Fifth Session

Production Targets for the Medical Radionuclides
Analytical Methods

Co-Chairs: J. Robert Dahl
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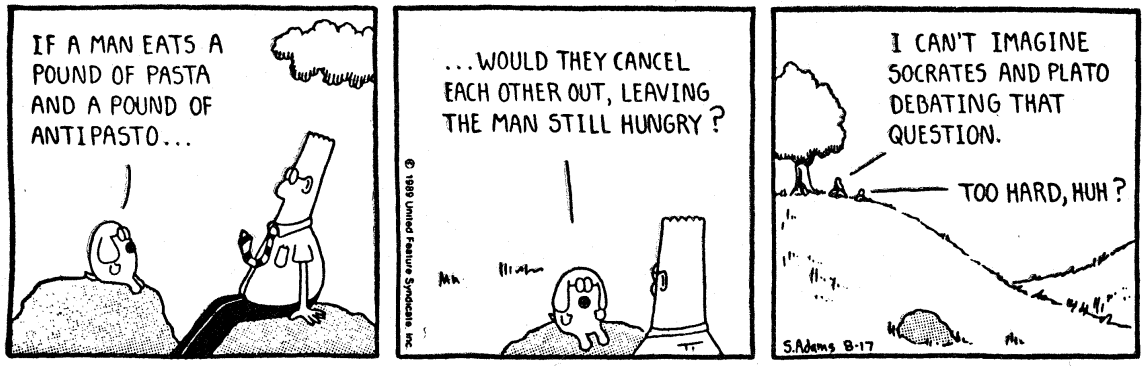

Introduction to Session V: Typical Production Targets for the Medical Radionuclides and Target Chemistry

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During the workshop planning stages this session, originally intended as the forum for discussion of systems for the routine production of a variety of medical radionuclides, became focused on targets for the production of ^{18}F fluoride ion. Prior to the workshop a survey was broadcast to the PET community to gain information which would hopefully provide a general picture of the various techniques used to produce ^{18}F fluoride ion, an action which further focused the session. The results of this survey are included here.

The material of which a target chamber is constructed remains a concern and was discussed specifically in two presentations, and was an important factor in several others. The increasing level of sophistication in calculations carried out to optimize target designs evident in the efforts of Pavan, Johnson and Cackette, who demonstrated the power of intelligent application of spreadsheet software to carry out iterative model calculations to predict heat flow through the target chamber body and an interesting discussion regarding heat transfer ensued.

In spite of these efforts there was not a real breakthrough to overcome the problems in daily maintenance of the water target system. Primarily this is due to the formation of silver colloids and leading to the secondary formation of silver particles originating from the target body. With regard to increasing dose on targets this remains a challenge for the future.

Target Survey results

Although there are several hundred medical cyclotron sites world wide, only twenty five responses to the questionnaire were received, including four responses from two facilities using two varieties of targets. All of the responders report using the $^{18}O(p,n)^{18}F$ reaction with a target of water enriched to >95 % abundance of ^{18}O.

The cyclotrons used for ^{18}F production had beam energies ranging between 10.5 MeV and 200 MeV, one facility at 10.5 MeV, six facilities at 11 MeV, one at 16 MeV, 9 at 17 to 17.5 MeV, one at 19 MeV, two at 30 MeV, one at 37 MeV, one at 42 MeV, and one at 200 MeV. Ten facilities reported deuteron beams were available, with energies ranging from 8 to 15 MeV, although none reported using these beams for ^{18}F- production.

Fifteen of the 25 reported targets were supplied by cyclotron manufacturers, “commercial” targets. All but two of the target bodies reported were made of silver. The exceptions used gold plated titanium and nickel plated copper. The volume of enriched ^{18}O water contained in the target during bombardment ranges from about 300 to 1500 mL.

Of the eleven facilities reporting entrance foil data, three use silver, six use Havar, two use titanium, all with nominal 0.001 inch foil thickness.

Eleven facilities reported data regarding overpressure gas. One used none, one used argon, the remainder, helium. Six laboratories used an overpressure of 5 atmospheres or less. Three used pressure between 28 and 35 atmospheres, and two reported using greater than 40 atmospheres overpressure.

Twenty two laboratories have been using their targets for between five months and five years, three of the for five years, eleven at least three years, and six of the laboratories have been using their targets less than one year.

Only five laboratories reported data on cleaning of the targets. The cleaning intervals reported are one month, five months, 16 months, 18 months, and 24 months. One laboratory, using a Ti entrance foil, reported a 12 month foil replacement interval, and two laboratories using Ag entrance foils reported replacement intervals of 1 month and three months.

The remainder of the data gathered is most easily presented in tabular form, shown in Table 1.

Table 1: Survey run data. Non-responses are not included in the statistics at the bottom of the table.

Response #	Runs /Week	Runs /Year	Usual Current [µA]	Max Current [µA]	Usual Time [min]	Max Time [min]	Activity @ EOB [mCi]	SSA @ EOSB [mCi/µA]
1			10.00	15.00				
2			25.00	40.00	60.00	75.00	750.00	110.00
3	2.00		14.00	15.00	120.00	120.00	1000.00	140.00
4	2.00		25.00		45.00	80.00	750.00	
5	2.00	75.00	10.00	25.00	30.00	100.00	175.00	100.00
6	3.00	120.00	14.00	25.00	35.00	60.00	500.00	162.00
7	3.00	150.00	13.00	20.00	60.00	150.00	950.00	185.00
8	4.00	180.00	20.00	26.00	90.00	132.00	2000.00	220.00
9	4.00	180.00	25.00	30.00	60.00	90.00	740.00	
10	4.00	200.00	13.00	20.00	60.00	120.00	1000.00	
11	4.00	200.00	20.00	20.00	75.00	120.00	1200.00	80.00
12	4.00	208.00	9.00	15.00	30.00	60.00	600.00	95.00
13	4.00	220.00	20.00	35.00	40.00	120.00	700.00	
14	5.00		15.00	15.00	38.00	75.00	700.00	148.00
15	5.00		15.00	20.00	90.00	140.00	1400.00	
16	5.00	250.00	20.00	20.00	120.00	120.00	900.00	
17	5.00	250.00	20.00	25.00	45.00	120.00	1000.00	200.00
18	5.00	250.00	22.00		60.00		525.00	
19	5.00	250.00	30.00	40.00	30.00	60.00	700.00	110.00
20	6.00	300.00	15.00	20.00	45.00	90.00	800.00	190.00
21	7.00		35.00	40.00	30.00	45.00	530.00	120.00
22	10.00		20.00		85.00		775.00	
23	10.00		25.00		90.00		1400.00	
24	15.00		40.00	50.00	60.00	120.00	1900.00	
25		250.00	20.00	20.00	60.00	120.00	1100.00	100.00
Average	5.18	205.53	19.80	25.52	60.75	100.81	920.63	135.38
Std Dev	3.05	58.45	7.62	9.99	26.80	29.99	423.84	43.03
Max	15.00	300.00	40.00	50.00	120.00	150.00	2000.00	220.00
Min	2.00	75.00	9.00	15.00	30.00	45.00	175.00	80.00

Comparison of Different Target Surface Materials for the Production of Carrier-free [^{18}F]Fluoride

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Introduction

Compounds labelled with the neutron-deficient isotope ^{18}F are widely used in nuclear medical diagnostics with positron emission tomography (PET). Proton irradiation of ^{18}O-enriched water is the most effective method for the production of no-carrier-added ^{18}F-fluoride. Many different targets have been designed to consume as little of the expensive ^{18}O-water as possible. Other important considerations are the required thickness of the water layer for optimum beam degradation, the selection of a suitable target body material, foils and seals, expected radiolysis in the water and efficient cooling of the target chamber. The produced micro-quantities of ^{18}F-fluoride can remain adsorbed on the metal surfaces of the target chamber which reduces the achievable yield. From all materials described, silver, titanium and gold have been found most favorable. Silver shows the best thermal conductivity, but under beam conditions it often forms colloids which contaminate the solution and interfere with the synthetic application. Titanium would be the material of choice since it is virtually inert, but effective cooling which is necessary for high beam currents can be technically difficult.

We wanted to investigate the feasibility of two equal small-volume targets manufactured from

- a gold / palladium alloy Au-Pd 90:10 and
- a silver body with 3 mm titanium on all internal surfaces (coated by ion beam assisted deposition - IBAD).

Both targets consist of a solid metal body with the front window electron beam welded onto the target chamber to avoid O-ring seals. The thickness of the front window is 0.8 mm. The target chamber holds 350 mL of ^{18}O-water (96 – 98 % enrichment).

Experimental

For each test run, the target was filled with water and pressurized to 20 - 70 bar with helium gas. The target was irradiated with proton currents of 1 μA to 15 μA for 30 minutes, 1 hr and 2 hrs. The proton energy from the cyclotron was varied from 32 MeV (maximum) to 25 MeV. After EOB, the target was emptied and the ^{18}F activity measured in an ionization chamber. A gamma spectrum was recorded after the decay of ^{18}F to measure the radioactive contaminants. Non-radioactive contaminants (metal traces) were determined by atomic absorption spectroscopy.

Summary of Results

Target	Proton Energy E_p [MeV]	Saturation Yield [mCi/mAh]	Radioactive Contaminants	Trace Metals [ng/mL]
Au – Pd	15.5	207	^{56,57}Co (< 100 Bq/mL)	Au < 1, Pd < 5
Ag / Ti	13.2	167	^{48}V (191 Bq / mL)	Ag 15.8, Ti < 10
Ag / Ti	16.2	230	^{48}V (185 Bq / mL)	Ag 11.5, Ti < 10
Ag / Ti	16.9	233	^{48}V (199 Bq / mL)	Ag 162, Ti < 10
Ag / Ti	17.6	228	^{48}V (190 Bq / mL)	Ag 151, Ti < 10
Ag / Ti	20.4	236	^{48}V (192 Bq / mL)	Ag 126, Ti < 10

Discussion
The results indicate that the targets tested are well suited for the production of aqueous ^{18}F-fluoride. The product solutions from both systems were colorless and transparent. The ^{18}F yields measured are in good agreement with the theoretical calculations and the values published by other authors [1,2].

Gamma spectrometry of samples from the Au/Pd target showed little radioactive contamination (cobalt radionuclides) caused by impurities from the stainless steel tubes connected to the target. Au and Pd did not appear in the product solution.

Samples from the Ag(Ti) target only contained a small quantity of ^{48}V which was inevitably produced from the titanium coating via $^{48}Ti(p,n)^{48}V$. No cadmium or silver radioisotopes were found which proved that in the beam area the target water was only in contact with the titanium layer which formed a perfect coating on the inner surface of the target chamber. The non-radioactive silver traces originated from the uncoated surface of the small volume bores in the target body.

References:
[1] T. Ruth and A.P. Wolf, Radiochim. Acta **26**: 21 (1979)
[2] M. Guillaume et al., Appl. Radiat. Isot. **42**: 749 (1991)

Discussion:

Q: T. Ruth: Frank, I noticed that you started with 70 bar, then you went up to 112 bar. Is a bar what I think it is? That seems awfully high for just one µA. So what do you think the limitation would be going up to 20, 30, 40 µA?

