A STATUS REPORT OF THE CYCLOTRON FACILITY AT THE KING FAISAL SPECIALIST HOSPITAL AND RESEARCH CENTRE

Presented by: J.W. Stetson, R.M. Lambrecht, M. Sajjad, F.W. Zielinski

Radionuclide and Cyclotron Operations Department
King Faisal Specialist Hospital and Research Centre
P.O. Box 3354, Riyadh 11211, Saudi Arabia

1. Summary

Operational experience gained since the commissioning of the CS-30 cyclotron at the Research Centre in 1982, has shown this facility to be a viable entity. The incidence of problems with major cyclotron systems has been low, thus allowing routine daily production of radiopharmaceuticals for distribution. Facility operating history, usage, and the radiopharmaceutical program is described.

2. Introduction

The cyclotron at the King Faisal Specialist Hospital and Research Centre (KFSH & RC) has now been operational for about four years. During this period, programs in research and medical service have been established. Areas of activity include: radionuclide production, radiopharmaceutical chemistry, radiopharmaceutical manufacture (and distribution to Arab States), positron emission tomography (PET), medical physics, radiobiology,1,2,3) and neutron therapy.4) A key factor in the continuing success of these programs has been the reliable performance of the Cyclotron Corporation (TCC) CS-30 cyclotron.

3. Cyclotron Operations

The CS-30 was assembled and tested at TCC in California before delivery to Saudi Arabia. General characteristics of the TCC compact cyclotrons have been adequately described elsewhere.5) Beam tests at the factory began in January 1977 and ended in October 1978. Beam energies measured during that period were as follows: protons = 26.5 MeV, deuterons = 14.8 MeV, ^{3}He = 38.1 MeV, and ^{4}He = 29.6 MeV.6) The cyclotron then was disassembled, shipped, and installed at the Hospital site by TCC personnel. The first beam on-site was achieved in January 1982. Maximum beam currents recorded during acceptance testing are given in Fig. 1. Commissioning tests were completed by the Fall of 1982, and the facility was declared operational.7)

	Internal	External	% Extracted
protons	92	71	77
deuterons	175	120	69
Helium-3	92	62	67
Helium-4	69	46	67

Fig. 1: Maximum beam currents recorded during acceptance testing, 1982, given in eμAmps.

Target stations are available on seven beam lines as well as on an internal target. A plan view of the facility is shown in Fig. 2. Beam line #1 (located in the "isotope production room") terminates in a standard TCC Model 4012 external target system, with remote transfer, which can be used with either solid or powder targets. Beam line #2 is presently assigned for a water target using either the $^{18}O(p,n)^{18}F$ reaction (with isotopically-enriched water), or the $^{16}O(p,{}^{4}He){}^{13}N$ reaction. Also mountable at this location is the astatine production target ($^{209}Bi({}^{4}He,2n){}^{211}At$). Both of these targets were made in-house. Beam line #3 terminates in a TCC Model 4048 tandem gas target and processing system, which was designed for production of the positron-emitters ^{11}C, ^{13}N, and ^{15}O. Beam line #4 consists of two end segments. The beam bent by the 101 degree dipole magnet is presently sent to a stacked-foil target. A secondary neutron beam has also been produced at this position, and provisions exist for a beam dump in the shielding wall. The straight part of beam line #4 is not used because of unacceptable levels of neutron leakage around the shielding door. Presently mounted on beam line #5 is an experimental krypton gas target, which provides for remote gas-filling and wash of rubidium-81 for krypton-81m generators. Beam line #6 goes to the "isocentric" neutron therapy system. Line #7 is used for daily ^{81}Rb production via a drop-off target that is transported under the floor to the hot cells by a "railroad". It is also used for a water target ($^{16}O({}^{3}He,p\ ){}^{18}F$). A TCC Model 4010 internal target system, with isorabbit transfer to the hot cells, is fitted to the cyclotron but has been substantially modified, as described below.

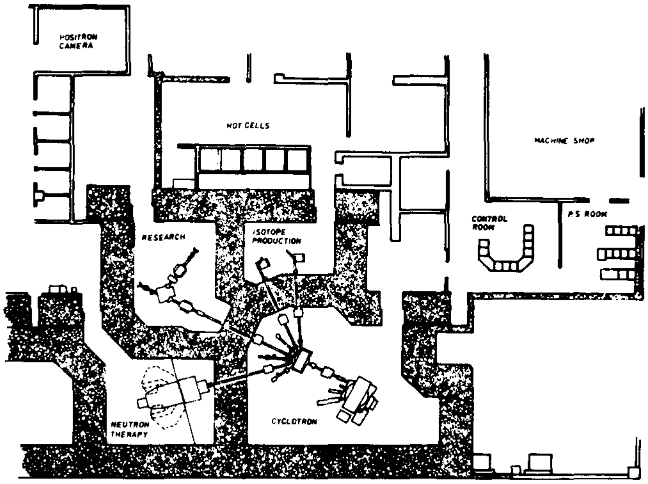

Fig. 2: Plan view of KFSH & RC cyclotron facility. Beam lines are numbered counterclockwise around the switching magnet.

