EXTERNAL CYCLOTRON TARGETRY SYSTEM FOR THE EFFECTIVE LOADING OF PRECIOUS GASES

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SUMMARY

The Cyclotron Facility at Mount Sinai Medical Center is involved in a program of radionuclide production culminating with the preparation of short-lived radiopharmaceutical agents requested for clinical evaluation. The increasing clinical "in-house" demand for short-lived, positron-emitting radiopharmaceutical compounds has necessitated an efficient production schedule requiring unique modifications to conventional external targets. One such project utilizes a low cost, minimal volume, air piston to effectively load enriched nitrogen-15 labelled nitrogen gas. The target yields oxygen-15 labelled oxygen from the $^{15}N(p,n)^{15}O$ nuclear reaction.

The operational characteristics of this target system and the chemical consequences encountered following the irradiation are presented.

INTRODUCTION

Over the past decade, the Cyclotron Facility at Mount Sinai Medical Center has been involved in a comprehensive program of radionuclide production and radiopharmaceutical preparation[1-6]. The emergence of positron emission tomography as an important clinical technique for the diagnosis of neurological abnormality has been a motivating factor for our renewed interest in short-lived, positron emitting, biologically important radionuclides. Consequently, the Cyclotron Facility production schedule has required flexibility in order to satisfy both demands from the clinical staff for large quantities and/or high specific activities of labelled compounds and the maintenance of the production of radionuclides possessing an intermediate half-life. Table 1 lists the radionuclides produced at the Cyclotron Facility.

TABLE I - RADIONUCLIDES PRODUCED AT MSMC

^{124}Te	(p,2n)	^{123}I
^{82}Kr	(p,2n)	$^{81}Rb \longrightarrow {}^{81m}Kr$
^{16}O	(p,pn)	^{15}O
^{16}O	(p,α)	^{13}N
^{14}N	(p,α)	^{11}C
^{203}Tl	(p, 3n)	$^{201}Pb \longrightarrow {}^{201}Tl$
^{112}Cd	(p,2n)	^{111}In
^{68}Zn	(p,2n)	^{67}Ga
^{18}O	(p,n)	^{18}F

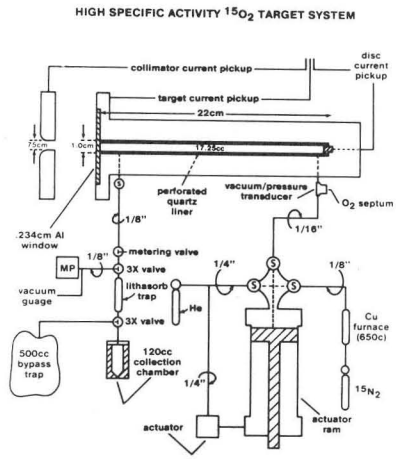
Although the accelerator is a model CS-30 (Cyclotron Corporation) with four particle capability (^1H, ^2H, ^4He, ^3He), the prudent choice of enriched target isotopes and attention to physical and chemical parameters, has allowed our needs to be satisfied by proton bombardments solely. The avoidance of the particle change results in time savings and minimized radiation exposure to the staff.

TARGETRY

Due to their short half-life, compounds labelled with oxygen-15 ($t_{\frac{1}{2}}$ = 123 s) are limited to those capable of being made "on line" via synthetic trains.[7,8]

The clinical request for a high specific activity oxygen-15 oxygen gas for blood component labelling required an alternative to the currently utilized nuclear reaction (Table 1). The $^{15}N(p,n)^{15}O$ reaction has been restudied by several investigators.[9,10] Enriched nitrogen-15 labelled nitrogen (Monsanto Research Corporation, Miamisburg, Ohio) offered a potential solution.

FIGURE 1 - TARGET SYSTEM



The proximity of the chemical processing area, the cyclotron and the clinical area effectively minimizes problems associated with the decay of the oxygen-15 radionuclide. The target chamber is fabricated from aluminum, and fitted with a sliced quartz sleeve to minimize the potential chemical problems with wall reactions. To ensure efficient target operations the beam current is monitored on the

front target window as well as on a terminal disc (Figure 1). The disc reading and theoretical thick target yields for the $^{14}N(p,\alpha)^{11}C$ and $^{14}N(p,n)^{14}O$ compare favorably with literature values.[10,11] Apparently significant scattering of the proton beam is caused by the thick front window[12] required for beam energy degradation (Table 2).

TABLE 2 - TARGET PRODUCTION

TARGET GAS	PRODUCT	ACTIVITY @EOB	*RUN PARAMETERS
$^{15}N_2$(98% enrichment)	^{15}O	163.9mCi	15μa/saturation
$^{14}N_2$(natural)	^{14}O	27.7mCi	15μa/saturation
	^{13}N	8.9mCi	15μa/3 minutes
	^{11}C	32.7mCi	15μa/3 minutes

*Nominal beam current on front target window

The target operational sequence begins with a helium purge of the system followed by evacuation of the system to approximately 60Pa. The system is isolated from the pump, and oxygen of sufficient volume to result in the presence of 0.5% carrier is added through a septum located downstream of the copper furnace. Enriched nitrogen-15 gas at 275mPa is released through the copper furnace into the target system. At equilibrium, the nitrogen-15 line is closed and the target ram (Schraeder-Bellows Econoram MS4) is actuated, increasing the pressure within the target chamber to 788mPa. Proton irradiation for 7 minutes with 15 μa of beam current placed on the front window and 1.0-1.5 μa of beam current indicated on the insulated disc are typical. At the end of bombardment, the target gas is released with a helium push into the collection vessel.

The irradiation of oxygen-nitrogen gas mixtures can lead to the formation of various oxides. Since oxidizing species could inhibit by competition the subsequent reaction of the oxygen-15 labelled oxygen with blood components, experiments with technetium-99m labelled red cells were undertaken. After exposure of the irradiated target gas to the labelled red cells, results from paper radiochromatography indicate the presence of both bound and unbound technetium-99m. Only bound technetium-99m was detected upon exposure of the labelled cells to irradiated target gas purified by passage of the enriched nitrogen-15 over copper at elevated temperature.

RESULTS AND CONCLUSIONS

The short half-life of oxygen-15 places a number of constraints on all aspects of the pharmaceutical preparation. The chemist responsible for the production of the final product must utilize the radionuclide in the form in which it is available from the target. To do otherwise would require additional time, requiring increased production of the radionuclide. A rise in personnel exposures and possible limitation of the production capability would be the end result.

An additional complication results from the radiation chemistry within the target. Apart from the nonlinearity of yield with beam current observed in many gas targets[13], seemingly due to density reduction within the beam strike volume, the radiation chemistry of oxygen-nitrogen systems has demonstrated the formation of various oxides of nitrogen.[14] The addition of a copper furnace operated at 650° C to the nitrogen supply line apparently minimized the oxide of nitrogen concentration within the target gas such that scavenger protection of the radiolabelled products is reduced.

The absolute cross section[10] for the $^{15}N(p,n)^{15}O$ indicates promise for the preparation of oxygen-15 labelled compounds within our facility. The actuator provides an alternative to cryogenic loading of the target and proved both efficient and effective in our target system. Work is continuing toward optimizing the recovery yields and designing of a remote handling system for the high specific oxygen-15 labelled oxygen.

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