A: We have only irradiated for a short time at higher temperature and it's not going higher than 180 bar. By about 10 µA, but not 30 min. But the target is so compact, there were no problems.

Q: What is the thickness of the gold window on the incoming side? It seems to be machined in the gold. What's the thickness?

A: The thickness of the front window is 0.8 mm.

Q: And on the rear side the same thing?

A: On the rear side it's about 1 mm.

Q: S. Preusche: A question to the target pressure during the irradiation. What you mentioned about 112 bar, is it a constant pressure over the whole time, or do you mention an increasing process in the pressure?

A: When the beam is coming on the target the pressure is increased not really in one step. It's increased up to 100 bar, then these figures are the figures which are practically on the same level.

Q: And if you reach the normal value of irradiation parameter, then you have a constant pressure.

A: Yes.

Q: K. Erdman: Is the target completely sealed? You pressurize it and then you seal it off, right at the target?

A: Yes. The pressure is, we have tried to give about over 300 bar at the target, and the rear part from the target is electronically welded on, it's from the same material.

Q: K. Erdman: I wasn't worried about that. When you pressurize it with the helium to 80 bar, then you valve it off at the target with that pressure in, or is the pressure line connected externally some distance?

A: No, we close the valves when the pressure in the target in this expansion room, we close the valves.

Q: A. Roberts: Just a question about the pressure change, when you irradiate it. Other people are running with sealed targets and not seeing that large a change. Correct? I was doing sealed targets at Hammersmith and did see a huge change, and it was just because I hadn't bothered to degas the water properly ahead of time. I was just wondering if those of you who are doing it right could comment on it?

C: Yes, I would like to comment on that. I do degas the water before irradiation, once a week, when I load the column. And certainly any increasing pressure has to be considered based on the whole volume, where you hold that, it's the sum of the target and all your plumbing. So if you see any increase of that magnitude, it means that your target volume it's a sizeable amount compared to the whole plumbing system. That's why you are moving up. But if your target volume is really small compared to the whole plumbing, then that increase could be much smaller.

C: A. Roberts: Yes, what I was doing at Hammersmith was, it was sealed up right up on the target. So the target volume dominated everything. And I was overpressuring to 600 psi and I'd see it go to 1300 before it blew things up the beam pipe.

C: F. Helus: I should mention one thing. We irradiated with a different energy. The initial energy of the target was 15, 14, 12 and 10 and the pressure is going to 112, 102, 95 and 84. So that was the results.

Q: J.-L. Morelle: I was just wondering if that alloy you were using, was a special mixture, prepared just for you?

A: Yes. But the cost of it is lower than the cost of enriched water, so I think it's worth it.

A Simple Heat Transfer Model of a Closed, Small-Volume, ^{18}O Water Target

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Abstract
The development of reliable, high-current, small-volume ^{18}O water targets have been desired by many in the PET community. To study a closed, solid block design, a test target was constructed and fitted with thermocouples to monitor the temperature through the target body and in the cooling water. Test runs were conducted while monitoring beam currents, and target pressures and temperatures. A simple, spreadsheet based computer model of the heat transport in the target was developed that matches the data obtained. The model indicates that heat transport through the back wall of the target cell is dominant when compared to heat transfer to the target body. Also, there are indications that closed, small-volume targets of similar design may prove problematic in trying to meet the goal of high current capability.

The Target Construction
The main body of the target is constructed in three parts:
1. The titanium body. This forms the major portion of the target, and encloses the target cell.
2. The target cell backing. This replaceable backing forms the back wall of the target cell. It is currently composed of a platinum foil bonded to silver.
3. The water plug. This aluminum fitting holds the cell backing in place and directs the cooling water directly against the cell wall.

A double-foil helium-cooled window and aluminum collimator are fitted to the front of the installed target. Three thermocouples are placed in holes drilled in line with the target center and the middle of the cell to 14, 11 and 7 mm depths, respectively. These positions are indicated in Figure 1 below. The cooling water temperature is monitored using two thermocouples, one each at the entrance to and the exit from the water plug. Target temperatures and pressure were monitored at various beam currents during bombardment. A simple schematic of the target appears in Figure 1.

Performance
Target testing is still in its initial phase. The target has withstood a maximum beam current of 30 μA, which resulted in a pressure rise of 420 psi (3 MPa). 35.3 mCi EOB of 476 Ci/(mmol) setoperone was recently produced after a short test run, indicating the suitability of the target for use in the preparation of patient doses.

The Target Model
The target was modeled using a Quattro Pro spreadsheet. However, none of the functions used were specific to Quattro Pro. Any modern spreadsheet would work as well. The program takes approximately 5 minutes to converge to a solution over approximately 10,000 iterations.

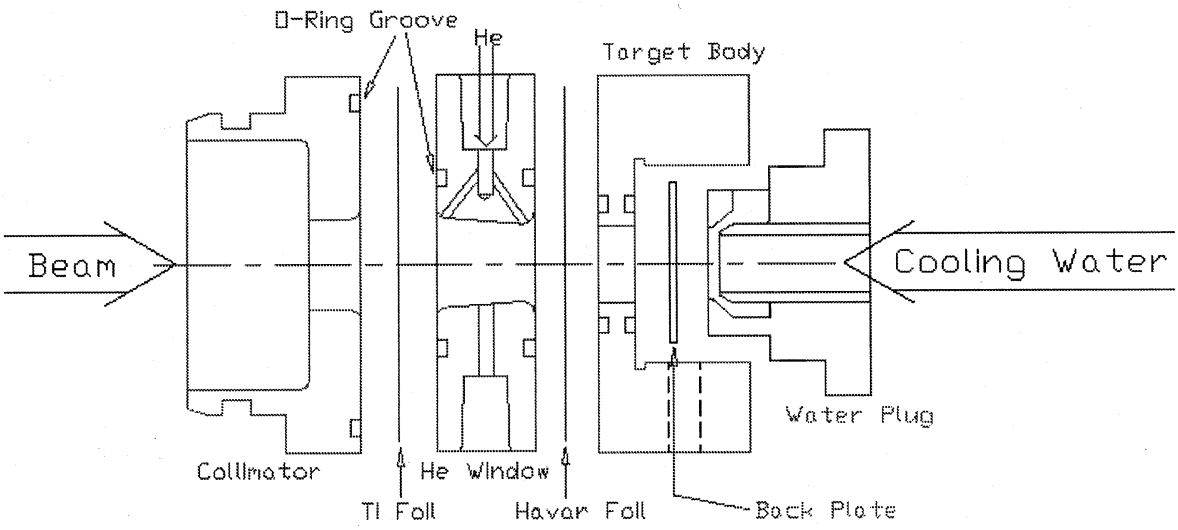

Fig. 1: Target Components. The diagram shows the order of assembly, the direction of the proton beam and the cooling fluid flow. Where necessary, helium-tight seals between components are achieved with polyurethane O-rings. The 13 MeV proton beam enters through a double-foil helium cooled window. 3-4 L/min of cooling water enters through the water plug at the back, strikes the back wall of the target cell, circulates around the target body, and then exits through the hole shown by the dashed lines. The target volume is 500 µL. The target body is composed of titanium. The windows are Havar foil, the back wall is platinum foil bonded to silver, and the water plug is constructed of aluminum.

Assumptions

1. The temperature of the water inside the target cell was assumed to be the saturated liquid water temperature at a given operating pressure.
2. The target was assumed to have equal temperatures at equal radii. This simplified the problem to a 2 dimensional nodal analysis, with the each node centered on a control volume.
3. Only conductive and convective boundary conditions on the target were evaluated. Radiation was not considered.
4. Heat transfer along the Helium cooled entrance foil was not considered.
5. The free convection coefficient on the outer surface of the target was assumed to be 10 W/(K m^2).

Physics

Control volume analysis using variable node spacing was used to determine the heat transfer through the target body. This process consists of dividing the target into nodal volumes, and determining the heat transfer into each node using the resistances to the surrounding nodes and their temperatures. In steady-state, the amount of heat energy entering any given control volume must equal the amount of heat energy leaving that control volume. The model consisted of 330 nodes centered on cylindrical control volumes, represented in individual cells. The nodal equations were entered into a spreadsheet and the boundary conditions were set. The program was then allowed to iterate until it relaxed into a stable solution.

The resulting temperature at any given node is given by the equation:

$$T_{ij} = \frac{\sum k_j T_j}{R_j} \qquad (1)$$

Target Heat Transfer Model — **Target Pressure** 130 [psi]

											Surface Avg dT	9.66	[C]	%Total			
h back		hair		Ucell		hw		K Tit			Q body	72.81	[W]	22.28			
34000	0.034	10	1E-05	50000	0.05	5000	0.005	22	0.022		Q back	253.96	[W]	77.72			
[W/m2K]	[W/mm2K]	[W/m2K]	[W/mm2K]	[W/m2K]	[W/mm2K]	[W/m2K]	[W/mm2K]	[W/mK]	[W/mmK]		Q total	326.77	[W]	Q actual	336	[W]	(@ 28 uA)

All dimensions in mm.

These areas are for the first set of dX data.
The rest get scaled.

