CURRENT STATUS RADIONUCLIDE DELIVERY SYSTEM

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INTRODUCTION

CTI has developed an integrated radionuclide delivery system (RDS) for the production of ^{11}C, ^{13}N, ^{15}O, and ^{18}F precursors and radiochemicals. The system includes a negative hydrogen ion cyclotron, targets, surface shielding and a radiochemical synthesis unit. Three RDS units have been installed in hospital settings (University of Tennessee Medical Center; San Raffaele Hospital, Milan, Italy; and Vanderbilt University Hospital). Following is some experience gathered from operating the RDS in both hospital and laboratory settings.

CYCLOTRON

The cyclotron produces an 11.4 MeV beam which may be extracted through four separate exit ports. Over 100 microamperes of proton beam may be extracted from the cyclotron. While this much beam current is excessive for any one target, it has been useful when large quantities of carbon-11 have been required. For example, using the dual simultaneous beam capability of the negative ion cyclotron, it has been possible to irradiate two ^{11}C targets with 40 uA of beam for 40 minutes. This resulted in the production of 2.3 curies of ^{11}C. The total beam extracted from the cyclotron was 120 microamperes with about 1/3 of the beam being collimated before it entered the target.

The cyclotron is operated by a microcomputer which permits fully automatic menu-driven operation. The computer system allows routine automatic operation of the cylotron, targets, and radiochemical synthesis units by technician level personnel. Dual simultaneous beams are automatically produced by computer control more quickly and accurately than by an experienced operator.

TARGETS

The targets are modular units which plug into the four cyclotron exit ports. The diameter of each target entrance window is 10 mm and is located about 20 mm downstream from a 10 mm collimator. The beam transmission through the collimator may be varied in the range of 60% to 90% to meet different target requirements. The uniformity and reproducibility of the beam has been more than sufficient to allow routine automatic operation.

Each of the targets has been tested in our laboratory and the results reported in Ref. 1-4. Subsequent operation of the system, including use in hospital settings, has resulted in the performance data given in Table 1.

TABLE 1

	Run Time (min)	Current (uA)	Recovered Activity (EOB mCi)	Species
F-18 (Gas)	60	30	870	F_2 (see Text)
F-18 (Water)	60	20	500	F^-
O-15 (Gas)	10	40	2000	O_2
N-13 (Slurry)	10	3	20	NH_4^+
C-11 (Gas)	20	40	1000	CO_2

At 40 uA, the $[^{15}O]O_2$ gas activity density is on the order of 20 mCi/cc. The target is fitted with low dead volume valves which can aliquot a fraction of the target activity into a helium stream which delivers it to a gas processing unit. For example, if 200 mCi (EOB) of $[^{15}O]O_2$ is required, only one-tenth of the target inventory needs to be dispensed. This corresponds to about 16.5 cc of target gas at STP or about $4.00.

The ^{13}C powder/water slurry target delivers $[^{13}N]NH_4^+$, thus avoiding subsequent synthesis. Most user operation to date has been at the three microampere level chosen because it produces 20 mCi in a 5 mL volume. Routine use at two hospitals at that level indicates a slurry bed life of about 20 hours (80 batches). The slurry bed can be renewed without disassembling the target. This target has also been operated at 15uA which produces batches of approximately 150 mCi of $[^{13}N]NH_4^+$. Under these conditions, the targets must be reloaded about every four runs.

Laboratory tests on the ^{11}C target indicate stable reproducible performance. The additon of O_2 (up to as much as 1%) to the N_2 target gas has been found necessary to achieve reproducible extraction of activity from the target (Ref.5). The specific activity of the $[^{11}C]CO_2$ from the target has been measured as greater than 50 Ci per micromole.

Development of other precursors includes production of $[^{18}F]F_2$ via proton irradiation of 1) a dilute fluorine in $[^{18}O]O_2$ gas mixture, or 2) a dilute F_2/He in $[^{18}O]O_2$ gas mixture. Recent results have shown that high yields of "reactive" fluorine can be produced with as little as 20 micromoles of carrier fluorine in the target during irradiation. In addition, the inert gas fraction has been measured at $\leq$ 10% of the total recovered ^{18}F. The activity generated by the proton irradiation of the above gas mixtures has been used in the synthesis of $[^{18}F]$2-FDG(Ref.6) and $[^{18}F]$ fluorobenzene from phenylmercuric acetate. As with the $[^{15}O]O_2$ gas target, the total EOB activity in the target can be aliquoted depending on user needs.

