MASTER

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ORNL/MIT-258

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SUBJECT: Design of a ^{18}F Production System at ORNL 86-Inch Cyclotron

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ABSTRACT

A target system for the production of ^{18}F by proton bombardment of $H_2{}^{18}O$ was designed for the ORNL 86-inch cyclotron facility. The system consists of concentric titanium and aluminum cylinders. Oxygen-18-enriched H_2O circulates through the inner titanium cylinder and through an external heat exchanger with cooling water flowing in the annulus. Yields of 5.0 curies are expected for a 250-μA proton beam current and 24-min irradiation time.

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1. SUMMARY

A fluorine-18 production system was designed for the ORNL 86-inch cyclotron using $H_2{}^{18}O$ as the target material. Design considerations were target geometry, materials of construction, heat removal, and ^{18}F recovery system. The Accelerator Target Simulation (ATS) computer program was used to determine yields and power dissipation within the target. Irradiation time was calculated based on available beam current and level of activity required. The system consists of aluminum and titanium concentric cylinders with target water flowing in the inner cylinder at a rate of 0.5 gpm to an external heat exchanger. Target cooling water flows in the annulus at a rate of 1.7 gpm removing the bulk of the dissipated heat. A proton beam current of 250 μA and an irradiation time of 24 min should be sufficient to produce ^{18}F with an activity of 5 curies without any heat removal problems. Cyclotron runs should be made using ordinary water ($H_2{}^{16}O$) and low concentrations of $H_2{}^{18}O$ to test the design specifications.

2. INTRODUCTION

The use of radionuclides in medicine has great potential in diagnostic and prognostic medical research (3, 5). Molecules labeled with positron emitting isotopes such as ^{11}C, ^{13}N, ^{15}O, and ^{18}F are important because they allow for a unique system of detection. The annihilation of an emitted positron, after collision with an electron in nearby tissue, yields two gamma rays which travel in opposite directions that can be detected to give an accurate spatial representation of the positron source (1, 3, 4, 12). Therefore, comprehensive mappings of individual organs can be obtained. Currently the isotopes ^{11}C, ^{13}N, and ^{15}O have been examined; however, their half-lives of less than 20 min are too short for practical purposes. Fluorine-18 with a half-life of 110 min is a good alternative (8, 9, 11, 13).

The objectives were to examine various target configurations and materials to determine the design specifications of the ^{18}F production system.

3. DESIGN OF THE ^{18}F PRODUCTION SYSTEM

3.1 Capsule Design

The evaluation of target configurations was aided by the Accelerator Target Simulation (ATS) computer code developed at ORAU for simulating proton bombardment of target systems (6, 7). In evaluating target geometries the following factors were considered:

1. Cyclotron hardware limitations constrain the internal irradiation zone to an area 6-cm wide and 0.6-cm long. The proton beam had an initial peak energy of 22 MeV with an uneven distribution (see Fig. 1) and a maximum beam current of 3000 μA internally and 30 μA externally (10,15).

2. Target configuration must allow protons in the proper energy range to collide with ^{18}O to maximize yields, which corresponds to the 4 to 12 MeV range as seen in Fig. 2.

3. The geometry should permit sufficient heat removal to prevent boiling of the water or overheating of the target system.

Table 1 summarizes the target geometries examined. The concentric-cylinders arrangement with cooling water in the annulus (Fig. 1) was the most suitable as it results in substantial ^{18}F yields, sufficient cooling capability, and the use of present facilities at the ORNL 86-inch cyclotron.

Target wall materials must be strong enough to use at relatively high pressures and also have low atomic densities for higher ^{18}F yields. Table 2 summarizes the wall materials examined. Although aluminum would be most suitable for outer walls, it could not be used for the inner walls due to ^{18}F adsorption (11). Titanium was the alternative as it did not have any ^{18}F adsorption problems. However, it has low thermal conductivity and forms ^{48}V.

