DUAL CHEMICAL STATION FOR CYCLOTRON PRODUCED ^{18}F

M.L. Mallory, G. Grimmett, D. Yang and R. Tilbury
The University of Texas, M.D. Anderson
Cancer Center, 1515 Holcombe Blvd.,
Houston, TX 77030

ABSTRACT

The demands for large quantities of 2[18F] fluoro-2-deoxy-D-glucose (FDG) for cancer diagnostics and the desire for 100% product delivery reliability has led us to develop a dual chemistry station. The irradiated target water (18O enriched) is transmitted to a counting vial located in the chemistry station hot cell and then is transmitted to either side of the dual chemistry processing station. The two stations are cleaned in the morning, when radioactivity has decayed from the previous day's runs, and then loaded for either two runs of FDG and/or one run of FDG and one run of another 18F-labeled compound. This station has over forty remotely operating valves. All gases from the chemical reactions are collected in a retaining bag and radioactive products are allowed to decay 24 hours. We have successfully achieved essentially zero radioactivity release. All operations are remote and little personnel radiation exposure is obtained. Since implementation of this dual station, we have greatly reduced failures due to chemistry station malfunction.

1. INTRODUCTION

PET (Positron Emission Tomography) has been used for medical purposes for many years. For example, D.K. Bewley's presentation at the Ninth[1] International Conference on Cyclotrons and Their Application, discussed the early uses of cyclotron produced PET isotopes. In our facility, a cancer hospital, PET imaging studies of tumors has existed for about three years. Recently (1991), the in house production of cyclotron produced PET isotopes has become available and the ready supply of these isotopes in large quantities has seen a tremendous increase in their use for medical diagnostic purposes. In particular, PET scans are now being offered for any part of the body. The medical findings at our institution are that PET does have a contribution to make in supplementing the other standard diagnostic modalities in the detection of cancer and also in the surveillance of the treatment progress of cancerous tumors.

The technical success of PET for cancer diagnostis depends on some type of differentiation in the biologic activity between cancer and noncancerous cells. This difference is not usually exploited by other diagnostic techniques. Figures 1 and 2 are diagnostic scans from two different techniques of the same breast tumor and illustrate the value of PET scans. Figure 1 is a standard mammogram and a possible neoplasm can be detected by the physicians. Figure 2, is a scan from a PET procedure and the cancerous tumor is readily apparent in the computer reconstructed image as indicated by the two dark spots. The success of these initial experimental PET scans at M.D. Anderson has put a demand upon the reliability of the cyclotron PET isotope production program and the conversion of the PET isotopes into the desired drug. Efforts at increasing the redundancy for failure items or a fast turn around after a failure have been implemented on the cyclotron, beam line and the target. In this paper, the efforts at increasing the redunancy in the PET chemistry station, where the desired drug produced is FDG, is reported in the following section.

2. FDG CHEMISTRY STATION

The process of making FDG in our chemistry station is the method first introduced by Hamacher.[2] This process involves, heating, cooling vacuum pumping, filtration and addition of chemicals, all done remotely in an enclosed hot cell. This process of producing FDG requires many operations and failures have occurred in various stages of this procedure, thus usually causing a total failure for that days production. To avoid this kind of failure, a dual station has been

built. Figure 3 is a schematic valve layout of this dual chemical station and it contains over forty valves. Figure 4 is a picture of the hardware (valves, test tubes, filter) all mounted on a rack inside the hot cell. The two stations are mounted side by side. The control panel for this process is depicted in fig. 5, where the valves are positioned on a graphic representation of the chemical process. A master valve switching the routing of the chemicals to either station is located at the top of the panel. The first step in either side of the process is a measurement of the radioactive yield of the target. This data is a check on the cyclotron and target performance and is also used in measuring the chemistry station efficiency.

A particular difficult problem has been sealing the chemical station against vacuum leaks. Our normal procedure is to test the system for leaks after cleaning and loading the chemicals for the days run. However, we still have on occasion, air leaks. These leaks interfere in the successful transfer of product thru the chemistry station, which is usually done by pressurizing the appropriate test tube. As a backup, we have found that applying vacuum in the appropriate areas can also cause the radioactive chemicals to be transferred and this option has been added.

It is well known that the process of making[3] FDG, gives off volatile radioactive gases that are not trapped out by standard air filters. Figure 6 is a graph of the detection of radioactivity being released from our air stack monitors. We have found that this activity can range up to 100 mCi of product. We now operate our system with total capture of all discharged gases into a bag. We have successfully contained all radioactivity for the FDG and also for all other PET radiopharmacutial production. The stack radioactive monitors are an excellent detection device for air leaks within our chemical station system and these leaks also interfere in the efficient production of FDG.

A potential problem in capturing the gas in our bag system is the buildup of pressure on the discharge side of our chemical operation. To avoid transfer of liquids due to this pressure buildup, we have built traps into the discharge lines.

