1.4. Target materials

Chairmen: J. R. Dahl (Manhassat) and D.J. Schlyer (Long Island)

The purpose of this paper is to selectively review the English language papers dealing with factors important to the selection and use of target materials for the production of biomedically useful radionuclides and to provide information on methods used to improve the purity of the precursor gases and liquids. An excellent introduction to the subject is given in Clark and Buckingham's book in the chapter discussing the processing of radioactive gases. To be of use in biomedical studies a radionuclide must be available in sufficient quantity and purity to be used as a tracer in an imaging agent, either as a product used directly from the target chamber, processed to a particular radiochemical, or as a tracer incorporated into a compound of biological relevance. Both quantity and quality of the radiochemical are strongly dependent upon the starting material; hence this review is principally concerned with the composition of the target material. Except for some consideration of the interaction between the target chamber material and the product radionuclide, the material from which the target chamber itself is constructed is not discussed here. Radiation dose has also been observed to effect the chemical form of the product, but this aspect is treated here only where the interaction of the radiation with the target material has been exploited to achieve a desired product or is illustrative of a particular point.

Matter in all three states has been bombarded with charged particles to produce bio-medically useful radionuclides. Gas and liquid materials have been the most common targets for the production of short-lived positron emitting radionuclides because these radionuclides are of relatively low atomic weight and the simple compounds of these elements are mostly either liquid or gas. Solid target materials are mostly used for the production of longer-lived radionuclides, especially metallic ions such as ^{67}Ga, ^{52}Fe, ^{207}Tl and ^{111}In. Although solid targets have been used for the production of ^{13}N, ^{11}C and ^{18}F, these targets are not in routine use at the present time. Therefore, this discussion is limited to gas and liquid target materials. The purity of the target material is usually a principal consideration. Small amounts of chemical impurities have been shown to profoundly effect the yield of the desired product. Carriers and additives are sometimes necessary for the efficient recovery of the product in a satisfactory yield and quality. Isotopically enriched targets are becoming increasingly important, especially in the production of the "physiologic" positron emitters ^{11}C, ^{13}N, ^{15}O, as well as ^{18}F, by use of cyclotrons with a proton energy less than 12 MeV exploiting the relatively large values of the (p,n) excitation functions.

When a gas target is bombarded with charged particles for radionuclide production, several events occur in addition to the activation of the target nuclei. The gas is ionized and highly excited states of matter exist. Any impurities present in the target gas are also ionized, dissociated and highly excited. The impurities therefore provide a potential source of reactive species which can reduce the yield of radiochemical by diverting some of the radionuclide to useless and undesirable radiochemicals. For example, $^{18}F-F_2$ is an electrophilic fluorinating agent of considerable interest due to its use in the synthesis of 2-[^{18}F]fluoro-2-deoxyglucose. It is conveniently prepared by bombarding neon gas

targets with deuterons to produce ^{18}F via the $^{20}Ne(d,\alpha)^{18}F$ nuclear reaction. Carrier fluorine gas is added to the target to aid recovery of the product following bombardment. The amount of carrier fluorine is minimized to maintain the specific activity of the $^{18}F-F_2$ as high as possible consistent with obtaining an acceptable yield. Highly purified Ne (up to 99.9999 % pure) is available to use as a target gas. Neon is relatively easy to separate from other materials due to its chemical inertness and to its physical properties. Fluorine, on the other hand, is a highly reactive material prepared by the electrolysis of flurospar and consequently contains many impurities. Commercially supplied fluorine contains up to several per cent of HF which must be removed before use as a carrier in $^{18}F-F_2$ production. HF present in the target gas will result in the diversion of ^{18}F from F_2, resulting in a reduction of yield and the contamination of the product with an impurity which must be removed to eliminate unwanted side reactions. HF is usually removed from the fluorine base by reaction with potassium fluoride, forming KHF_2. The KF must be very dry to prevent loss of the F_2 from the gas stream since F_2 reacts with water to produce HF. This treatment reduces greatly the amount of HF in the gas stream. Other materials, such as N_2 and gases containing carbon must be removed from the fluorine gas before it is used as a carrier or they will lead to the production of materials such as CF_4 and NF_3 which divert yield from F_2 and are not useful labeling materials. It has been shown that the presence of less than 0.03 % of N_2 and 0.01 % of CO_2 can reduce the purity of the $^{18}F-F_2$ product to 29 % compared to an expected 98 % under acceptable conditions <6,7>.

There are many potential sources of impurities in any target material. The first source considered is the impurities present in the gases as received from the supplier. Gases from one supplier work better in a target system than do gases from another supplier. A careful analysis of the target gas should be carried out. Most vendors will supply, for an additional fee, an analysis of the gases or gas mixtures as they are shipped. This is usually a worthwhile investment since it can save a great deal of idle speculation at a later date. Gases should also be analyzed when received to insure their purity. This analysis can easily be carried out on a gas chromatograph with a few carefully selected columns. Good choices for the analysis of the light gases used in most gas targets are Porapak Q, Molecular Sieve 5A, and Porapak P <1>.