The total amount of beam time on the machine since commissioning is now approaching 8,000 hours. A breakdown of the beam utilization through 1985 is given in Fig. 3. Beam time for isotope production has shown steady increases. Increased demand for PET radioisotopes is expected upon acquisition of a new positron emission tomograph. Resumption of neutron therapy also is expected in 1987.

Available beam intensities remain reasonably near those measured during acceptance testing. Maximum beam currents actually supplied to users during 1985/86 are shown in Fig. 4. The relatively poor performance given for the helium beams in 1982-1985 was due to lack of demand for higher intensities, difficulties in properly positioning the ion source quickly, and low utilization of helium beams. The run-to-run energy variability, as measured for protons and deuterons, using a NMR probe in the beam line #4 analysis magnet, is less than 1%. Apparently, no records exist that give on-site measurements of beam energies and emittances. A beam energy and intensity calibration check will be made soon, following the procedure given by Kopecky$^{8)}$ using proton reactions on a stacked-foil copper target.

A low-intensity beam of H_2^+ ions was developed in February 1986 for a user requesting a low-energy irradiation on an internal target. Intensity losses due to break-up of the H_2^+ ion by residual gas in the cyclotron tank were considerable, as can be seen in Fig. 5. From an unmodified ion source, there were over 50 eμA of H_2^+ available at small radius for acceleration. However, the beam intensities were intentionally kept low in order to avoid damage to unshielded components by the neutral beam. More intense H_2^+ beams might be achieved in a CS-30 by reducing the tank gas load, increasing the pumping speed, and installing neutral beam shields for critical components, as in a CP-42.$^{9)}$ Regardless of such changes, the heat loading on and radiation activation of the "closed" outer edge of the CS-30 dees will probably limit any such H_2^+ beam to a few tens of microamps.

	1982	1983	1984	1985
Isotope Production	66	569	958	1103
PET Radioisotopes	39	397	511	130
Medical Physics Research	5	103	90	210
Neutron Therapy/Research	81	972	346	42
CS-30 Maintenance, R&D	5	75	330	379
Total Hours	196	2116	2235	1864

Fig. 3: Cyclotron beam time by use and year.

	Internal	External	% Extracted, Avg.
protons	72	60	77.4
deuterons	180	100	53.8
Helium-3	40	25	55.2
Helium-4	20	14	59
H_2+	2.5	0.6	25

Fig. 4: Maximum beam currents used during 1985/86, given in eμAmps, and the average extraction efficiency.

A few significant modifications and additions to the cyclotron have been made by the operating crew. The original carbon pullers had a short lifetime, especially with helium beams. The pullers are now made of tantalum and last for several months of routine running. A vertical beam scraper has been added and functions over the outer 10 cm or so of orbit radius. The carbon tips of this device are placed 1.3 cm apart and somewhat reduce the activation of the dees by stray beam. The tungsten pre-septum blades, which were subject to cracking, are now fabricated from molybdenum. The blades now last well over a year. The drive for the magnetic channel extractor, as supplied by TCC, was positive in only one direction. The extractor used to be moved to a larger radius by a drive screw but depended on ambient air pressure to push it in the other direction. This system was replaced by a drive screw that was positive in both directions. A 50-turn coil of wire (computer data cable) was wrapped around the cyclotron magnet yoke. This was connected to a differential voltmeter, to provide a power-supply and shunt-independent indication of short-term magnet power supply stability by dB/dt induced voltage fluctuations.

