of Nuclear Physics NNC RK on the basis of isochronous cyclotron facility and radiochemical laboratory works are carried on for production of a set of radioactive isotopes for applications in medicine, ecology-related investigations, industry and other fields. These are radiopharmaceutical preparations "Thallium-201 chloride", "Gallium-67 citrate", sources ⁵⁷Co and ¹⁰⁹Cd, tracers ²³⁷Pu, ⁸⁸Y, ⁸⁵Sr. Nuclear reactions on protons with energies up to 30 MeV and alpha-particles with energies up to 50 MeV are used for their production. The irradiations are performed at the isochronous cyclotron U-150 with internal and external beams.

Target material is coated on copper substrate by the method of electrolytical deposition. At irradiation of a target of 8 cm² with proton beam of energy 30 MeV and current intensity 300 μ A the maximal density of heat flow is 1800 W/cm². Quality of the target material adhesion, high density of the heat flow can cause overheating of a target and its destruction.

The electron beam test facility was created for preliminary heat load targets examination before their irradiation at the cyclotron. This facility also enables to expedite development of technologies for isotope target production.

The electron-beam stand

The stand (fig.1) is represented by a vacuum chamber with an electron gun and a target unit situated at the end-walls with base of 600 mm. An electron tube was chosen as a heater due to several reasons [1]. It is possible to obtain high density of heat flow by means of an electron beam. At that, it is easy to adjust rate of the heat flow with time. Using beam forming systems and an external scanning device it is easy to change size and location of a heating zone.



Fig. 1. The general view of the stand.

Vacuum pumps provide vacuum in the working chamber of 10^{-4} Pa. A cathode of the tube is of lanthanum-boride with indirect heating. The tube is equipped with solenoid lens that makes it possible to get the minimal beam size at a target to be 1.5 mm. Maximal beam current is 200 mA at the electron energy up to 25 keV. Electronic power supply units are protected from emergency conditions.

Electromagnetic control system of the electron beam assures its moving over the whole target surface ($20 \times 40 \text{ mm}^2$) in manual and automatic modes. The beam scanning frequencies over a target (50 and 1200 Hz across and down, correspondingly) were chosen to provide uniform heating.

The target unit of the stand is identical with the same of the cyclotron. Their cooling systems are identical as well. Water pressure in the cooling system is 20 bar what provides water speed in the cooling channel up to 30 m/s.

The stand is equipped with TV system enabling to control the beam location on a target and control the irradiation process.

Electron beam density distribution influences considerably the results of the target thermal resistance estimations. Measurements performed by wire probes and by the method of small hole have shown that the best for the performed tasks is the beam of 4-5 mm in diameter. At that the current density distribution is close to the Gaussian one.

It should be pointed out that irradiation at the stand almost completely reproduces the target conditions at the cyclotron. At cyclotron irradiation the power deposition occurs at deeper layers. Cooling water is subjected to radiolysis with formation of active oxygen resulted in intensive oxidation of the cooling substrate surface.

Stand examinations make it possible to solve a set of practical tasks:

- 1. to perform regular preliminary examinations of targets prepared for irradiation at the cyclotron.
- 2. to test targets when develop technology of their production. There were performed tests of Ni, Zn and Ag targets. Electrodeposition modes for target materials were optimized using the examination results. A zinc target production technology for targets endured heat flows of ~38 W/mm² was developed as a result of investigations of zinc target with various intermediate layers.
- 3. to determine maximal possible heat flow rate in a target with further recalculation of this value for the cyclotron beam.

At irradiation with proton beam the power liberation occurs in the target bulk. The stopping range of 20 keV electrons in metals is about 1 μ m. That is why at irradiations with electron beam of materials with low thermal conductivity the melting temperature at the target surface is reached at lower heat flows. For example, thermal conductivity of thallium is 44 W/m×K. Melting temperature at the surface of thallium target (160 μ m thick) deposited on 2 mm copper substrate is obtained at irradiation with electrons of heat flow 1750 W/cm² when at irradiation with protons this value comprises 2300 W/cm². Temperature distribution in a target for both cases is presented in fig. 2.



Fig. 2. The calculated temperature distribution in the target induced by irradiation with protons (1) and with electrons (2). Maximal heat flow density in the first case is equal to 2300 W/cm^2 , in the second case 1750 W/cm^2 .

Conclusion

The electron beam stand is routinely used for cyclotron target tests before radioisotopes production. Such quality provides safe operation. This technique also provides wide possibilities for research and development of new target design and target preparation technologies.

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High Current Production of ¹¹C, ¹³N, ¹⁵O, ¹⁷F, and ¹⁸F for PET using a 3 MV Electrostatic Tandem Accelerator

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Target systems for the production of positron emitting radioisotopes used for medical research with positron emission tomography (PET) have been developed for a 3 MV electrostatic tandem accelerator (NEC 9SDH-2). While low current radioisotope production has been previously examined with this accelerator (Roberts et al., 1998, Ohlsson et al., 1996), high power target systems are presented for the production of [¹⁵O] H₂O (yield at saturation 9.8 mCi/ μ A), [¹⁷F]F₂ (25 mCi/ μ A), [¹⁸F]fluoride (11.1 mCi/ μ A),[¹⁸F]F₂ (15 mCi/ μ A), in target [¹³N] NH₃ from carbon (4.0 mCi/ μ A), [¹¹C]CO₂ (8.4 mCi/ μ A), and [¹¹C]CH₄ (5.3 mCi/ μ A). Water-cooled support grids for the entrance windows allow for beam currents in excess of 100 μ A on gas, liquid, or solid targets.

Methods

Accelerator

The National Electrostatics Corporation 9SDH-2 Pelletron was designed to provide 100 μ A of 6 MeV protons or deuterons within a maximum 10 mm diameter beam spot. The actual performance regularly exceeds these specifications. The Torvis multi-cusp negative ion source typically achieves more than 150 μ A. The two charging chains are rated at 150 μ A each, and accelerated beam currents in excess of 115 μ A have been demonstrated. The dome voltage of 2.97 MV required for 6 MeV single charge beams (with a 50 keV ion source voltage) is conservative, and the accelerator has been run up to 3.67 MV (for 7.4 MeV beam). The beam tuning components include low energy steering, and high energy quad focusing and steering magnets. The tuning capabilities coupled with an in-line rotating wire beam profile monitor allow for fine, continuous control of the beam shape and position. Independent adjustment of beam width in two dimensions is typically from 6 to 10 mm, with a full practical range of 2 to 20 mm FWHM.

Water cooled support grid

The support grid pattern consisted of circular holes arranged in a hexagonal pattern (Barnhart et al., 2002, Nickles, 1980; Schlyer et al., 1997). Trials were done with differing size holes to maximize the allowable beam current. Circular holes were made with 3.0 mm or 1.7 mm diameters, of which the smaller diameter holes withstood higher pressures and beam current. The aluminum between the holes was machined to a minimum of 0.18 mm while the grid thickness was approximately 12.5 mm along the beam direction. Thicker

grids have been used with no change in performance. The gas and solid targets for the tandem accelerator had the grid holes arranged inside a 1.9 cm diameter circle to minimize the heating on the grid. The water target grid was done inside 1.25 cm diameter circle, for the minimum volume of the enriched water. The grids are water cooled via two straight channels in opposite sides of the support grid. Chilled water at 18 c flows at 2.3 l/min through the cooling channels. The nec 9sdh-2 has a kf-40 quick connect flange designed to connect to the end of the beamline. Figure 1 shows the basic design of this grid with 80 1.7 mm diameter holes. Single entrance window foils varied from 12.7 to 25.4 μ m aluminum and 2.5 to 12.7 μ m Havar.



Fig. 1. Basic design of water-cooled support grid.

Gas targets

Flow-through gas target systems are used for the production of $[^{15}O]H_2O$, $[^{17}F]F_2$, $[^{18}F]F_2$, $[^{18}F]F_2$, $[^{18}F]F_2$, $[^{11}C]CO_2$ and $[^{11}C]CH_4$ (figure 2). Each product requires a mixture of gasses, summarized in Table 1. Target gasses are supplied to either a dual flow tube gas proportioner (Air Products) or a stainless steel manifold and feed the target via 1/8" O.D. stainless tube with a short PTFE section for electrical isolation. The gas enters the target at the downstream end though a stainless steel 1/8-NPT fitting, and exits through a 1/16-NPT fitting within 1 cm of the upstream end. The radioactive gas is then delivered to the analysis station though a short 1/16" PTFE tube followed by 30 m of HPLC grade 0.8 mm I.D. stainless steel tube or 0.8 mm I.D. PTFE tube. The target pressure is monitored with a corrosion resistant capacitance manometer (Entran) mounted on the gas line near the target feed. The target pressure is controlled by the gas flow (and supply pressure) and the impedance set by a needle valve on the outlet of the gas target. The water-cooled target body is 6061-T1 aluminum with a 12.7 cm by 1.9 cm I.D. Gas pressures of the targets typically operate at 15-50 psig O₂ or N₂ gas, although pressures to 450 psi are acceptable.

Isotope/ Form	Target composition	Reaction	Pressure (psi)	Flowrate (ml/min)
[¹¹ C] CO ₂	N ₂ /1 % O ₂	¹⁴ N(p,α) ¹¹ C	40	150
[¹¹ C] CO ₂	B ₂ O ₃ / He	¹¹ B(p,n) ¹¹ C	20	80
[¹¹ C] CH₄	N ₂ /5 % H ₂	¹⁴ N(p,a) ¹¹ C	50	200
[¹³ N] NH ₃	CH ₄ / 20 % H ₂	¹² C(d,n) ¹³ N	40-250	150-1000
[¹³ N] NH ₃	Carbon/ H ₂	¹² C(d,n) ¹³ N	10	40
[¹⁵ O] H ₂ O	N ₂ / 1 % H ₂	¹⁴ N(d,n) ¹⁵ O	40	150
[¹⁷ F] F ₂	O ₂ / 10 % He/ .5 % F ₂	¹⁶ O(d,n) ¹⁷ F	150	200
[¹⁸ F] F ₂	Ne/ 10 % He /< .5 % F ₂	²⁰ Ne(d,α) ¹⁸ F	150	200
[¹⁸ F] F-	Ne	20 Ne(d, α) 18 F	150	50
[¹⁸ F] F-	¹⁸ O-H ₂ O	¹⁸ O(p,n) ¹⁸ F	0	0

Table 1. Target Summary

The gas target for the production of [¹⁸F]fluoride via the ²⁰Ne(d, α)¹⁸F reaction varies from the other gas targets. The aluminum target body has been nickel-plated and a Niobium tube (15.7 mm I.D.) is inserted in the bore of the target. Holes drilled the niobium tube align with the gas ports at front and rear, and with a third port centered on the bottom of the target, to drain the water wash. Water is preheated to 85°C, and kept hot through the washing process with heat tape wrapped around the target. Total water volume is approximately 20 ml per wash. The [¹⁸F]fluoride target runs with a beam profile of 6 mm FWHM due to the smaller bore diameter whereas the beam profile for irradiating on the standard large bore gas targets is typically held from 8 to 10 mm FW<u>H</u>M.



Fig. 2. Basic design of gas target.

Liquid target

A liquid target system is also used for production of $[^{18}F]$ fluoride from $^{18}O(p,n)^{18}F$ on enriched water (figure 3). The water delivery lines are PTFE or HPLC grade stainless tubing (0.8 mm I.D.). The switch valves at the target are manual stainless steel ball valves with PTFE packing (Whitey, 40 series). The target body is Ag with stainless steel tubing top and bottom for water loading. The tubing is close fit to the silver, then silver soldered in place. The cylindrical beamstrike volume is 12.7 mm O.D. by 3 mm deep, sufficient to stop 6 MeV protons in water. The beamstrike volume is 380 µl, with a total of 500 µl required to fill between the switch valves. The target is completely filled, then sealed at atmospheric pressure before irradiation. Target pressure during irradiation is not monitored. The target mounts to the water-cooled support grid design used for the gas target, with the window foil compressed against a PTFE O-ring. A water jet at the back of the body cools the target. 6.0 MeV protons irradiated the water through Havar foil of thickness 10.1 to 12.7 μ m. Beam profile is kept to a maximum of 6 mm FWHM on the water target.



Fig. 3. Basic design of $[^{18}O]$ water target.

Solid targets

Two solid target systems are used for the production of $[^{11}C]CO_2$ and $[^{13}N]NH_3$. The first target (figure 4) is the same basic design as the gas target system, with the addition of a concave brass ramp cut to a 15-degree angle. The ramp is filled with B₂O₃ for $[^{11}C]CO_2$ (Clark and Buckingham, 1975) or with a form of carbon for $[^{13}N]NH_3$ production. 6.0 MeV protons or deuterons irradiated the target through single aluminum entrance window foils of 12.7 to 25.4 µm thick. Beam profile is kept to 8 to 10 mm FWHM while irradiating on B₂O₃ target to preserve integrity and reduced to 6 mm FWHM or less on carbon targets to increase the radiation induced diffusion.



Fig. 4. Water-cooled ramp target design for ¹¹C production.

The second target system was based on using a 19 mm o.d. quarts tube as the main target body so that the solid target (carbon) could be heated (figure 5). The quartz tube connected the same water cooled support grid using ³/₄" cajon ultra-torr fitting into a water cooled aluminum flange. The aluminum flange was water cooled via two straight channels in opposite sides of the bore. Sweep gas entered into the front aluminum flange through a 1/8-npt fitting. Gasses exited the target through another ³/₄" cajon fitting which was reduced down to 1/8-npt with stainless steel connectors. The quartz tube was heated to 950 c with a carbolite tube furnace mounted concentrically around the target material.



Fig. 5. Heated solid target design for ¹³*N production.*

Results

Gas targets

$^{14}N(p,\alpha)^{11}C, for[^{11}C]CO_2$

 $[^{11}C]CO_2$ ($t_{1/2}=20.3$ min) is produced by proton irradiation of natural N₂ plus 1 % O₂. This method is commonly used on most higher energy accelerators, but is attractive for higher current low energy accelerators because of target's simplicity(e.g. Heselius et al., 1987). With 6.88 MeV incident proton beam at 102 μ A, the $[^{11}C]CO_2$ is trapped in soda-lime at a saturation yield of 8.4 mCi/ μ A providing 850 mCi ^{11}C for practical use.

$^{14}N(p,\alpha)^{11}C$, for $[^{11}C]CH_4$

Where most ¹¹C is created in target as [¹¹C]CO₂ and then converted to [¹¹C]CH₄ for labeling as [¹¹C]CH₃I, flow through direct production of [¹¹C]CH₄ bypasses this step. [¹¹C]CH₄ is produced by proton irradiation of natural N₂ plus 5 % H₂ (Buckley et al., 2000). Although the yield is lower at 5.2 mCi/ μ A at 6.02 MeV, conversion efficiency and time favor its practical use with possible improvements in specific activity.

$^{14}N(d,n)^{15}O$, for in target[^{15}O]H₂O

Water labeled with ¹⁵O ($t_{1/2}$ =122 s) is formed in target by deuteron irradiation of natural N₂ plus 1 % H₂ (J.C. Clark 1995, Dahl et al. 1998). The total gas flow rate was maintained at 200 sccm. No flow control valve was used on the Teflon line out of the target as trapping occurs resulting in lower yields. Under these conditions with a 30 m, 0.8 mm i.d. delivery line target pressure is 40 psig. The gas is bubbled through 10 ml water in a calibrated dosimeter. The yield at 50 μ A gave 9.8 mCi/ μ A and produced 491 mCi of activity. Higher beam current test have not been done since this yield far surpasses the need in blood flow imaging.

$^{16}O(d,n)^{17}F$, for[^{17}F]F₂

 $[^{17}F]F_2$ (t_{1/2}=65 s) is produced for the production of $[^{17}F]CH_3F$ by the deuteron irradiation of natural oxygen gas with 10 % of a mixed gas containing 5 % F₂ in He (Mulholland et al, 1987, Roberts et al. 1998). This results in a nominal 0.5 % F₂ mix in 150 psig oxygen flowing at 200 sccm. The thick target yield for 100 μ A of deuterons is 25 mCi/ μ A, totaling 2.5 Ci of ^{17}F .

$^{20}Ne(d,\alpha)^{18}F$, for $[^{18}F]F_2$

Production of $[{}^{18}F]F_2$ is similar to that of $[{}^{17}F]F_2$, where the same 10 % by volume mixed gas of helium/fluorine except that instead of oxygen, a 90 % neon is used as the main target gas. Using this gas mixture throughout the irradiation, 15 mCi/µA was the yield at 90 µA. Further trials will be performed to minimize the amount of carrier F_2 required to maintain a sufficiently high specific activity so that the $[{}^{18}F]F_2$ is useful as a precursor and comparable to $[{}^{18}O]$ gas target systems (Nickles et al., 1984; Roberts et al., 1995b).

²⁰Ne(d, α)¹⁸F, for aqueous [¹⁸F]fluoride

 $[^{18}F]$ fluoride (t_{1/2}=110 min) is used in the production of $[^{18}F]$ FDG, the most commonly used PET tracer. Using ²⁰Ne has both cost advantages as well as advantages in targetry consideration over $[^{18}O]$ H₂O targetry (Helus et al., 1994). Operating gas pressures of 150 psig used here are much lower than sealed or over pressurized targets. Low gas flows using a needle valve stabilize target pressure during the irradiation. Water washes of the target have given yields of 11.1 mCi/µA at 85 µA.

Liquid targets

$^{18}O(p,n)^{18}F$, for aqueous [^{18}F]fluoride

The ¹⁸F is produced by ¹⁸O(p,n)¹⁸F using highly enriched [¹⁸O]water as the target material (Roberts et al., 1995a). While the reaction yield at <6 MeV is significantly less than that e.g. at 11 MeV, amounts sufficient for on site PET use can be produced without difficulty. The saturation yield for ¹⁸F at 100 μ A is 8.9 mCi/ μ A on fully enriched ¹⁸O water, lower than the reported 44 mCi/ μ A at 10 μ A (Ohlsson et al., 1996).

Solid targets

$^{12}C(d,n)^{13}N$ for $[^{13}N]NH_3$

¹³N ($t_{1/2}=10$ min) is produced by deuteron irradiation of a solid carbon target. This a highly efficient means for ¹³N production for PET, even at incident energies <1.5 MeV (Dence et al., 1994; Ferrieri et al., 1983;Shefer et al., 1994). Several forms of carbon have been tested, with the best so far being coconut charcoal in a quartz tube heated to 950°C gives a saturation yield of >20 mCi/µA with 4 mCi/µA collected as in-target [¹³N] NH₃ at 60 µA.

${}^{11}B(p,n){}^{11}C for[{}^{11}C]CO_2$

The ¹¹B(p,n)¹¹C theoretical yield of ¹¹C from protons on ¹¹B is nearly twice that from ¹⁴N(p, α)¹¹C in the 6 MeV range, but we have been able to only coax slightly more than half of ¹¹C yield from it. At this time, no more than 42 μ A of protons have been successfully irradiated the B₂O₃ on the ramp with a yield of 5.3 mCi/ μ A. ¹¹C is still more effectively produced in the gas target. A water-cooled ramp target is in production, so that variable cooling may be added to optimize the extraction of ¹¹C from the B₂O₃ melt.

The developments in target systems have already improved production of currently desired isotopes. Table 2 below summarizes where the current status of the accelerator targets for the 9SDH-2 with theoretical yields shown for 6 MeV protons or deuterons.

Isotope/ Form	Target Type	Max Beam Current (µA)	Yield (mCi/ μA)
[¹¹ C] CO ₂	Gas	108	8.4(@6.88 MeV)
[¹¹ C] CO ₂	Solid	42	5.3
[¹¹ C] CH₄	Gas	50	5.2
[¹³ N] NH ₃	Solid	60	4
[¹⁵ O] H₂O	Gas	50	9.8
[¹⁷ F] F ₂	Gas	100	25
[¹⁸ F] F ₂	Gas	100	15
[¹⁸ F] F-	Gas	85	15
[¹⁸ F] F-	liquid	100	8.9

Table 2. Measured Target Beam Currents and Yields.

Conclusion

The NEC 9SDH tandem accelerator is ideal for reliable production of ¹⁷F and ¹⁵O precursors for blood flow tracers, and the high beam current allows production of a number of other useful radioisotopes for PET. Developments of targets capable of withstanding the 100 μ A of 6 MeV deuteron and proton beams demonstrate practical production of lower yielding isotopes such as ¹¹C, ¹³N, and ¹⁸F. The target hot atom chemistry operating inside the target simplifies post irradiation production of [¹⁵O]H₂O, [¹¹C]CH₄ and [¹³N]NH₃.

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COSTIS: Compact Solid Target Irradiation System

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Aim

Dedicated PET cyclotrons have a great potential for the production of interesting positron emitting radionuclides of medium Z via (p,n) reaction. The aim of this work is the development of a dedicated target unit for irradiating TeO₂ for the production of radioiodine via the Te(p,n)I reaction. Most interesting in this concern is ¹²⁴I, but ¹²³I or ¹²⁰I would be accessible using the same technology.