Light gases such as hydrogen and helium often concentrate heavier impurities in the bottom of the tank due to a density gradient in the tank. It has been noted by several groups that targets using hydrogen gas sometimes change their characteristics when pressure in the tank runs low.

Table 1

Effect of impurities in Neon target gas

Composition of target gas (balance Neon)					% ^{18}F appearing as ^{18}F labelled–		
% F_2	% N_2	% O_2	% CF_4	% CO_2	F_2	NF_3	CF_4
1.00	0.49	0.60	N.D.	0.13	29	54.1	16.9
0.62	0.30	0.037	N.D.	0.008	29	50.7	20.3
0.047	0.002	N.D.	N.D.	0.001	98	--	--
0.076	0.0002	0.009	0.008	N.D.	15	--	85.0

A second source of impurities is provided by the valves, seals, and other components of the apparatus. A notable example occurs in the production of ^{11}C from a nitrogen target: Carbon occurs in the product obtained from the target system even though meticulous care has been used in excluding any form of carbon from the system. Nearly all manufacturers use hydrocarbon solvents to clean metal pieces prior to shipping and it is extremely difficult to remove the last traces of these solvents from the pieces. The best method for removing carbon from metal pieces is to bake the piece at 550 to 600°C in a flowing oxygen atmosphere. This procedure is, of course, limited to those parts which can withstand such treatment without damage. Ultrasonic cleaning with aqueous solvents offers the next best solution.

Careful attention must be given to selection of the apparatus used in the handling of the gas. For instance, an improperly selected regulator may have a diaphragm which allows atmospheric gases to contaminate the target gas or may introduce impurities themselves to the gas stream. It is widely accepted that the elasticizers in synthetic and natural rubbers are slowly released to a gas stream sweeping over them. Most elasticizers are organic compounds, and may provide a source of contamination when present in apparatus used to regulate the pressure of nitrogen to be used for ^{11}C production, thereby limiting the specific activity <8>.

Several radionuclides are recovered from the target chamber by washing the target chamber with water. Examples of this recovery method are the preparation of ^{18}F fluoride ion from the proton bombardment of ^{18}O-gas, ^{123}I from ^{124}Xe, and ^{81}Rb from Kr. The water used in the recovery will introduce impurities if demineralized water is used instead of distilled water. Deionized water also typically has a lower pH than distilled water, and this detrimental to the recovery of fluoride and iodide.

In the bombardment of enriched krypton in the production of ^{81}Rb for use in generators for the preparation of ^{81m}Kr, the target must be washed with an aqueous solution to remove the ^{81}Rb. If care is not taken in the design, construction, and use of

the target chamber, impurities will be introduced into the target gas which will result in the production of radionuclidic impurities which will contaminate the generators <9>. In the cited reference, detrimental contaminants resulting from the accumulation of oxygen and nitrogen which entered the target chamber during post-bombardment processing caused corrosion of the target chamber. When, during the removal of the ^{81}Rb from the target chamber, these corrosion products were washed from the target chamber onto columns for the preparation of generators for ^{81m}Kr production, reduction of the loading efficiency of ^{81}Rb produced via the $^{82}Kr(p,2n)^{81}Rb$ reaction resulted.

Gases used to purge the target after irradiation should be of the same high purity as the target gases. Inert gases and nitrogen should be scrubbed of hydrocarbon impurities to prevent contamination of the target gas, especially in the case of carbon. If possible, the target should be evacuated between runs to help remove the lighter hydrocarbon impurities.

When preparing a target chamber for initial use, it is normal for the cleaning to be as rigorous as possible. A question arises with respect to the best cleaning method for use with a particular radionuclide production process. One worker customarily used a sequence of dilute acids, highly purified water and acetone to clean a nickel target chamber for use in preparing $^{18}F-F_2$. The results of the first few bombardments usually had to be discarded due to contamination with ^{18}F labelled fluorocarbons. When the cleaning procedure was simplified to cleaning by ultra-sound and rinsing with high-purity water, and allowing the target chamber to air dry, the amount of fluorocarbons produced in the initial bombardments was drastically reduced <10>. Another method which has been found very effective at Brookhaven National Laboratory is cleaning with increasingly polar solvents (a typical sequence might be hexane, acetone, methanol, water) with several rinses with water, a rinse with dilute HCl, several more rinses with water and a final drying in a vacuum oven.

When a single chamber is being used for the production of more than one nuclide in more than one chemical form, it is essential to insure that the second target gas will not be contaminated by residues from the preceding experiment. A recent publication <11> details the use of a single target chamber for the sequential preparation of a variety of radionuclides by proton bombardment of different target gases in the same target chamber. Although no difficulties resulting from cross-contamination of the different target gases were reported, it remains a factor to consider, especially when the sequence of target gases is different from that reported. Probably the most effective method of preventing contamination of the second experiment by residues from the first is to evacuate the target chamber between irradiations. This is often not possible and the next best course of action is to purge the target chamber. At BNL it has been our experience that purging the target chamber at a flow rate of 200 to 300 cm^3/minute will remove most of the unwanted gases.