[mm2] Ar+	Ar-	As	dR	R	0	0.6	1.2	1.8	2.4	3	3.6	4.2	4.8	5.4	6	6.6	7.2	7.8	8.4	8.7	9	10	15	20	
				dT	7.81	8.52	10.22	11.37	11.71	11.26	10.04	8.34	7.64												
				dX		0.6														0.3		1	5		
				X																					
					179.8	179.8	179.8	179.8	179.8	179.8	179.8	179.8	179.8												
19.04	18.85	1.57	0.1	5	172.0	171.3	169.6	168.4	168.1	168.5	169.8	171.5	172.2												
19.42	19.04	3.20		5.1	170.2	169.4	167.3	165.9	165.4	166.0	167.5	169.6	170.5												
19.79	19.42	3.27		5.2	168.6	167.5	165.0	163.3	162.8	163.5	165.3	167.8	168.8												
20.17	19.79	3.33		5.3	167.0	165.8	162.7	160.8	160.2	161.0	163.0	166.1	167.3												
20.55	20.17	3.39		5.4	165.6	164.1	160.5	158.3	157.6	158.5	160.8	164.5	165.9			T@11mm		39.04	C						
20.92	20.55	3.46		5.5	164.2	162.5	158.2	155.8	155.1	156.0	158.6	162.9	164.6												
21.30	20.92	3.52		5.6	162.9	161.0	156.0	153.2	152.5	153.5	156.4	161.5	163.3					39							
21.68	21.30	3.58		5.7	161.8	159.7	153.7	150.7	149.9	151.0	154.2	160.1	162.2												
22.05	21.68	3.64		5.8	160.8	158.4	151.3	148.2	147.3	148.5	152.0	158.9	161.3												
22.43	22.05	3.71		5.9	160.0	157.3	148.9	145.6	144.7	145.9	149.7	157.9	160.5												
22.81	22.43	3.77		6	159.3	156.4	146.4	143.0	142.1	143.4	147.3	157.0	159.8												
24.88	22.81	21.86		6.1	158.8	155.7	143.8	140.4	139.4	140.8	144.8	156.3	159.3												
28.65	24.88	44.61	1	7.1			115.9	112.8	112.0	113.0	116.2														
32.42	28.65	50.89		8.1			83.3	83.3	83.2	83.2	83.2														
35.25	32.42	42.29		9.1			54.6	57.2	57.8	56.8	53.9														
38.08	35.25	45.83	0.5	9.6	41.4	42.3	45.4	47.2	47.6	46.6	44.3	41.0	38.5	20	20	20	20	20	20						
42.22	38.08	73.61	1	10.6	39.8	40.0	40.6	40.9	40.8	40.0	38.5	36.7	34.8	20	20	20	20	20	20						
46.75	42.22	88.97	1.2	11.8	36.3	36.3	36.2	36.0	35.6	34.8	33.8	32.5	31.1	20	20	20	20	20	20						
49.20	46.75	51.97	0.1	13	33.1	33.0	32.8	32.5	32.0	31.4	30.5	29.4	28.0	26.0	24.7	23.8	23.1	22.5	22.0	21.5	21.3	21.0	20.7	20.3	20
49.57	49.20	8.23		13.1	32.8	32.7	32.6	32.3	31.8	31.1	30.3	29.2	27.9	26.1	24.8	23.9	23.1	22.5	22.0	21.6	21.3	21.0	20.7	20.3	20
53.16	49.57	81.33		13.2	32.6	32.5	32.3	32.0	31.5	30.9	30.0	29.0	27.7	26.1	24.9	23.9	23.2	22.6	22.1	21.7	21.3	21.0	20.7	20.3	20
60.32	53.16	179.67	1.8	15	29.1	29.1	28.9	28.7	28.3	27.9	27.4	26.8	26.1	25.3	24.7	24.0	23.4	22.9	22.4	21.9	21.5	21.1	20.7	20.3	20
67.86	60.32	213.63	2	17	26.7	26.7	26.6	26.4	26.2	25.9	25.6	25.2	24.8	24.4	24.0	23.5	23.1	22.7	22.2	21.8	21.4	21.0	20.7	20.3	20
75.40	67.86	238.76		19	25.2	25.2	25.1	25.0	24.9	24.7	24.5	24.2	23.9	23.6	23.3	23.0	22.7	22.3	22.0	21.7	21.3	21.0	20.7	20.3	20
82.94	75.40	263.89		21	24.3	24.3	24.3	24.2	24.1	23.9	23.8	23.6	23.4	23.1	22.9	22.6	22.4	22.1	21.8	21.5	21.2	20.9	20.6	20.3	20
90.48	82.94	289.03		23	23.9	23.8	23.8	23.7	23.7	23.5	23.4	23.2	23.1	22.9	22.7	22.4	22.2	21.9	21.7	21.4	21.2	20.9	20.6	20.3	20
94.25	90.48	150.80		25	23.7	23.7	23.7	23.6	23.5	23.4	23.3	23.1	23.0	22.8	22.6	22.4	22.1	21.9	21.7	21.4	21.1	20.9	20.6	20.3	20
					20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	

Fig. 2 : The target model as implemented on the Quattro Pro spreadsheet. Nodal coordinates can be interpreted from the column marked R and the row labelled X. The numbers within the cells represent the nodal temperatures of the target body. The columns labelled Ar+, Ar-, As and dR, indicate the surface areas between the nodes in the positive and negative radial directions, in the x-direction and the radial nodal spacing, respectively. The numbers along the row labelled dX indicate the horizontal nodal spacing. The shaded area below the x-coordinates represents the target cell water temperature. Dark shaded areas represent insulated surfaces. The lightly shaded rectangular area to the right-center of the figure represents the cooling water as it passes through the channel formed between the interior of the target body and the water plug. The results of the model appear in the top-right corner of the spreadsheet.

where, R_j and k_j , respectively, are the resistances and conductances between nodes *i* and *j* and T_i and T_j are the temperatures at nodes *i* and *j*.

The conductances between internal nodes and fluid-surface boundaries respectively, are given by the equations:

$$k_j = \frac{K_{ij} A_{ij}}{L_{ij}} \tag{2}$$

$$k_j = \bar{h}_j A_{ij} \tag{3}$$

where, K_{ij} is the conductivity of the material between nodes *i* and *j*, A_{ij} is the area of the interface between nodes *i* and *j*, L_{ij} is the distance between nodes *i* and *j*, and $\bar{h}_j$ is the convective heat transfer coefficient at the fluid-surface boundary.

Convective heat transfer coefficients for the cooling water were calculated using the Dittus-Boelter formulation for the determination of the Nusselt number, Nu:

$$Nu = \frac{\bar{h}_c D}{k} \cong 0.023\,\mathrm{Re}^{0.8}\,\mathrm{Pr}^{0.3} \tag{4}$$

where, *k* is the conductivity of the fluid, in this case water, Re and Pr are the Reynolds Number and the Prandtl Number of the convecting fluid of the convecting fluid, and L is the film thickness of the fluid. In some cases, a quantity called the hydraulic diameter, *D*, must be employed in channel flow in place of L.

The convective heat transfer coefficient at surfaces inside the target cell was modified in the spreadsheet until the temperature at the innermost measured point matched the results taken during a test run. Heat transfer through the body was measured by summing up the heat conducted through the boundary nodes to the cell. Heat transfer through the target backing was determined analytically. The sum was then compared against the known energy input to the target. A screenshot of the target model appears in Figure 2.

Results

Measurements

Temperatures measured during bombardment remained consistent under similar beam currents. Cooling water temperatures under beam indicated that > 95 % of the beam energy was taken up in the cooling water, supporting the assumption that no heat was transferred through the foil window to the helium coolant. Temperature variation in the target body proved to be negligible. In fact, the measured temperature of the outer radii were consistently greater than that of the innermost measured point. It is speculated that this is due to conduction from the beam striking the collimator. For this reason, the innermost temperature was used as the reference point to which the target temperatures were matched in the model.

Model

A comparison between the power transmitted in the modeled target, and that of the real target is shown in Figure 3. One can see that good agreement exists between the spreadsheet model and the real system.

The target model indicates that, as expected, most of the heat energy is transmitted through the back wall of the target cell. This fraction varied from 60 – 75 % over beam currents ranging from 5 - 30 µA, with the lowest values occurring at the lowest beam currents. The model also indicates that the greatest resistance to heat flow occurs in the target cell boundary and at the cooling water interface. The resistances due to convection determined

by using the model were, in general, an order of magnitude greater than resistance in the material of the back wall of the target. Future target designs will take this into consideration. The agreement between the model and the physical system indicates that In the absence of more sophisticated modeling software, simple control volume analysis on a spreadsheet can be a useful tool in evaluating target designs.

Increased heat transfer rates can be achieved by increasing the exposed surface area inside the target cell, which would increase the cell volume, and by increasing the exposed surface area of the target cell to the cooling water.

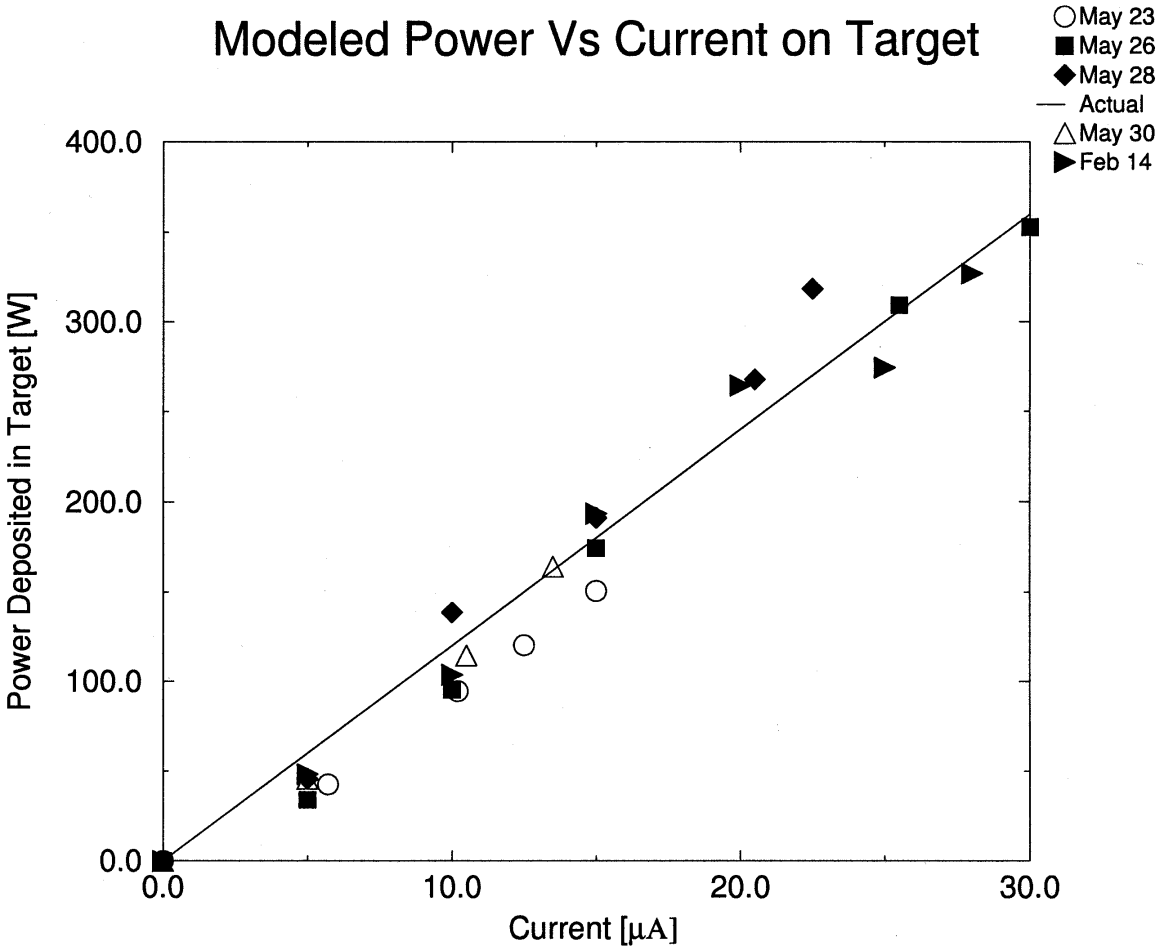

Fig. 3: Results of modeled target runs. The figure shows the result of modeled targets runs vs. input current for these runs. The solid line representing the actual beam energy deposited on target for a given beam current is shown for comparison.

Discussion:

Q: Can you orient the system, where is the beam ?