Method

We selected the experiences of the Rossendorf Cyclotron Group in the eighties [1]. The target is a circular Pt-disk that carries the TeO_2 melted into a circular grove in the center of the disk. This target coin is mechanically very stable and easy to handle in both phases: irradiation and radiochemical processing. The target coin is inserted into the station, fixed pneumatically in the irradiation position, deblocked remotely after irradiation and falls down driven by gravity into the transport container. The irradiated target disk is then inserted into a dedicated furnace of the separation module developed by Nuclear Interface and the radioiodine is released by applying a special temperature program, transported in an air stream, and trapped in a pH=8 buffer solution. The target disk can be re-used for the next irradiation without further treatment.

Results

The target unit has five main components:

- 1. Connecting flange, which fits to the standard IBA target connection. This flange can be customized to fit virtually any other cyclotron.
- 2. A water-cooled graphite collimator that is electrically isolated, in order to monitor the beam spill.
- 3. The target assembly, including the exchangeable window foil which can be used as a degrader, isolating the closed He cooling loop from the cyclotron vacuum. The He stream is cooling the window foil on the one side and the TeO₂ surface on the other side in the same time. The target plate is electrically isolated for current monitoring.
- 4. The water-cooling jet directed to the rear of the target disk.

5. A remotely controlled pneumatic locking mechanism that holds the target disk in place during irradiation and releases the target disk so that it can fall down into a transport container. The complete target unit has been manufactured and tested.

Conclusion

This compact target unit for irradiation of sensitive materials, with He cooling that is common in PET target technology, can be easily adapted to the target ports of any PET cyclotron. Earlier experiences illustrate that one can apply a proton beam of around 15 MeV up to 20 μ A/cm² density to such a target. The target area depends on the local beam parameters; most suitable is 1 cm², which can carry 250–300 mg of the enriched ¹²⁴TeO₂. Batches of 30–50 mCi ¹²⁴I are accessible under optimal conditions.

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A Recoil-Escape Fiber Target using ⁹⁴Mo(p,n)^{94m}Tc to Produce ⁹⁴TcO₄⁻ Precursor for Radiolabeled Compounds Useful in Positron Emission Tomography

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Introduction

The purpose of this project is the design a cyclotron target system for producing Technetium-94m (^{94m}Tc), to be used as a radiochemical labeling agent for Positron Emission Tomography (PET) imaging.

In target approaches prior to this work, 94m Tc was recovered by chemical separation from the oxide target material, which involves a high exposure dose to the production chemist. The proposed fiber target system to produce 94m Tc will not only reduce the radiation dose to the chemist, it will also make pertechnetate (TcO₄⁻) readily available after end of bombardment (EOB), without chemical processing.

PET agents have been successfully produced with a slurry target and a fiber target, using the principle of recoil escape. This method consists of maintaining the target atoms in a permanent chemical and geometric form, while recovering the product radionuclide ion by stopping it in a liquid or gas. The product radionuclide is then transported out of the target while leaving the target atoms behind to be used in subsequent production runs We have used this approach to design the novel ^{94m}Tc target system which is the focus of this thesis.

The positron-emitter ^{94m}Tc can be used for PET in numerous radiochemical forms that have been developed for ^{99m}Tc, avoiding the usual extensive animal and metabolic studies that must precede the use of any radionuclide application. The advantages of PET include high resolution and quantitative tissue concentrations. The subsequent availability of kinetic data for compartmental modeling is extremely useful in studies to understand the mechanism of drug action.

Materials and methods

The proposed target is designed with thin molybdenum fibers distributed in a container of gas (steam or a noble gas). The advantage of steam is that the final product is pertechnetate (TcO_4) , which is the labeling agent used in the pharmaceutical kits widely available and used by almost every nuclear medicine department.

Nuclear reaction cross section data are needed for optimizing the production of a radioisotope, especially for calculating production yield and impurities as well as for target design and chemical processing. Reaction cross-section data are obtained from published work. Ranges of protons in the target mixtures and stopping power of the mixtures are

calculated using TRIM, a program that allows a quick calculation of parameters for any type of mixture.

Information about the mechanism of a nuclear reaction is often obtained from the distribution of recoil range of its product nuclide. This distribution is frequently required in charged particle activation analysis and radionuclide production. These measurements have been done using catcher foil technique methodology, such as results published by Iwamoto et al [17]. They will be used in this work to analyze the energy of the ^{94m}Tc nuclides recoiling from the molybdenum fibers. From the conservation of energy and momentum, the maximum and minimum recoil energy can be calculated for a reaction that proceeds via the compound nucleus (it is assumed that the recoil nucleus is formed solely by the decay of the compound nucleus).

Target Nuclide + Incident Particle \downarrow Compound Nucleus \downarrow Product Nuclide + Emitted Particle

 $^{94}Mo + p^{+} \rightarrow ^{94m/g}Tc + n^{\circ}$

This concept takes the following mathematical form:

$$E_{pmax} = M_c^{-2} \{ [M_e M_i E_i]^{0.5} + [M_e (M_c Q + M_i E_i)]^{0.5} \}^2$$

$$E_{pmin} = M_c^{-2} \{ [M_e M_i E_i]^{0.5} - [M_e (M_c Q + M_i E_i)]^{0.5} \}^2$$

 E_{pmax} and E_{pmin} are the maximum and minimum recoil energies of the product nucleus (^{94m}Tc) in this case. A negative sign will indicate that the recoil is backward (does not occur in our case). Following the same criteria the most probable recoil energy is the kinetic energy of ^{94m}Tc and is expressed as

$$< Ep > = M_p M_i E_i M_c^{-2}$$

 $M_e = 939.56$ MeV (mass of the emitted particle) $M_c = 174948.37$ MeV (mass of the compound nucleus) $M_i = 938.27$ MeV (mass of the incident particle) $M_p = 87476.31$ MeV (mass of the product nuclide) $M_t = 87472.06$ MeV (mass of the target nuclide) $E_i = 6$ to 13 MeV (energy of the incident particle)

Production of ^{94m}Tc recoil energies for 6 to 13 MeV protons are tabulated below

E	Epmin	<ep></ep>	Epmax
6	6 46E-05	0.063	0 244
7	7.91E-05	0.073	0.264
8	2.19E-05	0.084	0.283
9	4.14E-04	0.094	0.302
10	6.55E-04	0.105	0.321
11	9.36E-04	0.115	0.339
12	1.25E-04	0.126	0.357
13	1.59E-03	0.136	0.375

Tab 1	Energy	of the	recoil io	n in	function	of incident	proton energy.
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These values will be used to calculate the range of ⁹⁴Tc in Mo. These ranges require the use of fibers with diameters smaller than one micron. Using this data we evaluated the thick target yield and a tentative geometry for the system.

Since the target material is expensive and not readily available, a totally experimental approach is not feasible. Thus the system was simulated using FIBTAR (a computer code, based on the Monte Carlo Method, that has been written specifically for fiber targets). The code provides the total yield of the system, and the recovered yield (from recoil escape and subsequent fluid region capture) of the radionuclide of interest. It predicted successfully the behavior of previous fiber targets, with experimental results in good agreement with the simulations. FIBTAR results will be used to design a prototype target geometry to be experimentally tested. If the fibers contain any material other than the target atoms, or if the target atoms are coated onto a support fiber, the influence of this material on the target behavior must be investigated.

Technetium-94m produced by the ${}^{94}Mo(p,n){}^{94m}Tc$ reaction on natural molybdenum is accompanied by several radionuclidic contaminants. Enriched ${}^{94}Mo$ is available from vendors in the USA and Russia at prices from \$4 to \$6 per mg. It is available with different grades of enrichment, and as metal or oxide. The trioxide (${}^{94}MoO_3$) can be chemically dissolved and reoxidized for reuse as target material.

The impurities produced in the target influence toxicity of the product. Different types of radioactive emissions will contribute to the dosimetry of the agent while not providing any image information. Gamma emissions will contribute little to patient radiation dose compared to β^{-} and α emissions which lose all their kinetic energy in tissue. High energy β^{+} will blur the image degrading the quality of the study.

The thermal characteristics of a target system are influenced by the chemical form of the isotope to be used as the target material, its physical form, and the material used for windows and target containers. Metallic Mo has one of the highest melting points of the naturally occurring elements. Window materials may require special cooling provisions. Excessive heat will affect the physical and chemical properties of the target.

Water and steam were first considered as stopping fluids. Heat deposited in the system may cause water to be present in more than one physical phase, which affects the length of the target. Water vapor behaves as an ideal gas between 480 and 1000 K. Helium or argon (also candidate fluids) have no chemical influence on the ^{94m}Tc ion, but must be evaluated for radionuclidic impurities produced by proton irradiation in the selected energy range.

The advantage of the noble gases is that they stay in the gaseous state, but they must be mixed with enough water vapor to produce the pertechnetate ion. The chemical form of the recovered product will determine if separation of undesired byproducts is necessary. Technetium in the form of pertechnetate is chemically the most desirable form, since it is the labeling agent used in pharmaceutical kits. The monographs of the US Pharmacopoeia (USP) are the standards that establish the limits of radionuclidic contaminants, and the amount of carrier allowed for human use applications of radiochemicals.

One published target system employed molten Mo, extracting the technetium ion by sublimation. This method may be useful for fast recovery of the technetium ion, but the target must be irradiated using a vertical beam (not usually available), and the efficiency of the product recovery is problematic.

Results and conclusions

A target (porosity = 0.963) was modeled with the Monte Carlo code FIBTAR for 0.2 micrometer diameter Mo fibers in steam at a pressure of 6.8 atm and a temperature of 800 K. A Gaussian proton beam was collimated to a diameter of 7 mm before entering a target body with inside diameter of 14 mm. Figure 3-1 shows the ^{94m}Tc yield as a function of incoming proton beam energy up to 14 MeV (maximum energy for practical small cyclotron applications). The 14 MeV total thick target yield at saturation is 74 mCi /µA as compared to 117 mCi/µA for a pure Mo target as published by Rosch, et al (see reference 8, Chapter 2). This reduction in yield to 63 % is a reasonable concession to obtain the recoil escape into steam necessary to recover the radionuclide product. The yield recovered in the fluid is about 20 % of the total fiber target yield, which is reasonable. Based on this promising result, an extensive heat transfer analysis was performed on fiber target geometries.

Following the completion of the heat transfer analysis and preliminary design, it was decided to extend the fiber/steam yields of Figure 1 to the maximum extent of cross section data at 18 MeV (for completeness). As shown in Figure 2, the cumulative yield showed a decrease above 14 MeV (not physically possible unless the target has an excessive exit energy). In order to resolve this discrepancy, a much simpler analytical model based on solid Mo compared to homogenous mixtures of Mo/fluid was undertaken. A homogenous option of FIBTAR was also used for modeling the same cases. The resulting comparison is shown in Figure 3, showing that the Monte Carlo modeling gave good results for a solid target, but gave homogenous Mo/fluid results that were about ten times too low, and also turned down above 14 MeV. Figure 4 shows an expanded version of the homogenous Monte Carlo data, from which another discrepancy is obvious. The various fluids vary greatly in magnitude, where the analytical model fluids are tightly grouped as expected.

At this point, attention was directed back to the Monte Carlo Mo-fiber/steam modeling. Volumetric heating as a function of distance into the target was calculated from FIBTAR results as shown in Figure 5. Since stopping power increases as proton energy decreases, we expected an increasing heating rate as proton energies decreased with penetration. Since this was not the result, the same case was treated analytically for a homogeneous

target as shown in Figure 6. This shows heat generation increasing with penetration as expected, and a target length for 14 MeV down to 2 MeV proton energy of about 45 cm. The magnitude of volumetric heating is much less than the Monte Carlo fiber/fluid target, which had a corresponding length of only 4.3 cm (Figure 5). Figure 7 shows the FIBTAR-based heat generation result for a homogenous target, which indicates yet another inappropriate combination of shape, magnitude, and depth. Figure 8 compares the widely varying results of Figures 5 to 7. FIBTAR was reluctantly temporarily abandoned at this point, with the conclusion that the submicrometer fibers and very high porosities required by this design (not to mention the billions of histories required) will require extensive code modifications that are beyond the scope of this thesis. FIBTAR had worked in the past where fiber dimensions were in the several micrometer range for the nuclear reactions and target materials involved.

At this point, the Monte Carlo modeling was replaced with and analytical model shown in Figure 9, based on a unit cell with a 0.022 micrometer Mo layer followed by a 44.5 micrometer steam layer at 10 atm and 800 K (porosity = 0.9776). Target length is 45 cm. This configuration was used to recalculate the heat transfer model, resulting in the radial temperature profile shown in Figure 10. The 25°C temperature rise from bulk cooling water to the target centerline for a 1 μ A beam is based on averaging the volumetric heat generation rate over the length of the target. The target will easily tolerate a 10 µA beam. more than adequate to produce enough ^{94m}Tc-pertechnetate which for is radiopharmaceutical labeling. It is possible that the target pressure could be increased to 30 atmospheres, reducing target length to 15 cm. Fiber temperatures would be high enough to vaporize liquid water pumped into the target through small orifices in the walls and/or back. Using a HPLC pump (high pressure capability), water could be metered in at a controlled rate, expanded into steam, and removed through a small bore teflon tube (approximately 0.25 mm). The tube would provide an appropriate pressure drop to maintain the target at high pressure while providing a recovery delivery flow of a few hundred cm³/min without the use of a metering valve. Vaporization of the water by the hot fibers would also result in considerable evaporative cooling via the change in state. If nonenriched Mo or MoO₃ fibers become available, this design approach can be evaluated experimentally prior to beam testing.

In summary, the feasibility of an enriched ${}^{94}Mo(p,n)^{94m}Tc$ target to deliver ${}^{94m}Tc$ pertechnetate on-line has been established. The detailed choice of fiber size for a prototype target must await the revision of the FIBTAR Monte Carlo code to accurately model the high-porosity submicron fiber/steam configuration needed to construct an efficient prototype target for beam testing. As a parallel effort, the identification of an appropriate fiber material fabrication process must be accomplished. These steps must precede the construction and beam testing of a prototype target system.



Fig. 1. FIBTAR Monte Carlo model of fiber target to 14 MeV.



Fig. 2. FIBTAR Monte Carlo model of fiber target to 18 MeV.



Fig. 3. Comparison of solid Mo and homogenized Mo/fluid targets anlytically modeled with TRIM, and Monte Carlo modeled with FIBTAR.



Fig. 4. Homogenized Mo/fluid targets, Monte Carlo modeled with FIBTAR (not valid).



Fig. 5. Volumetric heat generation in a Mo-fiber/STEAM target Monte Carlo modeled with FIBTAR (not valid).



Fig. 6. Expected volumetric heat generation in a homogenized target.



Fig. 7. Volumetric heat generation in a homogenized Mo/steam target Monte Carlo modeled with FIBTAR (not valid).



Fig. 8. Comparison of volumetric heat generation in a Mo/steam target modeled three ways.



Fig. 9. Thick target yields of solid Mo and homogenized Mo/fluid targets analytically modeled with TRIM.



Fig. 10. Radial temperature profile for a Mo/STEAM target for 1 μA of 14 MeV protons.

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Gravity Can Offer Help: Stable Production of C-10 by Bombarding a Molten Sea of Boron Oxide with a Vertical Proton Beam.

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Why C-10

C-10-CO₂ has shown improved performance over ¹⁵O labelled water in the rendering of brain and kidney perfusion (I. Law et al, J. Cereb.Blood Flow Metab, 21, 1003-1012, M. Jensen et al, J Nucl Med, 41, 1363) but the actual use has been hampered by the long term instability of the target. The molten glass of enriched boron oxide slowly creeps out of the beam strike area under the action of gravity when using standard horizontal beam geometry. We have set out to investigate the use of a vertical beam on a molten horizontal target for C-10-CO₂ production.

How to make C-10

The production method and cross section are described by Alves (JARI 52,899ff). The method mimics old fashioned boron ¹¹C production, but in our case target temperature and release conditions have to be optimised because of the much shorter half life. Titanium was chosen for the crucible because of the high melting point and stability of the oxide (Common experience to anyone having tried to hard solder Ti, even using B₂O₃ as flux).

Methods

300 mg of B₂O₃ enriched to 99.5 % in ¹⁰B was melted as a homogeneous glassy disc into at Titanium crucible with an internal diameter of 14.9 mm, giving a target thickness of 172 mg/cm². The crucible was positioned in a stainless steel target canister with an internal volume of 90 cm³. The target was flushed with 99.996 % pure Helium with a flow of 200 cm³/min through a CuO converter CO-->CO₂ at 400°C and an NOX trap (T. Tewson, JARI 40,765ff), carrying the C-10-CO₂ through 10 meters of 1/16" Teflon tubing to an Ascarite trap mounted in a dose calibrator. Vertical proton beams at 15, 21 and 28 MeV were incident on the Boron Oxide surface. The beam diameter and profile was initially inspected with a beam viewer showing aprox. 10 mm FWHM diameter. This beam was collimated down to 8 mm directly in front of the target, yielding an almost uniform circular beam about 8 mm diameter.

Power balance

Only the target entrance window flange was water cooled. The target housing was allowed to heat up during bombardment until radiative and convective heat loss from the target canister surface (300°C?) balanced beam power input. A deliberately poor thermal contact between target crucible and target body allowed the radiative stabilisation of target surface temperature. Assuming black body cooling conditions the crucible reached 1500°C at our maximally tested beam power of 420 W (20 microA @21MeV).



10-CO2 Steady state

Yield

Release of C-10-CO₂ is a very steep function of beam power. Little variation was seen in yield across the tested energy range, consistent with the data of Alves, JARI 52, 899ff and the fact that the present B_2O_3 target is "thin" to the vertical beam (incident 21 MeV protons leaves at 17 MeV). The observed Ascarite trap yields were all decay corrected for a total of 70 sec delay (30 sec hold up in the target, 40 sec delay in converter, trap and tubing).

The best performance was obtained with 21.5 MeV @12 microA, where we found 46 % of the theoretical yield calculated from the Alves data. Both target and CuO converter temperatures were probably on the low side of optimum, and more improvement could be expected. The target was inspected after about 2 hours bombardment at currents between 10 and 20 microA. The Boron glass had lost less than 2 mg of mass. The glass still formed an integral disc in the crucible.
Optimisation Studies on the Production of High-Purity I-124 and I-120g at a Small-Sized Cyclotron

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Aims

The radionuclides ¹²⁴I ($T_{\frac{1}{2}} = 4.18$ d) and ^{120g}I ($T_{\frac{1}{2}} = 1.35$ h) are interesting positron emitting analogues of the therapeutic radionuclide ¹³¹I ($T_{\frac{1}{2}} = 8.0$ d) and the single photon emitting diagnostic radionuclide ¹²³I ($T_{\frac{1}{2}} = 13.2$ h), respectively. It has been shown that both ¹²⁴I and ^{120g}I can be produced at a small-sized cyclotron. However, several production parameters needed detailed investigations. The aim of this study was to optimise those parameters to be able to produce the two radionuclides in high purity.

Methods

The TeO₂-target technology and dry distillation method of radioiodine separation were studied. A target system involving He cooling in front and water cooling in the back was developed for medium scale production. The removal of radioiodine was studied differentially as a function of time. The integral loss of TeO₂ from the target was investigated as a function of oven temperature and time of distillation. A determination of the positron emission intensity in the decay of ¹²⁴I was done using a very pure source and comparing the intensities of the annihilation and X-ray radiation. Production of ¹²⁴I was carried out using 200 mg targets of 99.8 % enriched Te-124-O₂ on Pt-backing, 16 MeV proton beam intensities of 10 μ A, and irradiation times of about 8 h. For the production of ^{120g}I only a thin 30 mg target of 99.9 % enriched Te-120-O₂ was available. Irradiations were done with 16 MeV protons for 80 min at beam currents of 5 μ A. The radiochemical purity of both ¹²⁴I and ^{120g}I was checked via high performance liquid chromatography (HPLC), thin layer chromatography (TLC) and a few known iodinating reactions. Regarding the chemical purity, the Te content in radioiodine was determined spectrophotometrically.

Results

The TeO₂-target withstands 16 MeV proton beams up to 15 μ A. A distillation time of 15 min at 750°C was found to be ideal both from the viewpoint of radioiodine removal and TeO₂ loss. The positron emission branching in ¹²⁴I was exactly determined as 22.0 +/- 0.5 %. The batch yield of ¹²⁴I at EOB was 550 MBq (15 mCi). At the time of application the radionuclidic impurity ¹²³I (T_{1/2} = 13.2 h) was <1 %. The levels of other impurities were negligible (¹²⁶I < 0.0001 %; ¹²⁵I = 0.01 %). Special care was taken to determine the ¹²⁵I impurity via X-ray spectrometry. The ^{120g}I batch yield achieved at EOB was 700 MBq (19

mCi), and the only impurity detected was the isomeric state 120m I (T_{1/2} = 53.0 min) at a level of 4.0 %. The radioiodine collected in 0.02 M NaOH solution existed > 98 % as iodide. The amount of Te in all the radioiodine samples was found to be < 1 µg.