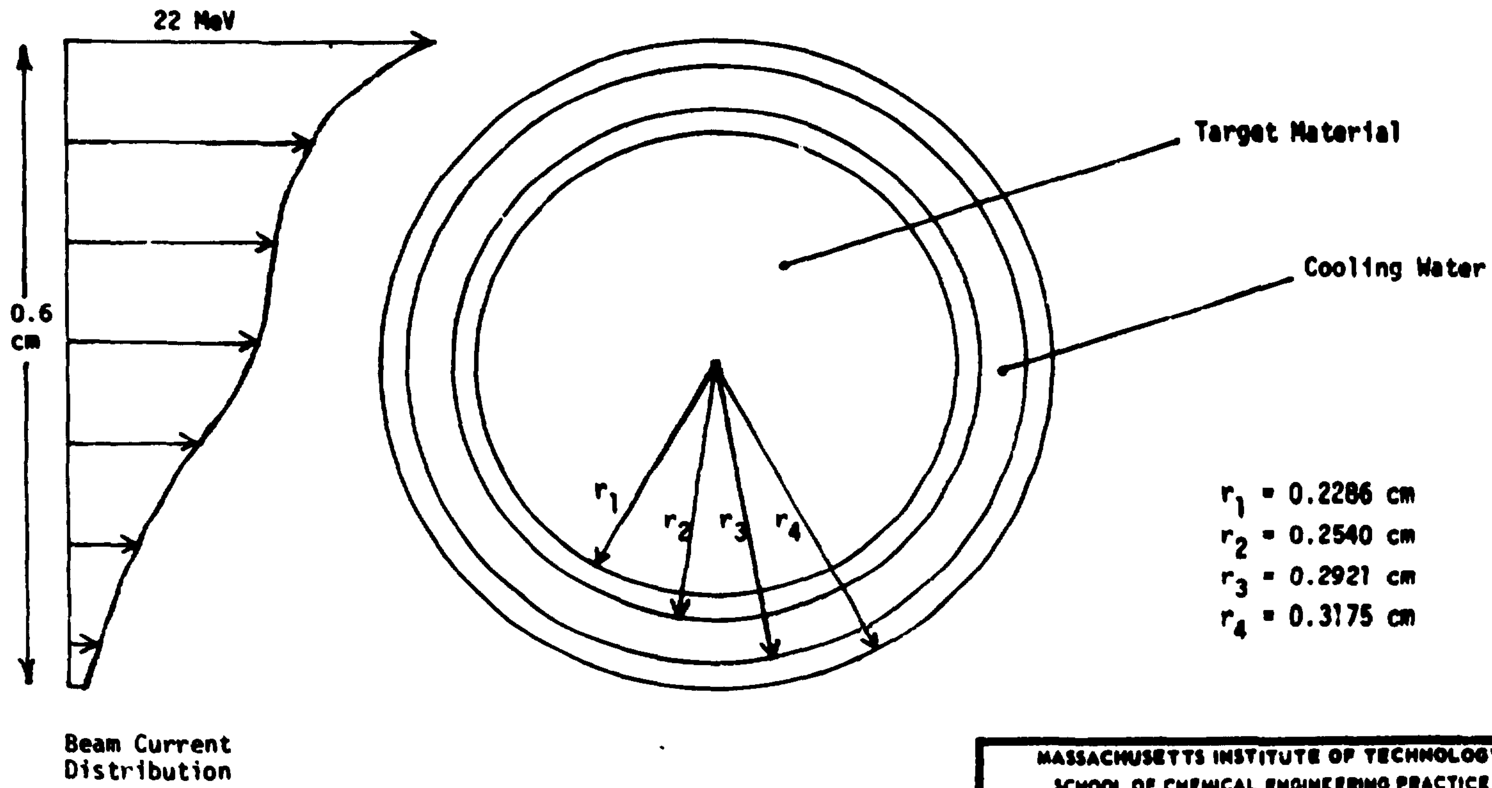
Target compounds examined were water, boron oxide, and oxygen gas. Table 3 summarizes their advantages and disadvantages. Oxygen-18 enriched water was the most suitable as it had large yields without any heat removal problems. However, the formation of H_2 and O_2 due to proton radiolysis as well as the recovery of ^{18}F from the solution should be examined (see Appendices 7.1 and 7.2).