SHIELDS

The targets and the cyclotron are enclosed in a "surface shield". Radiation measurements around the perimeter of a 16 foot by 16 foot square surrounding the cyclotron give radiation levels below 4.0 millirem per hour when a $[^{18}O]H_2O$ target is irradiated with 20 microamperes. Ninety-seven percent of the dose equivalent is due to gamma radiation; the

remaining 3% is due to neutron radiation. The shield can be opened to service the cyclotron and targets. Radiation level at the target surface with the target material removed is several hundred millirem per hour just after irradiation. Isotopes removed from the cyclotron for subsequent use also generate radiation fields far greater then the prompt radiation experienced around the operating cyclotron. The three medical units installed to date are enclosed in rooms not designed for radiation shielding. Outside these rooms it is not necessary to restrict access due to radiation.

CHEMISTRY SYSTEMS

Radionuclide-labeled precursors generated by the cyclotron are chemically converted to other precursors or radiochemicals. $[^{15}O]O_2$, for example, is converted to $[^{15}O]H_2O$ with 85% efficiency while $[^{15}O]CO$ and $[^{15}O]CO_2$ are synthesized with $\geq$ 50% efficiency. $[^{11}C]CO_2$ is converted to $[^{11}C]CO$ with 90% efficiency. The Chemical Process Control Unit (CPCU) is a user programmable device which can produce a range of radiochemicals (Ref.7). To date it has been used to synthesize 2-deoxy-2-[^{18}F]fluoro-D-glucose (FDG), [^{18}F]fluoro-D-mannose, [^{18}F]fluoroacetate, and N-[^{18}F] fluoroethylspiperone from [^{18}F]fluoride ion. Over 650 runs producing FDG have resulted in an average radiochemical yield of 50% (corrected to EOB).

CONCLUSION

Developments reported here make PET isotopes available to a wider range of users than in the past. This is due to simplified precursor production and synthesis. It is likely that further simplification and automation will play a critical role in the development of clinical PET.

REFERENCES

1.) Wieland BW, Hendry GO, Schmidt DG, Design and Performance of Targets for Producing ^{11}C, ^{13}N, ^{15}O, and ^{18}F with 11 MeV Protons, J Label Cmpds Radiopharm, 23:1187-1189 (1986).

2.) Wieland BW, Hendry GO, Schmidt DG, Bida GT, Ruth TJ, Efficient Small-Volume ^{18}O Water Targets for Producing ^{18}F Fluoride with Low Energy Protons, J Label Cmpds Radiopharm, 23:1205-1207 (1986).

3.) Wieland BW, Schmidt DG, Bida GT, Ruth TJ, Hendry GO, Efficient, Economical Production of Oxygen-15 Labeled Tracers with Low Energy Protons, J Label Cmpds Radiopharm, 23:1214-1216 (1986).

4.) Bida GT, Wieland BW, Ruth TJ, Schmidt DG, Hendry GO, Keen RE, An Economical Target for Nitrogen-13 production by Proton Bombardment of a Slurry of ^{13}C Powder in ^{16}O Water, J Label Cmpds Radiopharm, 23:1217-1218 (1986).

5.) Clark JC and Reiffers S, Proceedings of the First Heidelberg Workshop on Targets and Target Chemistry, Oct. 4-7, 1985, pages 17-27.

6.) Bida GT, Satyamurthy N, Wieland BW, Ruth TJ, Proceedings of the 2nd Heidelberg Workshop on Targets and Target Chemistry, Sept. 22-25, 1987, pages 19-23.

7.) Padgett HC, Schmidt DG, Luxen A. Bida GT, Satyamurthy N, Barrio JR, Computer-Controlled Radiochemical Synthesis: A Chemistry Process Control Unit for the Automated Production of Radiochemicals. Appl Radiat Isot, in press, (1989).