Conclusions

High purity ¹²⁴I and ^{120g}I can be advantageously produced on a medium scale using the low-energy (p,n) reaction at a small-sized cyclotron. The yield of ^{120g}I can be considerably increased by using a thicker taget.

The Present Status of a High Current Inclined Target and Solid Target Changer at Washington University

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Aims

Solid targets have gained great importance in nuclear medicine with the production of novel isotopes such as ⁷⁶Br, ⁷⁷Br, ¹²⁴I, ^{94m}Tc, ⁴⁵Ti and various copper isotopes. With limited beam time available on the CS-15 cyclotron to produce these isotopes, an automatic solid target changer for the JSW cyclotron has been designed and fabricated to be used in conjunction with a recently installed conveyor system for remote target retrieval.

An inclined target design has been described previously for use in the production of halogen isotopes (1). In-beam tests have been performed with this target to study the target material properties such that the maximum beam current could be determined. Present disk targets for the production of Br and I allow for irradiation up to a maximum of 5 microAmps of beam current.

Methods

The target changer comprises a target cassette that can hold up to six disk targets, or two disks combined with the inclined target described above. Target loading and unloading is under computer control, comprising a user-initiated predetermined sequence of steps. The control software includes multiple safety interlocks to ensure reliable target loading, irradiation, and unloading onto the conveyor. We anticipate testing the target changer on the JSW cyclotron in the next several months.

The inclined target (20 degrees) was prepared with [76 Se]Cu₂Se material by placing 70.8 mg of material into a Pt-coated depression of a tungsten target. The material was heated in an induction furnace to melt and adhere it to the platinum. The target was irradiated on four occasions at 2, 6, 10 and 13 microAmps for 10 minutes. The activity was monitored over several days to determine the amount of 76 Br produced.

Results

The production rate measured from the irradiations is 1.1+/-0.2 mCi/microAmp hour for ⁷⁶Br. This production rate is about 35 % of the predicted value from published cross-section data assuming a uniform spread of the target material over the inclined surface.

Additionally, the measured yield decreased monotonically with current. Experiments are planned to investigate the source of these discrepancies.

Conclusions

The results of the target irradiation show that with this target design, higher beam currents will be permissible compared to the conventional disk targets that are currently being used for the halogen isotopes. Further irradiation will be performed in order to determine if the beam current can be increased further.

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The Production of I-121 at the Vertical Beam-Line of the MC32NI Cyclotron at the DKFZ Heidelberg

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Introduction

Radionuclides of iodine have been widely used in nuclear medicine as tracers in diagnostics, therapy and research. Positron emitting iodine isotopes, i. e. ¹²⁴I ($T_{1/2} = 4.15$ d) and ¹²¹I ($T_{1/2} = 2.12$ h) have been requested by our PET group for labelling of specific carriers used in investigations of molecular mechanisms with short- and long-term dynamics. First work on ¹²¹I was done on enriched ¹²²TeO₂ in our institute using the former AEG compact cyclotron (22 MeV p, 11 MeV d) many years ago (Helus et al. 1979). This compound as well as metallic Te which we are using at present is prone to melt and may run off a perpendicular target under proton bombardment. Hence, the yield may vary substantially. We built a vertical beam-line at our Scanditronix MC32NI



Fig. 1. Design of the vertical beam-line (upper left) with 90° deflecting magnet (Scanditronix Magnet AB); sketch and picture of target body with water cooled entrance flange (right);



cyclotron (32 MeV p, 16 MeV d) where meltable samples can be irradiated in horizontal position without the risk to escape from the beam spot (Fig. 1).

Aim

This feasibility study aimed at collecting data and experience in optimizing the target and procedures. Ultimate goal is to achieve reproducible yields over long irradiation times at elevated beam currents.



Fig. 2. Decay curves taken with dose rate monitor of the 17.7 and 21.5 MeV protons on 128 Te/ 122 Te mixture (left).

Temperature dynamics in the target body (lower left).

Target crucible showing beam spot with covering net aside. This carries some small crystals of sublimated Te (lower right)



Materials and methods

Target design: The target housing is made from stainless steel (Fig. 1). It contains a platinum crucible filled with metallic Te covered by a platinum net to prevent loss of material by sputtering (Fig. 2). Te has a lower melting point (452° C) and higher atomic density compared to TeO₂ (m.p. 760°C). The target bottom is warmed up to 400°C by a temperature-controlled heater and the beam current. At operating temperature the upper part of the target assembly acquires about 220°C, just above the sublimation point of iodine (185°C).

Radiochemistry: The volatile iodine is flushed to a NaOH receiver or a cold trap by warm helium, which prevents oxidation of Te during bombardment. To save cost, we used a 50 mg/1000 mg mixture of 99.6 % enriched ¹²²Te/¹²⁸Te (euriso-top) in preliminary experiments and recalculated the yield to 100 % ¹²²Te. ¹²¹I is probably produced most effectively via ¹²²Te(p,2n) in analogy to the ¹²⁵Te(p,2n)¹²⁴I reaction investigated recently by Hohn et al., 2001. The proton energies on target were set to 17.7, 21.5 and 26 MeV around the expected cross-section maximum.

Results

- Variation of the He flux showed a distinct maximum at 40 ml/min.
- At 17.7 MeV on target , 1 μ A the yield at EOB was approximately 3.2 mCi/ μ Ah; at 21.5 MeV, 1 μ A the yield rose to 9.4 mCi/ μ Ah inline with earlier results (F. Helus 1979)
- The platinum net covering the crucible turned out to be very essential to minimize losses by evaporation of Te (Fig. 2).

Outlook

Next steps will focus on optimizing the energy window with respect to yield and radionuclidic purity and the estimation of the radiation burden from the daughter nuclide 121 Te (EC, 16.8 d).

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Subliming Activity from White Hot Targets. A General Method, Tested and Rationalized by ¹⁰C Production

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Introduction

Release of product radioactivity during bombardment is often regarded as one of the many perils threatening the target chemist. In fortunate cases, this release can be turned in to good use, not only providing steady state supply of ultra-short lived radionuclides beyond the reach of batch processing, but also offering elegant and maintenance-lean possibilities of in-target separation. Among the mechanisms used for release, heat is by far the most popular method. From early internal target probes with activity detection on the cyclotron fore-pump outlet to the state of the art targetry for on-line isotope-separators, the method is perhaps more used than it is understood.

Theory

Transport and release of a tracer formed in the interior of a solid target matrix follows an Arrhenius temperature relationship, dominated by diffusion as characterized by $D = D_0 \exp(-E_a/kT)$. Charged particle reactions deposit the initial radioactive product distribution into the depth of the solid target matrix. This profile follows the energy dependence of the excitation function $\sigma(E(x))$, from the surface to a Q-dependent depth where the cross section goes to zero, generally a few hundred microns in. This diffusion path length to the surface, x_0 , represents a diffusion time t of the order of x_0^2/D , greatly favoring shallow grazing angles or finely divided powder targets and incandescent temperatures. The decay losses during this diffusion voyage results in the log-log relationship between the activity arriving at the surface A and the initial activity A_0 deposited at depth, x_0 such that:

(1)
$$\ln [D_o/\lambda x_o^2] + \ln \ln (A_o/A) = E_a/kT.$$

At the surface, a sweep gas can entrain the sublimed activity for tuned pipeline transport to the distant collection sites. The initial activity A_0 is proportional to the neutron counting rate, an easily observable measure of the true target nuclear yield. The recovered activity A becomes a steep function of target temperature, often tempting the designer to use the beam for target heating. Typical target performances for the known examples of heat-release (p,n) reactions are listed in Table 1 below, with expected yield A_0 at EOSB on 100 % enriched elemental material.

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Reaction	<u>t1/2</u>	<u>Target</u>	<u>mp (°C)</u>	A _o (EOSB)
${}^{10}B(p,n){}^{10}C$	19 sec	$^{10}B_2O_3$	473	10 mCi/µA @ 11 MeV
${}^{11}B(p,n){}^{11}C$	20 min	$^{nat}B_2O_3$	473	93 mCi/µA @ 11 MeV
$^{12}C(d,n)^{13}N$	10 min	С	3400 (subl)	$25 \text{ mCi/}\mu\text{A}$ @ 7 MeV
76 Se(p,n) 76 Br	16 hr	⁷⁶ Se	217	$37 \text{ mCi/}\mu\text{A} @ 11\text{MeV}$
124 Te(p,n) 124 I	4.2 d	124 TeO ₂	733	$36 \text{ mCi/}\mu\text{A} @ 11 \text{MeV}.$

We have observed the above derived relationship (1) for thermally driven target release in the case of ultra short lived ($t_{1/2} = 19 \text{ sec}$) ^{10}C formed in molten boron oxide glass. The target temperature in the beam strike was monitored by the use of an IR thermocouple (Exergen IRtc.3AMF), with germanium optics (helium-swept target window, lenses) to pass the necessary 8-12 μm wavelengths. The extraction efficiency $e = A/A_o$ is proportional to the ratio of the trapped activity (eg. $^{10}\text{CO}_2$ in soda lime) to the measured neutron counting rate. If ln ln 1/ ϵ is plotted against 1/T , the proposed relationship should yield a straight line, as shown in Fig. 1 below.



In spite of the scatter due to crowbars and fluidic irregularities in the boiling ${}^{10}B_2O_3$ melt, the log-log relationship is evident, with a steep slope indicating a diffusion enthalpy that suggests bulk convection effects, such as noted by Beyer and Pimentel (Radiochim Acta **88**, 175 (2000)).

Harvesting radionuclides from incandescent solid or molten targets poses a set of serious challenges to the target chemist. Their successful resolution will provide new feedstock for applications ranging from PET imaging to radioactive ion beams for nuclear

astrophysics. A theory allowing a first-principle calculation of the necessary operating point is the now available.

Methods

Carbon-10 dioxide is used as an example of fast sublimation because of its potential importance in the PET imaging of regional blood flow (I Law, et al: J Cereb Blood Flow Metab 21, 1003-1012 (2001)). The yield from the ${}^{10}B(p,n){}^{10}C$ reaction (Alves et al: Int J Appl Rad Isotopes 54, 899-903 (2000)) favors high proton energy and thick targets of elemental ¹⁰B, while successful sublimation from the target substrate strongly favors the use of the molten boron oxide. To maintain the molten glassy target material in a horizontal beam (see Jensen et al: Gravity can offer help: Stable production of ¹⁰C by bombarding a molten sea of boron oxide with a vertical proton beam; these Proceedings). the enriched boron oxide is sintered onto a woven mesh angled at 30° to the horizontal. Mesh materials include rhenium, molybdenum, Monel and 304 stainless steel, ordered in preference, based on their refractory nature and inertness to the melt. The mesh, spot welded to a stainless support tube, is thermally cantilevered away from contact with the water-cooled target housing, shown in Figure 2, in order to allow its surface temperature to reach white heat with the dissipation of several hundred watts of beam power. The helium gas flow enters upstream of the beam strike, serving to clear any condensate from a germanium window, coated to pass the 8-12 micron infra red on to a focussed IR thermocouple that monitors the surface temperature of the melt. The IRtc was calibrated by simultaneous measurement against a conventional thermocouple in the beam. The helium stream then passes, or around, through the molten boron oxide and leaves the target through a 1/16" SS tube (0.020" ID) for a 10 second tranport to the traps and furnaces of the chemical processing station, shown in Figure 3.



Fig. 2. Target chamber for the production of $^{10}CO_2$.



Figure 3. Schematic of the flow-through chemical processing of $^{10}CO_2$.

First the contaminating ¹³NO_x is removed by an indicating trap of silica gel, treated with $CrO_3 + CuSO_4$ (T Tewson et al: Int J Appl Rad Isotopes **40**, 765-768 (1989)). The approximately even split between ¹⁰CO₂ and ¹⁰CO is evident in gas chromatography as well as the trapping efficiency of the activity in soda lime. For this reason, the CuO furnace at elevated temperature insures that the label will be in the form of ¹⁰CO₂ for patient administration. Recent work has succeeded in cryotrapping the ¹⁰CO₂ for pulsed inhalation, as well as trapping the majority of the activity in 0.155 mM NaOH across a dialysis membrane for subsequent neutralization to injectable saline. This work presages studies to determine whether a spike input may be preferable to the steady state administration of ¹⁰CO₂ in cerebral activation studies.

As an independent investigation of the sublimation of labeled CO₂ from boron compounds at high temperatures, ballistic thermochromatography was performed on proton-irradiated natural boron compounds. After bombardment, the elution of ¹¹CO₂ into a helium stream was followed, as the temperature was ramped linearly from room temperature to 1100° C in a muffle furnace. The release of ¹¹C-activity was dramatic for B₂O₃ and its hydrated form H₃BO₃ at 280°C, but barely perceptible for the refractory elemental boron, BN, B₄C₃ and AlB₂. This behavior was fit to a STELLA (High Performance Software,Lyme, NH) model searching for the diffusion constants, but confounded by imperfect knowledge of the grain size distribution.

Conclusions

Nearly eighty years ago, the pioneering cyclotron chemists (Calvin et al: Isotopic Carbon, John Wiley and Sons, New York, (1949)) were boiling $^{11}CO_2$ away from B_2O_3 cyclotron targets. Today, new radioisotopes enter new applications, ranging from the basic to the life sciences. Nuclear engineers study radiation enhanced diffusion that embrittles fusion reactor walls. Nuclear astrophysicists coax short-lived radionuclides out of primary targets become radioactive ion beams, mimicking the stellar interior of supernovae. For the biological scientist, Table 1 lists just a few of those candidates for which ready access from incandescent targets would be welcome.

Some Aspects on Tellurium Targets for Iodine-123 Production

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It is well known that ¹²³I is one of the best radionuclides for medicine. V.G. Khlopin Radium Institute cyclotron MGC-20 gives protons with the energy of 2-18 MeV. At these conditions we can use only proton irradiation of ¹²³Te to produce iodine-123. Tellurium-123 dioxide used to prepare the target is not a convenient material. It is not firm under proton bombardment, it takes special measures to attach to the platinum background, it remains radioactive a long time after irradiation; besides, it should be of high enrichment on ¹²³Te. For more than 10 years we have tried to investigate some questions, part of which may be of interest for iodine-124 production too.

Target preparation

Tellurium target is prepared by a well known method of tellurium dioxide melting on a platinum plate. The key point here is attachment of tellurium dioxide to platinum. It is very important to have a high chemical purity of the starting material. Also very important to make a background surface rough enough. Some authors scratches the surface, others makes special profile of the plate bottom. We are preparing background surface by acid (hydrochloric and sulphuric) pickling, and we try to use not new platinum foil for background.

Target regeneration and purification

Enriched tellurium-123 is rather expensive material, so it is important to collect all losses of tellurium (from extraction device, after accidents with the target) and to recover tellurium-123. Tellurium regeneration and purification method is based on TeO₂ volatility at high temperature. Technology includes stages of evaporation and dissolving [1]. The procedure of purification allows to obtain high quality TeO₂ suitable for iodine-123 production. Tellurium losses during purification are 3-5 %.

Radionuclide purity dependence on tellurium-123 enrichment

It is well known that the highest radionuclidic purity for iodine-123 may be achieved by proton irradiation of Xenon-124 as a target. We have made efforts to improve radionuclide purity for iodine 123 produced via proton irradiation of tellurium-123. We have started our activity with tellurium-123 enrichment >95 %. Then we employed starting material more high quality – 98.5 % and 99.3 % enrichment. For tellurium-123 enrichment of more than 95 % there is only impurity of iodine-124. On the face of it, there is no limitation to get radionuclidic purity (RNP) close to 100 % with the increasing tellurium-123

enrichment. Actually, it is easy to show that there is a relation between RNP and content of tellurium-124 in the target:

$$\text{RNP} = \frac{\text{A}_{123}}{\text{A}_{123} + \text{A}_{124}} \times 100\% \approx (1 - \frac{\text{A}_{124}}{\text{A}_{123}}) \times 100\%$$

where A_{124} is iodine-124 impurity activity and A_{123} is iodine-123 activity.

In the case of tellurium target irradiation during t hours at the proton energy of E_p we have at the end of bombardment (EOB):

$$\frac{A_{124}}{A_{123}} = \frac{C_{124}}{C_{123}} \times \frac{(1 - \exp(-\lambda_{124} \times t))}{(1 - \exp(-\lambda_{123} \times t))} \times F(E_p)$$

 $\begin{array}{ll} \lambda_{124}, \lambda_{123} & - \mbox{ are constants of decay for iodine-124 and iodine-123,} \\ F(E_p) & - \mbox{ is a function of proton energy} \\ For t=1 \mbox{ hr} \end{array}$

$$\frac{A_{124}}{A_{123}} = \frac{C_{124}}{C_{123}} \times 0.136 \times F(E_p)$$

And for E_p constant $F(E_p) = F$

$$\frac{A_{124}}{A_{123}} = \frac{C_{124}}{C_{123}} \times 0.136 \times F$$

Fitting to experimental data gives F ≈ 1.0 . This formula shows: diminution of tellurium-124 content should lead to the decrease of iodine-124 impurity. But it appeared that the decrease of the tellurium-124 content in 50 times decrease the impurity only in 15 times. We can propose that there is another reaction for iodine-124 production - $^{123}\text{Te}(p,\gamma)^{124}\text{I}$ [2]. An estimation of the RNP limitation reached by diminution of tellurium-124 content gives us 99.983 (for Ep = 15 MeV, irradiation time of 1 hr and tellurium-123 enrichment of 99.3 %). Thus it is not necessary to get tellurium-123 with very high enrichment for iodine-123 production.

Target activitation

It is important to investigate target activation under particle beam bombardment. It is especially important in the case a manual target operation (without manipulators) to reduce occupation dose. There are three stages of iodine-123 technology where target activity is essential.

- *First* Iodine-123 production technology demands manual positioning of the irradiated target into the extraction tube.
- *Second* The same target is usually used for iodine-123 production for many times. So it will accumulate activity in spite of iodine extraction and manual target positioning into the target device becomes dangerous.
- *Third* Telurium-123 dioxide is an expensive material. During proton irradiation its purity may by deteriorated by ion implantation for instance (aluminum atoms and clusters knocked out by beam from window before target) and target may have mechanical damage. Moreover small amount of target material is evaporated into the iodine extraction device every extraction. That material may by gathered from the device and used for target preparation again. It is preferable that target material regeneration and purification, as well as following target preparation are realized at low activity.

We have investigated activities of targets used to produce iodine-123 via proton irradiation of tellurium-123 dioxide. The main results are:

- 1. Target activity after iodine extraction is mainly conditioned by gamma-radiation of aurum isotopes and of tellurium isomers. Aurum isotopes Au-194, 195, 196, 198 are produced through ^{nat}Pt(p,n) reaction; tellurium-123m is a result of inelastic proton scattering; tellurium-121m is obliged to ¹²²Te(p,d) reaction.
- 2. Right after irradiation backing activity is obliged to 194 Au.
- 3. Right before target positioning in the target device target activity is determined by decay of isotopes produced in the target during previous irradiations. At periodic irradiations there are different contributions to the total activity from tellurium dioxide and from separate backing isotopes depending on frequency of irradiations.
- 4. When the target is "cooling" for more than 6 weeks its activity is being determined by ¹⁹⁵Au and ^{123m}Te independently from the "history".

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Remote and Automated Solvent Extraction of Gallium-66

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We are now producing a number of non-conventional positron emitting nuclides for potential use in nuclear medicine at Washington University. The positron-emitting radionuclide ⁶⁶Ga ($t_{1/2} = 9.49$ h; β^+ 56.5 %; EC 43.5 %) can be used as a substitute for the photon emitter ⁶⁷Ga in a large number of labeled compounds. Gallium-66 has potential for radiopharmaceutical labeling in PET imaging and for targeted radiotherapy of cancer. The production of large quantities of ⁶⁶Ga requires the development of a remote/automated system for the routine processing of large quantities of this radionuclide.

A solid target holder designed and built for the cyclotron production of 64 Cu ${}^{[1]}$ is used to hold a thin zinc foil. This foil is mounted on a 1-cm diameter threaded platform in the center of an aluminium target disk and held in place with a 1-cm diameter aluminum screw cap with a 6-mm diameter window in the center. A depression in the back of the disk provides efficient cooling during irradiation with water flowing through it. 66 Ga is produced by the 66 Zn(p,n) 66 Ga nuclear reaction, by irradiating this thin zinc foil with 14.5MeV protons using a Cyclotron Corporation CS-15 cyclotron.