3.2 Beam Current and Irradiation Time

Analysis of the temperature distribution for the target system indicates that higher temperature would occur within the walls of the inner cylinder (see Fig. 2). The maximum allowable beam current was determined by setting the target water outlet temperature below the boiling point to 90°C. The maximum beam current was then back calculated to be 250 μA with a 50% margin for safety. Therefore, to produce ^{18}F with 5 curies of activity 24 min of irradiation time would be required.

3.3 Heat Transfer Characteristics

The proton beam current dissipates 5 kw of heat within the target capsule. To keep the temperature of the target water below its boiling point, it was circulated through an external heat exchanger at a rate of 0.5 gpm,



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TARGET GEOMETRY

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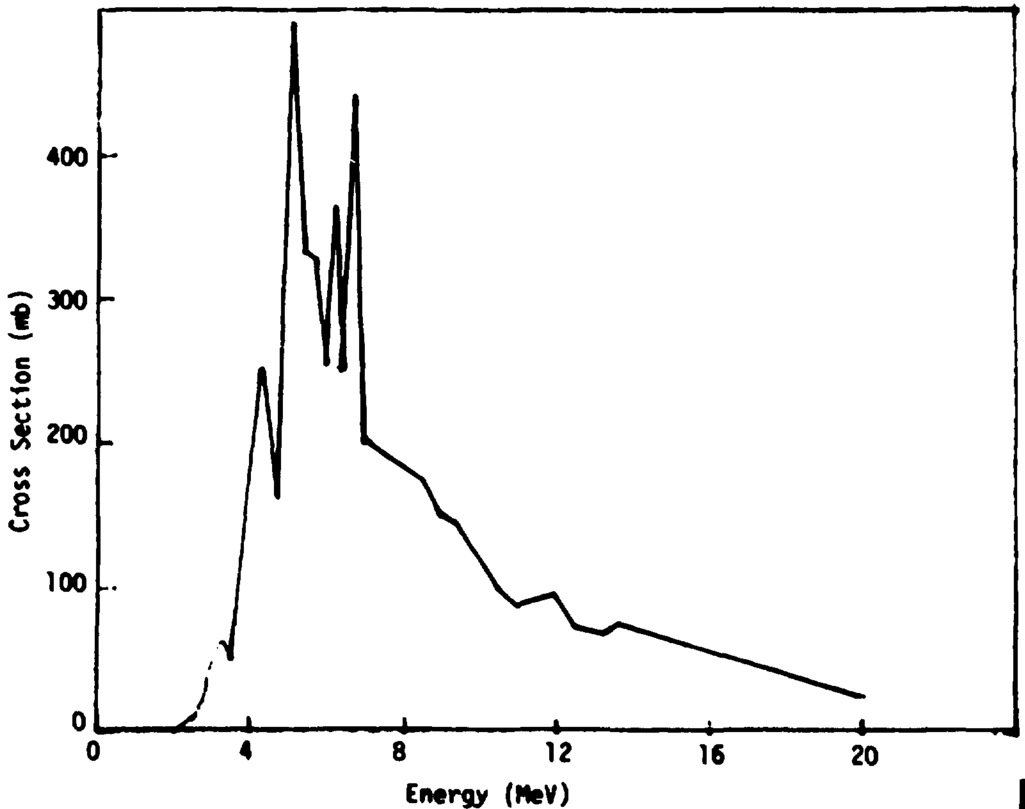
10-18-77	BAB	CEPS-X-258	1



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NUCLEAR REACTION CROSS SECTION of $^{18}O(p,n)^{18}F$

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10-18-77	FB	CEPS-X-258	2

Table 1. Target Geometries

Geometry	Advantages	Disadvantages
Concentric cylinders, cooling water in annulus	Sufficient cooling Substantial ^{18}F yield Uses existing header blocks	Inefficient proton beam utilization ^{18}F recovery may be difficult
Concentric cylinders, target material in annulus	Sufficient cooling Uses existing header blocks	Inefficient proton beam utilization Low ^{18}F yields ^{18}F recovery may be difficult
Single cylinder	Sample design High yields	Inefficient proton beam utilization High target compound inventory High heat load New header blocks ^{18}F recovery is difficult
Flat Plate	Sufficient cooling Utilizes beam effectively	Low ^{18}F yields Difficult to hold target material