Several methods are used to remove impurities from gases to be used as targets. The selection of the appropriate method depends on the type and concentration of the impurity in the target gas. Particulate matter and liquids may be removed from the gas stream by passing the gas through a 0.22 micron filter. Gaseous impurities are more serious and must be removed by chemical purification. The gases most commonly used as targets for the preparation of short-lived positron emitters are nitrogen, oxygen, and neon. Nitrogen can be cleaned just prior to flowing into the target chamber by first flowing it through a furnace containing hot copper/copper oxide and then through a soda lime trap. The copper will remove oxygen, the copper oxide will convert CO to CO_2

and the soda lime will remove the CO_2. There are commercial catalysts for the removal of impurities from target gases. These include "BTS Catalyst", a product from BASF Co., which will remove oxygen, hydrogen, hydrogen sulfide, and carbon monoxide from a gas stream of nitrogen or neon. "DEOXY", "OXYSORB", and "RIDOX", are other commercially available deoxygenation catalysts on the market. All of these catalysts lack ability to remove the last traces of oxygen from nitrogen or neon <12>. The removal of nitrogen traces from oxygen is very difficult. The only effective method employs a rhodium catalyst to oxidize the nitrogen to nitrogen dioxide which can then be scrubbed out. Alumina gel or silica gel may be used to remove water from nearly all gases. Hot sulphuric acid may also be used to dehydrate several gases including gaseous HF <13>.

Materials may be added to the target material to aid in the recovery of the product radionuclide in the desired chemical form. Stable isotopes of the product element may be added as carrier, as in the addition of stable $^{19}F-F_2$ to aid in the recovery of $^{18}F-F_2$ when neon gas is bombarded with deuterons <5, 6, 7>. Other materials may be added to the target material to influence the form of the compound recovered from target chamber. Finn and Christman <14,15> used hydrogen as an additive to nitrogen which was bombarded with protons for the production of ^{11}C via the $^{14}N(p,\alpha)^{11}C$ reaction. The recoiling ^{11}C atoms reacted with the hydrogen to produce $^{11}CH_4$. Ammonia was also produced in the target chamber by reaction between the excited hydrogen and nitrogen. The $^{11}CH_4$ plus NH_3 mix was converted to $H^{11}CN$ by catalytic conversion with platinum at 1000°C placed in the stream of flowing gas. Trace amounts of oxygen present in "zero gas" <16> are sufficient to convert to $^{11}CO_2$ all of the ^{11}C produced by the proton bombardment of nitrogen <15>. Some workers report more reliable recovery when small amounts of O_2 are added to the target gas <17>. There has been much private discussion <8> among investigators regarding the choice of target chamber material for containing nitrogen for the production of ^{11}C via the $^{14}N(p,\alpha)^{11}C$ reaction, but published references are scarce concerning the determination of which material will not retain ^{11}C or add unacceptable levels of carrier. One group <17> identifies quartz as the material of choice. However, this study is not exhaustive and it is quite likely a more suitable material may be found. A particular advantage of this target chamber system is the ability to produce $^{11}CO_2$ from 100 ppm O_2 in N_2 for radiochemical synthesis using a 14.9 MeV proton beam; and immediately thereafter with a remotely controlled beam energy degrading foil in place, produce $^{11}CO_2$ contamination from 100 ppm O_2 in N_2 or produce ^{11}CO from UHP N_2, both without ^{13}N contamination, for direct use in patients by reducing the energy of the proton beam from 14.9 MeV to 8 MeV (Figure 1). The target chamber can also be used to make $H^{11}CN$ by bombardment of 5 % H_2 in N_2. All of these products are produced in a linear yield with respect to incident beam (Figure 2). Although no carbon comes from the quartz tube, the use of an elastomer O-ring to seal the front provides a source of carbon to reduce specific activity. We have measured the specific activity of HCN produced with this target system at approx. 1 Ci/μmol. Two recent studies <18,19> have focused on optimizing the yield and specific activity of ^{11}C, but the principal focus has been on the target. Little data describing the target gas is available.