Fig. 1. Solid Target Holder and Foil Target Holder

Gallium-66 is purified by an ether extraction method. Briefly, the irradiated zinc target material is dissolved in 12 M HCl and subsequently diluted to 7 M HCl. The diluted sample is extracted three times into diisopropyl ether. The organic phases are combined and washed once with a small amount of titanium chloride to reduce the Fe³⁺ ion contaminants. A second wash with 7 M HCl removes any traces of Zn and Cl ions. Finally, ⁶⁶Ga is recovered by three back-extractions into milliQ water. The final product is evaporated to dryness and resolubilized into 150 μ L 0.05 M HCl. In the work by Lewis *et al.* ^[3] this purification procedure was shown to be superior to purification by cation-exchange chromatography in terms of processing time, concentration of stable contaminants and radiopharmaceutical labeling yields. We have now designed a remote system to perform these purification steps.

The inherent differences in the electrical conductivity of each layer of the biphasic system are the basis for our automated extraction system. Two electrodes immersed in the biphasic solution are capable of detecting the presence or absence of the highly conductive aqueous medium. Two gold wires extending to the bottom of a conical-bottom plastic tube are used as the electrodes. Using a digital voltmeter as a preliminary setup, the transition between the two-phase aqueous/ether mixture to a single-phase ether solution can be detected during the course of multiple back-extractions. Preliminary data collected, using a 9V battery, has shown that the potential difference between the aqueous and organic layers is sufficiently large to detect the end point of extraction. Mosaic Industries' (Newark, CA) components ("Quick Easy Design" QED package, QED boards and stepper motors) have been selected to implement the remote extraction of the different layers. A touchscreen front panel system, the Panel-Touch Controller[™], with a QED-Flash board has been chosen to interface with four small stepper motors mounted on two printed circuit boards. This powerful real-time controller includes a graphical user interface, 48 analog and digital I/O lines, eight 12-bit A/D inputs. Two digital I/O boards control the motors. These four stepper motors activate the syringes for liquid displacement. The QED board and two small resistors are set to read the voltage. Built-in software is being used to specify the different parameters during extraction.



Fig. 2. Schematic of the Automated System.



Fig. 3. Mosaic Industries Components.



We are currently making progress on the electrolytic deposition of Zn material on a

Fig. 4. Preliminary Data – Experimental Potentials.

solid target. This will permit the recovery of this target material. The electrolyte for Zn plating is a ZnCl₂ solution at pH = 5-6, which has a small amount of hydrazine hydrate (NH₂NH₂) added as a depolarizer. Final Zn concentration of the electrolyte is ZnCl₂ = 0.46 M. Approximately 7-8 mL of electrolyte is needed to plate an area of ϕ 10mm on a gold target and approximately 2-3 mL of electrolyte is needed for an area of ϕ 5mm. Following a method from P. Van den Winkel *et al.*^[2] constant current electrolysis technique is used to deposit the target material at a constant rate. A single bipolar chopped sine wave is the desired waveform for the zinc electrodeposition. Preliminary plating experiments using natural Zn target material on large and small solid gold disks showed promising results: the electroplated material was evenly distributed with no obvious dendrite formation, of a shiny metallic coloration and appeared to be well adhered to the substrate.



Fig. 5. Electroplating Setup.



Fig. 6. Chopped Sine wave.

- Bipolar chopped sawtooth (f_{st} = 100 Hz)
- Chopper frequency ($f_{ch} = 1000 \text{ Hz}$)
 - Net cathodic constant current



 $(160.2 \text{ mg/cm}^2, 4 \text{ h plating})$

Fig. 7. Plated Zn target.

To test the adhesion between the gold disk and the zinc layer, the above plated Zn target (figure 7) was irradiated for 5 minutes at 10 μ A. Its appearance remained unchanged. However at a higher proton beam current of 15 μ A during a 5 minutes irradiation, the plated materiel volatilized. The porosity of the electroplated Zn material needs to be reviewed for higher beam current.

In conclusion, preliminary results show that using the ionic strength of aqueous layers for the solvent extraction is a dependable way to identify a good separation of phases. The combination of voltage level, with sufficient duration between measurements, provides a reliable method to delimit the overall layer endpoint during the extraction process. Careful implementation of remote and automated processes will reduce the amount of mechanical and quality control variation and decrease the radiation dose to personnel.

Acknowledgments

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Preparation of Carbon-13 Target Material from C-13-Benzene

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Summary

In an effort to prepare an improved carbon-rich target material for the accelerator production of N-13-labelled ammonia, pyrolyzed C-13-enriched sulfonated poly(styrene/divinylbenzene) has been under investigation. The preparation of this target material using naturally abundant carbon-12 was investigated in order to optimize conditions for the preparation of the analogous carbon-13-target material which may provide a cost-effective method for producing nitrogen-13 via proton irradiation. Porous C-13-enriched poly(styrene/divinylbenzene) was synthesized in four steps starting from C-13-benzene. Sulfonation and pyrolysis of the copolymer has been accomplished to afford a carbon-13-rich target material.

Introduction

For the purpose of improving nitrogen-13 production for use in medical imaging, pyrolyzed C-13- enriched sulfonated poly(styrene/divinylbenzene) has been under investigation. In order to prepare the C-13-enriched copolymer, the corresponding styrene monomer was synthesized in three steps starting from C-13-benzene in approximately 50 % yield¹ and polymerized by emulsion polymerization using divinylbenzene (DVB) as a cross-linking agent² (Fig. 1).



Fig. 1.

Cross-linking with DVB, and the addition of sulfonic acid groups on the styryl ring³ impart strength and thermal stability to the polymer for the pyrolysis stage which involves heating the material from room temperature to 800°C at a rate of 0.5°C/min. to afford a carbon-rich matrix (Fig. 2).



Fig. 2

Initially, styrene, prepared using naturally abundant carbon-12-reagents, was polymerized by suspension polymerization to afford small, spherical, glassy beads that were functionalized and pyrolyzed. Carbonized beads ranging from approximately 1-300 μ m in size were evaluated with deuteron irradiation.⁴ As anticipated for beads of these sizes, the recovered nitrogen-13 yields at end of bombardment (EOB) were low suggesting that a high fraction of the produced nitrogen-13 remained in the carbon particles. The problem of low recoil fraction should now be alleviated through the use of emulsion polymerization which is used to create macroreticular polymers. The porous structure may allow for escape of the produced nitrogen-13, thus increasing the yield at EOB.

Experimental

General

When required, glassware and cannula were flame-dried prior to use. NMR spectra were recorded on a Bruker AC 250 MHz FT-NMR spectrometer. GC analyses were performed on a Gow-Mac Gas Chromatograph Series 350 equipped with a Thermal Conductivity Detector using a 20 % DC 200 on Chrom.-P 80/100 mesh column. All yields reported in the C-13-styrene synthesis were determined by GC and corrected for purity.

$[^{13}C_6]Bromobenzene^1$

To a 250-mL pear-shaped flask equipped with magnetic stirbar and condenser with drying tube attached were added [$^{13}C_6$]benzene (4.94 g, 58.8 mmol), freshly distilled dichloromethane (70 mL), triflic acid (99⁺ %, 5.03 g, 33.5 mmol), and 1,3-dibromo-5,5-dimethylhydantoin (DBMH) (9.73 g, 34.0 mmol). During the addition of the DBMH, the

flask was covered with aluminum foil. The cloudy, yellow mixture was allowed to reflux in the dark for 2 h. A saturated solution of sodium bisulfite (35 mL) was then added to the product mixture until the amber organic layer was decolorized, and the mixture was neutralized with aqueous sodium carbonate (60 mL, 2 <u>M</u>). The organic layer was separated, and the aqueous layer extracted with dichloromethane. The combined organic extracts were dried over magnesium sulfate and distilled to afford 7.47 g of $[^{13}C_6]$ bromobenzene (77.9 % yield, 96.7 % GC purity); ¹H NMR: δ 7.50 (m, 2H, *ortho* H's), 7.25 (m, 3H, *meta* and *para* H's).

$\int^{13}C_6$ sec-Phenethyl Alcohol¹

Magnesium turnings (3.30 g, 138 mmol), a crystal of iodine, and a magnetic stirbar were placed in a flame-dried 100-mL three-necked round-bottomed flask equipped with thermometer, reflux condenser, and addition funnel. The apparatus was then carefully flame-dried again, and kept under an argon atmosphere. Ether (21 mL) was introduced to the flask through the addition funnel by cannula. [13C6]bromobenzene (4.45 mL of mixture, 4.30 mL, 40.8 mmol) was transferred to the funnel via cannula and carefully added to the mixture at room temperature. The beginning of the reaction was evidenced by the disappearance of the iodine color which changed from light yellow to gray, then finally to dark brown. The flask was placed in a warm water bath to induce reflux. After 30 min. of continuous reflux, the mixture was placed in an ice bath and allowed to cool to 0° C. To the addition funnel was added a mixture of ether (7 mL) and acetaldehyde (5.0 mL, 89 mmol) by cannula. The acetaldehyde solution was slowly added to the mixing Grignard reagent over a 63 min. period with the temperature held below 15°C. The reaction mixture then became milky yellow and viscous. Ice water was added to quench the reaction, and the magnesium salts were dissolved with 15 % sulfuric acid. The organic layer was separated, and the aqueous layer extracted with diethyl ether. The combined organic layers were dried over magnesium sulfate and concentrated in vacuo to yield 4.31 g of $[{}^{13}C_6]$ sec-phenethyl alcohol (82.6 % yield, 89.8 % GC purity); ¹H NMR: δ 7.30 (m, 5H, Ar H's), 4.85 (g, 1H, methine H), 2.10 (s, 1H, OH), 1.40 (d, 3H, CH₃).

$[^{13}C_6]$ Styrene¹

 $[^{13}C_6]$ sec-Phenethyl alcohol (4.55 g mixture, 4.08 g, 31.9 mmol), potassium bisulfate (0.28 g), copper metal (0.08 g), and hydroquinone (spatula tip) were added to a 15-mL pearshaped flask equipped with short-path distillation apparatus with thermometer, and magnetic stirbar. The flask was wrapped with aluminum foil and placed in an oil bath. With a vapor temperature <150°C and oil bath temperature >200°C, the distillate was collected. The organic layer was separated, and the aqueous layer extracted with diethyl ether. The combined organic phases were dried over magnesium sulfate and concentrated to give 2.54 g of $[^{13}C_6]$ styrene (72.4 % yield, 81.7 % GC purity); ¹H NMR: δ 7.69 (m, 2H, *ortho* H's), 7.53 (m, 3H, *meta* and *para* H's), 6.99 (dd, 1H, CH), 6.03 (dd, 1H, H *cis* to ring), 5.15 (dd, 1H, H *trans* to ring).

$[^{13}C_6]$ Poly(Styrene/38 % DVB)²

Freshly distilled [$^{13}C_6$]styrene (0.80 g, 7.3 mmol), divinylbenzene (1.05 g containing 45 % ethylvinylbenzene, 4.25 mmol DVB), and sorbitan monooleate (0.45 g) were added to a 1-L plastic commercial reagent bottle equipped with an overhead stirrer. The bottle was covered with plastic wrap. Potassium persulfate (0.15 g) was dissolved in deionized water (77 mL), and the solution was added dropwise to the reagent bottle with stirring. A white,

creamy emulsion formed. The stirrer was removed, and the bottle was loosely capped and placed in a 50°C oil bath overnight. After heating, the creamy emulsion had hardened into a porous, white solid. The solid was chipped out of the bottle in 1 cm³ blocks, oven-dried at 40°C overnight, then washed with isopropanol (250 mL) using a Soxhlet extractor and oven-dried at 40°C overnight to afford [$^{13}C_6$]poly(styrene/38 % DVB) (0.64 g, 35 % yield).

$[^{13}_{-}C_6]$ Poly(Styrene Sulfonic Acid/38 % DVB)³

 $[^{13}C_6]$ Poly(styrene/38 % DVB) (0.59 g) and a catalytic amount of silver sulfate were added to a three-necked 500-mL round-bottomed flask equipped with thermometer, addition funnel containing chlorosulfonic acid (15 mL), and rubber stopper with exit valve. The acid was added to the contents of the flask with stirring, and the reagents were allowed to stir for 3 h at 100°C. The mixture was then allowed to cool with stirring overnight. The copolymer was washed with deionized water until a neutral pH was attained, then dried overnight at 100°C. In order to determine the extent of sulfonation, the exchange capacity was measured by titration of hydrochloric acid, generated by potassium exchange with the sulfonic acid proton.⁵ [$^{13}C_6$]Poly(styrene sulfonic acid/38 % DVB) (0.021 g) was washed with aqueous potassium chloride (4.3 mL, 1.0 <u>M</u>) for 1 h, and the solid was collected by vacuum filtration. Sodium hydroxide (0.95 mL, 0.050 <u>M</u>) was used to titrate the filtrate, and the exchange capacity was calculated (2.2 mol/kg, approx. 41 % sulfonated).

Pyrolysis of $[^{13}C_6]$ *Poly*(*Styrene Sulfonic Acid*/38 % *DVB*)⁶

 $[^{13}C_6]$ Poly(styrene sulfonic acid/38 % DVB) (0.36 g) was weighed into an alumina boat and placed in a quartz tube furnace. The furnace was purged with argon to maintain a slight positive pressure, and the argon was released into a hypochlorous acid trap. The copolymer was heated from room temperature to 800°C at a rate of 0.5°C/min., held at 800°C for 1 h, and then allowed to cool to room temperature under argon. This afforded 0.16 g (approx. 60 % yield) of carbonaceous material.

Conclusion

C-13-enriched poly(styrene/38 % DVB) has been synthesized in four steps starting from C-13-benzene. The copolymer has been sulfonated and pyrolyzed to afford a porous carbon-13-target material. The material's packing density (0.30 kg/L) was determined by placing a weighed sample into a stainless steel cylindrical device with a hollow center, closed on one end, gently inserting a stainless steel plug into the opening, and measuring the volume with a vernier caliper. As anticipated, the packing density of porous poly(styrene/DVB) made by emulsion polymerization is significantly lower than that of glassy poly(styrene/DVB) made by suspension polymerization.⁷ It is anticipated that the porous C-13-matrix will allow for greater yields of N-13-labelled ammonia at EOB due to a higher recoil ion escape.⁸

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High-energy Irradiations of Solid and Gas Targets

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A New Method for Cu-64 Radioisotope Production Theoretical and Experimental Results

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Aims

⁶⁴Cu is a radioisotope of great interest for PET and radiotherapy. It decays by the emission of β⁺ (17.4 %), which allows PET imaging, and by the emission of β⁻ of 0.579 MeV (39 %) making it especially suited for targeted radiotherapy. Moreover, its half-life of 12.7 h matches the requirements for a reasonable uptake of larger tumour targeting molecules like monoclonal antibodies or antibody fragments. The therapeutic potential of Cu-64 has been demonstrated in a colorectal tumour-bearing hamster model where complete tumour regression could be achieved with therapeutic doses of ⁶⁴Cu-labelled mAb 1A3 without observed toxicity. In clinical PET using Cu-64-TETA-Octeotide the compound showed high sensitivity in lesion detection of neuroendocrine tumours with favourable dosimetry and pharmacokinetics.

Methods

Several production methods have been investigated for the production of this radioisotope, such as those using neutron irradiation of Cu and Zn (natural or enriched targets) and also proton beam irradiation of an enriched ⁶⁴Ni target. The latter method yields a high specific activity product, however ⁶⁴Ni is obviously very expensive. Irradiation with neutrons is nowadays problematic since the nuclear reactors are shutting down one after the other. The new method for N.C.A ⁶⁴Cu production (where also ⁶⁷Ga radioisotope of medical interest is produced) based on natural Zn irradiated with deuterons (19 MeV) is promising and preliminary results have been already presented elsewhere.

Results

In this paper we compared experimental thick target yield of the ⁶⁴Cu and other produced radioisotopes with the calculated results obtained using Monte Carlo simulation of the excitation functions and the stopping power. The table below shows a good agreement between the experimental and the theoretical results.

Conclusion

This paper presented experimental and theoretical results of a new method for the production of N.C.A ⁶⁴Cu radioisotope. Using the same theoretical approach, an investigation for deuteron irradiation of enriched Zn is planned for further improvement of the purity of the ⁶⁴Cu radiochemical product.

Radioisotope	Half life	Nuclear Reaction	Theoretical	Experimental
	(h)		Yield	Yield (MBq/µAh)
			(MBq/µAh)	
64 _{Cu}	12.7	64Zn(d,2p), 66 Zn(d,2p2n),	24,171	30,821
		⁶⁷ Zn(d,2p3n), ⁶⁸ Zn(d,2p4n)		
61 _{Cu}	3.4	64Zn(d, 2p3n)	163,733	104,007
67 _{Cu}	61.9	⁶⁷ Zn(d,2p), ⁶⁸ Zn(d,2pn),	0	Not det.
65 _{Zn}	5863.2	⁶⁴ Zn(d,p), ⁶⁶ Zn(d,p2n),	0,276	0,481
		64Zn(d,n) and b+ decay		
69m _{Zn}	13.8	⁶⁸ Zn(d,p)	26,557	14,504
66 _{Ga}	9.4	$^{66}Zn(d,2n), ^{67}Zn(d,3n),$	101,426	138,38
67 _{Ga}	78.3	$66_{Zn(d,n)}, \overline{67_{Zn(d,2n)}},$	19,010	16,28
		68Zn(d,3n)		

Excitation Functions of Proton Induced Reactions on Enriched Rb-85 up to 100 MeV: Yields of Sr-82 and Sr-83

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Aims

The radionuclide ⁸³Sr (T¹/₂ = 32.4 h) is a positron emitting analogue of the pure electron emitting therapeutic radionuclide ⁸⁹Sr (T₁/₂ = 50.5 d). The radionuclide ⁸²Sr (T₁/₂ = 25.5 d) is widely used for preparing the ⁸²Sr/⁸²Rb positron emitting generator system. The cross section data base for the formation of both ⁸³Sr and ⁸⁵Sr was rather weak. The aim of this work was to determine the excitation functions of all the (p,xn) reactions on ⁸⁵Rb up to 100 MeV and to calculate therefrom the integral yields of ⁸³Sr and ⁸²Sr as well as the level of the long-lived impurity ^{85g}Sr (T₁/₂ = 64.9 d).

Methods

Excitation functions were measured by the coventional stacked-foil technique. Thin samples of 99.4 % enriched ⁸⁵Rb-chloride were prepared by sedimentation on copper foils. Irradiations with protons up to 45 MeV were done at the CV28 and injector of COSY at Jülich, up to 71 MeV at PSI (Villigen), and up to 100 MeV at the cyclotron of NAC (Faure). The beam current was measured via monitor reactions. The radioactivity of the products was determined using high-resolution gamma-ray spectrometry. In the case of ⁸²Sr, a high-performance liquid chromatographic separation and X-ray spectrometry were also applied. The cross sections were calculated using the well-known activation equation. From the measured excitation functions the integral yields of ⁸³Sr, ⁸⁴Sr and ⁸⁵Sr were calculated.

Results

The data obtained using the four cyclotrons have maximum uncertainties of about 15 % and are consistent. The transition from the low-energy region to the high-energy region is smooth. The excitation function for the formation of ⁸⁵Sr above 30 MeV has been studied for the first time. The data for ⁸³Sr agree with the literature results up to 70 MeV, but the cross sections for ⁸²Sr are appreciably lower than the published values. For the energy range 30 to 37 MeV the ⁸³Sr yield amounts to 160 MBq/µAh and the level of the long-lived ^{85g}Sr and ⁸²Sr impurities to < 0.25 %. The yield of ⁸²Sr over the proton energy 40 to 60 MeV amounts to 10.5 MBq/µAh and the level of the ^{85g}Sr impurity to < 10 %.

Conclusion

The radionuclide ⁸³Sr can be advantageously produced via the ⁸⁵Rb(p,3n)-reaction, provided a 40 MeV cyclotron is available. The yield of ⁸²Sr via the ⁸⁵Rb(p,4n)-reaction is about 30 % lower than the literature value.

Production Plans for the New 100 Mev Isotope Production Facility at Lanl

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To ensure that U.S. researchers have a steady supply of medical isotopes, the U.S. Department of Energy's Los Alamos National Laboratory is building a new Isotope Production Facility (IPF) to replace an existing facility. Once operational, the new IPF will support eight months of isotope production annually. Combining its output with similar isotope production capabilities at Brookhaven National Laboratory in New York will ensure doctors and researchers an adequate, year-round supply of accelerator-produced medical and research isotopes. Construction of the new IPF began in February 2000 and the first production runs are planned for October 2003.

Isotopes such as ⁸²Sr and ⁶⁸Ge have been produced at LANL for more than 20 years using 800 MeV protons. The new facility will use a 100 MeV proton beam with beam currents of up to 250 µA extracted from the existing LANSCE accelerator by means of a pulsed kicker magnet. This lower proton energy is much more suitable for radioisotope production and will lead to products with substantially higher purity. The facility will irradiate a wide range of materials to produce a variety of radioisotopes of value to the DOE's Office of Isotopes including ⁸²Sr, ⁶⁸Ge, ⁶⁷Cu, ²²Na, ³²Si, ⁴⁸V, ⁸⁸Zr, ⁷³As, ¹⁸⁶Re, etc.