Table 2. Target Wall Materials (2, 14)

Material	Thermal Conductivity (cal/cm-sec-°C)	Atom Density (atoms/cc x 10^{-22})	Advantages	Disadvantages
Aluminum	0.531	6.02	High thermal conductivity Low atom density Inexpensive No radiation byproducts	Adsorbs ^{18}F
Nickel	0.187	9.13	High thermal conductivity Inexpensive	Yields ^{57}Co ($t_{1/2}$ = 272 days)
Stainless steel	0.060	8.54	Inexpensive	Low thermal conductivity Radioactive byproducts
Titanium	0.039	5.67	No ^{18}F affinity	Low thermal conductivity Yields ^{48}V ($t_{1/2}$ = 16 days)

Table 3. Advantages and Disadvantages of Oxygen-18 Compounds

Target Compound	Advantages	Disadvantages
$H_2{}^{18}O(\ell)$	Acts as a heat sink High yields of ^{18}F Commercially available	Proton radiolysis No proven separation technique
$B_2{}^{18}O_3(s)$	Target system in use Can be used together with ^{11}C production	Low ^{18}F yields Heat removal problems Batch recovery of ^{18}F Not commercially available
$^{18}O_2(g)$	Yields $^{18}F_2$ Commercially available	Requires external irradiation Low yields Long irradiation times

corresponding to a temperature rise of 22°C (40°C inlet to 62°C outlet). Heat exchanger specifications were calculated using a computer program to evaluate the necessary heat transfer areas at different cooling flow rates, vessel dimensions, and beam currents. A countercurrent double-pipe heat exchanger with specifications given in Table 4 was sufficient for a 240 μA proton beam current.

Table 4. Target Water Heat Exchanger Specifications

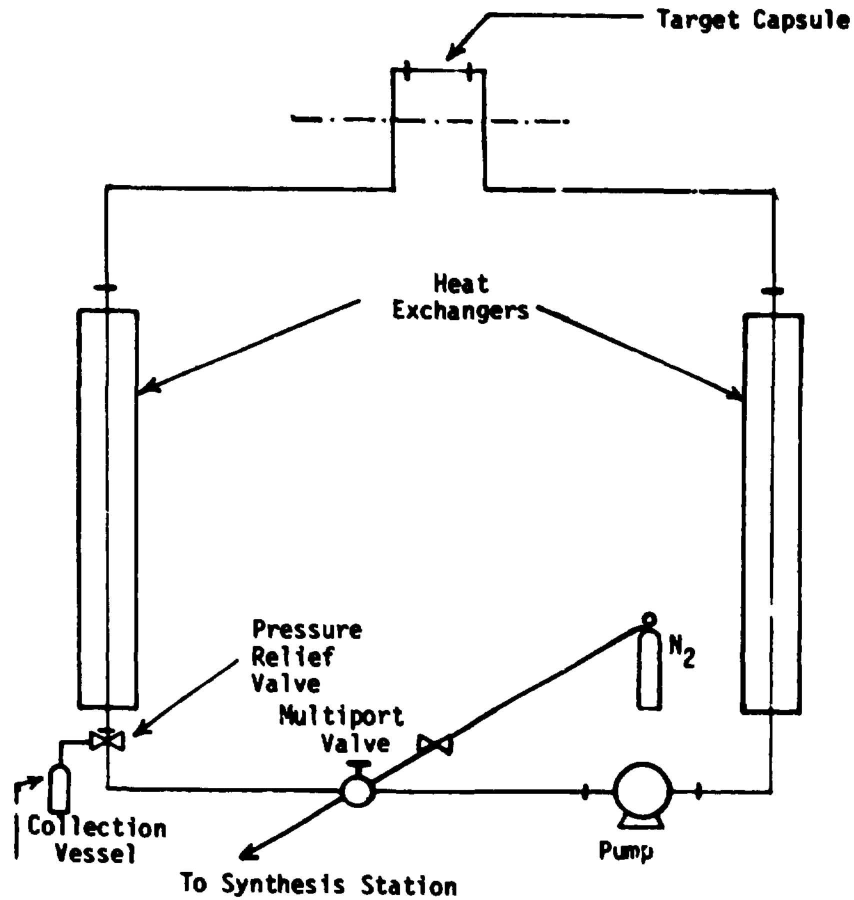
T_{in} = 62°C; T_{out} = 40°C; Cooling Area = 304 cm^2