A: The beam would be here. The target cell would extend up. It doesn't really matter, it's a constant temperature surface, I wasn't worried, what was above. I not modeling heat transport within the water, I'm just saying, if you have water at a certain temperature, you have a certain heat transfer coefficient along the fluid/metal interphase.

Q: As you are going down, you are going radially away from the center?

A: Yes.

Q: So what you're looking at the red line across the top is actually the narrow edge of the cylindrical volume ?

A: Yes.

Q: K. Dowsett: Two things. One is, what proportion of the heat was lost through the body and what did you say through the back ?

A: That's right here, on the totals. About 25% through the body, about 75% through the back.

Q: K. Dowsett: And did you make any assumption about the temperature gradient in the water between the top an the bottom or did you assume it was uniform?

A: I assumed it was uniform. When you look at the pictures with the water ...(inaudible)

Q: A. Roberts, Wisconsin: Did you say what the beam current limit is, on what you can put on that target?

A: I've put 30 µA on it.

Q: A. Roberts: At 13 MeV?

A: It's 12 MeV in the target water, so that's 360 W.

Q: A. Roberts: Did you try winding up the energy on that thing ? I think you guys can do that?

C: T. Ruth: No, we kept fixed energy. This is the 13 MeV machine.

A: I can't go any higher then 500 psi on a target, because the pressure transducer readouts ramp out at 500 psi, I don't know what's going on after that and I don't want to risk anything.

Q: J. Clark, Cambridge: In a real world of course your foil is not really that flat. So your water shape is going to be very different from that. And the beam of course is never a square wave.

A: Yes. Maybe I didn't make myself clear. I didn't say I'm putting in a certain amount of energy. What I said was, the water is at a certain temperature, what's the energy that's getting transmitted. So I assumed a constant temperature in the water. I didn't say I've got a source of Q here and where is it going? What I said was, I've got a temperature here, how much heat is getting transmitted that way?
The nodal equations look like this. So the temperature at a given node is the sum of the conductance is times of the adjacent node temperatures over the conductances. And I did this for each node at each interphase and this just describes the conductances in between. It needs a lot more work, I mean, if you don't have a finite element analysis package to work with or whatever, you just want to play around and get an idea of what you are doing. Get an idea of where you are making mistakes, where your gases arrive. I think a spread sheet and a simple model like that is a good place to start. I don't think I'm making any grand statements like I know what's going on in there. But I think it's not a bad tool to work with in the beginning.

Experience with a High Pressure Silver Water Target System for [^{18}F]Fluoride Production using the CTI RDS-111 Cyclotron

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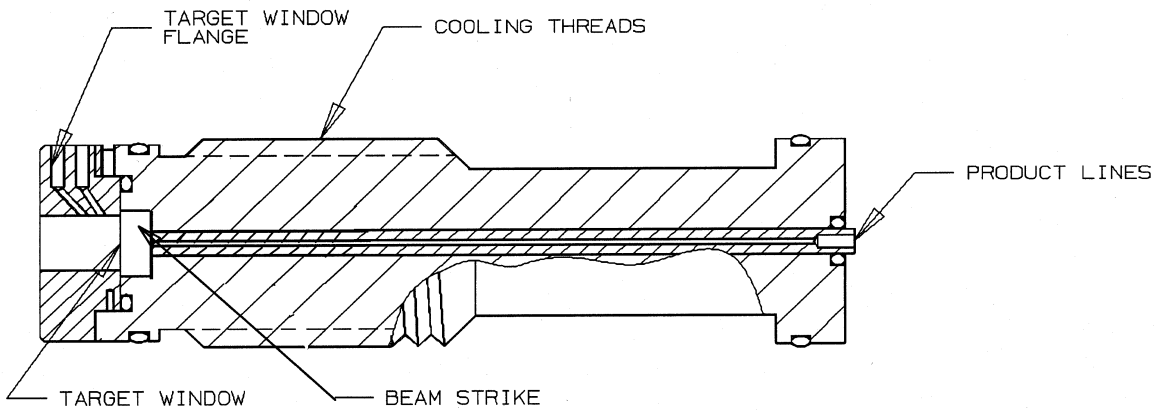
One of the newest low energy cyclotrons for the production of positron emitting isotopes was sited at Lawrence Berkeley National Laboratory in July 1995. This prototype CTI RDS-111, proton only, 11 MeV, negative ion machine is producing GBq quantities of fluorine-18 for radiopharmaceutical applications. A CTI designed target changing system developed for this cyclotron can hold up to eight small targets. We report on the use of a CTI high pressure silver target design for the production of [^{18}F]fluoride ion and compare the results to a CTI RDS-112 low pressure silver body target, first used for production on our machine. The fluoride ion produced from this machine is routinely used to label fluorodeoxyglucose to trace glucose metabolism in patients as well as for new radiopharmaceutical development.

High pressure targets for the production of fluoride ion with both gas and water overpressure have been previously described [1 – 4]. The CTI RDS-111 high pressure target uses argon gas overpressure at 48 bar on a completely filled target cavity which is shaped like a baseball diamond (triangular base and rounded top). This shape provides a reflux area above the beam strike area. The cavity is 5 mm deep with a volume of ~500 µL. The target is over-filled with 750 µL of enriched $H_2{}^{18}O$, using a Cavro syringe pump, then pressurized with argon gas to 48 bar. The extra 250 µL of water is used to fill the dead volume between the load/unload valve along with 100 µL excess in the vent/overpressure line. When the bombardment has ended, the target is allowed to rest for 1 min. then a 3-way valve is switched to allow the target material to unload, through 9 meters of 0.8 mm ID poly tubing, without venting the target. The pressure in the system is monitored and found to drop off rapidly, reaching near atmosphere pressures in under 1 min.. We have also collected time-activity data by unloading the target into a LabView monitored Capintec dose calibrator. Using this unload procedure we can recover 90 – 100 % of the 750 µL of water loaded into the target. Conversely, venting the target down to 13 bar prior to unloading causes migration of radioactivity back into the unshielded target support unit; most of the radioactivity is pushed back through the target by argon gas during the unload sequence. Target yields (i.e. recovered activity) by either method are comparable.



While the low pressure silver body fluoride targets have a beam current limitation of 20 µA, due to potential voiding, boiling and radiolysis at higher currents, the high pressure targets have been designed to suppress these phenomena and support higher beam currents. We

have irradiated $H_2{}^{18}O$ in the high pressure silver target over a range of 20 - 40 µA for irradiation times up to 60 min. We experience a loss in saturation yield as a function of both increased time and increased beam current. This is most likely due to insufficient target cooling and/or voiding as previously described by Heselius, et alt [4]. Even though the saturation yields from the high pressure target at all beam currents and irradiation times exceed those from the low pressure target and satisfy our present needs, we are working to improve our yields at higher beam currents and longer irradiation times.

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Discussion:

Q: J. Nickels: Do you do any pretreatment of your target water? Degassing or anything ?

A: No, we don't degas or anything. It gets filtered through a millipore filter, but weeks in advance often, or weeks later we use it.

Q: J. Clark: People just naturally say they clean their targets. We've heard people say, don't, whatever you do, get organics in. I think GE use baking powder or something similar to dry.

A: We end up avoiding that. If that's real, we faulted it by avoiding it completely. We typically scrub the inside of the target with a Q-tip or cotton swab and baking powder / methanol slurry. Then we go back, rinse the target out and then we go through a series of 1 hour sonications at about 50 °C on the solvents, that will handle that. But we use chloroform or methylene chloride, acetone. Then we turn around and sonicate in Milli-Q water for 1 hour at 60 °C and blow the target dry with helium. We don't oven-dry it or anything, because we've always been afraid of getting a bunch of AgO in there to start with.

C: J. Steinbach: I got a hint from the Zürich group, Westera. He told me to clean up the targets with ammonia solution and it would work very well. Only pump through ammonia solution and clean enough for the next run. Of course, additional pure water after, but that seems to be enough.

C: J. O'Neil: That's essentially the same procedure we use for cleaning our F_2 gas target.

Routine Production of [^{18}F]Fluoride with a High Pressure Disposable [^{18}O]Water target

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Increasing demand for the glucose analogue 2-[^{18}F]fluoro-2deoxy-D-glucose (FDG) for PET and SPECT, continue to challenge investigators to develop more efficient methods to produce and incorporate short-lived radioisotope. Integration of the radiopharmaceutical into an exigent clinical program and the potential for regional distribution demand highly reliable systems involving: short, simple and cost effective production and maintenance procedures.

Small target volume is desirable given the high cost of highly enriched (> 95 %) ^{18}O-water. To accomodate irradiations at high beam currents, target cooling conditions can be improved by raising the target pressure. Given the relatively low thermal conductivity of water, heat dissipation in water targets through conduction and convection is limited [1]. Recently, a high power ^{18}O water target operating at 40 bars He overpressure was described for the CTI/RDS cyclotron [2]. They report mean [^{18}F]fluoride recovery yields at saturation close to 80 % of theoretical maximum, in agreement with those values reported by Wieland et al. [3].

We describe results after one year operations with a new high pressure Ni plated Cu target for routine production of [^{18}F]fluoride. Target size and fabrication costs have been reduced to a level that the concept of *disposable target* can be applied. A newly designed target loading system that reduces the number and complexity of components required is also described.

Target Design

The 32 mm diameter by 25 mm long target is made from oxygen-free high-conductivity (OFHC) copper. The ^{18}O water cavity is 4 mm deep, 13 mm wide at the front and narrows down to 10 mm in the back. Slightly more than half the cavity is filled with ^{18}O water, leaving the rest as overhead pressure space. The ^{18}O water cavity is nickel plated (typically 5 µm thick).

Two pieces of stainless steel tubing I.6 mm o.d. by 0.5 mm i.d. by 10 cm long are press fitted through the top and bottom ports and epoxy sealed on the external side. A 50 µm thick PEEK (Polyetheretherketone) gasket seals the target front to a 32 µm thick Ti foil. A 1.0 mm thick aluminum plate support, the Ti foil while reducing the beam energy entering the water target from 23.2 MeV to approximately 18 MeV. Beam diameter on target is 10 mm. The target is cooled with 10 °C deionized water flowing at 2.5 L/min. Six bolts are used to compress the PEEK gasket to the target and front foil. The entire assembly has been successfully tested with He gas for pressures up to 55 bars.

A schematic of the newly developed system is shown in Figure 1. Spring loaded back-pressure regulators -V3, V4 and V5- minimize dead volume and simplify target operation as compared to bulkier electropneumatic valves. Loading valve V3 is adjusted to open near 17 bars (250 psi) while regulator V4 and delivery valve V5 are adjusted to open at 35 bars (515 psi) and 45 bars (660 psi) respectively. All three pressure settings refer to differential values.
Target loading cycle begins by pressurizing the target with UHP He at 46 bars (680 psi) through valve V1 (normally closed valve) for 5 seconds. Venting to operating pressure (35 bars) is accomplished through pressure relief valve V4 and valve V2 (normally open valve). Metering pump -MP- is switched on for a pre-established period of time (30 sec), the ^{18}O-water is loaded and the target is ready for irradiation. After irradiation, high pressure valve V1 is opened and V2 closed. The irradiated water can only move back through delivery valve V5

since valve V3 is rated to withstand backpressures up to 68 bars (1000 psi). Target content is delivered through a 15 m long polyethylene tubing 1.6 mm o.d. by 0.8 mm i.d.) in less than one minute. The loaded/recovered ^{18}O-water target volume is 0.5 cm^3 with approximately 0.1 cm^3 of water sitting above the top of the beam strike. Only 0.020 cm^3 of ^{18}O water (4 % of total load) does not occupy the water chamber.