Up to three targets can be irradiated simultaneously utilizing the production energy windows 90-70 MeV, 65-45 MeV and 30-10 MeV. Targetry and target preparation facilities and techniques are being developed in order to ensure that the facility output meets the quantity and variety demanded by researchers and commercial suppliers worldwide. Production schedules are designed to minimize overall production cost by maximizing the occupation of the three energy slots in such a way that a good mix of long- and short-lived isotopes are made available on a regular basis. As an example expected production quantities for continuous operation over an eight months period is given below for one such proposed production schedule.

Isotope	Half-life	Target	Quantity produced
⁸² Sr	25.5 d	RbCl	2.5 Ci per month
⁶⁸ Ge	270 d	Ga	1.8 Ci per month
⁶⁷ Cu	2.6 d	Zn	500 mCi twice a month
⁷³ As	80.3 d	Ge	1 Ci per year
²² Na	2.7 y	Mg	1.4 Ci per month
³² Si	172 y	NaCl	160 μCi per year
48 V	16 d	Cr	6 Ci per month
⁸⁸ Zr	83.4 d	Nb	2.7 Ci per month
¹⁸⁶ Re	3.2 d	^{186}W	250 mCi twice a month

⁶⁷Cu Production by Proton Induced Reactions on Enriched ⁶⁸Zn

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Aims

At present we produce up to 3.7 GBq of 67 Cu in the 72 MeV accelerator at Paul Scherrer Institute by irradiating nat Zn. We tested the use of 68 Zn in order to scale up the 67 Cu production.

Methods

Cross sections were measured using the reactions 65 Cu(p,n) 65 Zn of monitor foils, nat Zn(p,2pxn) 67 Cu, and 68 Zn(p,2p) 67 Cu in the proton-energy range 67 to 45 MeV. Preparation of *thin Zn-targets*: 5 to 10 mg/cm² nat Zn or 68 Zn were electroplated on discs of Al at 3.6 V and 20 mA/cm² for 5-10 min. *Thick Zn-targets*: 30 mL 1.5 M 68 ZnSO₄, 0.1 M H₂SO₄ solution was electrolysed at 4.5 V and 125 mA/cm², 892 mg/cm². 68 Zn was electroplated on disc Ag. A rotary Pt-rod (1/s) served as anode. Electrolysis was stopped after 400 min. The pH of the solution at the start of electrolysis was 1.6, the final pH was 0.8. Current efficiency was 85 %.

Irradiations and proton flux: The entrance proton energy was 67.7 MeV after degradation in the cooling water. Beam intensity was determined via monitor reaction and by Farady cup. Proton beam: 1-4 μ A, 5-60 min and strong 70 μ A, 2 h. Radioactivity was measured after 2-5 days and measurements were repeated up to 23 days, to allow decay of interfering short-lived isotopes, especially of ⁶¹Cu.

Radiochemical separations: The thin 68 Zn-targets were dissolved in 0.5 ml 65 % HNO₃. The Zn-solution was washed off the surface, evaporated to dryness, re-suspended in 1 mL 7 M HCl and dried. The residue was taken up in 3 mL 7 M HCl and applied (0.25 mL/min) to a Dowex 50W X 8 (2.5 mL H-form). The Zn/Cu/Co/Ni-isotopes were eluted to a total volume of 10 mL of 7 M HCl. Under these conditions the Ga-isotopes remain on the cation exchange resin.

Work up of irradiated production-targets: Work up and separation of 67 Cu was accomplished (total mass per target = 2.8 g 68 Zn) over a combination of ion exchange catridges (Bio-Rad AG 50W-X8 /Chelex-100 /Bio-Rad AG1-X8). Recovery of 68 Zn: The 67 Cu / 68 Zn solution was evaporated to dryness. The residue was then taken up in 20 mL 2 M HCl and washed over Dowex 1X8 with 180 mL 1 M HCl. Co/Ni/Fe pass the column, whereas 68 Zn eludes with 80 mL 0.01 M HCl. The electrolysis was performed in sulfuric acid solution. Thus, chloride in the 68 Zn-solution was exchanged by sulfate via a Dowex 50W X 8 ion exchange column using 400 mL H₂O followed by 0.5 M H₂SO₄ to wash off the 68 Zn. The solution was then evaporated. The residue was dissolved in 5 mL H₂O and

used for further electrolysis. More than 90 % of ⁶⁸Zn can be recuperated by this method. Contain of ⁶⁵Zn: ⁶⁵Zn accumulates in the targets, when the targets are recovered. The use of the enriched ⁶⁸Zn results in a two-fold increase in the yield of ⁶⁵Zn compared to ^{nat}Zn. Yield of ⁶⁵Zn decreases with higher proton-energy up to a maximum of 30 MeV. At above energies the amount of ⁶⁵Zn declines, whereas the production of ⁶⁷Cu increases. The formation of ⁶⁷Ga reaches a maximum at 30 MeV and decreases at higher proton energy as well. Compared to ^{nat}Zn, the formation ⁶⁷Ga was higher by a factor at 4.1.

Conclusion

⁶⁷Cu production: in the 67 to 45 MeV energy range the yield of ⁶⁷Cu from the enriched ⁶⁸Zn was found to have 4.5 fold increase compared with the ^{nat}Zn. The specific activity of ⁶⁷Cu should increase by means of using Chelex-purified Zinc. Currently the specific activity of ⁶⁷Cu is $3.7 \times 10E+8$ Bq /10E-6 g.





Fig. 1: ⁶⁸Zn -target after electrolysis

Fig. 2: 67 Cu depending on the p-energy and ${}^{nat}Zn / {}^{68}Zn$ -isotopes

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Reports from the Laboratories

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Status of Cyclotron based Radioisotopes Production in Kazakhstan. Report from the Laboratory

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Introduction

The variable-energy isochronous cyclotron U-150 M has been in routine operation in Almaty since June 1967. It was designed and manufactured by the D.V. Efremov Institute in Leningrad as "classical" machine with a single beam line and fixed energy per nucleon 10 MeV/nucleon for protons, deuterons and alphas. In 1971-72 it was converted to variable-energy isochronous mode of operation [1]. Now it is a compact pole, three spiral sector, positive ion machine with K=50 MeV. The cyclotron generates beams of protons 6 – 30 MeV, deuterons 12,5 – 25 MeV, helium-3 ions 18,5 – 62 MeV, helium-4 ions 25 – 50 MeV.

Radioisotope ²⁰¹Tl has been manufactured in Kazakhstan since 1986 [2]. The short-lived radoioisotope and its labeled compound was supplied to hospitals and research institutes in Almaty and Medical Centers in nearby countries for use as tracers for diagnostic and research purposes.

Now also radionuclides such as ⁶⁷Ga, ⁵⁷Co, ¹⁰⁹Cd, ²³⁷Pu, ⁸⁸Y, ⁸⁵Sr are produced upon request. Wet chemical procedures have been developed for the recovery and purification of various radionuclides from the irradiated targets.

Target preparation

At the present time for isotopes production only solid targets are used at the internal and external beam of the INP isochronous cyclotron. The schematic view of internal target head is shown in Fig.1. Metallic targets prepared by electrodeposition of corresponding metal on a copper substrate of special design are used for production of 201 Tl, 67 Ga, 109 Cd, 57 Co.



Fig. 1. Schematic view of the internal target.

Choice of the method for electrolytic deposition depends on the type of metal to be deposited. When a nickel one (57 Co) is prepared the galvanostatic mode of deposition with insoluble platinum anode is used. For getting silver (109 Cd) and zinc (67 Ga) layers electrolysis with soluble anode and reverse current is used. This enables to control simultaneously thickness of the deposited layers and spent anode material.

A technology developed by P. Van den Winkel (VUB) and handled over within IAEA Technical Co-operation Project is used for the production of thallium targets.

Below, in Table 1, one can find detailed data on metallic targets. Powder targets produced by pressing at ~2500 N/cm² of RbCl, SrO and UO₂ into a metallic capsule are used for production of the nuclides ⁸⁵Sr, ⁸⁸Y and ²³⁷Pu, correspondingly. In all cases the thickness of the pressed powder is 1-1.5 mm.

Radionuclide	Target	Metal layer	Presence	Electrolyte type	Current mode
	material	thickness, µm	of sublayer		
²⁰¹ Tl	²⁰³ T1	160	-	Alkaline EDTA	chopped,
					sawtooth
⁶⁷ Ga	^{nat} Zn	350	-	Subacid chloride	Direct with reverse
¹⁰⁹ Cd	^{nat} Ag	290	Ag, 2 μm	Thiocyanatous	Direct with reverse
			C/ .	-	
⁵⁷ Co	natNi	240	Au, 10 µm	Sulphate-chloride	direct
				-	

Tab. 1. Summary data on the internal targets prepared by electrolysis.

For assessment of adhesion due to presence of a diffusion layer a set of experiments was carried out for investigations of the diffusion rate for metal electrically deposited on a copper substrate matrix at different temperatures. Profile of the coated layer prior and after the annealing is determined at the Electrostatic tandem with 1.5 MeV protons by the PIXE method [3]. The investigations have shown that thickness of the diffusion layer comprises

 $0.5-1 \mu m$ at target annealing temperature of 250-300°C. Therefore, to remove bulk stresses in metal and to increase the diffusion layer thickness the targets are annealed in vacuum at temperature 180-250°C during 3-5 hours before the irradiation.

Target irradiation

For radionuclides production both external and internal target irradiation are used. Beam intensity on the external target now is equal to 30 μ A for protons and deuterons and limited by beam power dissipation in the electrostatic deflector. In some cases during target irradiation the beam is swept across the target surface in a circular fashion by means of a stator of electro-motor in order to ensure an even power distribution.

Beam power distribution for the extracted beam spot and for the circularly scanned beam are shown in Fig. 2. When irradiating targets with high intensity internal beam the target is inclined with respect to the beam axis at the angle of 18° in order to reduce beam power density on the target. Thin layer 0,5 mm thick of cooling water, flowing at a velocity of approximately 30 m/s along the target surface is employed to ensure necessary cooling of the target. Cooling water pressure is equal to 20 bar which enables to use irradiation with internal 30 MeV proton beam and intensity up to 500 μ A. Summary of the produced radioisotopes is presented in the Table 2.

Radioisotope	Production route	Energy of	Beam	Average	Yield of activity
		incident	intensity,	heat flow,	(for nat),
		ions, MeV	μA	kW/cm ²	mCi/µA*h
²⁰¹ Tl (72,9 h)	203 Tl (p,3n) 201 Pb $\rightarrow ^{201}$ Tl	28,5	125	0.7	≥ 0.2
⁶⁷ Ga (78,2 h)	⁶⁸ Zn(p,2n) ⁶⁷ Ga	30	125	0.8	≥ 1.3
109 Cd- (463 d)	109 Ag (p, n) 109 Cd	22	250	1.1	≥ 2.6e-3
⁵⁷ Co (270 d)	${}^{58}\text{Ni} (p, 2p) {}^{57}\text{Co}$ ${}^{58}\text{Ni} (p, pn) {}^{57}\text{Ni} \rightarrow {}^{57}\text{Co}$	22	300	1.3	≥ 0.3
$ \begin{array}{c} ^{237}\text{Pu} \\ (45,2 \text{ d}) \end{array} $	235 U(α ,2n) 237 Pu	48 (α)	10	-	≥1.7e-10
⁸⁸ Y (106,6 d)	⁸⁸ Sr (p,n) ⁸⁸ Y	22	10	0.044	≥ 0.103
⁸⁵ Sr (64,8 d)	⁸⁵ Rb(p,n) ⁸⁵ Sr	22	10	0.044	≥0.076

Tab. 2. Summary of the produced radioisotopes.



Fig. 2. External beam spot (a). Circularly swept beam spot (b).

Radiochemical extraction of radionuclides:

Classical methods of ion exchange and extraction chromatography are used at radiochemical processing of the irradiated targets. Developed on their basis techniques enable to obtain high rate of purification of a desired product both from macrobacking, the irradiated target material, and from accompanying radioactive impurities.

I. Thallium-201:

- Extraction of ²⁰¹Pb (T_{1/2} = 9.3 hours) by co-depositing on SrSO₄ collector and optimal exposure of the extracted ²⁰¹Pb during 26 hours for ²⁰¹Tl accumulation.
 Separation of the accumulated ²⁰¹Tl from the parent radionuclide ²⁰¹Pb by the
- extraction method.
- 3. Thallium-201 transfer to isotonic solution, a base for production of the radiopharmaceutical preparation (RPP).

II. Gallium-67 [4]:

- 1. Chemical dilution of a zinc layer at the substrate in 12N HCl.
- 2. Separation of ⁶⁷Ga from macroamounts of Zn and microelements Fe and Cu by the method of extraction chromatography.
- 3. Gallium-67 transfer to isotonic solution in form of citrate complex, a base for production of RPP.

III. Cobalt-57:

- 1. Anode dilution of a nickel layer at the substrate in 9N HCl.
- 2. Separation of ⁵⁷Co from Ni, Fe, ⁶⁵Zn by the method of ion exchange chromatography.
- 3. Cleansing of Cu residue by electrolysis.

IV. Cadmium-109:

- 1. Chemical dilution of a silver layer at the substrate in 7N HNO₃.
- 2. Separation of ¹⁰⁹Cd from silver macroamounts by the method of cementation on copper.
- 3. Separation of ¹⁰⁹Cd from ⁶⁵Zn, Fe and macroamounts of Cu by the method of ion exchange chromatography.
V. Yttrium-88 [5]:

- 1. Dilution of the irradiated powder in weak HNO₃
- 2. Separation of ⁸⁸Y from ⁶⁵Zn, Fe, Cu and macroamounts of Sr by the method of extraction chromatography.

VI. Strontium-85 [5]:

- 1. Dilution of the irradiated powder in weak KOH and filtration.
- 2. Separation of ⁸⁵Sr from ⁶⁵Zn and macroamounts of Rb by the method of ion exchange chromatography at activated charcoal.

VII. **Plutonium-237** [5]:

- 1. Dilution of the irradiated powder in concentrated HNO₃.
- 2. Pu (III) oxidation to Pu (IV).
- 3. Extraction of Pu by the method of extraction chromatography.

Recovery

Recovery of the target material occurs in two cases only:

- 1. Recuperation of enriched ²⁰³Tl in metal form to the Tl target production cycle from the spent solutions and the electrolyte. The procedure implies electrolysis with controlled cathode potential (CCPE). The recovery rate is ≥99.5 %.
- Recuperation ^{nat}Ag in metal form to the Ag target production cycle from the worked out for ~80 A h/l thiocyanate electrolyte. The reductioned silver is used as dissolved anodes. The recovery is also carried out by CCPE with the recovery rate ≥99 %.

Electron beam stand

The electron beam test facility was created for preliminary heat load targets examination before their irradiation at the cyclotron.

This facility also enables to expedite development of technologies for isotope target production.

Electron blocks of beam focussing and deflection in vertical and horizontal directions provide obtaining of beam dimensions of diam. 1.5 mm and its scanning against the target surface. Scanning frequencies are the horizontal one -50 Hz and vertical one -1200 Hz that provides homogenous target heating. There is an opportunity of fixed beam spot moving at any point of the target surface. Electron beam has following parameters: electrons energy up to 25 keV, beam intensity up to 200 mA. The water pressure in cooling system is equal to 20 bar that provides water velocity in the cooling channel equal to 30 m/s.

Target tests at the stand enable to determine maximal allowed heat flows which are fixed in melting point of target material. Energy loss caused by reflected and second electrons are accounted on basis of known reference data.

Conclusion

Cyclotron internal beam intensity is increased up to 500 μ A for 30 MeV protons. Internal target design enables to irradiate it for some materials with beam current of 350 μ A. Sweeping system is inserted in the beam line to produce homogeneous irradiation of the external target. Many radioisotopes to be used in medicine, industry etc. can be produced in Kazakhstan using K = 50 MeV cyclotron to meet need of the Republic.

Acknowledgement

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Performance of a Flow-Through Target for the Production of $[^{11}C]CH_4$

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Previous work at TRIUMF (Buckley et al.) on static irradiations of a H_2/N_2 target gas for the production of methane indicated that recoverable yields at 13 MeV plateaued at about 750 mCi at EOB. The relatively poor yields were attributed in part to hot atom interactions with the target chamber walls. In order to try and overcome this limitation an aluminum bodied flow-through gas target was implemented and tested for the production of [¹¹C]CH₄ on the TR13 cyclotron at TRIUMF. Nitrogen gas with varying quantities of hydrogen has been used to investigate the optimum ratio for methane production. Comparison of the flow through target with the static-target irradiations for production of methane are given.

Methods

Aluminum body gas targets were designed with cylindrical bores of 12.7 mm ID and 120 to 127 mm lengths. A water-cooled support grid shown in figure 1, with 34 X 1.59 mm holes arranged in a hexagonal pattern with 1.78 mm between centers supported aluminum target window foils 25.4 micrometre thick (Barnhart et al.). Transmission through the grid was calculated to be approximately 70 percent. Beam transmission studies indicated 64 % transparency. Mixtures of N₂ with up to 12 percent H₂, pressurized up to 3.1 MPa were used to make [¹¹C]CH₄. For comparison, [¹¹C]CO₂ was produced in the same target system with a mixture of N₂ and 0.5 percent O₂, pressurized at 0.69 to 2.28 MPa. Gas flow in each case was 200 to 600 ml/min. Irradiations of up to 32 μ A lasted up to 60 minutes. The radiolytic production of ammonia could be a concern for post production processing, e.g. [¹¹C]CH₃I synthesis. To measure the ammonia this system produced, we passed the target gas through a series of HCl traps and back-titrated to a phenolphthalein end point.



Fig. 1. Schematic of Grid Window Support.

Results

Testing of the flow-through target gave a saturation yield of up to 2.89 GBq/ μ A (79 mCi/ μ A) [¹¹C]CH₄ at 32 μ A with a correction for the grid transmission (both beam current on target gas and saturation yields). For comparison, [¹¹C]CO₂ was produced with a saturation yield of 2.66 GBq/ μ A (73 mCi/ μ A) at 27 μ A with correction for grid losses. Yields improved to approximately 12 % H₂ as is shown by the colleted activity in figure 2. Higher concentrations of H₂ may increase the saturation yield of [¹¹C]CH₄. The maximum [¹¹C]CH₄ produced after a 35 minute run at 30 μ A was 57.3 GBq (1.55 Ci), shown in figure 3. Comparison of the flow through target with the static-target irradiations for production of methane are given in figure 4. Results for 5 % hydrogen in the flow-through target show a marked reduction in methane production over the 10 % hydrogen gas mix.



Fig. 2. Collected activity vs. percent hydrogen.



Fig. 3. Flow-through target total activity and saturation yields vs. time.



Fig. 4. Comparison of ¹¹*C*-*CH*₄ *yields in static and flowing target systems with varying hydrogen percentages. On-target beam current is the beam current corrected by transmission losses of the grid.*

Preliminary measurements of the specific activity (SA) via the synthesis of [¹¹C] raclopride indicate that the EOS SA is approximately 13.5 GBq/µmole (500 mCi/µmole). Further conditioning of the target system should improve the specific activity. In the static target we found that ammonia production reached equilibrium quickly resulting in a production of 0.13 mmoles. The flow through target generated 8 mmoles of ammonia for a 50 μ A X 20 minute irradiation, however the NH₃ should be quanitatively removed with sufficient HCl traps in the gas stream.

Conclusion

The flow-through target system for the production of $[^{11}C]CH_4$ provides increased radioactivity over single shot low volume, high pressure gas targets. The $[^{11}C]CH_4$ saturation yield is within experimental errors to that for $[^{11}C]CO_2$ under similar conditions and is 72 % of calculated theoretical maximum yield, allowing for the support grid transmission. The cause for the relatively low specific activity is under investigation. The high quantity of ammonia co-produced will adversely affect the production of $[^{11}C]CH_3I$ and must be removed for a useful system.

Acknowledgements

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Qualitative Evaluation of Helium-Cooling Windows

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Aim

To support the quest for higher beam current deposition on gas or liquid targets we set out to evaluate the effectiveness of our helium cooling windows.

Methods

The parameters explored included flow rate, pressure and direction of the jets. In order to rank the different designs of helium flow paths across the target window we built a simple jig to deposit a reproducible amount of heat into a plate coupled to the He cooling chamber and observed the temperature change to the plate as a function of differing helium cooling window designs and conditions. In addition to this work a computational fluid dynamics (CFD) analysis of helium flow and heat transfer was performed to investigate our "standard" helium cooling window and supposed near "ideal" helium window geometry.

Results

We will present the results of the mathematical analysis and the qualitative ranking of the different designs.

Conclusions

Modelling of the He window can lead to improved designs for more efficient cooling.