With so many valves in the system, it is to be expected that we have experienced valve failures. Initially, we used 30 psi valves in the system. We have determined that on occasion the pressure can exceed this value. We are retrofitting the valves to 100 psi. Our second concern is that some of the valves must operate for time period of 1-2 hours. The high power applied to the valves' control solenoid causes them to become thermally hot in this time period. We are implementing an electronic circuit that reduces the power to these valves after initial opening.

3. CONCLUSION

The redundant chemistry station has been utilized 4 times since the first of the year (~ 6 months) hence, providing a greater reliability in PET drug product delivery for our patients. In the process of making our chemistry station perform, we have encountered some interesting technical problems, but have devised solutions. We are most encouraged that we can make PET isotope drugs without releasing any radioactivity to the environment during a normal production run.

4. ACKNOWLEDGMENT

We acknowledge the dedicated work of the cyclotron staff in designing, construction and debugging this apparatus. We acknowledge the funding by the Division of Diagnostic Imaging. We thank B. Taylor, and V. Forward for their help in producing this manuscript.

5. REFERENCES

1) Bewley, D.K., "Medical Uses of Cyclotrons: Treatment and Diagnosis," in Proceeding Ninth International Conference on Cyclotrons and Their Applications" (les editions de physique, Caen, France, Sept. 7-10th, 1981) pp 653-660.

2) Hamacher, K., Coenen, H.H. and Stocklin, G., "Efficient Stereospecfic synthesis of no-carrier-added 2 - [18F] fluoro-2-deoxy-D-glucose using

aminopolyether supported nucleophilic substitution," J. Nucl. Med. 27, 235, (1986).

3) Kleck, J.H., Benedict, S.H., Cook, J.S., Birdsall, R.L., Satyamurthy, N., "Assessment of 18F Gaseous Releases During the Production of 18F-Fluorodeoxyglucose," Health Physics 60, No5, pp. 657-660, (1991).

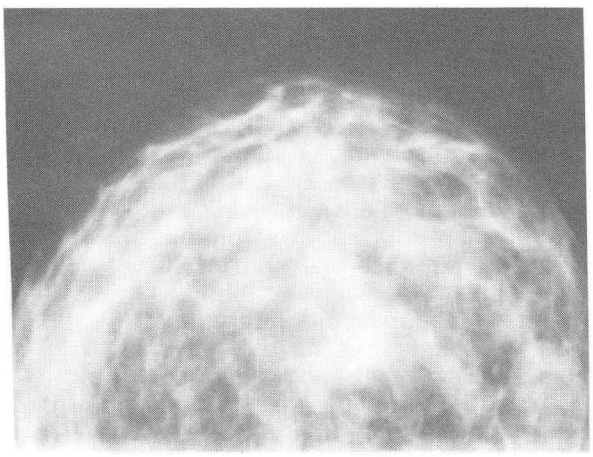

Fig. 1. A standard mammogram of a breast cancer patient is shown. This diagnostic method depends upon a density difference between cancer and noncancerous tissue. A trained expert could detect a potential problem with this patient.

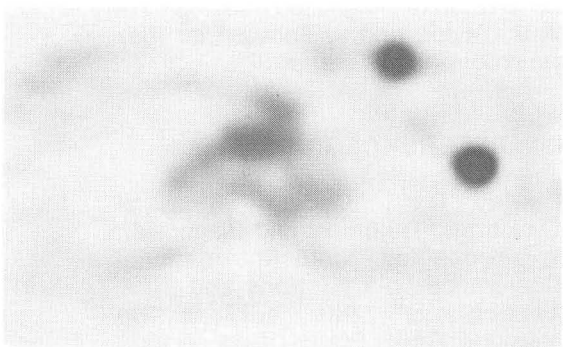

Fig. 2. PET scan of the same patient shown in fig. 1 is displayed. The two dark spots located in the patient right breast areas where 18F has accumulated, are diagnosed as cancerous cells and were later verified by needle biopsy and pathology. This remarkable clarity in diagnosing breast cancer with PET scans have in part motivated the subject of this paper, increased reliability in the production of FDG by a dual redundant chemistry station.

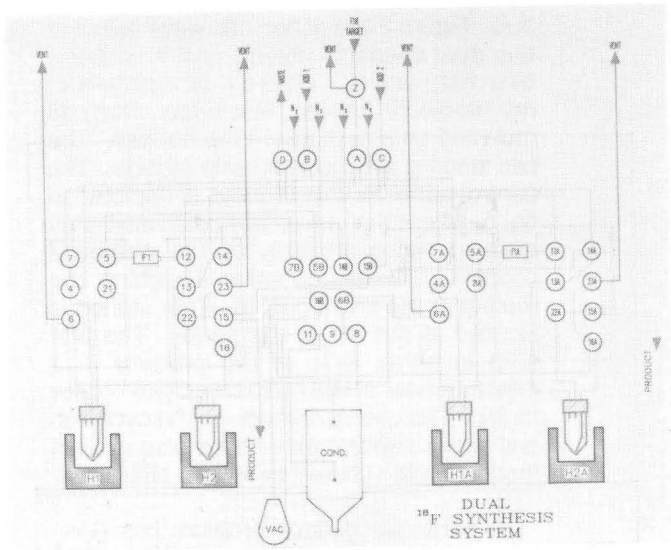

Fig. 3. A schematic drawing of the FDG dual processing chemistry station showing over forty Teflon valves. The first step in this process is to measure the radioactivity from the target.