During irradiation, we observe a small pressure increase of 1 to 2 psi maximum at 20 µA. This increase correlates with the ratio of displaced He -on the overhead volume- to the full He overpressure volume by water vapor and evolved gases from radiolysis.

Experimantal Results

Results for 18 MeV incident proton energy are presented in Figure 2. The solid curve was obtained using an average saturation yield of 195 mCi/µA. All data points except for the highest integrated current value fall between a ±5 % interval for the saturation yield. The longest run shown deviates only 7 % from the average value. Within our margin of error we do not observe any variation in the saturation yield as a function of beam current for currents all the way up to 25 µA. A decreasing trend seems to appear for runs in excess of 90 min. A curve similar to that displayed in Figure 2 is shown on Figure 3 displaying total ^{18}F recovered when a target rinse was performed after collection of initial irradiated products. Again, the solid curve is the predicted ^{18}F activity at EOB using a saturation yield of 228 mCi/µA. Less than 1 % of the initial recovered activity was collected after a second target rinse was performed.

Up to 59 GBq (1.6 Ci) of [^{18}F]fluoride were trapped with 99.98 % efficiency when the irradiated ^{18}O-water was circulated through a strong anion exchange resin. Comparable efficiency was observed when the product was eluted from the resin with a potassium carbonate solution. Average radiochemical yields of 37 ± 13 % (> 200 runs) decay corrected at EOB are currently obtained in the production of [^{18}F]FDG with a Siemens/CTI CPCU system using this new target system.

Conclusion

Our mean saturation yield of 195 mCi/µA (200 mCi/µA corrected for 97.5 % ^{18}O-water) at 18 MeV represents approximately 86 % of theoretical maximum. The cost to build each of these targets, including plating procedures, is less than US $100. Targets are currently replaced after approximately 75 runs (~ 4 months). Target servicing takes less than 1 hour including leak target configuration is currently being implemented production of ^{13}N-Ammonia.

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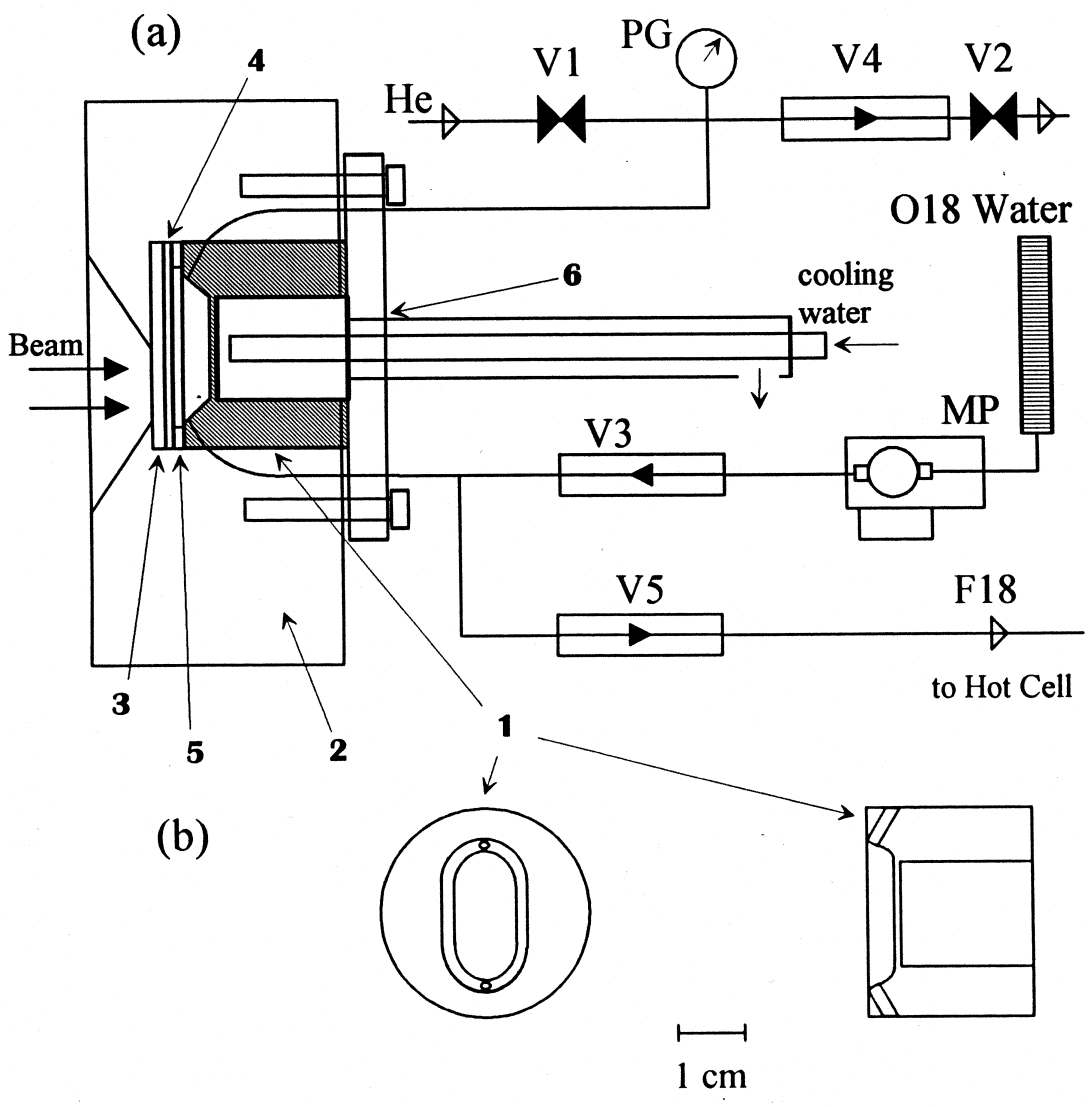

Fig. 1: a) schematic of the new target system including:

1) Ni plated Cu disposable target (shaded)
2) Target autochanger aluminum adapter flange
3) Energy degrader
4) Target foil
5) PEEK gasket
6) Coaxial water cooling flange. For details regarding target loading/delivery system see text.

b): Front and side view of disposable target.

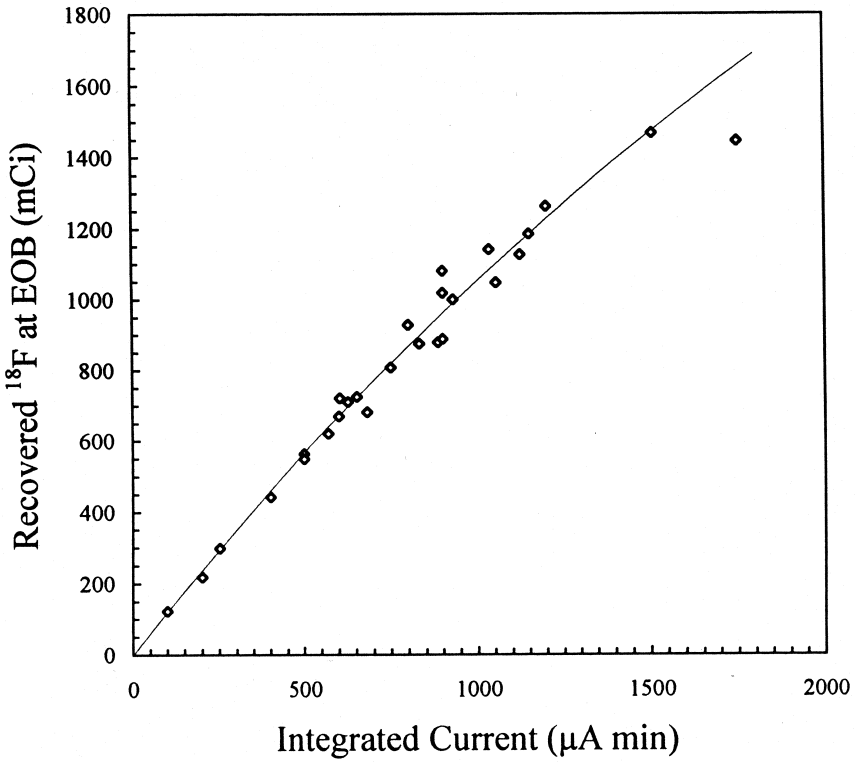

Fig. 2: Production of ^{18}F with disposable Target (18 MeV protons on 97 % water);
Solid curve: saturation Activity = 195 mCi/µA

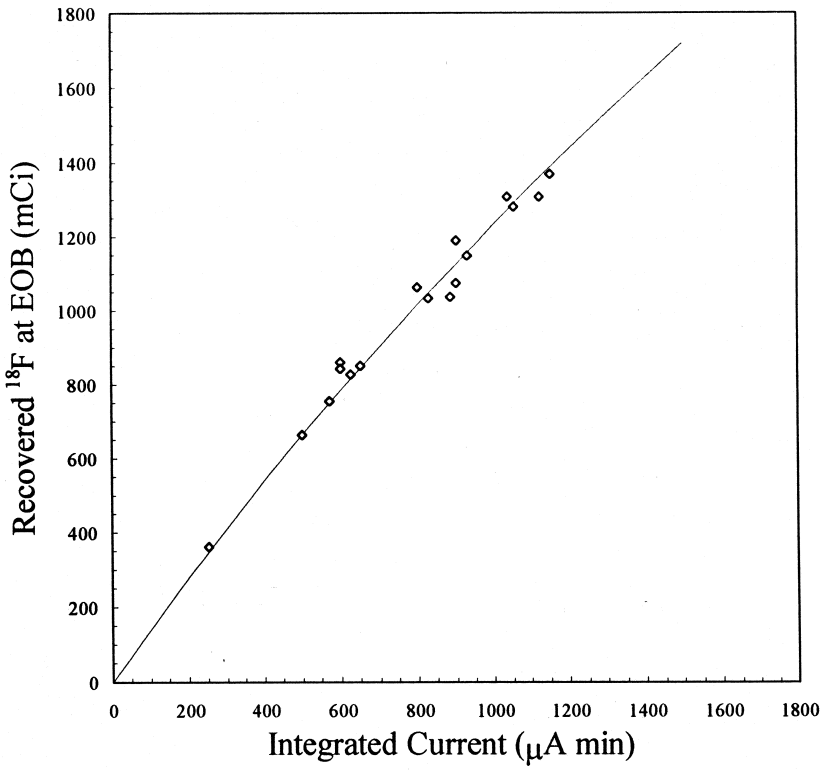

Fig. 3: Production of ^{18}F with disposable Target (18 MeV protons on 97 % water + target rinse);
Solid curve: saturation Activity = 228 mCi/µA

Olof Solin, Turku: Comment on Silver Targets

Just a brief comment that is connected with the earlier talk. We use a fluoride target at our place, a low volume silver target with a volume of 400 µL and it's running in an unpressurized mode, so it's just an open target. The depth of the cavity is 3 mm and width is about 11 mm. The reason why we don't use overpressure, is that we are limited in beam current, we can't get much more than 10,11 µA. The yields from this target are for 2 hour normal irradiation is about 1040 mCi per run. So that constitutes a saturation activity of about 195 mCi/ µA. The target, if it is a new machine target it works well for about almost a year, it slowly starts to deteriorate and when the yield drops about 5 %, we mechanically scrape it out, we don't clean it chemically. And after that you can use it again, but it goes bad again sooner than before and actually on the average I think, the lifetime of these targets is about 2 years, than we replace the silver body and use a new target.