The Turku PET Centre Medical Compact Cyclotron CC-18/9

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Introduction

A medical compact cyclotron CC-18/9 has been designed and manufactured by the D.V. Efremov Scientific Research Institute of Electrophysical Apparatus (NIIEFA). The cyclotron has been designed for the production of radionuclides applied in positronemission tomography (PET) as well as for the production of other radionuclides used in nuclear medicine. The cyclotron will be installed at Turku PET Centre, Finland, in 2003-2004. Negative ions of hydrogen and deuterium (H⁻ and D⁻) are accelerated in the cyclotron. A multi-cusp ion source will be used for external injection of the negative ions into the central part of the cyclotron. The particle beams of protons and deuterons are produced by stripping the negative H⁻ and D⁻ ions in carbon foils in the cyclotron vacuum tank. Efficiency of the extraction is approximately 100 %. Specified beam currents of protons and deuterons are 100 μ A and 50 μ A, respectively.

General description

The cyclotron accelerates negative ions of hydrogen (H⁻) to 18 MeV energy and deuterons (D⁻) to 9 MeV energy. The magnet of the cyclotron is of shell type with a vertically located median plane. Four sectors per pole form an isochronous magnetic field in the working area of the cyclotron. The gaps in hills and valleys are 27 mm and 118 mm. The shape of the sectors maintains the isochronous acceleration of the H⁻ beam. The isochronous acceleration of the D⁻ beam is achieved by movable ferromagnetic shims which are installed in special recesses inside the hills. The cyclotron has no trim coils.

The cyclotron vacuum tank consists of a casing and two lids. The tank casing is a hollow thick-walled cylinder made of carbon steel that also is part of the magnet yoke. The tank lids are pole tips of the magnet with flanges of stainless (non-magnetic) steel welded to them. The accelerating double-dee resonant system is located inside the vacuum chamber and fixed to the side of the tank casing.

The particle beams of protons and deuterons are produced by stripping the H⁻ and D⁻ ions in thin carbon foils. There are three stripping foil mechanisms for extraction of H⁺ and D⁺ beams out of the vacuum tank, two of which are for targets mounted on the cyclotron, the third one is for the beam extraction and beam delivery to four distant target stations. The location of the stripping mechanisms and extraction foils in the tank casing provides besides single target irradiation, also the possibility for irradiating simultaneously one of the near and one distant target, or alternatively two near targets. The near targets are mounted on the gate valves 13 and 14 (Fig. 1). The layout of beam extraction and equipment in the cyclotron tank is shown in Fig 1.

The beam-transport system delivers the particle beam to four distant target stations (Fig. 2). The system consists of an ion guide, a doublet of quadrupole lenses, a switching magnet and after that four ion guides diverging at angles of $\pm 12^{\circ}$ and $\pm 36^{\circ}$ with reference to the initial beam direction. Doublet quadrupole lenses mounted on all the four ion guides focus the beam to the target stations. A beam-positioning magnet (11 in Fig. 1, and 2 in Fig. 2) is installed at the beam outlet of the cyclotron to correct for the beam direction. The layout of beam transport system with appropriate equipment is shown in Fig. 2.

The beam diagnostics in the cyclotron vacuum tank is done by using a probe, and in the delivery system by using scanners and Faraday cups. To gain access to equipment inside the cyclotron vacuum tank half of the magnet yoke together with the tank lid can be moved away from the tank casing 800 mm by an electrical gear.

The operating pressure in the cyclotron tank is ensured by two cryogenic pumps with a capacity of 3200 liter per second each and by a rough pump. The performance of the cyclotron and beam delivery system are controlled from the control panels and by computer.

The technical data of the CC-18/9 cyclotron are summarized in Table 1.

Table 1. Technical data of the CC-18/9 cyclotron.

Accelerated particles	H^{-}, D^{-}
Extracted particles	H^+, D^+
Energy of particles H/D, MeV	18/9
Extracted beam currents for H^+/D^+ , μA	100 / 50
Electromagnet:	
Pole diameter, cm	115
Average induction at the final radius, T	1.25
Power consumption, kW	7
Weight of magnet, ton	22
Resonant system:	
Frequency, MHz	38.2
Number of dees	2
Dee voltage, kV	35
RF-generator power, kW	30
General power consumption	
of the whole cyclotron complex, kW	90



Fig. 1. Equipment layout inside the vacuum chamber of the cyclotron: 1-vacuum chamber; 2-RF system; 3-power input; 4-trimmer; 5, 6, 7- carbon stripper units; 8-probe; 9, 10-baffle-boards; 11-steering magnet; 12, 13, 14- valves; 15-cryogenic pump; 16-RF probe.



Fig. 2. Equipment of the cyclotron. 1- cyclotron; 2- steering magnet; 3- magnetic corrector; 4- scanner; 5- Faraday cup; 6- doublet quadrupole lenses 7LK; 7- switching magnet; 8- doublets quadrupole lenses 4LK;9- target stations; 10- rough vacuum pump; 11- pneumatic station; 12- cryogenic pump power supply; 13- external injection system.

Website for Proceedings of the Workshops on Targetry and Target Chemistry

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Aim

To make all past WTTC Proceedings available on line to the target community and beyond.

Methods

TRIUMF hosts a website for the proceedings of the WTTC. The website is at http://www.triumf.ca/wttc. Proceedings of past workshops that were not available in electronic format have been scanned and converted to Adobe portable document format (pdf) files. Proceedings that were available in electronic format have been converted directly to pdf files. Suggestions on further content for the website (such as useful links) are welcome and may be directed to the Advisory Committee or webmaster as obtained from the website.

Results

All Proceedings are now available for viewing and downloading.

Conclusions

Electronic access to the previous Targetry Workshops makes the historical record on the progress of target development available for the wider community.

GE PETtrace Mel Microlab: Six Years' Experience with System*

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Aims

We wish to describe our six years' experience with the GE PETtrace MeI Microlab (the box) since its installation in March, 1996. We are particularly interested in describing the problems encountered after receiving the unit and our approach to solve them. We will detail the use of the box in our current radiosyntheses.

Overview

The GE PETtrace MeI Microlab is a fast and reliable system to synthesize C-11 MeI by free radical formation from C-11 methane in the presence of iodine at 720°C. The box was acquired in March of 1996, one of the early units on the market. Soon after receiving the unit we started to have problems with the Process Unit because of clogging of the needle piercing the lower septum of the iodination column. This problem was traced to condensation of iodine around the needle at the end of synthesis during the cooling phase. This problem caused considerable downtime while cleaning the faulty piece and reconditioning the column. A permanent solution involved the elimination of the septa/needles in favor of O-rings located around the Teflon piece, where the quartz column (containing the iodine) is inserted by gentle pressure from above. This simple solution later appeared in a newer model of the box by GE Medical System (GEMS), as described in their manual Rev.1D November 30, 1998. We have also adapted an inexpensive clear plastic tube to act as a holder for refilling the quartz iodination tube. This plastic tube is marked permanently with the distances to be refilled with quartz wool, ascarite and iodine, thus making the preparation of a new iodination tube a quick and accurate operation from run to run. Another change in our system has been the elimination of water from the ascarite on top of the quartz. Wet ascarite was a cause for plugging of the iodination tube, and slow recirculation during C-11 MeI production. At the present time, we consistently use the iodination column for 10-12 runs before a new column is installed. We do not remove the iodination column from the system during longer periods of non-use (such as weekends), thus increasing the chemical safety for the operator.

The box is located in a hot cell at a distance of about 35 feet from the methylation gantry currently in use. The C-11 MeI is transported with a polyetherether-ketone (PEEK) line 0.010" ID x 1/16" OD, the flow from the box is modulated with a flow controller to 8-10 mL/min and the total tranfer time in the box is reset to 350 seconds. The radioactivity is first passed through a glass tube 15 cm long X 1.2 cm ID filled with NaOH pellets. From May 2000 to the present, we have used this methylation system to produce over 400 batches of MeI with a yield of approximately 355 Ci. We routinely run a short bombardment (30 sec or less) to check the box after a new column is installed. Some of

the applications of this device have been for the labeling (n=number of preparations) of raclopride (114), lactic acid (29), omega fatty acids (41), flumazenil (45), NMB (19), and a number of other tracers. Specific activities at EOS for clinical batches have exceeded 92.5 GBq (2.5 Ci)/umol for raclopride and 55.5 GBq (1.5 Ci)/umol for flumazenil.

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The Installation of a Multi-Radiopharmaceutical P.E.T. Facility at Washington University in St.Louis, Mo, USA.

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A new compact PET pharmacy has been installed at Washington University to meet impending FDA regulations and increased demand for radiopharmaceuticals used in clinical PET. The new pharmacy was installed at the site of the tandem cascade accelerator that was decommissioned in April of 2001. The 1880 square foot pharmacy consists of a production lab, quality control lab, reagent preparation lab, shipping and storage area and an office. A CTI RDS111 cyclotron installed in the fall of 2001 supplies precursors in the following form for radiopharmaceutical compounding and use, ¹⁸F fluoride, ¹⁸F fluorine, ¹¹C carbon dioxide, ¹¹C carbon monoxide, ¹³N ammonia, ¹⁵O oxygen, ¹⁵O carbon dioxide and ¹⁵O carbon monoxide.

The pharmaceutical production facility consist of eight minicells BBS2 and one general hotcell MIP-1 from Comecer. Radiopharmaceutical production is accomplished using chemistry modules from CTI. F-18 FDG is produced using the CTI QuadRx module. C-11 acetate and C-11 Methyliodide are produced using the CTI grinard module. We also installed the CTI hydrogen cyanide and methylation module. This leaves us with three minicells for further expansion.

The quality control lab has a general purpose fume hood, and a laminar flow hot cell MIP1-1P LAF 1250 from Comecer used for dispensing. The quality control lab is equipped with a Bioscan AR2000 TLC, an Agilent 6890 gas chromatograph and a Agilent 1100 high performance liquid chromatograph for chemical and radiochemical purity analysis. A Capintec CRC-15W and a Aptec-NRC multi channel analyzer are available for dose measurement and radionuclidic purity testing. Finally a Fisher Scientific isotemp incubator is used for pyrogen and sterility testing.

The reagent lab houses a general fume hood and a class II laminar flow hood from Labconco. An isotemp explosion proof refrigerator/freezer is used for reagent storage. The equipment used in the reagent preparation lab consists of a dry oven from Fisher Scientific and a Napco 9000D autoclave.

The facility began processing FDG for patient use in February 2002. ¹⁵O oxygen carbon monoxide and water can be shipped to three different PET suites. The furthest PET suite from the RDS111 cyclotron is 2500 feet away. ¹¹C acetate and ¹³N ammonia are both proceeding through the approval process for patient use.

A Research Resource in Radionuclide Research

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Aims

Since September 1999, Washington University has been funded as a Research Resource in Radionuclide Research by the National Cancer Institute. The goals of the Resource include providing novel radionuclides for collaborative research and other applications. In addition, imaging facilities at Washington University, including the microPET (Concorde Microsystems, Knoxville, TN), the first commercial device based on the design of Cherry and colleagues (1), are being made available to collaborators to assist in the evaluation of radiotracers for both diagnosis and therapy.

Introduction

⁶⁴Cu is a medium half-lived positron emitter, whose positron energy is similar to that of ¹⁸F. This makes ⁶⁴Cu a very attractive isotope for imaging studies utilizing the microPET. Currently, ⁶⁴Cu is being made available to researchers at Washington University and to 14 other institutions. Since the start of the Resource, 56 Curies of ⁶⁴Cu have been produced for studies at Washington University and for shipping to investigators across the country.

We are also making progress on the production of ⁷⁶Br, ⁷⁷Br, ¹²⁴I, ⁸⁶Y and ⁶⁶Ga. We have shipped small quantities of ⁷⁶Br and plan to ship ¹²⁴I and ⁷⁷Br in the near future. In addition, we are making available several short lived isotopes for collaborative studies carried out at Washington University: ^{94m}Tc, ⁶⁰Cu and ⁶¹Cu.

Due to the high energy positrons, some of these non-standard isotopes are less than ideal for imaging. The imaging characteristics of these isotopes is being evaluated using a mini Derenzo phantom and other phantoms (2, 3).

Conclusions

The National Cancer Institute's funded Research Resource in Radionuclide Research has provided nonstandard isotopes to investigators at Washington University as well as investigators at other institutions. The resource has also made available imaging facilities, such as the microPET, to collaborators. In addition, progress has been made in the production of ⁷⁶Br, ⁷⁷Br, ¹²⁴I, ⁸⁶Y and ⁶⁶Ga. These isotopes are being evaluated for their imaging properties on the microPET.

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Modified Module for the Production of C-11-Methyl lodide from C-11-Methane, Produced in Target

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Aims

Carbon-11 labelled methyliodide is a frequently used labelling agent for the production of PET-tracers. Besides the classical 'wet' production method, i.e. reduction of C-11-CO₂ to C-11-methanol followed by hydrolysis to C-11-methyl iodide, the so-called 'gasphase' production method is being applied. Several groups published data on this production method, in which C-11-methane is iodinated to form C-11-methyl iodide. The commercially available GE-module is being widely applied for routine production. This module uses C-11-CO₂ as starting agent, which is being converted to C-11-methane.

The presently reported home-built module uses C-11-methane as input being produced intarget in order to achieve maximal specific activity. The target is a Scanditronix aluminium C-11-target, filled with $N_2 + 5$ % H₂. The 'gasphase' production of C-11methyl iodide from C-11-methane produced in target has been published earlier by Larsen et al., but our module has been adapted to be optimal compatible with the MC-17 cyclotron environment.

Methods

C-11-Methane produced in target is trapped on a liquid nitrogen cooled Porapak N trap located in the cyclotron vault. The target and the trap were evacuated by a vacuum pump to remove the hydrogen gas. The trap was warmed to ambient temperature. The C-11methane-in-target production has been implemented in the STEP-5 software. The C-11methane was transferred to the helium preconditioned module in the hot cell over a distance of 20 m using a helium flow of 500 ml/min. A carbosphere column equipped with two radioactivity detectors at both ends was used to collect the C-11-methane. When all C-11-methane was present on the carbosphere, the recirculation process was started by activation of the membrane pump. The following parameters were used. Temperature of empty tube: 675°C, temperature I2 85-90°C. Recirculation flow 400 ml/min. The formed C-11-methyl iodide is being trapped at the top-end of the same carbosphere column. Accumulation of C-11-methyl iodide was followed by the top-end radioactivity detector. The radioactivity profile is a result of a gradually increasing C-11-methyl iodide accumulation and still unreacted C-11-methane. The latter component shows an oscillating pattern. C-11-Methyl iodide is released from the carbosphere by heating the carbosphere to >300°C and using a helium flow of 20-30 ml/min in the opposite direction. Heating of carbosphere is achieved by moving the column into a preheated furnace pneumatically. After the production the column is moved outwards to ensure fast cooling down and short preparation time for the next run. The module was controlled by Labview software.

Results

Using this system, C-11-methyl iodide is produced with a radiochemical yield of 50-60 % (EOB) with a synthesis time of 15 min and specific activities of >20,000 GBq/mmol (EOB) were achieved. The system is ready for the next run within 10 min.

Conclusions

A fully automated 'gas phase' methyl iodide system has been developed that uses C-11methane as input, producing C-11-methyl iodide with high specific activities.

A Cryo-Buncher Based on a Ten-Port Switching Valve

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Introduction

A device was constructed based on a 10-port switching valve developed for the administration of gaseous $C^{14}O_2$ in concentrated form to the lung for cerebral activation studies. The oxygen-14 tracer has desirable characteristics ($t_{1/2} = 71 \text{ sec}$, β^+ , 2314 keV γ), which allow for repeated studies at an increased throughput. The 10-port switching valve is plumbed in the "column regeneration" mode where a steady stream of the $C^{14}O_2$ tracer is trapped at LO₂ temperatures while the other loop is subsequently heated and eluted into a stream of He gas. The trap and release mechanism permits repetitive patient studies with a controllable delivery time between each administered dose. The delay time between trapping and subsequent elution of the columns allows for 1-2 minute acquisition periods followed by several minutes of delay time without any loss in activity for the column in the "trapping" phase of the cycle.

Methods

A target gas mixture of natural nitrogen with one part per hundred oxygen is irradiated with protons and monitored by a ruthenium-based optical probe. The irradiation is done on a CTI RDS 112 negative-ion cyclotron at fixed proton energy of 11 MeV. Oxygen-14 is produced by the following reaction with natural nitrogen, ${}^{14}N(p,n){}^{14}O$, with a measurable thick target yield of 2 mCi/ μ A. Several contaminants are present in the output stream and are summarized in the table below.

Reaction	Q(MeV)	A(ESOB)	Chem Form	Action
$^{14}N(p,\alpha)^{11}C$	-2.92	60 mCi/µA	CO ₂ , CO	Trap for later
				use CO ₂ , "
$^{14}N(p.n)^{14}O$	-5.93	2	O ₂	Pass on
$^{14}N(p,pn)^{13}N$	-10.55	0.1	N ₂	Can't trap,
				innocuous
			NO _x	Trap out
$^{15}N(p,n)^{15}O$	-3.54	0.2 @ 0.3 %	O ₂	Can't separate
				from ¹⁴ O ₂

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The target output stream is dominated by ${}^{11}\text{CO}_2$ formed directly in the target chamber and by oxidation of ${}^{11}\text{CO}$ with the first CuO furnace. Any ${}^{11}\text{CO}_2$ formed in the target chamber



is immediately trapped in soda lime coupled to the output stream before reaching any furnaces. The remaining activity is piped into a hood, stripped of ¹³NO_x (Tewson et al), and sent though a CuO furnace to convert the remaining ¹¹CO to ¹¹CO₂, which is then trapped in soda lime or LO₂ for later use. The residual activity stream, consisting of ¹³N₂, ¹⁵O₂ and ¹⁴O₂, is then sent to a charcoal furnace to convert the oxygen species to carbon monoxide and dioxide products. Finally, the activity streams are passed through another CuO to convert any last remaining carbon monoxide compound to carbon dioxide. The final activity stream is then sampled and evaluated on a GC system (PORPAK Q) showing an approximate 10:1 mixture with ¹³N₂. Upon evaluation of the final product, the activity stream is passed through the cryo-concentrator based on to the 10-port switching valve shown in Figure 1. The

trapping column is submerged in LO_2 while the other loop is resistively heated to elute the trapped $C^{14}O_2$ into a He stream.

Results

Production of $C^{14}O_2$ followed flow-through chemistry where the target gas was piped through a series of traps and furnaces as discussed in the previous section. The trapped activity was monitored with a heavily shielded BGO crystal coupled to a photomultiplier tube. Energy windows were set to monitor the 511 keV annihilation photon and 2314 keV coincident gamma. Figure 2 shows a drawing of the inline chemistry and graph of the activity trapped over time. An approximate 6-fold increase in the concentration of activity is achievable compared to a steady state delivery. It was observed that 2.5 mCi could be trapped in a volume of 60 ml with a trapping time of 6.5 half-lives (rise time seen on graph) and elution of the trapped activity is on the order of several seconds. This is an ideal time period for a patient scan of 2-3 min and an interscan delay of several minutes for decay and clearance of the remaining activity.

 $C^{14}O_2$ that enters the lung is rapidly transported across the alveolar membrane and into the blood stream. The transport of CO_2 out of the lung and into the blood stream depends on which element in the compound is labeled. Oxygen-14 labeled CO_2 transfers its label to the water pool, forming carbonic acid, labeled bicarbonate, HCO_3 -, and labeled water, $H_2^{14}O$ on a time scale of milliseconds. Figure 3 compares some various inert diffusible tracers detailing their physical characteristics and lung clearance that dictate the shape of the arterial input function. The dominant characteristics when choosing to administer the activity by pulsing rather than steady state is the clearance time of the tracer in the lung. The behavior of the $C^{14}O_2$ distribution in the lung, brain, and expired breath are shown in Figure 4. The fast clearance kinetics and delta function input is evident by the initial decrease in activity in the lung and expired breath tracers.



Why would you want to pulse C14O2 ?!?

Horses:	¹⁰ C	¹⁷ F	14(D	15O	
t _{1/2} (sec)	19	64	7	1	122	с. — С.
A. (nCV/A)	8	14	1	2	70	
Tracer:	10CO2	CH317F	C14O	2 H ₂ ¹⁴ O	C15O	H ₂ ¹⁵ O
t _{1/2} (lung)	≈7 sec	$\approx 45 \text{ sec}$	≈4 se	c	$\approx 4 \sec \theta$	
Pulsed/SS?	1	Î	11	Î	Ť	1
How?	сгуо	dissolved	cryo	dissolved	сгуо	dissolved
Bulk gas:	He	Ne, O2 + CH.	N ₂	N2 + H2	(15)N ₂	(15)N2 +H2
Trap:	LN ₂	C-18 (-78° C)	LO,	saline	LO,	saline

rep rate, known p, PS,..conventional targetry, chemistry

Fig. 2. Schematic of flow through chemistry for the production and trapping of $C^{14}O_2$.