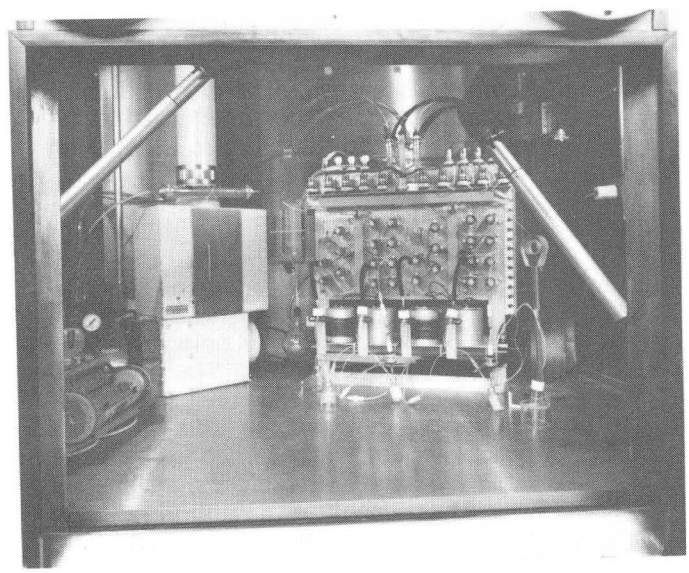

Fig. 4. A picture of the chemistry station mounted on a rack inside the hot cell. The two chemistry station are mounted side by side. The stations are cleaned and loaded with chemicals before the processing start each morning.

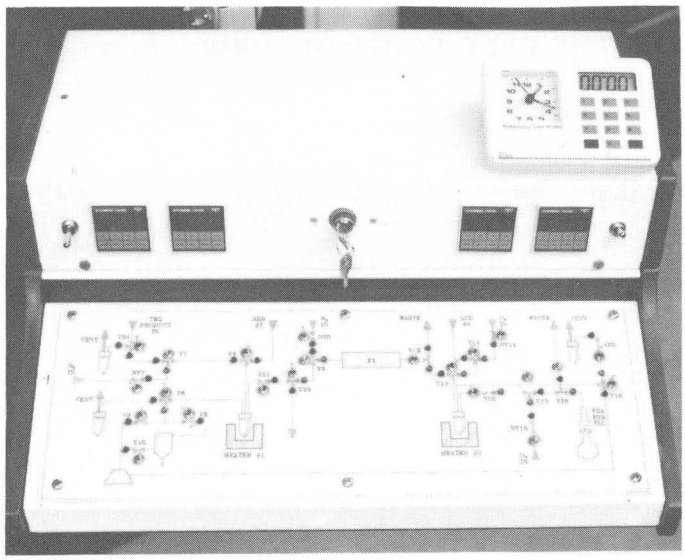

Fig. 5. The chemistry control panel is depicted in the following photo. Only one side of the chemistry station is shown. The switches are located on a graphical layout of the process. A master switch for either side is located at the top of the panel.

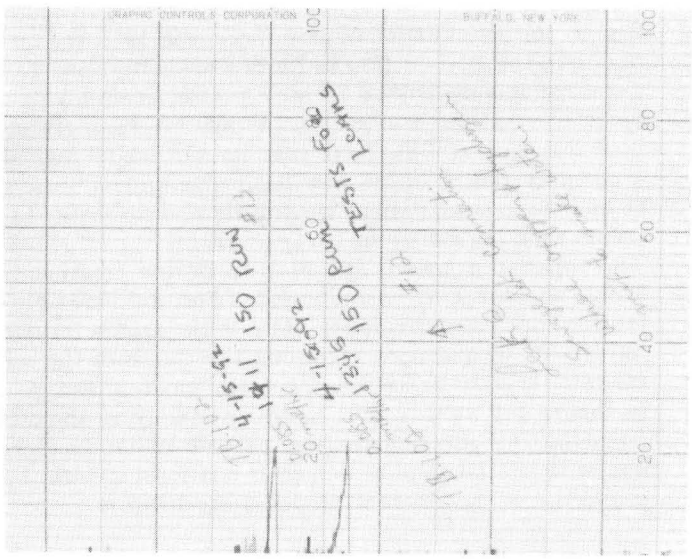

Fig. 6. The radioactivity of two peaks of 15O released up the stacks of the cyclotron hot cells are shown. The radioactivity takes approximately one minute from release to detection by the stack monitors. The stack monitors are G.M. detectors. All gas released from the chemistry station hot cell is now bagged and allowed to decay for 24 hours, hence decreasing our released radioactivity to essentially zero.