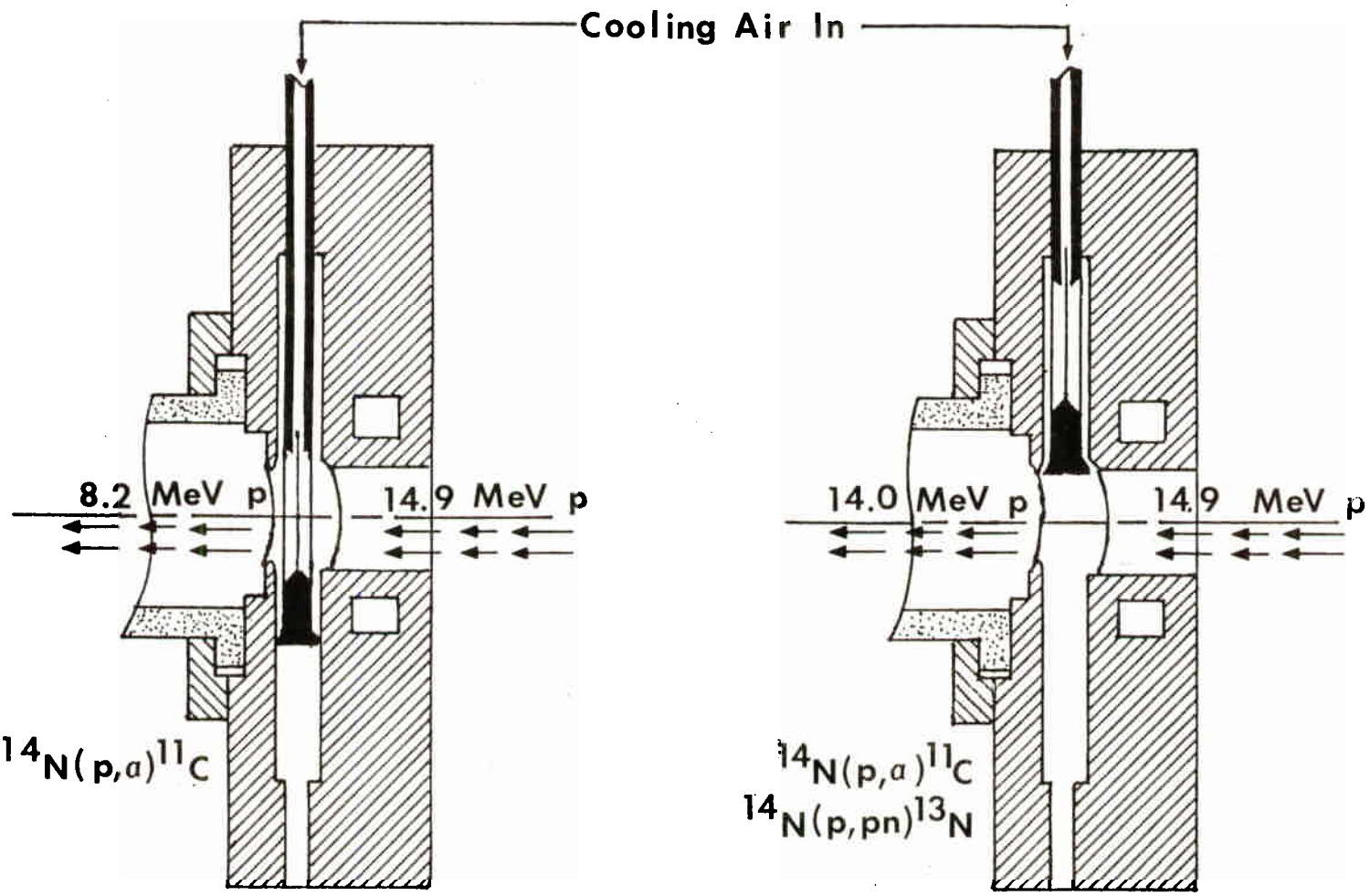

Figure 1
Beam Window Arrangement of SKI ^{11}C Target Chamber.