Weigh



Fig. 4. Clearance of $C^{14}O_2$ *from the lung, brain, and expired breath.*



Steady state delivery of isotopes used for cerebral brain mapping have suffered in their ability to show sufficient contrast in activated regions. The sensitivity in steady state of several CO₂ analogues is shown in Figure 5. A peak in the sensitivity occurs with $C^{14}O_2$ where the physical decay rate $\lambda_p = \ln(2)/71$ sec is perfectly matched to the gray matter flow rate f=60 ml/min-dl. The short half-life, fast lung clearance, and ability to cryogenically trap $C^{14}O_2$ allows delivery of an instantaneous gas pulse to a patient's lungs. This is ideally suited for dynamic imaging of the impulse response function of regional cerebral blood flow. The breath of gas is then held for several seconds and cleared from the lung by normal breathing with a half-life of 4 sec. The bolus then travels through the heart undergoing turbulent mixing and on to the blood brain barrier.

Conclusions

Cyrogenically trapping $C^{14}O_2$ for bolus injection to the lung takes advantage of the short lung half-life and flow-through chemistry. In addition, delivery of the activity can be automated for quick and repeated brain mapping studies. Oxygen-14, either as CO_2 or water, promises faster study cycling and more efficient utilization of the PET scanner. These issues are becoming critical in today's clinical setting.

Targetry and Chemistry for the Production of [O-14]: Application to Radioactive Ion Beam Experiments

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A number of interesting problems in nuclear astrophysics as well as nuclear structure are best studied with radioactive ion beams. BEARS is an ongoing project to provide light-ion radioactive beam capability to the 88-inch Cyclotron at LBNL. To date work has focussed on the production of accelerated Carbon-11 with beams of more than 10⁸ ions/sec being used for various experiments.

Development of Oxygen-14 as the second BEARS beam has presented considerable technical challenges due to the short half-life of 71 seconds, the in-target radiation chemistry of oxygen as well as the chemical processing of the target gas. The standard techniques developed for the medical uses of Oxygen-15 involve the addition of significant amounts of carrier oxygen not compatible with the high vacuum needs of the 88-Inch Cyclotron's ion source.

We have developed a method for the production of Oxygen-14 as carrier-free water, followed by a two-step chemical conversion to carbon dioxide, a gaseous carrier of the Oxygen-14 compatible with the BEARS transport system.

Targets and chemical processing equipment have been incorporated into the CTI RDS-111 medical cyclotron and initial tests of producing and accelerating an Oxygen-14 beam have been performed.

In addition to the uses of Oxygen-14 for nuclear science research, this short-lived, positron emitting isotope shows potential in nuclear medicine imaging. For example: Fast PET scanning for brain activation studies with [O-14]water. (Sajjad et al. J. Nucl. Med. (2000) 5, 244.)

Development of capabilities

Involvement of the Department of Functional Imaging in the BEARS project includes but is not limited to:

Target design for the BIF CTI RDS-111 cyclotron Target chemistry and post irradiation chemistry Radioactive species production

In order to provide the capability to run continuous and automated production sequences for days, modifications to the RDS-111 cyclotron and support facility have been made. As a result, enhanced performance and reliability have been achieved.

The original BEARS system has been modified to allow the production of Oxygen-14 radioactive ion beams. National Instruments LabVIEW software and FieldPoint modules are used to control the post irradiation chemistry as well as the gas tranfer between

cyclotrons. In addition the LabVIEW software monitors environmental safety interlocks and is interfaced with the RDS control system to coordinate unload timing.

Initially, a Carbon-11 beam was developed as previously reported (J. Powell et al., Nucl. Instr. and Meth. A 455 (2000) 452). The most recent Carbon–11 experiment ran continuously for 60 hours and delivered over <u>100</u> Curies of [Carbon-11]CO₂ to the ion source of the 88" cyclotron over 300 meters away.

Development of an oxygen-14 radioactive ion beam

Oxygen-14 presents the challenges of a 71 second halflife and high reactivity.

To realize a working beam, a target and target material are needed which provide Oxygen-14 that is:

- 1) Easily extracted from the target.
- 2) Quickly and efficiently converted to a chemical form suitable for rapid gasphase transportation to the 88" cyclotron.
- 3) Amenable to efficient trap and release with low carrier gas loading on the ECR ion source.

Due to intense radiolysis within the target (>50 eV deposited per molecule in 40mA, 90 sec run), initial attempts at exchange reactions with additives such as CO failed.

Carbon monoxide radiolysis: $4CO \rightarrow CO_2 + C_3O_2$.

In addition, radical species, especially oxygen, have strong interactions with the target walls and thus we have not been able to extract appreciable amounts of O-14 from aluminum targets.

Adding even small amounts of stable oxygen as a carrier, as is routinely done in the case of ¹⁵O production for medical, was not feasible since dilution with stable oxygen exceeds pressure limitations of the high vacuum ECR ion source.

However, after additional experimentation, a mixture of 1-5 % hydrogen in nitrogen irradiated in a gold plated target body produced $H_2^{14}O$ in good recoverable yield.

Conversion: $H_2^{14}O \rightarrow C^{14}O \rightarrow [^{14}O]CO_2$

¹⁴O labeled carbon dioxide can be made from target produced ¹⁴O labeled water as follows:

- A) Separate H₂¹⁴O from other target gases including ammonia, hydrogen and ¹¹CH₄ through momentary freezing at -40°C followed by resistive heating of the trap.
- B) Convert $H_2^{14}O$ to carbon monoxide by flowing over 1000°C graphite in a helium stream.
- C) Oxidize $C^{14}O$ to carbon dioxide over platinum at 180°C (add some O_2 for this step).



Fig. 1. Diagram of the apparatus used to produce O-14 labeled cabon dioxide

Efficiencies:	Oxygen-14	Carbon-11				
Thick-target production 5×10^{9} /s 1×10^{11} /s						
Recovery from target	~50 %	~50 %				
$\mathrm{H_2}^{14}\mathrm{O} \rightarrow [^{14}\mathrm{O}]\mathrm{CO_2}$	~60 %	n/a				
Activity decay	~30 %	~80 %				
Ionization 3.6 % (6+) 11 % (4+)						
Other efficiencies similar						
From known ¹¹ C ⁴⁺ beam o estimate ¹⁴ O ⁶⁺ b	n target $\Rightarrow 1-2 \times 1$ beam $\Rightarrow 5 \times 10^5$ ion	0 ⁸ ions/s ls/s				
Early test runs with poor beam diagnostics (tuned on ¹⁴ N) provided ¹⁴ O ⁶⁺ beam => $\sim 1 \times 10^5$ ions/s						

Acknowledgements

Due to the hard work of both the 88" Cyclotron staff and the BIF staff as well as support from the U.S. Department of Energy (DE-AC03-76SF00098), a means of producing Oxygen-14 RIBs has been developed and tested at Lawrence Berkeley National Laboratory.

A Versatile and Ready-to-Automate Set-Up for Research and Development of Radiopharmaceuticals

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Aims

Automated systems for the production of radiopharmaceuticals are usually 'dedicated' and not very flexible. We designed a versatile set-up to perform research and development (R&D) of a wide range of labelled molecules. The set-up allows easy monitoring during R&D and step-by-step full automation.

Methods

The main functions of the set-up are:

- transport of gases and liquids by a series of 7 multi-port rotary valves (Hamilton), using Ar-pressure (liquids) and sometimes by peristaltic pumps,
- moving the reaction vessels by 2 hydraulic units for heating and cooling, driven by tapwater-pressure,
- purification by high pressure liquid chromatography with automated injection,
- monitoring and recording temperature, gas flow, valve position and radioactivity via PLC-(Programmable Logic Controller) to personal computer,
- process control by PLC.

Results

The set-up has already been applied for ¹¹C labelled molecules: ¹¹C-thymidine, ¹¹C-flumazenil, and ¹¹C-acamprosate, produced from ¹¹C-carbondioxyde via ¹¹C-iodomethane or ¹¹C-acetyl chloride, as previously described (1, 2, 3). The optimisation of the process parameters and the automation went side by side. The reliability was outstanding.

Conclusion

The design of the set-up - the combination of the multifunctional valve-system and PLCcontrol - proved to be very suitable for the fast development of a series of carbon-11-based radiopharmaceuticals.

The main innovation of the set-up is the use of a series of multi-port rotary valves. The combination of these valves avoids the use of a very large number of separate 1- and 2- way valves, tees and tube-fittings. This reduces significantly the dead volumes. Our

experience proved they are very reliable and the feedback assures safe operation. The flexibility of the system allows easy switching between different types of synthesis.

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Ten Years Oxygen-15 Production at the Turku University Central Hospital

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In 1990 a decision was made to install an oxygen generator at the Turku University Central Hospital. The Turku PET Centre has its PET-isotope production and radiochemistry facilities at Åbo Akademi University which is located about 800 m from the hospital. A low-energy (3.5 MeV) deuteron accelerator Cyclone 3 (IBA sa., Belgium) was our solution for oxygen-15 production at the hospital.

Installation of the Cyclone 3 started in the beginning of January 1992. First beam was found in the end of April and the machine was preliminary accepted in the end of June 1992. However, the performance of the machine was not satisfying because the magnet poles and sectors were still experimental. The magnet had to be rebuilt. After rebuilding the magnet the performance of the machine was improved considerably. The final acceptance tests were performed in August 1993. During the first year, 1992-1993, after the preliminary acceptance, oxygen-15 production and oxygen-15 chemistry was established. First patient study was done 28th of April in 1993.

The Cyclone 3 was installed in a vault about 60 meters form the hotlab and the PET scanners. This installation was in use about six years until the scanners were moved into the new PET building in March 1999. Cyclone 3 is still operated from the old vault and the present distance between Cyclone 3 and hotlab is about 180 m. Target gas flow rate can be maintained at 500 ml/min in the three times longer FEP tube (o.d. 1/4", i.d. 2 mm) with increased target gas preussure of 2.1 bar againts the 7 μ m thick titanium target window. Because of the long distance between the hotlab and cyclotron the data communication of the cyclotron control system had to be improved with a RS-232 converter (Westermo, Access MA-44).

When the distance was 60 m a target gas pressure of 1.9 bar was used and the oxygen-15 saturation yield was about 260 MBq/ μ A. The oxygen-15 saturation yield in the new laboratory is about 190 MBq/ μ A which has been satisfying for PET studies. Naturally the main oxygen-15 product has been oxygen-15 labelled water for blood flow studies. During the last few years we have developed a new radiowater production system (1) which is more safe and easier to use for different kinds of blood flow studies.

10001.00000000000000000000000000000000	Table 1. (Oxygen-15	studies	during	the years	1993 -	2001
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	Brain	Heart	Muscle	Oncology	Other	Total
H ₂ O	3578	2207	469	39	46	6339
CO	83	879	106	19	8	1095
O_2	74	232	261		7	574
Total	3735	3318	836	58	61	8008

Rerference

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CS-30 Cyclotron Operation at the Duke University PET Facility: Report from the Labs

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The Duke CS-30 cyclotron is a positive-ion four-particle machine accelerating protons to 27 MeV, deuterons to 15 MeV, ³He to 39 MeV and alphas to 30 MeV. The external beam is magnetically switched to seven different target stations, which are currently outfitted with two proton ¹⁸F targets, a deuteron ¹⁵O target, a proton ¹³N ammonia target, a proton ¹¹C target, a tandem proton ¹⁵O water / ¹³N ammonia target, and a beam port for experimental targets. We have previously produced ¹²⁴I from proton bombardment of enriched tellurium targets, and have bombarded a porous carbon target with ³He. We operate an instrumented internal beam target station that has been used for six years for the high level production of ²¹¹At (monoclonal antibody label for glioblastoma therapy) by bombarding bismuth targets with alpha particles.

The cyclotron is currently operated approximately1000 hours per year, the majority of which is used to produce ¹⁸F for clinical PET. F-18 FDG is typically synthesized three times a day Tuesday through Friday to support a PET scanner throughput of about 3000 patients per year. ¹⁵O water and CO, and ¹³N ammonia are produced for 250 research studies per year. ²¹¹At production averages about an hour per week for chemistry studies, with a four-hour run for patient therapy dose when required. Two new ¹⁸F target systems are under development using the experimental beam line: a thermosyphon batch target and a regenerative turbine recirculating target. The purpose of these targets is to significantly increase the beam current that a target can tolerate, thus increasing the ¹⁸F produced and making more effective use of the high beam power available from current and future generation cyclotrons.

The cyclotron staff consists of Bruce Wieland, PhD/PE, Claudio Illan, MSEE/MSNE, and operators Shawn Murphy, BSNE, and Michael Dailey, AE Mechanical/Electronics. The cyclotron is typically staffed from 4 AM to 6 PM. Two part-time operators (physics graduate students) are also available for late night runs as required.

Radiochemistry and Automation

OPC Based Control Software

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Aim

To develop a method of implementing chemistry module control systems that allow simple and rapid development of a graphical user interface and supports sequencing for automation tasks.

Methods

I reported at the previous WTTC meeting (http://www.triumf.ca/wttc) on our use of Lookout (National Instruments http://www.ni.com) control software for our chemistry control systems. Lookout is a commercial software package that allows the rapid development of graphical user interfaces to control hardware. Lookout lacks a simple environment for implementing scripting or sequence execution necessary to effectively implement automated synthesis. A software model known as component object modelling implemented by Microsoft (http://www.microsoft.com) as object linking and embedding (OLE) allows for the communication of multiple software processes running on one host or distributed hosts. This model has been adopted by the process control community and implemented as OLE for Process Control (OPC) (OPC Foundation http://www.opcfoundation.org). The practical effect of this is to provide a software layer (the OPC server) that interacts with the control hardware and interacts with any other software program (the OPC client) that implements the OPC protocol. In this way multiple software programs (on the same or different computers) can communicate with a single hardware system via the OPC server.

Results

I have implemented this model on our chemistry synthesis systems to partition the GUI tasks to Lookout and the automation tasks to Visual Basic (Microsoft Corporation http://www.microsoft.com) programs. In this way the strengths of each environment are utilized without the weaknesses.

Conclusions

OPC provides an add-in for computer control systems which allows implementing automation tasks outside commercial software packages which may not support such tasks.

Radiochemical TI-201 Production Process

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Aims

²⁰¹Tl, in spite of the previsions, continuous being the most frequently used cyclotron produced radionuclide in SPECT nuclear medicine; in the present work was sought to obtain a productive chromatographic process, that permit to obviate the classic lead precipitation and extraction step.

Methods

The distribution K_D constants, were determined for Tl⁺, Tl³⁺ and Pb²⁺ in cationic exchange resins of different crosslinked, particle sized and different concentrations of HCl and HNO₃. Thallium was labelled with ²⁰¹Tl and correlated by atomic emission at 3446 Å (sensibility 1 ppm). Lead was labelled with ²¹⁰Pb and by atomic absorption at 2170 Å sensibility 0.01 ppm. Chromatographs were developed using a peristaltic pump, a fraction collector coupled to a NaI(Tl) detector with an integrative and registering system.

Chromatographic Development

The simulated cyclotron target used for development was prepared with 700 mg of TlNO₃, 1 mg of PbNO₃ and labels of ²⁰¹Tl and ²¹⁰Pb. With a low pressure chromatographic equipment, these targets were eluted using different types of columns, resin bulks, gradients and solvent flows. This development was based on optimising Pb-Tl separation, seeking the greater number of theoretical plates getting the following conditions: Resin type :AG 50W-X12 200-400 Solvent : HNO₃ 0.1 M Resin bulk : 120 g Flow: 1.3 ml/min. Temperature : 25°C



These conditions give the best relationship for $K_D Pb^{2+} / K_D Tl^+$ in HNO₃ 0.1 M. More than 99.9 % of Tl⁺ was eluted and all Pb²⁺ remained in the column. The production process is the charge of the dissolved irradiated ²⁰³Tl in the column, washed the column with HNO₃ 0.1 M, 32 Hs decay time, elution of ²⁰¹Tl produced in column with HCl 0.1 M, dryness, and physiological solution.

Results

This method was tested in the laboratories of Ezeiza Atomic Centre Cyclotron, Buenos Aires and is working from -97 up to now in ²⁰¹Tl production. Earlier test were performed with natural Tl as target. In these conditions large quantities of ²⁰³Pb (which was used to evaluate withholding of Pb into the column), were produced.

Yields obtained: Withholding of Pb^{2+} into the column: 99,8 %; Radionuclidic purity : ²⁰¹Tl: 100 % ²⁰⁰Tl: 1 % ²⁰⁰Tl: 0,4 %; Ratio ²⁰¹Tl exp./ theor.: 87-95 %; Recovery of ²⁰³Tl: 99,9 %

Conclusions

The radiochromatographic method has great advantages, avoids precipitation and extraction, is simple, easy to automate and low maintenance. The high number of theoretical plates of the column produces high Tl quality. In the other contribution submitted (G.J. Maslat and G.A. Casale) we are presenting an automated system for this method.

Synthesis of C-11-Labelled Acamprosate for Pharmacodynamic Studies by PET

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Aims

Although acamprosate is used therapeutically in Europe for several years to reduce relapse in weaned alcoholics, the mechanisms by which acamprosate decreases alcohol ingestion and relapse rates of alcoholics are still not clear. It is suggested that acamprosate acts by reducing neuronal hyperexcitability, responsible for the acute alcohol withdrawal syndrome, on the level of both excitatory glutamate type and inhibitory GABA (gammaaminobutyric acid) type neurotransmitter pathways. (1)

An interesting method of investigation of the pharmacodynamic properties of acamprosate is to look for the drug action site. Since PET has made it possible to examine the biodistribution of certain compounds in vivo, this imaging technique might be a powerful instrument for the characterisation of these binding sites in the human brain. For this application it is necessary to label the molecule of interest with a short-lived, positronemitting radionuclide as carbon-11 ($T_{1/2}$ =20.4 min). Therefore, this study aimed to develop a synthesis for C-11-labelled acamprosate. From the structure of acamprosate or calcium-N-acetyl homotaurinate, the acetyl group is considered to be the most accessible position.

Methods

Carbon-11 radionuclide was produced by irradiation of pure nitrogen with 18 MeV protons accelerated in a cyclotron for 20 min at 15 μ A beam intensity. During irradiation carbon-11 reacts with traces oxygen to form [C-11]carbon dioxide. After irradiation [C-11]carbon dioxide was collected in an automated set-up and transformed into [C-11]acetyl chloride, according to the method described by Luthra et al. (2) This labelling agent finally reacted with homotaurinate to form [C-11]N-acetyl homotaurinate.

The [C-11]N-acetyl homotaurinate was separated from the reaction mixture on a semipreparative reversed phase C18 column. Finally, the collected fraction was purified by SPE (solid phase extraction), sent through a 0.22 μ m sterile filter and formulated for intravenous administration.

Results

The radiosynthesis lasted 45-50 min from the end of the radionuclide production to provide [C-11]N-acetyl homotaurinate ready for intravenous injection. The radiochemical yield was about 1.10 GBq. This corresponds to 12 % of initial [C-11]carbon dioxide radioactivity, decay-corrected. The specific radioactivity at the end of synthesis was more
then 8 GBq/ μ mol. For the assessment of radiochemical purity and chemical purity analytical high pressure liquid chromatography (HPLC) and gas chromatography were used.

Conclusion

The ability to produce radiochemically pure [C-11]N-acetyl homotaurinate with a sufficient specific radioactivity enables a study of the distribution of acamprosate in the brain with PET.

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Rapid Screening of PET Volatile Organic Infusions Generated from 2-F-18-FDG Synthesis by Solid Phase Microextraction Coupled with GC/MS

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Aims

2-F-18-Fluoro-2-Deoxy-D-glucose (2-FDG) is the most important commonly used radiopharmaceutical in PET imaging. The F-18-FDG synthesis involves the conversion of nucleophilic 18F- into F-18-FDG. The mannose triflate precursor, dissolved in acetonitrile, is introduced in the reactor. A nucleophilic substitution reaction occurs, in which the trifluoromethane sulfonate group is replaced by the F-18 atom, and results in 2-F-18-fluoro-1,3,4,6-tetra-O-acetyl-D-glucose. During this time the reverse phase cartridges are conditioned with ethanol and water. This study aims to develop an experimental method using headspace solid phase microextraction (HS-SPME) coupled with GS/MS to quantitatively determine the amounts of volatile organic solvent (VOC) that may be present in clinical preparations of aqueous 2-FDG manufactured at the Paterson.

Methods

Pre-conditioned fused silica fibers (1 cm long, 75 µm diameter) coated with a PDMS/Carboxen polymeric stationary phase were bonded with a high temperature epoxy resin, to a stainless steel plunger that was installed in a syringe type holder. The syringe type device allow penetration of the F-18-FDG sample vial septa in order to sample directly from the vial head space. Organic analytes then absorbed/adsorbed onto the fiber coating from the head space. Once removed from the head space the fiber was then transferred to an Optic 2 injector fitted to a GC, where the analytes were thermally desorbed from the coating and entered the GC column for separation and analysis.