The TCC pneumatically-actuated shaft system that inserted targets into the cyclotron vacuum tank for irradiation was beset with problems. These problems often caused the hot target to be "lost" upon removal from the tank. This mechanism was recently replaced by an electrically-driven system, designed and constructed in-house,$^{10)}$ that is somewhat less prone to catastrophic failure. The new system has also allowed for much higher cooling-water flow through the target holder, more than 5 gpm @ 75 psi. The rabbit transfer system was not changed and remains a problem. Remote

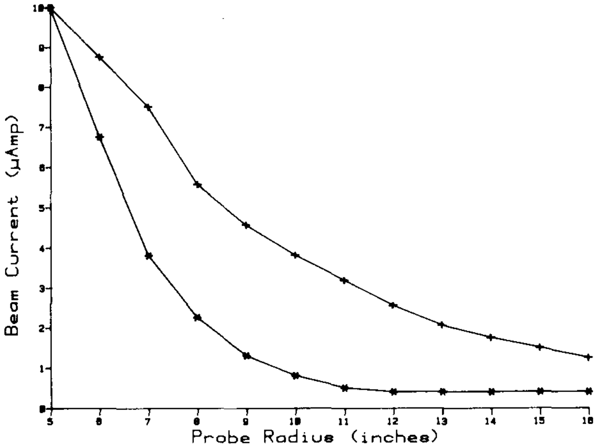

Fig. 5: H_2^+ beam current as a function of radius. The upper curve was obtained at a nominal tank pressure of 3.8×10^{-5} Torr, and the lower at 7.0×10^{-5} Torr.

transfer of the target shuttle from the hot cells to the target station in the cyclotron vault results in damage to the target or the shuttle. Consequently, targets for internal irradiations must be loaded by hand.

Few machine problems have resulted in cancellation of scheduled runs, but there have been more numerous minor problems. One of the worst was a fire in 1983 in the RF anode power supply (APS), caused by a faulty A.C. contactor. The damage was limited to the power supply cabinet. Another interruption occurred in 1986 after the cracking of a RF feedthrough insulator--the first such failure. Upon removal of the dee strap assembly during repair, it was found that the clamp of the shorting strap was worn and required shimming. Earlier, the timing of the release/clamp sequence had to be modified to ensure the strap was not driven while the clamp was still engaged. It is unknown whether drag caused by this malfunctioning of the clamp or whether normal use was the cause of the clamp wear.

One recurring problem with the APS is the relatively short life of the Eimac CX350A driver tubes. The cause of this appears to be that the tubes are operating at a greater-than-recommended temperature.

The "cold cathode" internal ion source, as supplied by TCC,11) is basically quite reliable. The lifetime of the tantalum cathodes is often greater than 100 hours when producing protons. For helium beams, however, the lifetimes are greatly reduced. If user demand for helium beams warrants it, use of alternative cathode materials such as hafnium12) will be investigated. In contrast to the ion source itself, the source drive system creates some problems. It allows the source to move from effects of heating on the source support structure. Also, the system lacks the means for reproducible positioning and for control of the rotational angle of the source. Precise axial alignment to better than 1 degree is necessary for proper control of source output. The helium beams require distinctly different alignment from that needed for protons and deuterons.13,14) These factors mean that operators must manually (at the cost of time and accuracy) adjust the axial angle after source changes and between energy changes. Computer Technology and Imaging (CTI), which supports TCC machines, offers a new drive system that addresses these problems and can be retrofitted to older CS-30's.15) Modification or retrofit of the drive system is now being considered.

One difficulty in making modifications at the KFSH & RC facility involves the feedthroughs from the control room directly into the cyclotron vault. The total area available is only about 0.2. m^2 and it is already completely filled with existing cables. Future cable runs will require either more feedthrough access or elimination of some cables which are no longer used.

In the context of running an active cyclotron-based research and service program in a developing nation, several special factors need to be mentioned. It is essential to have an easy-to-operate cyclotron of proven reliability and performance. Stable electrical power is now available from the local grid in Riyadh, but may be a problem in other developing countries.16) A large number of items must be kept in inventory, due to the long delays in deliveries of spare parts and technical support equipment. A machine shop dedicated to cyclotron operations, as at KFSH & RC, is a necessary requirement in order to have instrument development and cyclotron maintenance performed in a timely manner. Similarly, technically experienced personnel must also be available on-site.

4. Positron Emission Tomography

A state-of-the-art Positron Emission Tomograph is in the late stages of procurement. The PET site is located in close proximity to the cyclotron-radiopharmaceutical chemistry laboratories of the Research Centre and connects to the Hospital for easy patient access. (See Fig. 2)

Targetry and radiochemistry is being developed for ^{18}F, ^{38}K, ^{75}Br, ^{78}Br, ^{15}O, ^{11}C and ^{13}N synthetic precursors to prepare conventional and to evaluate potential radiopharmaceuticals labeled with positron emitting radionuclides. Emphasis is being placed upon automation and process control of all radiochemical operations.17) Projection is to use 45% of the PET for the clinical studies, 45% for the tracer kinetics and physiologic modeling in the animal studies, and 10% for maintenance and instrument development.