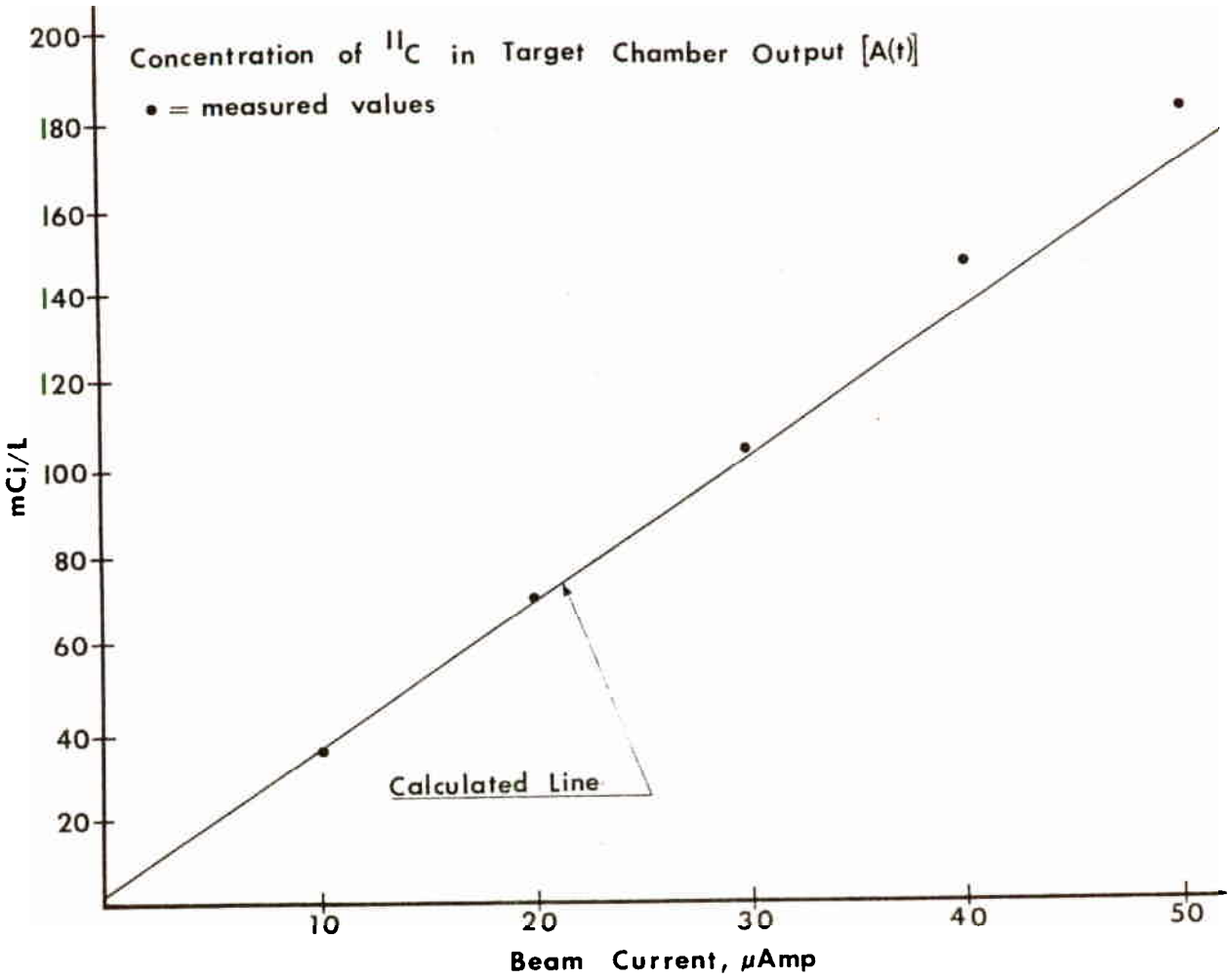

Figure 2
Yield and Equation Slide.

The amount of carrier added to a target gas is usually minimized to maintain the specific activity as high as possible. In cases where carrier is required to effect efficient recovery of the radionuclide, the yield is frequently dependent on the amount of carrier added. For instance, in the production of $^{18}F-F_2$ by the proton bombardment of enriched ^{18}O gas and subsequent recovery of the ^{18}F by rebombardment of a neon–fluorine mix in the target chamber, Nickles, Daube, and Ruth <20> found the minimum effective concentration of carrier was 0.1 % F_2. They observed that this level of carrier seems to be generally required since the same results were obtained in experiments with the deuteron–neon system. Previously unreported work in our laboratory at Sloan–Kettering Institute has shown that a carrier level of about 0.3 % F_2 is necessary to obtain a consistent 65 % recovery of $^{18}F-F_2$ from a nickel chamber filled with neon plus F_2. The target is not re–bombarded in this case. Other work would tend to bear out this observation <21>. A measure of the yield of ^{18}F recovered from a nickel target was reported in <5> when the technique for producing this precursor was first described (Table 2).

Occasionally the radionuclide product desired can be best produced by means of a reaction which may, due to interfering reactions on other nuclides in the target, yield a marginally pure product. In some cases it is possible to minimize the impurities present in the output from the target chamber by carefully selecting the energy thickness of the target. Gas targets provide an easy method to do this. Proper selection of foil and target chamber allows control of the energy thickness of the target to minimize contaminating activities. Thus the need to separate oxygen and nitrogen was avoided in a process to produce ^{14}O, a positron emitting oxygen isotope with a 70 second half-life, as $^{14}O-O_2$. Carrier gas (5 % CO in He) was added to the gas from the target before it was purified, for efficient removal of ^{11}C containing gases <23>.

Liquids have been used as target materials for the production of positron emitting radionuclides with considerable success, largely because of the ease of handling of the target material and due to the usually simplified procedures for the recovery of the radionuclide. Pure liquids are most commonly used, although experimentation with solutions is gaining importance and attention. Water is probably the most commonly employed liquid target material, usually selecting ^{16}O as the target nuclide, either in the production of ^{18}F via a helium ion induced reaction <24> or in the production of ^{13}N when bombarded with protons. For the production of ^{18}F it is usually sufficient to use water for injection (USP) without any added preservative as the target material. Such water is usually extremely pure and the product is used directly <24>. This is also true of water which is to be used for the preparation of ^{13}N although it has been shown that relatively small amounts of additives to the target solution can profoundly effect the nature and distribution of the labelled chemical species <25>.

Table 2
Dependence of $^{18}F-F_2$ recovery on the amount of F_2 added to $^2H^+$ bombarded Neon target gas

% F_2 in Ne target gas	relative recovery of $^{18}F-F_2$
0.0	7.7
0.1	37
0.7	48
2.0	63
7.5	100

(Lambrecht et. al., <5>).