These are not of course expensive targets, silver is really very cheap and easy to machine. One special thing that we do at our place is of course that we utilize that fluoride from the water target not only as an anion for radiochemistry, but we also synthesize F_2 from this anion. We were first synthesizing fluoromethane, methylfluoride in a good yield, about 80 % chemical yield in a short time. And then we react this fluoromethane in an electrical discharge with some amount of carrier F_2. Very low amounts, between 150 nmol to maybe 1 µMol and get in this exchange reaction at maximum 60 % of ^{18}F-labeled F_2, and the specific activity is for F_2 in a normal run a bit less than 1 Ci/µmol. It's rather high for F_2, much more than you can get from the oxygen or neon targets. If we accept a low yield in the exchange reaction we can get specific activities of about 2 Ci/µmol, the yield is then lower. At the 1 Ci/µmol level we can get about 450 mCi of F_2.

Q: Do you have a publication on the gas method?

A: Yes, it's coming out soon in Nuclear Medicine and Biology.

Andy Roberts, University of Wisconsin: High Pressure Silver Body Targets

About four years ago we went from the low pressure Ni-plated copper targets that were originally from CTI for the 112, replaced it with a silver body with a gold back target that ran at much higher pressures. We had the thing running at 600 psi, about 40 bar. Not much to say about it, the beam comes in this way, this is a view of what it looks like. Havar foil, 1 thou. It does have a head space, we overpressure it to about 40 bar and then leave it open to the back to the regulator, so it's a big volume and the pressure doesn't change when you irradiate it. This whole section here is the silver part, the tubes are just 16 stainless, that's a tight fit and then soldered in place. And then on the back you've got just a Cu cooling assembly. This is 1/8" Cu tubing that puts the jet of water right at the back. The original idea was that we wanted to have a gold back, so that we could use the neutron monitoring as a very accurate way of knowing whether we're irradiating all the water. Especially when you go up to high beam currents and you can see your relative neutron rate going down, because you're not activating as much your whacking into the walls, gold is extremely good for that. There were problems with it, we don't use it any more, that's a good sign. The problems are as you can imagine, when you start trying to take those mixed metal things, when you try to put them together somehow. And the way I did it, was to solder the gold to the back to the silver and ended up getting some junk around the outside and that messed up the reactivity of the fluoride which we got all back by Ni-plating it. So now you have a gold back, silver body, Ni-plated target, which is, you don't want to do that. We scrapped all that, but this is still the basic design that we use, we just make it out of a single silver piece. The only loss

from that is, the neutron counting is not nearly as sensitive. The relative neutron production at this energy when you're hitting just straight your silver is I think 1/3 of ^{18}O or so.

So we are running these things with silver, still same parameters, still same high pressure, typical runs, we ran it at 40 µA to get a couple of Ci out of it. It doesn't like to do that. You can do that a couple of times and then you get the black crud. Interestingly when we did that on the gold target, you get yellow crud and it changes color with days, it's really neat. So even if we had done it all out of gold, you still have some crud problems coming out. The way we operate it now, we never go above about 25 µA and under those conditions, we haven't seen the black crud for years. It just never shows up. And 20 µA for a couple of hours you are going to end up with 1100, 1200 mCi out of this thing. And that's where it stands. The crud issue is there, if you really want to go to 35 or 40 µA. It doesn't like to do that, but at 30 or below, I think it's fine. So we don't have to routinely clean it.

C: K. Erdman: We've had in operation a titanium target now for 2 years at 25 µA that hasn't been cleaned and the yield hasn't fallen off. And it's totally sealed, it has no headspace, it goes up to 460 psi with 25 µA on and returns down to within 15 psi of the pressure it started at.

A: Yes, I guess the comment about having a two year lifetime on a target. I think the silver one we've got on there now we've been running for about three and haven't really seen a change.

Q: What is the target volume?

A: K. Erdman: The target volume in that one is about 0.6 mL.

Dave Schlyer: Heat Transport

You saw this already, the 5 µA beam and the 10 µA beam on the water target. And this is a target we built to take advantage of the fact, that Sven described a little bit this morning. What we did was connect a light guide back here, a light sensor in the back of the target, so we can see, when the beam made it into the cooling water of the target. So when you do that, here is the target temperature vs pressure, so this is looking at the pressure in kPa and this is the temperature in °C inside the target with 14.7 MeV protons on a 15 µA beam current. And as you raise the pressure, indeed you do see the water temperature go up above 100 °C, where it would normally start boiling.

We were also able to show in that study, that if you look at that light emission from the cooling water indeed as you raise the pressure you essentially stop the penetration of the beam through the target. So it all stops inside the target and quits coming out into the cooling water, for the most part. This is essentially dark current back here. The target we are using now we've been using since 1991 I think. Silver target, it's solid silver. We cleaned it I think just recently, but before that it's been at least six months since the last time we cleaned it. We don't use any O-rings, we use a titanium front foil. We close it off with Rheodyne valves above and below. Solid water, no airspace whatsoever, no overpressure. And just let it go to whatever it goes to. And we use polyethylene gaskets to seal the foils. We don't have a pressure sensor on the target, but we can tell by the bowing of the titanium window and yield strength, that we are getting up around 300 psi, somewhere around that.

Jörg Steinbach, FZ Rossendorf: Heat Transfer by Convection

In the same time we did some very simple experiments. That means we irradiated an open target at atmospheric pressure and had inside a thermocouple. It measured the temperature in dependence on the beam current. We measured that we reach 100°C, the boiling temperature at normal pressure at about 3 µA. And we added some calculations about this beam transport. And we found the following. The pure heat conduction, the heat conduction in this case is quite low, because we have a very thin target of about 2 mm thickness. It's only 6.8 W/cm^2. And this is a quite low heat current density. Another mechanism is the heat transfer by free convection. It's also not so good, that's a small slit, it should be a little bit better in thicker targets. But it's also only 14 W/cm^2 in this case. If you add these two values, you come to 2.5 µA. And this is near to the value we found here and if you calculate this heat transfer by boil cooling, then you find for this additional heat transfer you need a temperature difference of about 20°C between the target water and the wall. That means as you mentioned, the boiling is a prerequisite for the heat transfer and it's not recommended to suppress. The target does in any case. That means, if you want to increase the beam and the heat into the target and to transfer this energy away, you should press up the target as all of us do and in this case this water boiling temperature is going up and the temperature difference is going up too. But the message is, a target must boil.

C: D. Schlyer: When we did these experiments we also took video of the target when it started to boil. And we watched the convection currents, you could see the convection currents building up to a pretty good clip just before the first bubble came across. And although it's not free convection at that point, I think there may be something in these overpressurized targets where the bubbles are actually forming and then, because of the pressure that's caused by the bubble forming they recollapse back in things, especially with no added gas. So you may get some situations in between free convection and boiling that's saving us in these other targets. But I think you don't necessarily have to have it freely boiling.

A: J. Steinbach: It's a theoretical assumption to have this convection. And it shows that it can not work to cool this target out.

A: D. Schlyer: But I think the free convection that you are using may not be an accurate representation of the convection events that are actually occurring in the target.

C: J.Steinbach: I think it works at very low beam currents.

C: I just wanted to add that certainly at least very high pressures and there is a huge temperature difference between a layer of water touching the wall at least in most targets like that layer is at 20 °C and a few microns it's probably at 200 °C. So there's a huge difference in density. That might also contribute to a better convection force or that might be the pump that we are looking for to move the water inside the target but I still agree with you that we do need to have boiling to take care of the other 300 W that we dump in there.

C: K. Erdman: Just one comment. If you look at the power level that you're putting into the target, you realize the temperature of the water inside is going up at the rate of 300 °C/s and it can't convect that fast under any kind of convection conditions that you can imagine, except if it's under the kinds of conditions that Dave was talking about, where some kind of forced convection due to bubbles forming and collapsing. So it's not boiling in the usual sense, it can't in that water. The heat can't get to the top any other way.

Home-Made Routinely Used Targets for the Production of PET Radionuclides

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Medizinische Hochschule Hannover

The systems have been constructed for the production of ^{11}C, ^{13}N, ^{15}O and ^{18}F. The radiopharmaceuticals prepared from these radionuclides are used for in-house applications only. Therefor the targets have been optimized for performance reliability in terms of withstanding long periods of beam time in combination with a minimum maintenance (in order to minimize the radiation dose to the staff), rather than for optimum performance in terms of maximal beam current toleration.

The following tables give an overview of the general system and of the targets in some detail (construction, operation parameters and yield). A summary is presented in the last table to show the production yield in percent of the theoretical yield.

The relatively low value for $13NH_3$ is caused by bubbles in the target water under beam conditions. As with the water target for the production of ^{18}F the purity of water is essential.

First tests with the conically shaped neon target for ^{18}F production using 0.1 % F_2 gave relatively poor results. A recovery of 30 % of the theoretical yield was observed. The large surface of the target may need a higher amount of carrier in general since tests runs with 0.8 % F_2 yielded good results.