Results

In order to develop a quantifiable experimental method for the analysis of VOC's contained in F-18-FDG samples, it was necessary to optimise the SPME parameters such as extraction time, extraction temperature and phase-volume ratio (volume of sample to headspace). This was done in order to establish which of these parameters gave the greatest extraction efficiency for the VOC's. It was found that an extraction time of 10 minutes, extraction temperature of 60°C and a pahse-volume ratio of 1.00 gave the greatest extraction efficiency. Both the calibration curves generated for the acetonitrile and ethanol samples and for low acetonitrile concentrations were found to be linear with correlation coefficients calculated to be 0.9963, 0.9913 and 0.8227 respectively. The detection limits

for the experimental method developed were in the order of 2.52 ppm for ethanol and 0.49 ppm for acetonitrile.

Conclusion

This study has established that this experimental method is fast, inexpensive and solvent free. It has also demonstrated an ability to analyse ppm residues of both acetonitrile and ethanol contained within clinical preparations of F-18-FDG.

Direct PC Automation of Radiochemical TI-201 Process

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Aims

In order to continue our chromatographic radiochemical method for cyclotron irradiated Thalium targets, an automated system was developed. The philosophy was an equipment with both possibilities: auto/manual, commanded by an open software, with a radiochemical friendly script language. We called it "Direct PC" because all the systems are directly interfaced to a common PC without PLC or dedicated electronics systems. The PC microprocessor has all the information of the radiochemical process.

Methods

Two main programs drive the module: "Main Control Program" and "Radio-chemical Editor Program". Both developed in Visual Basic 3.0 for 16 bits machine or 6.0 for 32 bits. The radiochemical module has an active part in a hot cell (150mm lead) and an inactive one outside the hot cell with different reagents pumps and manifold selection valves without risk of radiation damage. The active module consists only of a dissolver, two Rheodyne PEEK valves, exchange column and an evaporator plumbed by tygon/teflon lined tubes. These valves are excellent in high radiation fields.

All the components are interfaced directly to the PC via In/Out ports made with the well known 8255PPI directly interfaced to the PC bus, drivers and relays for the electrovalves action. The analogs ports with the MAX147, (12bit, 8 channels) measures the temperatures of target, TI^+/TI^0 potential during dissolution, valves position and bubble detector. The pump GILSON 402 Dilutor, is interfaced via RS232.





Results

The equipment was tested in cold and hot chemistry, all the radiochemical parameters were repeated obtaining the same laboratory results:

Pb ²⁺ Column retention: >99.5 % ²⁰³ Tl recovery: >99.9 % ²⁰³ Pb in batch(with postcolumn):0.003 %	²⁰¹ Tl elution after decay time: >95 % Tl ⁺ total in batch: < 2 ppm ²⁰⁰ Tl/ ²⁰² Tl in batch: 1-2 % / 0.1 % (depends of irradiation parameters)
	or multicle parameters)

Processing Times: First Process: Dissolution, load, wash column: 1.45 h Second Process: Tl elution, dryness, batch extraction: 3 h

This equipment has been working since 1997 up to now. The average of activity has been 55.5 GBq/batch (1.5 Ci/batch) (80-90 μ A, 10-12 h irradiation).

Conclusions

The direct PC automation has great advantages: is simple, not too much electronic involved, the microprocessor has all the parameters with total control. The graphical interfaces are easily operated, the chemist can change differents radiochemical parameters, like flows, volumes, temperatures, reagents, etc. The accuracy, repeatability, minimum sizes, low personal dose, low maintenance (only a column by process and o-ring dissolver each 6 process) during these years, make the whole system very successful.

Experiences with the Amercare Syringe Fill Station

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Aims

Because of the increasing demand for FDG and the concomitant manual dispensing of patient doses, the finger radiation burden has become a serious issue that had to be adressed. To reduce the finger radiation dose, the Amercare dispensing unit had been selected for several reasons: 1) patient doses are being delivered in a shielded 10 ml syringe, 2) fast preparation of a bolus (< $3 \min$), 3) application to other PET-tracers, 4) use of sterile disposables only, 5) accuracy of radioactivity measurement within 10 %, 6) GMP compliance. Here we present our experience with the dispensing unit over the last year of full operation.

Methods

The fill station has been developed to completely replicate the manual syringe filling process. It has a central syringe and multidose vial position and is capable of handling shielding up to 20 mm of tungsten. The calculated volume of product is entered by the operating console (FILL-action). We use the option to fill the syringe to 8 ml with saline (ADD-action). To measure the activity (MBq/ml) a PIN silicon photodiode is integrated, which signal is translated to absolute radioactivity on a LCD display. The photodiode is linear in the range of 50-1000 MBq and is located in such a way that air bubbles > 0.5 ml are detected by appearance of discrepancy between measured and calculated amount (>15 % deviation). The shielded syringe can easily be taken out of the system and put in a lead shielded transport system. At the PET-camera the shielded syringe is connected to the injection cannula. After installation of the fill station, several optimation actions have been carried out to increase accuracy and repeatability. During the last year the following parameters were documented: accuracy of the FILL-action, correlation between radioactivity as measured by a dosecalibrator and by the photodiode after the ADD-action.

Results

The overall accuracy of the FILL-action is $95 \pm 6\%$ (n=224). This number fell below 90 % at fill volumes < 0.5 ml. On average, at volumes of 0.3-0.5 ml 86 % of the calculated volume was dispensed, whereas at volumes < 0.3 ml this number was 73 %. The relatively low accuracy below 0.5 ml forced us to split the FDG-multidose vial in two portions when the concentration of FDG was > 400 MBq/ml. This splitting action is also performed by the Amercare syringe fill station. On a few occasions (3 % of the total), a substantial

amount of air (1-3 ml) was observed in the syringe. In this case, a discrepancy between the LCD-readout and the desired dose was observed. The correlation coefficient between the radioactivity in the syringe as measured by the dose calibrator and the photodiode is 0.94 +/- 0.06 (n=55). Because the radiation dose is 15-20 μ Sv/h at 1 m distance from the tungsten shielded syringe, containing 500 MBq FDG, the fill station has been put in a lead-shielded laminar air flow hood to create a safe working environment from radiation protection point of view.

Conclusions

We successfully implemented the syringe fill station, which plays a crucial role in the daily manipulations with FDG. The finger radiation dose has been reduced to almost zero during dispensing and injection into the patient.

Radiopharmaceutical Production Quality Control Considerations

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A large number of radiopharmaceuticals are being utilized for routine clinical, clinical research and development. At Washington University in St. Louis we operate three cyclotrons for patient/animal imaging on six PET scanners in four separate buildings. They are a Cyclotron Corporation CS15 cyclotron which currently can only accelerate protons, a Japan Steel Works 16/8 cyclotron which can accelerate protons and deuterons and a RDS 111 cyclotron which produce only protons. These cyclotrons produce radiopharmaceuticals for two clinical PET scanners, three research human. Currently 18 radiopharmaceuticals are produced routinely for human use. Quality control often becomes the limiting factor in scheduling. Our QC division has two HPLC systems, a Waters and an Agilent[®], one Varian[®] GC, a Waters LC/MS, an ion chromatography system, a dose calibrator, and a germanium detector. BET and sterility testing are also performed on all injectable human radiopharmaceuticals.

DATE/TIME	LOCATION	RaPh	QC SYSTEM
3/20/02	7 MIR	FDG (8 patients)	LC
: 0800	Clinical PET		GC-residual solvents
	ECAT and C-PET		Dose Calibrator
: 0830	East Bldg	FDOPA	HPLC System 1
	Siemens 943		Dose Calibrator
: 0900	7 MIR	O-15 Water	GC
	Research HR+		Dose Calibrator
: 0900	4CSRB MicroPET	FDG dose	NA
: 0915	7 MIR	C-11 Acetate	HPLC System 2
	Research HR+		GC residual solvents
			Dose Calibrator
: 0915-1000	4CSRB Research	Tc-94m target	
: 1300	7 MIR	C-11 Glucose	HPLC System 2
	Research HR+		Dose Calibrator
: 1300	7 MIR	F-18 FES	HPLC System 2
	Research HR+		Dose Calibrator
: 1400	10 NICU	C-11 FMZ	HPLC System 1
	ECAT		Dose Calibrator

Table 1 - Examples of Daily Scheduling

An example of a typical production schedule is shown in Table 1 above. Given the number of radiopharmaceuticals produced on a daily basis, it is necessary to schedule production of isotope, synthesis of the compound, and the quality control to make sure that all can be accomplished pre-release as required.

Synthesis of Fluorine-18 Labeled Recombinant Annexin-V Derivative, for Identification and Quantification of Apoptotic Cells with PET

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Apoptosis has been recognized as an important process for the cardiovascular system. Acute cardiovascular incidences (myocardial infarction, myocarditis and heart failure) as well as other cardiovascular diseases (atherosclerosis, vascular - and cardiac allograft rejection and diabetes) are characterized pathologically by apoptosis. Increasing knowledge of the apoptotic process in relevance to the cardiovascular system, may develop new strategies for the of cardiovascular diseases. therapy Apoptosis is a form of programmed cell death, which is gene-regulated. During phosphatidyl-serine apoptotis. externalizes from the inner leaflet of the plasma membrane to the outer leaflet. An endogenous human protein that has high affinity for binding to phosphatidylserine is Annexin V. In this report, we describe the synthesis of fluorine-18 labeled recombinant Annexin-V derivate (4-[18F]-FBA).

In a four step procedure (figure 1), 4-[18F]-FBA synthesized is in а microcomputer controlled, automated module (figure 2) within 90 minutes. The radiochemical yield is in the range of 15-20 % (corrected for decay) with a specific activity of more than 3.5 GBq/µmol. The radiochemical purity is higher as 95 %. Batches of 4-[18F]-FBA of up to 2000 MBg were prepared from 25 GBg [18F]fluoride.



4-[¹⁸F]fluorobenzoyl-Annexin-V Figure 1. Synthesis of 4-[18F]-FBA

Radiation Sources and Radiodetectors

Compact, Solid-State Radiation Detectors for use in PET Isotope and Radio-Chemistry Laboratories

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<u>Abstract</u> We present a collection of compact and novel solid-state radiation detector systems used to monitor the quantity, position, and flow of activity in radioactive fluids and gasses in radio-chemistry laboratory processes, apparatus, and applications. The detectors described below include:

- 1) Multichannel systems incorporating relatively low-sensitivity, subminiature Si diode probes for use in tight spaces inside process-automation apparatus;
- 2) High-sensitivity systems with compact probes incorporating small (1 cu cm) scintillating crystals coupled to Silicon PIN diodes for analytic high-performance liquid chromatography (HPLC) and gas chromatography (GC);
- 3) Very high-sensitivity probes incorporating large (50 mm x 50 mm x 25 mm) CsI(Tl) crystals for use as stack-effluent monitors; and
- 4) A compact bench-top scanning detector system for thin-layer chromatography (TLC) applications. The TLC scanner incorporates a multi-mode Si diode detector is designated *OMNI-RAD*tm and is intended for use with any of the commonly-used beta-emitting, positron-emitting and low-energy gamma-emitting radio-nuclides.

<u>Multi-Channel Radiation Detector</u> The model 101-HDC3 is a radiation detector system intended for process monitoring applications in laboratory hot cells. The system comprises a set of up to three miniature detector probes, plus a three-channel trans-resistance (current-to-voltage converter) amplifier. The maximum gain of the amplifier in each detector channel is nominally 5×10^9 ohms, that is, a diode current of one nano-ampere produces a voltage of 5 volts at the output of the amplifier. A multi-turn trim potentiometer on the output of each amplifier chain allows the user to adjust the overall gain of the system over a range of approximately 10:1.

The active element in the detector probe is a silicon PIN diode which is enclosed in a small metal capsule to shield it against light and stray electro-magnetic fields. Each probe is connected to its amplifier through a length of small-diameter cable. The probes operate in "DC" mode and are intended to be used in close proximity to concentrated sources of gamma-emitting radio-nuclides. The output of each detector channel may be monitored by any high-input-impedance recording device: voltmeter, chart recorder, computer data acquisition system, etc.



<u>High-Sensitivity Radiation Detector</u> The model 105-S is a high-sensitivity radiation detector system used for HPLC, flow monitoring in radiochemical synthesis, monitoring of stack effluents, and similar applications.

In HPLC and flow-monitoring applications, the system employs a compact detector probe (2 cm x 2 cm x 3 cm) in conjunction with a bench-top amplifier / console unit (7.75"W x 7.5"D x 2.5"H). The sensitive element of the detector probe is a 1 cm³ CsI(Tl) scintillating crystal, optically coupled to a 1 cm² silicon PIN diode which, in turn, is connected to a charge-integrating¹ preamplifier.



Stable, reliable operation at low photon fluxes is enhanced by operating the detector in AC-coupled pulse-mode. In this mode of operation, individual gamma ray photon interactions in the scintillating crystal are converted to flashes of light which are then converted in the diode / preamplifier to discrete pulses of current. The pulses of current are amplified, thresholded, and integrated to produce a "DC" signal which is proportional to the count rate of photons which exceed threshold.



¹Covered by one or more of the following US Patents: 5,990,745; 6,054,705.

For stack-monitor applications, the same console unit is used with a larger, more sensitive probe: a 50 mm x 50 mm x 25 mm CsI(Tl) scintillating crystal which is optically coupled to a 10mm x 20mm silicon PIN diode plus charge-integrating preamplifier. The probe is epoxy-cast for protection against moisture incursion, and sealed into a compact 65 mm x 65 mm x 35 mm aluminum enclosure for convenient shielding.

<u>**OMNI-RAD**tm</u> Detector for thin-layer chromatography This versatile, PIN-diode-based module is used for scanning TLC plates which have been 'spotted' with compounds labeled with commonly-used medical and research isotopes, including low-energy gamma emitters, positron-emitters, or beta (-) emitters.

<u>Beta Detection</u>: In beta (or positron) mode the detector module utilizes anti-parallel (opposed-polarity), back-to-back, 1 sq. cm. PIN-diodes mounted behind a 3mm wide slit in a 1/4" thick lead plate centered over the scanning bed. The diode which is closest to the TLC plate responds to both beta's and gamma's emitted from the sample; the second diode, which is "shadowed" by the first diode, responds only to gamma's. By electronically subtracting the second (gamma) signal from the first (beta plus gamma) signal, we have a composite detector which, in effect, responds to beta's only, providing excellent spatial resolution for beta + (positron) or beta (-) emitters, but without the need for bulky lead shielding -- even in the presence of an intense gamma background.

The effectiveness of the concept is illustrated in the 'Mock" TLC scan, where the sample under test (56 Co) emits both positrons ($E_{max} = 1.459$ MeV) as well as intensely penetrating gamma rays (846, 1240, 1760, 2600 keV, 3260 keV and others).

<u>Gamma Detection</u>: In gamma detection mode, the signals from the two detector diodes are summed instead of subtracted. Spatial resolution for low-energy gamma-emitters (\sim 140 keV max.) is provided by a 3 mm wide slot cut in the 1/4" thick lead bottom plate.





<u>**EZ-SCAN**</u> tm is a compact, bench-top TLC scanner / detector system that occupies a relatively small foot-print on scarce lab-bench real-estate. The system is designed for routine use in a busy lab environment. Using <u>**EZ-SCAN**</u> with the **Omni-Rad** detector module, one can 'spot' a small sample drawn directly from a production run, without requiring any dilution. The annotated thumb-nail image at the right is reproduced from a time-record from PeakSimpletm – a computer-based Chromatography data acquisition system. This was a 'mock' scan using a TLC plate on which small drops of ¹⁸F-labeled

fluoride were placed by hand. The plate was later cut up and the pieces assayed in order to ascertain the amount of activity represented in each peak. Total width of the plot represents 5 minutes time duration for a 10 cm scan.



Estimating the Radiation Source Term for PET Isotope Targets

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<u>ABSTRACT</u> An estimate of the source term - the neutron fluence and spectra for nuclear reactions commonly used for producing PET isotopes - is required to validate the design of shielding, and to estimate the potential for activation of materials and components in and around the cyclotron.

We present data on neutron fluence and spectra for the most commonly used (p,n) PET isotope nuclear reactions, including ¹⁸O(p,n)¹⁸F for proton energies of 11 MeV and 17 MeV. Data were obtained from our own neutron measurements on bare and partially-shielded targets at 11 MeV. At the higher proton energy we conducted computer simulations utilizing the program *ALICE-91*.

<u>Neutron spectra at 11 MeV</u> The Energy spectrum of neutrons from un-shielded RDS-112 Targets (CTI, Inc., Koxville, TN, USA) were measured using an NE-213 Protonrecoil Spectrometer^{*}. Pulse-shape discrimination produced separate and distinct energy spectra for gamma-ray events versus neutron-induced proton-recoil events. The raw detector data were 'unfolded' using our own algorithm which incorporates a correction



* Beam energy on target -- accounting for energy loss in the foils – was 10.4 MeV.

detector data were 'unfolded' using our own algorithm which incorporates a correction for the intrinsic non-linearity of response of the scintillator at low recoil energies, a correction for the energy-dependent fall-off in detector efficiency and, finally, channel-by-channel discrete differentiation to extract spectral information from the (more-or-less) featureless continuum of the raw data. The algorithm was validated by comparing an 'unfolded' AmBe neutron spectrum against examples from the literature¹.



<u>Angular distribution of neutrons</u> This was measured by fast-neutron activation of small material samples placed at several angles around (and close to) bare RDS -112 targets: Small pellets of P_2O_5 were activated via the reaction ${}^{31}P(n,p){}^{31}Si$ to record neutrons above 2 MeV; small iron bolts were activated via the reaction ${}^{56}Fe(n,p){}^{56}Mn$ to record neutrons above 6 MeV. In the figures below, data for respective threshold reactions are normalized – *not according to relative intensity* (which is apparent from the above figures) -- but rather for ease of visualization of angular distribution.



<u>Spectrum and Fluence for Ep = 17 MeV</u> For bombarding energies greater than Ep = 12 MeV, a number of additional neutron-producing reaction channels open up. However, to the best of our knowledge, direct experimental data on total neutron fluence and spectrum for reaction energies higher than ~12 MeV is not available at this time.



Discussion: The reaction ¹⁸O(p,n)¹⁸ F is today -- by far -- the most widely used reaction for PET isotope production. Below $E_p = \sim 12$ MeV the rate of neutron production is virtually identical to the ¹⁸F saturation yield, i.e., the rate of production of 'new' ¹⁸F atoms².

Above $E_p = 11$ MeV a number of additional ¹⁸O(p,x) neutron-emitting reaction channels become energetically possible³, but experimental cross-section data are not readily available to help us determine rates of 'excess' neutron emission. We turn, therefore, to computer codes, such as *ALICE 91* to help us make these estimates.



The plots above show that below $E_p = -8$ MeV *ALICE 91* underestimates ¹⁸F saturation yield and– by inference – also underestimates neutron production per uA on an ¹⁸O water target.

Above $E_p = 8$ MeV, *ALICE 91* begins to overestimate both ¹⁸F saturation yield and neutron yield.

At 17 MeV *ALICE 91* plausibly predicts approximately 1.5 times as many neutrons per second relative to its own internal model calculation for ¹⁸F saturation yield, but this is almost 4 times as many neutrons per second relative to experimentally-measured -- and widely accepted -- ¹⁸F yield data⁴ scaled for a 100 % enriched water target.

Thus, between 11 MeV and 17 MeV *ALICE 91* provides a credible – albeit highly conservative – upper bound for neutron yield per uA from this reaction, offering a wide safety margin relative to enriched water targets as well as higher-performance ${}^{18}O_2$ gas targets for use in shielding and activation calculations.

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Potential of TIBr Semiconductor Detector for Nuclear Medicine

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Aims

During the last years space organizations in Europe and USA have actively developed new high density semiconductor detectors for the energy range 30-200 keV. Both position and energy resolution are important. All those specifications are important in nuclear medical applications as well.

TlBr is one of the material developed. Because TlBr has a high mean atomic number and a density of 7,6 g/cm³, its radiation absorption properties are comparable with BGO. The material is still in the development phase but very promising spectroscopic properties has been demonstrated. Main effort is put to the purification and growing of detector grade single crystals.

Methods

The purity of the crystal and a low density of defects are critical properties for the detector grade crystals. Purification is done using several steps. The raw material is usually purified by the multiple distillation and crystallization method. Liquid distillation is studied. Trace element concentrations from different process steps are analyzed. The crystals are chracterized by several methods including X-ray diffraction and IR reflection spectroscopy. Electron collection properties are measured.

Results

Several detectors are produced from TlBr single crystals. X-ray spectra are measured using ⁵⁵Fe, ¹⁰⁹Cd and ²⁴¹Am sources. Energy resolutions 800 eV at 22 keV and 3 keV at 60 keV have been measured.

Conclusions

According to our studies TlBr is a potential detector material for nuclear medicine. It is a wide band semiconductor which can operate at room temperature. Because TlBr has a high atomic number and a high density its properties match well to the medical applications. Good energy resolution can be used for the background suppression in imaging applications. Next step is to refine the detector grade crystal growing process.

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