	Outer Tube	Inner Tube
Length (cm)	153	153
O.D. (cm)	-	0.635
I.D. (cm)	1.021	-
Flow rate (gpm)	6 (annulus)	0.5
Material	aluminum	nickel

4. PRODUCTION SYSTEM - DESIGN SPECIFICATIONS

The production system (see Figs. 1 and 3) consists of concentric cylinders with $H_2{}^{18}O(\ell)$ as the target isotope. The outer cylinder (250 mil OD, 10 mil thick) is aluminum while the inner cylinder (200 mil OD, 10 mil thick) is titanium (see Table 5). The target water flows through the inner tube at a rate of 0.5 gpm, entering at 40°C. Cooling water enters at 24°C with a rate of 1.7 gpm, passes through the annulus countercurrently, and provides the bulk of the cooling.

The cooling system for the target water consists of countercurrent, double-pipe heat exchangers to be used with existing facilities at ORNL 86-inch cyclotron facility, specifications of which are given in Table 4. Table 5 summarizes the results of the final target system design. Circulation of the target water will be provided by a peristaltic pump. The loop will have the capability for collection of radiolysis products and a catalytic unit for recombination of O_2 and H_2. A multiport valve permits loading and removal of target water.



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PROPOSED TARGET SYSTEM

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10-17-77	BAB	CEPS-X-258	3

Table 5. Design Specifications of the Target System

(See Table 4 for Heat Exchanger Specifications)

	Target Water (100 ml holdup in the loop)	Coolant Water (Annulus)
Flow Rate (gpm)	0.5 ($\Delta P \sim 0.3$ psi)	1.7 ($\Delta P \sim 128$ psi)
Inlet Temperature (°C)	40	24
Outlet Temperature (°C)	62	-
Target Dimensions Existing at ORNL		
	Inside Tube	Outside Tube
Length (cm)	20	20
I.D. (cm)	0.4572	0.5842
O.D. (cm)	0.5080	0.6350

Pump: Peristaltic type, Masterflex No. 7549-19

5. RECOMMENDATIONS

1. Heat transfer equipment specifications should be tested with cyclotron runs using tap water.
2. Titanium proton bombardment products should be examined.
3. ^{18}F yields should be tested using dilute $H_2{}^{18}O$.
4. ^{18}F recovery techniques should be developed.

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7. APPENDIX

7.1 Fluorine-18 Concentration in Target Water

Fluorine-18 with an activity of 5 curies should be produced at the cyclotron facility (see Appendix 7.2). This corresponds to 185 x 10^9 decays/sec. Using the definition

$$\text{activity} = \frac{0.693}{t_{1/2}} N$$

where $t_{1/2}$ is the half life of the radioisotope (6600 sec for ^{18}F), the number of ^{18}F atoms, N, can be calculated:

$$N = 185 \times 10^9 \frac{6600}{0.693} = 1.76 \times 10^{15} \text{ atoms of } ^{18}F.$$

For 100 cm^3 of target water inventory, the molal concentration of ^{18}F is then

$$[^{18}F] = \frac{1.76 \times 10^{15}}{6.02 \times 10^{23}}\left(\frac{1}{0.1}\right) = 2.9 \times 10^{-8} \text{ mole/liter.}$$

7.2 Fluorine-18 Recovery and Level of Activity

Fluorine-18 produced in the proposed target system will be in the form of aqueous fluoride ion. Production of anhydrous $H^{18}F$ from this solution would be possible by making the mixture alkaline, distilling to recover the $H_2{}^{18}O$, and acidifying to release the anhydrous $H^{18}F$ (16). Two possible schemes exist for the synthesis of ^{18}F-2-fluoro-2-deoxyglucose. The first method involves the fluorination of triacetyl glucal with $^{18}F_2$; however, this reaction requires $^{18}F_2$. The second method involves nucleophilic displacement of fluorine using 2-iodo-2-deoxyglucose to form the fluorinated form of the compound.