References:

[1] H.-J. Helmeke, T. Harms, K.H. Matzke, G.-J. Meyer, H. Hundeshagen, Routinely Produced [^{13}N]NH_3 for PET Examinations with a Continuous Flow Water Target, Applied Radiation and Isotopes **45**: No. 2, 274-276 (1994)
[2] H.-J. Helmeke, H. Hundeshagen, Design of Gas Targets for the Production of Medically Used Radionuclides with the Help of Monte Carlo Simulation of Small Angle Multiple Scattering of Charged Particles, Appl. Radiat. Isot. **46**: No. 8, 751-757 (1995)

Table 1: General information about the target system in use

beam sweep	a few millimeters horizontally
beam line foil	0.025 mm Ti (2-3 foils per year / depends mainly on the amount of deuteron beams)
He – cooling	~ 35 °C, 65 L/m beam line foil, 180 l/m target foil
collimator	movable collimator in front of the He-cooling, hole diameter: 14 mm
water cooling	~ 19 °C, $9x10^5$ Pa, conductivity << 4 µSiemens (1/Ω)
maintenance	foils and seals are changed during the annual cyclotron maintenance in January. Ni-targets are washed with HCl, pure water and acetone. Other targets are cleaned with pure acetone only. Additional foil changes are carried out after leakage or a visual check of the foils. An additional foil change next morning after scheduled beam time yields a personal dose of ~ 40 µSievert (4 mrem)
manufacturing	machine shop of the Medizinische Hochschule Hannover

Table 2: ^{11}C target

material	Al-Mg-Si 0,5
foil	0.05 mm Havar
seal	1 mm teflon disk
target diameter (mm)	20
target length (mm)	240
volume (cm^3)	75,4
cyclotron energy (MeV) /particle	17 / p^+
target material	N_2 + 5 ppm O_2
current on target batch/max (µA)	20 / 30
current on collimator, batch (µA)	5
MCoulomb per batch	36
pressure no beam/$beam_{max}$ (10^5 Pa)	20 / 34
MCoulomb (1996)	590
number of irradiations for PET (1996)	27
number of foils per year	1
^{11}C yield per batch (GBq)	65.8 (EOB)
impurities (EOB)	21.6 % ^{13}N (EOB)

Table 3: ^{13}N target

material	Ti > 99 %
foil	0.05 mm Ti
Seal	2 mm teflon O-ring
target diameter (mm)	17
target length (mm)	3.5
volume (cm^3)	0,8
cyclotron energy (MeV) /particle	17 / p^+
target material	H_2O + 5 mmol/l ethanol
current on target batch/max (µA)	12 / 12 *
current on collimator, batch (µA)	8
MCoulomb per batch	6 or 10
pressure no beam/$beam_{max}$ (10^5 Pa)	10, continuous flow
MCoulomb (1996)	1463
number of irradiations for PET (1996)	167
number of foils per year (1996)	1
continuous flow (mL/m)	200
$^{13}NH_3$ yield (GBq), 6 mCoulomb	4,2 ** (EOB)
impurities (Bq) 3 h past EOB in the target water (6 mCoulomb batch)	^{43}V: 3021 ^{47}Sc: 135 ^{44m}Sc: 138 ^{44}Sc: 323

* rapidly increasing number of gas bubbles
** average / minimum 2,3 / maximum 5,2

Table 4: ^{15}O target

material	Al-Mg-3
foil	0.025 mm Havar
seal	1 mm teflon disk
target diameter (front-, backside) (mm)	16 , 20
target length (mm)	57
volume (cm^3)	15.9
cyclotron energy (MeV) /particle	8,5 / d^+
target material	N_2 + 1 % O_2
current on target batch/max (µA)	20 / 20
current on collimator, batch (µA)	5
MCoulomb per batch	10.8
pressure no beam/$beam_{max}$ (10^5 Pa)	13 , continuous flow
MCoulomb (1996)	1123
number of irradiations for PET (1996)	104
number of foils per year (1996)	1
continuous flow (mL/m)	100
$H_2{}^{15}O$ yield (GBq), 9 minutes, 20 µA	7,7 (EOB=EOS)
(yield: bedside in the PET room! tubing: ~ 50 m, 0,5 mm diam.)	

Table 5: ^{18}F target (> 96 % $H_2{}^{15}O$)

material	Ti > 99 %
foil	0,05 mm Ti
seal	2 mm teflon O-ring
diameter, length, volume	see ^{13}N target
cyclotron energy (MeV) /particle	17 / p^+
target material	> 96 % $H_2{}^{18}O$
current on target batch/max (µA)	8 * / 15
current on collimator, batch (µA)	4
MCoulomb per batch	27
pressure no beam/$beam_{max}$ (10^5 Pa)	14 * / 15
MCoulomb (1996#)	1377
number of irradiations for PET (1996#)	51
number of foils (1996#)	1
^{18}F yield (GBq)	14,1 ** (EOB)

* depends extremely on the purity of the water
** average / minimum 8,3 / maximum 17
\# last 5 month of the year

Table 6: ^{18}F target (neon, shape: straight round cylinder)

material	Ni > 99 %
foil	0.05 mm Havar
seal	1 mm teflon disk
target diameter / length (mm) / volume (cm^3)	16 / 104 / 20,9
cyclotron energy (MeV) /particle	14 / d^+
target material	Ne + 0.1 % F *
current on target batch/max (µA)	20 / 20
current on collimator, batch (µA)	15
MCoulomb per batch	18 .. 54 **
pressure no beam/$beam_{max}$ (10^5 Pa)	21,5 / 32
MCoulomb (1996)	8308
number of irradiations for PET (1996)	235
number of foils per year (1996)	3 #
^{18}F yield (GBq), 36 mCoulomb	5.8 ## (EOB)

* 1996: 0,8 % F_2 since 1997 : 0,1 % F_2 with preirradiation (18 mCoul.) for FDG

\# dirt on the target body and especially on the foil caused by the old gas cylinder/regulator required two extra foils; yield decreased rapidly within a week → target cleaning!

** due to patients time schedule and NaF or FDG

\# # incl. Preirradiation (additional 18 mCoulomb) with 0,8 % F_2 and no preirradiation 6,6 GBq (EOB)

Table 7: ^{18}F target (neon, conically shaped)

material	Ni > 99 %
foil	0,025 mm Havar
seal	1 mm teflon disk
target length L (mm)	200
target diameter D (mm) entrance (L=0 mm) linear increase to L=100 L>100: D(L)=9,2*(0,02*L*L/100-0,3*L/10+3,18)	16 20 L = 200 : 47,6
volume (cm^3)	103,5
cyclotron energy (MeV) /particle	14 / d^+
target material	Ne + 0.8 % F_2 *
current on target batch/max (µA)	25 / 25
current on collimator, batch (µA)	10
MCoulomb per batch	36
pressure no beam/$beam_{max}$ (10^5 Pa)	8.5 / 13.5
^{18}F yield (GBq), 36 mCoulomb	7.6 (EOB)

* after a test phase it is planned to decrease to 0,1% F_2 and use the target for $Na^{18}F$ and ^{18}F-uracil

Table 8: routine and theoretical yield

Production	MCi (EOB)	mCoul	µA	Time (m)	$T_{1/2}$ (m)	A_{sat} theor. (mCi/µA)	mCi theor. yield	%
^{18}F/T3 /0.8%F_2	205,4	36	25	24,0	109,70	74,0	260,3	79
^{18}F/T1 /0.1%F_2	156,8	54	20	45,0	109,70	74,0	366,3	43
^{18}F/T1 /0.8%F_2	178,4	36	20	30,0	109,70	74,0	255,5	70
^{18}F/ >96% $H_2{}^{18}O$	381,1	27	8	56,3	109,70	193,0	461,8	83
$^{13}NH_3$	113,5	6	12	8,3	9,963	28,5	150,5	75
$H_2{}^{15}O$	695,9		20	9,0	2,03	52,1	993,8	82
bedside!	285,0							
^{11}C	1778,4	36	20	30,0	20,30	176,0	2256,1	79

Data for ^{15}O pipeline:	4	time (m) target-PET for ^{15}O
	1	volume reactor vessel (mL)
	5	volume valves (mL)
	50	length tube target -PET (m)
	0.5	diameter tube target-PET (mm)
	392.7	tube volume (mL)
	100	flow in mL/m

FDG PETtrace MicroLab®: Average [^{18}F]FDG EOS Activity Compared to the Source of the [^{18}O]Water Used

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Fludeoxyglucose F-18 Injection ([^{18}F]FDG) is prepared in our institution using the commercially available unit, the GE PETtrace MicroLab®. The synthesis employs nucleophilic exchange on a quaternary 4-aminopyridinium resin [1]. [^{18}F]fluoride is produced via the ^{18}O(p,n)^{18}F nuclear reaction by irradiating isotopically enriched [^{18}O]water with 15-16 MeV protons (beam current: 20-40 µA). Following irradiation times of 60-90 minutes the [^{18}F]fluoride is collected on the resin, and the irradiated target water is eluted to a collection vial. GE indicates that distilled [^{18}O]water is acceptable for use in [^{18}F]FDG production using the MicroLab®.

Over the last 18 months our demand for [^{18}F]FDG has increased to ~250 mCi/day. We have observed that this is easily achieved using [^{18}O]water obtained directly from the manufacturer, but not when using distilled [^{18}O]water. This posed a problem to us since a second fluoride irradiation and production of FDG not only adds to our costs, but also disrupts the daily cyclotron production schedule.

We have compared the [^{18}F]FDG end of synthesis (EOS) yields using "virgin" (obtained from supplier) [^{18}O]water (both 70 % and 98 % isotopically enriched) and distilled [^{18}O]water. The synthesis has been tested using [^{18}O]water from Swan Chemicals, Isotec, and Cambridge Isotope Laboratories (CIL). The statistical comparison was performed on batches without any mechanical delivery problems, or problems identified with "box" chemistry.

For syntheses using "virgin" water we found yields of 197±49 mCi (Isotec 98 %; n = 24), 239±51 mCi (CIL 98 %; n = 23) to 250±68 mCi (Swan Chemical 98 %; n = 49). As a measure of the effect of isotopic enrichment we have determined an average yield of 192±50 mCi for 70 % virgin water (CIL; n = 50).

In comparison we have found some interesting differences for the yields using distilled water. We have been careful to ensure that different batches of water were not mixed before distillation. On average Swan distilled water gave a lower average EOS for [^{18}F]FDG yield, 173±60 mCi (n = 24) compared to virgin 250±68 mCi (n = 49). The isotopic enrichment of the 98 % water after distillation is known to be in the range of 85-89 %, indicating the decreased yields are not directly due to the difference in isotopic enrichment. Additionally, comparison of Isotec 98 % virgin and distilled water samples did not show a decrease in EOS yields. Further analysis of our data revealed when distilled water was used, less activity was retained on the MicroLab® resin and was found in the [^{18}O]water collection vessel. This [^{18}O]water, when collected and resin treated according to the Brookhaven method [2] was found to be reactive when tested on other chemistry. This would indicate to us the presence, either ionic or organic, of a species in the distilled water that is preventing the radioactivity from binding to the FDG resin in the GE MicroLab®.

We have analyzed selected batches of virgin and distilled [^{18}O]water for selected ions using a Waters Ion Chromatography system as detailed previously [3]. These analyses included mono and divalent cations (Li, Na, NH_4, K, Mg, Ca, Sr, Ba), anions (F, Cl, NO_2, Br, NO_3, HPO_4, SO_4) and transition metal ions (Cu, Pb, Zn, Ni, Co, Cd, Fe(II), Mn). We have found no

statistically significant correlation of these ions and batch yields. These findings are in agreement with many other groups who have tried to evaluate these contaminants.