The areas of emphasis of the KFSH & RC cyclotron/PET Program are categorized as: differential diagnosis of intracranial masses, cardiopulmonary studies, leukemia and other cancers, neurological disturbance and disorders, and a variety of special projects.

5. Radiopharmaceutical Production and Distribution

Routine production of radiopharmaceuticals at KFSH & RC began in April 1983. To date, 159 batches of Thallium-201, 36 batches of Indium-111, 187 batches of Gallium-67, 633 batches of Rubidium-81, and 560 batches of Iodine-123 have been prepared and distributed to hospitals in the Middle East. Each batch of radiopharmaceuticals released for distribution consists of many individual patient doses, manufactured and tested according to FDA guidelines and specifications. Presently, during a typical week, 11 individual targets are irradiated in order to be able to make 13 or 14 different batches of radiopharmaceuticals suitable for administration to patients. Production yields and chemical processing at KFSH & RC have been described.18)

The KFSH & RC weekly distribution includes 2.2 mCi vials of ^{201}Tl, 3 mCi vials of ^{111}In-chloride, 5.0 mCi vials of ^{67}Ga-citrate, ^{81m}Kr/^{81}Rb generator systems ($\geq$4.0 mCi each), 3.0 mCi vials of ^{123}I ortho-iodohippurate, 5.2 mCi vials of ^{123}I iodide solution, and 0.2 mCi capsules containing ^{123}I iodide. Routine deliveries of all these products are continuing.

Products that will soon be available from KFSH & RC for distribution to hospitals and/or research centers include: ^{111}In-oxine, ^{123}I-meta-iodobenzyl guanidine (mIBG), ^{211}At-astatide, and ^{124}I-iodide. ^{111}In-oxine will be used primarily to prepare radiolabeled leukocytes for the detection of inflammatory disease. Labelled mIBG with ^{123}I, ^{124}I, or ^{131}I will be useful for the diagnosis and treatment of for the diagnosis of malignant pheochromocytoma and neuroblastoma. ^{211}At is being developed for research in radiopharmaceutical chemistry and for distribution to other research institutions.

6. Acknowledgments

Clearly, the work described in this report would not have been possible without the commitment and dedication of the staff, both past and present, of the King Faisal Specialist Hospital and Research Centre.

References

1. M.A. Hannan, et al., Mutation Res., 149, 1985, pp. 353-358.
2. M.A. Hannan, D.P. Gibson. Radiation Res., 1044, 1985, pp. 94-101.
3. M.A. Hannan, et al., Int. J. Radiation Biol., 1986, (in press).
4. A. Aissi, J.M. Feola, B.S. Clubb. Int. Sym. on Radiotherapy in Developing Countries, Int. Atomic Energy Agency, 1986, IAEA-SM-290/7.
5. G.O. Hendry. AIP Ninth Con. Proc., 1972, pp. 616-626.
6. Project 779 Data Sheets, The Cyclotron Corporation.
7. R.C. Barrell, et al. IEEE Trans. on Nucl. Sci., NS-30, April 1983, pp. 1777-1783.
8. P. Kopecky. Int. J. Appl. Isot., Vol. 36, No. 8, 1985, pp. 657-661.
9. G.O. Hendry, et al., Ninth Int. Con. on Cyclotrons and their Applications, 1981, pp. 125-127.
10. W.O. Meyers. (internal report)
11. D.K. Wells. IEEE Trans. on Nucl. Sci., NS-14, No. 3, 1967, pp. 70-71.
12. T.A. Antaya, P.S. Miller. CH-1996-3/84/0000-0341, IEEE, 1984, pp. 341-344.
13. T.Y.T. Kuo, R. Lee, J.S. Laughlin. IEEE Trans. on Nucl. Sci., Vol. NS-22, No. 3, 1975, pp. 1711-1714.
14. T.Y.T. Kuo, J.S. Laughlin. Proc. Seventh Int. Conf. on Cyclotrons and their Applications, 1975, pp. 381-385.
15. C.G. Smith, CTI communication, July 10, 1986.
16. S. Chattergee, et al. Ninth Int. Con. on Cyclotrons and Their Applications, 1981, pp. 75-79.
17. R.M. Lambrecht in: Applications of Nuclear and Radiochemistry (R.M. Lambrecht & N.A. Morocs, Eds.) Pergamon, 1982, pp. 5-14.
18. H.B. Hupf, et al. Nucl. Instr. and Meth., B10/11 (1985) pp. 967-968.