Although it is unlikely that the effect is due to target impurities, an interesting observation is the failure of $^{13}NH_3$, produced by the reduction of the ^{13}N-nitrates by the use of $TiCl_3$ in basic solution, to label amino acids by reactions with immobilized enzymes as well as $^{13}NH_3$ produced by reduction using deVarda's alloy and NaOH. In the process of implementing a remotely controlled apparatus for reduction of the ^{13}N

using $TiCl_3$, the yields of ^{13}N-glutamate were less than one half that obtained using $^{13}NH_3$ prepared from deVarda's alloy. Treatment of the $^{13}NH_3$ with hot NaOH did not improve this yield <26>. Investigation of this question continues.

In early work with helium ions for ^{18}F production, the interaction between target water and target chamber was a matter of special concern. The tendency of fluoride ion, the anticipated chemical form of the ^{18}F, to form complexes with various metal ions is well known, and the possibility of introducing deleterious metal ions into the target water by interaction with the target chamber material was of considerable concern. Several studies were carried out before Titanium was selected as the most suitable material <24,26,27>.

Pure liquids other than water have been used as target materials. In particular, Chloroform has been used to produce ^{38}K by $^{4}He^{++}$ bombardment although sodium chloride evaporated from solution onto a Tantalum plate proved superior <28>. Similarly, Bromoform was used as the target material in the preparation of ^{79m}Kr by the $^{79}Br(p,n)^{79m}Kr$ reaction. Several problems were associated with this production method. The ^{79m}Kr is removed from the target as it is produced by sparging the target with Helium during bombardment. The Helium also sweeps many radiolytic decomposition products from the target and these must be removed by subsequent processing. The increase in the internal volume of the delivery apparatus due to the additional processing requirement delays the transmission of the product to the site of use unacceptably <29>.

The bombardment of solutions for the preparation of radionuclides offers the opportunity to exploit radiation induced reactions which take place in the target to produce radiolabeled compounds otherwise difficult to prepare. It also provides the opportunity to recover gaseous products by sparging the target solution with helium during or after bombardment to recover the activity.

An especially interesting example is the bombardment of a liquid ammonia-nitrous oxide target to prepare ^{11}C-guanidine <30>. It was shown that the yield of ^{11}C-guanidine varied with the concentration of N_2O in the target, and suggested that the yield of ^{11}C-guanidine could be optimized by devising a method of maintaining a constant level of N_2O in the target during bombardment.

A method for preparaton of ^{13}N-N_2 in a stream of flowing Helium has been reported. Aqueous solutions of ammonia are bombarded with protons while the target is being sparged with helium <31>. It was found that without the addition of carrier ammonia to the target solution the yield of ammonia released to the sparging gas was about 6 % of the value obtained when the target solution contained 2×10^{-2}M ammonia. Using N_2 as the sparging gas to maintain saturation of the target solution with ammonia had no effect.

Liquid target materials are not problem-free. A principal problem with liquid target materials, cavitation or bubble formation, derives from causes similar to the causes of the phenomenon of density reduction in gas targets and has much the same results: seemingly thick targets are suddenly thin. At low beam currents convection within the target, in short bombardments at least, seems to be sufficient to carry away the energy deposited by the beam. As the beam intensity increases, the energy deposition rate increases and the liquid will momentarily vaporize. In addition to this phenomenon, the liquid will decompose due to radiolysis, and the products can be gases. If the gases are allowed to build up in the solution, or accumulate in the target chamber indefinitely, the results will be reduction of the yield of radionuclide through loss of target thickness in the beam path, or rupture of the target chamber entrance window foil, due to gas pressure build-

up. At least two designs for recirculating liquid targets have been tested <32,33>. Rapid recirculation of the target liquid was shown an effective means of maintaining the yield of radionuclide directly proportional to the beam current at beams as high as 60 μA <32>. Methods for calculating target thinning due to local boiling of the liquid in the beam path are very few, in spite of the fact that in static target systems it is probably as large a factor in density reduction as radiolytic decomposition. Recently, a method was published for density correction in cryogenic liquid target materials, and the approach is applicable to calculate the density correction which must be accounted for when bombarding materials which are liquid at more usually encountered temperatures <34>.

Interest in designing a target chamber to hold a very small amount of $^{18}O-H_2O$ for the production of ^{18}F via proton bombardment has increased. In addition to save expensive isotopically enriched target material, several of these targets minimize decomposition of the target material through deposition of energy in cooling H_2O rather than in the target water by means of target thinness <35,36>. Target volumes as low as 0.6 ml have been reported <37>.