Our distillation technique (on batches of 25-40 g water) was a simple atmospheric method using a 14 cm vacuum-jacketed Vigreux column and fraction collector. We used a very slow "boil up" time and collected the first 5 mL as a separate fraction, before distilling the remaining water into a separate vial. It has been speculated that the initial distillate contains a significant percentage of organic materials. We attempted to analyze this by gas chromatography with little success. Comparison of the UV spectrum of these samples compared to virgin water revealed large absorbances in the 200-280 nm range for the initial distillate. The spectrum of the bulk distillate compared to the virgin water were very similar, but suggested that there may be slightly more organic material present in the redistilled water. We are currently attempting to further analyze and characterize these impurities.

References:

[1] S.A. Toorongian, G.K. Mulholland, D.M. Jewett, M.A. Bachelor and M.R. Kilbourn, Routine production of 2-deoxy-2[^{18}F]fluoro-D-glucose by direct nucleophilic exchange on a quaternary 4-aminopyridinium resin, Nucl. Med. Biol. **17**: 273-279 (1990)
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[3] C.S. Dence, T.J. McCarthy and M.J. Welch M, Ionic contaminants (radioactive and non-radioactive) in irradiated [O-18]water. Preliminary results of a comparative study, Proceedings of the Sixth Workshop on Targetry and Target Chemistry, Vancouver, B.C., Canada, 1995, 199-205

Discussion:

Q: T. Ruth: The source of your nitrates and nitrites is just dissolved air that's then converted into...?

A: Positively.

Q: J. Nickles: Because I see that if you use nitrogen overpressure for producing ^{13}N, you do change the specific activity dramatically.

A: It's just that we don't see it in our "virgin", the only place we see it is in the distilled.

Q: Do you check the pH of the water when you distill it?

A: The final pH ? No, I don't.

Q: J. Steinbach: What are the costs for one mLof water or 1 g of water in the US?

A: $60 from Swan. We sell it back then.

C: J. Steinbach: That's comparable than, it's DM 95.00.

C: M. Welch: I think it's worth making a comment, that at least in the States, with the whole business of writing an NDA I'd rather not have to put in the requirements and everything for distilling water, I'd much rather simply say I buy water of a certain standard. I think that is one reason why I am for using virgin water.

Q: R. Ferrieri: Does Swan provide a certificate of analysis?

A: Yes, they do.

Q: J. O'Neill: Do you know Sally, if they do an organic analysis though?

A: I don't know that, they don't send that analysis, I haven't asked.

C: J. O'Neill: That's along Welch's line what's the guarantee to the FDA, what are they going to do with the water and how is Swan going to deal with contamination problems of water coming back?

C: They are taking it all the way back ...(inaudible)

Q: M. Welch: I have a general question for people using water targets. Those of us that go back a long way and if your read the original Tilbury, Laughlin et al. paper, they had a catalyst on top of that original target to reconvert the hydrogen, oxygen made radiolytically back to water. Do people think that one of the advantages of the high pressure is that at 50 atmospheres you cut down the radiolysis or you somehow through pressure reconvert the hydrogen, oxygen, because if you don't see a pressure rise with this amount energy you're somehow reducing radiolysis from those original targets.

C: K. Erdman: We found in the titanium target that if we did not have really clean water and we got radiolysis and the pressure rose and never came back down. But if you're putting in really clean water into the target and seal it off, the pressure goes up, basically it's related to the temperature of the water inside, and then when you turn the beam off, it cools down, it goes right back down again. So you are not really producing any gas inside.

C: R. Dahl: There's probably some sort of equilibrium set up there, Mike.

C: J. Steinbach: We have the experience, in dependance on the beam current the pressure is going up at low beam currents and stays stable over a very long time at very high beam currents. Maybe it's depending on this.

C: C. Gonzales: One of the things that I've looked for was the amount of water volume recovered after irradiation. That could also give you an idea, how much water you lost there. And as I said, at least with our high pressure target we recover the volume of water that we are loading within 4-5 %.

C: J. Nickles: Mike, I'd like to address your concerns. We're sure of them. We're all paranoid in the US about the FDAs compliance. But I've got to say another word distilling our water to get it back. We get about 80 % recovery, we always get an improvement up to about over 6 MΩ/cm resistivity. And this is our criteria that we've done a good distillation. And as a result our synthesis yield and every criteria of quality it's better with distilled water for us than virginal.

Q: S. Schwarz (to J. Nickles): What are you using for your FDG synthesis?

A: J. Nickles: Cryptocarbonate or cryptoammonium, tetrabutyl ammonium.

C: S. Schwarz: This box, this resin I think that's being affected by distilled water.

C: J. Steinbach: Another comment. We didn't speak about the problem contaminations in water today. Contaminations in the water after irradiation and to have the same contaminations in the final product or not. Are there any comments to that?

Q: M. Jensen: I would like to know how people deal with the possibility of biological contamination if you store your ready-to-use ^{18}O water next to the target. How long do you store them and how do you look at regulatory items there and all that?

A: S. Schwarz: If you are making preparations for human use, I mean, you're final filtering and sterile filtering, so you are removing biological contamination. There wouldn't be a problem at the end.

Q: So nobody cares?

A: Yes, I think you should think about it. And I think that you probably need to store it appropriately.

C: K. Dowsett: We've definitely had problems with contamination with water left on the target. And we now take any waters off that's been more than a week on the target and take it down, because at one point we had bugs growing in it. And more than it comes out alive, bits come through even after irradiations there's pyrogens. We've got some fragments of proteins and things left from the edge of the target, where it stopped. They may were remains of things that were living in our water.

Q: S. Schwarz: How frequently do you do pyrogen sterility testing?

A: I think the FDG gets a pyrogen test fairly regularly.

C: S. Schwarz: Ours do it every day.

C: But now we store our water in the fridge all the time and only take it out for a week.

C: S. Schwarz: So you just have a weeks worth in the vault?

C: We have a weeks worth loaded and if we don't use, we take off.

C: D. Schlyer: We've seen that too, if we had a bottle of water sitting on the shelf, it'll grow little critters inside which go into the target, make crispy critters, but if you are careful about the distillation and do it reasonably often, you can keep that kind of bacterial growth down. But I agree, after that you do your sterile filtration.

C: S. Schwarz: And if you don't store your over... I mean if you have enough there for a shorter period of time, you don't really store the ^{18}O water near the cyclotron.

Cross-Sections for the $^{11}B(p,n)^{11}C$ and the $^{11}B(d,n)^{11}C$ Nuclear Reactions

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Introduction

Carbon-11 is a short-lived (20.4 minutes) radioactive isotope of carbon which is widely used to track organic molecules in the human body using Positron Emission Tomography (PET). One of the factors in the future expansion of PET into routine clinical practice is the availability of carbon-11 and other short-lived positron emitters at a reasonable cost to centers in major cities. Though the $^{14}N(p,\alpha)^{11}C$ reaction is widely used for carbon-11 production on cyclotrons where the proton energy is typically 11 MeV or higher, the only nuclear reaction available for producing C-11 at very low energies (< 5 MeV) is the $^{11}B(p,n)^{11}C$ reaction on either enriched or natural boron. Boron-11 targets have been used in the past using cyclotron bombardments, but the problem has always been the recovery of the carbon-11 from the boron matrix. The purpose of this study was to directly examine the nuclear reaction yields over a wide energy range encompassing the 0-5 MeV range available on low energy accelerators with both protons and deuterons to determine the theoretical yields so that they could be compared to actual yields from the prototype targets.

Experimental

All irradiations were carried out on the BNL 60" cyclotron using the target assemble shown in Figure 1.

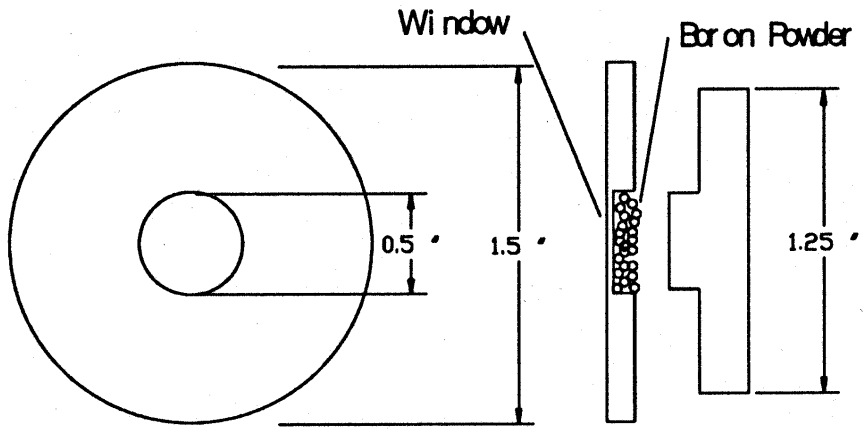

Fig. 1: Target Assembly; Material of Construction: Aluminium

The target holders were constructed of aluminum and each contained 50 mg of boron powder to achieve high energy resolution but with sufficient material to ensure accurate cross section measurements. Carbon-11 yields were determined by decay curve analysis.

Results

The results from the measurements for the $^{11}B(p,n)^{11}C$ nuclear reaction are shown in Figure 2.

Summary

The yields fom the $^{11}B(p,n)^{11}C$ nuclear reaction have been measured over the energy range of 0 to 28.6 MeV. The yields from the $^{11}B(d,n)^{11}C$ nuclear reaction have been measured over the energy range of 0 to 21.5 MeV. Cross section values were derived from the yield data.

The yield measurements were carried out on sealed samples of boron powder isotopically enriched to greater than 93 %. Our data show that at energies below 5 MeV, the $^{11}B(p,n)^{11}C$ nuclear reaction can be expected to produce 250 mCi of carbon-11 (based on a 30 minute irradiation at a beam current of 100 µA).

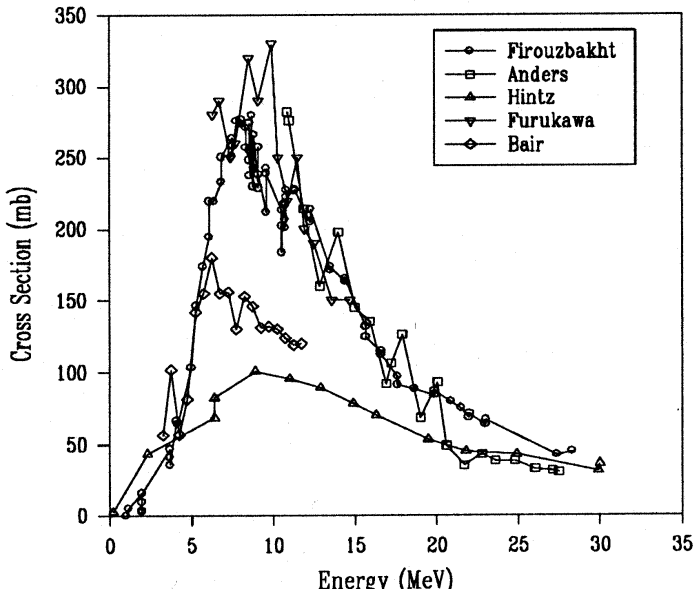

Fig. 2: $^{11}B(p,n)^{11}C$ Reaction Cross Section

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