The level of activity that must be generated in the target is determined by the required activity at the time of patient injection. Since a full synthesis method has not been developed yet, the method using fluorinating agents will be discussed. At the time of patient injection, 20 mCi of ^{18}F activity are required. Twenty minutes must be allowed for patient management. The chemical yield for the fluorine-substitution of 2-iodo-2-deoxyglucose is 20%. Assuming that the fluorinating agent has four fluorine atoms, the activity could be decreased by 75% as only one in four fluorine atoms would be labeled. These two factors alone increase the required initial activity by a factor of 20 up to 460 mCi. The time for transportation and other synthesis can be estimated to be one half-life or 110 min, thus doubling the required starting activity to 920 mCi. Allowances must also be made for losses in separation processes and for removal of the target water from the capsule. Using an overall 20% efficiency for these steps will result in an initial activity requirement of 5 curies.

7.3 Literature References

1. Clark, J.C., and D.J. Silvester, "A Cyclotron Method for the Production of Fluorine-18," Int. J. Appl. Rad. Isotopes, 17, 151 (1966).

2. Etherington, H., "Nuclear Engineering Handbook," McGraw-Hill, New York, 1958.

3. Highfill, R.R., B.W. Wieland, L.C. Washburn, and R.L. Hayes, "System for Synthesis and Use of Positron-Emitting Radiopharmaceuticals," proposal to National Institute of Health (1977).

4. Huxtable, W.P., letter to B.W. Wieland dated 3-4-77, "ORNL-ORAU Carbon-11 Cyclotron Target Fluid Flow and Heat Transfer Design and Analysis."

5. Lambrecht, R.M., and A.P. Wolf, "Cyclotron and Short-Lived Halogen Isotopes for Radiopharmaceutical Applications," in "Uses of Cyclotron in Chemistry, Metallurgy and Biology," Butterworth, London, 1970.

6. Lemon, R.A., B.W. Wieland, R.S. Howell, and J.P. Casillo, "ATS-Accelerator Target Simulation," Oak Ridge Associated Universities (1977).

7. Lemon, R.A., "ATS User's Manual," Oak Ridge Associated Universities (1977).

8. Linder, L., G.A. Brinkman, T.H.G.A. Suèr, A. Schimmel, *et al.*, "Accelerator Production of ^{18}F, ^{123}Xe(^{123}I), ^{211}At and ^{38}S," in "Uses of Cyclotrons in Chemistry, Metallurgy and Biology," Butterworth, London, 1970.

9. Linder, L., T.H.G.A. Suèr, G.A. Brinkman, and J.T. Veenboer, "A Dynamic 'Loop'-Target for the In-Cyclotron Production of ^{18}F by the $^{16}O(\alpha,d)^{18}F$ Reaction on Water," Int. J. Appl. Rad. Isotopes, 24, 124 (1973).

10. Livingston, R.S., and A.L. Boch, "The Oak Ridge 86-Inch Cyclotron," ORNL-1196, Oak Ridge National Laboratory (1952).

11. Marsh, W.R., "An Apparatus for the Proton Irradiation of Supercritical Water in a Flow System," in "Uses of Cyclotrons in Chemistry, Metallurgy and Biology," p. 101, Butterworth, London, 1970.

12. Martin, J.A., and F.L. Green, "Cyclotron Target for the Irradiation of Chemical Compounds," Nuc. Sci. Eng., 1, 185 (1956).

13. Palmer, A.J., J.C. Clark, and R.W. Goulding, "The Preparation of Fluorine-18 Labelled Radiopharmaceuticals," Int. J. Appl. Rad. Isotopes, 28, 53 (19[illegible]).

14. Perry, R.H., and C.H. Chilton, "Chemical Engineers' Handbook," 5th ed., McGraw-Hill, New York, 1973.

15. Pinajian, J.J., and T.A. Butler, "ORNL 86-Inch Cyclotron Facility for Isotope Production," Isotopes Rad. Tech., 1(2), 137 (1963-64).

16. Washburn, L.C., personal correspondence, Oak Ridge Associated Universities, Oak Ridge, TN (October 6, 1977).