Various isotopically enriched target materials have been used when the natural abundance of the target nuclide has been so small that significant gains in the yield of the product radionuclide could be realized. In the past these enriched target materials have commonly been metals from which the product obtained was a radionuclide in an inorganic ionic form. Recent interest in cyclotron production of positron emitting radionuclides via the (p,n) nuclear reaction has focused attention on $^{18}O-H_2O$ due to the large average value of its (p,n) excitation function at proton energies less than 16 MeV. Due to the expense inherent in using any isotopically enriched target material, it is usually recovered and used continually, replenishing the inevitable mechanical losses with new material and exercising care in handling to minimize the introduction of deleterious contaminants. Kilbourn <35,36> reports the contamination of the recovered target is mostly with metal ions from the target chamber material or from the foil windows. Nickel and copper ions were found to leach from a nickel plated copper target chamber and contaminate the solution with about 10 ppm of each ion. When a titanium target chamber was used with Havar entrance foil, cobalt, iron and chromium were found to be the principal contaminants, at much reduced levels. When titanium foils were used, the level of the contaminants was reduced from 50 to 100 fold over that obtained with the nickel-plated target chamber. The use of Ti as a material for containing liquids, particularly water for the production of ^{18}F, has been well established <24,26>.

Conclusions

A primary consideration in designing, building, using, and maintaining quality control of radionuclides for bio-medical use produced by bombarding liquids or gases with cyclotron beams is the chemical composition of the target material. Careful consideration of the constituents of the target, and meticulous control of the handling and processing to prevent the intrusion of extraneous materials will aid greatly in obtaining reproducible yields and maintaining the required level of radiochemical purity.

References

1. Clark, J.C. and Buckingham, P.D., Short-lived Radioactive Gases for Clinical Use. Butterworths, London, 1975, p46ff.
2. Ferrieri, R.A., Schlyer, D.J., Wieland, B.W., and Wolf, A.P., On-line Production of ^{13}N-Nitrogen gas from a Solid Enriched ^{13}C-Target and its on to ^{13}N-Ammonia Synthesis using Microwave Radiation. Int. J. App. Rad. Isot. 34:897-900, 1983.
3. Buckingham, P.D., and Forse, G.R. The Preparation and Processing of of Radioactive Gases for Clinical Use. Int. J. Appl. Rad. Isot. 14:439-445, 1963.
4. Bakker, C. and Kasperson, F., Production of ^{18}F by Alpha Particle Bombardement of SiO_2 Int. J. App. Rad. Isot. 30:61-62, 1979.
5. Lambrecht, R.M., Neirinckx, R., Wolf, A.P., Cyclotron Isotopes and Radiopharmaceuticals XXIII. Novel Anhydrous ^{18}F-Fluorinating Intermediates. Int. J. Appl. Radiat. Isot. 29:175-183, 1978.
6. Bida, G.T., Ehrenkaufer, R.L., Wolf, A.P., Fowler, J.S., MacGregor, R.R., Ruth, T.J., The Effect of Target Gas Purity on the Chemical Form of ^{18}F during ^{18}F-F_2 Production Using the Neon/Fluorine Target. J. Nucl. Med., 1:758-762, 1980.
7. Casella, V., Ido, T., Wolf, A.P., Fowler, J.S. MacGregor, R.R., Ruth, T.J., Anhydrous ^{18}F Labeled Elemental Fluorine for Radio-Pharmaceutical Preparation. J. Nucl.Med. 21: 750-757, 1980.
8. Lore: A particular goal of this symposium was to bring into focus credible hearsay which may have some basis in fact, with the hope that it may be fruitfully attended to, either in proof or disproof. Items of lore are thus identified.
9. Finn, R., Vora, M., Boothe, T., Campbell, J., Carroll, S., Clark, J., Radiation-Induced Defects as Illustrated by the ^{81}Rb-^{81m}Kr Target System. Int. J. Appl. Radiat. Isot. 33:349-353, 1982.
10. Wieland, B., Personal communication.
11. Ruth,T.J., The Production of ^{18}F-F_2 and ^{15}O-O_2 Sequentially from the same Target Chamber. Int. J. Appl. Radiat. Isot. 36:2, 107-110, 1985.
12. Gordon, A.J., and Ford, R.A., The Chemists' Companion. Wiley Interscience, New York, 1972, p428ff.
13. Ehrenkaufer, R.L.,et al., Production of $H^{18}F$ by Deuteron Irradiation of a Neon-Hydrogen Gas Target. Radiochimica Acta 33: 49-56, 1983.
14. Finn, R.D., Christman, D.R., Ache, H.J., Wolf, A.P., The Preparation of ^{11}C-Cyanide for Use in the Synthesis of Organic Radiopharmaceuticals. Int. J. Appl. Radiat. Isot. 22:735-744, 1971.
15. Christman, D.R., Finn, R.D., Karlstrom, K.I., Wolf, A.P., The Production of Ultra High Activity ^{11}C-labelled Hydrogen Cyanide, Carbon Dioxide, Carbon Monoxide and Methane via the $^{14}N(p,alpha)^{11}C$ Reaction (XV). Int. J. Appl. Radiat. Isot. 26:435-442, 1975.
16. Braker, W. Mossman, A.L., Matheson Gas Data Book 5th Ed., Matheson Gas Products, E. Rutherford, N.J., 1971.

17. Dahl, J.R., Drumm, P., Lee, R., A Quartz Target Chamber for ^{11}C Production. 186th Nat'l. Am. Chem. Soc. Meeting Washington, D.C. Aug. 28–Sept. 2, 1983, paper NUCL27.
18. Vandewalle, T., and Vandecasteele, C., Optimization of the Production of $^{11}CO_2$ by Proton Irradiation of Nitrogen Gas. Int. J. Appl. Radiat. Isot. 34:10, 1459–1464, 1983.
19. Heselius, S.J., Malmborg, P., Solin, O., Langstrom, B., Production of Carbon–11 With Respect to Specific Radioactivity– A Target Study. Proc. 5th Int. Symp. on Radiopharm., Chem., Tokyo, Japan, July 9–13, 1984, 272–274.
20. Nickles, R.J., Daube, M.E., Ruth, T.J. An $^{18}O_2$ Target for the Production of $^{18}F–F_2$. Int. J. Appl. Radiat. Isot. 35:2, 117–122, 1984.
21. Target built by Chemistry Department Brookhaven National Laboratory, on Loan to Sloan–Kettering Institute Core Cyclotron Facility.
22. Dahl, J.R., Tilbury, R.S., Russ, G.A., Bigler, R.E., The Preparation of Oxygen–14 for Biomedical Use. Radiochem. Radioanal. Lett. 26:2, 107–116, 1976.
23. Tilbury, R.S., Dahl, J.R., Mamacos, J.P. Laughlin, J.S., Fluorine–18 Production for Medical Use by Helium–3 Bombardement of Water. Int. J. Appl. Radiat. Isot., 21:277–281, 1970.
24. Tilbury, R.S., and Dahl, J.R., ^{13}N Species Formed by Proton Irradiation of Water. Rad. Rsch. 79:22–33, 1979.
25. Dahl, J.R., Drumm, P., Lee, R., Gelbard, A.S., Rosenspire, K.C., A Remotely Controlled Semi–Automatic System for the Preparation of ^{13}N–Ammonia. Symp. on Chem. Considerations in the Labelling of Radiopharmaceuticals with Short–lived Radionuclides. 187th Nat'l. Am. Chem. Soc. Meeting, St. Louis, Mo., Apr. 8–13, 1984, paper NUCL89.
26. Clark, J.C. and Silvester, D.J., Title Unknown, Int. J. Appl. Radiat. Isot. 17: 151, 1966.
27. Mudrova, B., Svoboda, K., Adsorption of ^{18}F on Glass, Polyethylene, Titanium and Aluminum Surfaces. Radiochem. & Radioanal. Lett., 11:3–4, 177–185, 1972.
28. Tilbury, R.S., Myers, W.G., Chandra, R., Dahl, J.R., Lee, R., Production of 7.6–minute Potassium–38 for Medical Use. J. Nucl. Med., 21: 867–871, 1980.
29. Dahl, J.R., Myers, W.G., Graham, M.C., Production of Krypton–79m for use in Nuclear Medicine, Proc. 190th Am. Chem. Soc. Meeting, Chicago, I11., Sept. 8–13, 1985. Paper UCL 138.
30. Iwata, R., Ido, T., Tominaga, T., The Production of ^{11}C–Guanidine by the Proton Irradiation of the Liquid Ammonia–Nitrous Oxide System and its use in the Synthesis of ^{11}C–Pyrimidines. Int. J. Appl. Radiat. Isot. 32: 303–308, 1981.
31. Suzuki, K., Iwata, R., A Novel Method for the Production of ^{13}N by proton irradiation of an Aqueous Solution of Ammonia. Radiochem. Radioanal. Lett. 28:263–268, 1977.
32. Lee, R., Drumm, P., Dahl, J.R., Radioisotope Production in Recirculating Liquids Using a Retractable Target Chamber. 186th Nat'l. Am. Chem. Soc. paper NUCL28.
33. Parks, N.J., Krohn, K.A., The Synthesis of ^{13}N Labelled Ammonia, Dinitrogen, Nitrite, and Nitrate Using a Single Cyclotron Target System. Int. J. App. Radiat. Isot. 29:754–757, 1978.
34. Tate, M.W., Sadler, M.E., Density Correction for a Boiling Liquid Hydrogen Target. Nucl. Instr. Meth. 204:295–298, 1983.

35. Kilbourn, M.R., Hood, J.T., Welch, M.J., A Simple ^{18}O Water Target for ^{18}F Production. Int. J. Appl. Radiat. Isot. 35:7, 599–602, 1984.
36. Kilbourn, M.R., Jerabek, P.A., Welch, M.J., An Improved ^{18}O–Water Target for ^{18}F–Fluoride Production. Int. J. Appl. Radiat. Isot., 36:4, 3 27–328, 1985.
37. Wieland, B.W., Wolf, A.P., Large–scale Production and Recovery of Aqueous ^{18}F–Fluoride Using Proton Bombardement of a Small–Volume ^{18}O–Water–Target. J. Nucl. Med. 24:5, p122.