THE OPERATIONAL STATUS OF THE NATIONAL INSTITUTES OF HEALTH CYCLOTRON COMPLEX

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Nearly ten years ago realization of the escalating role for cyclotron produced radionuclides for medical applications prompted the consideration of an on-site cyclotron facility at the Clinical Center of the National Institutes of Health. The facility was originally designed around a single, variable energy cyclotron capable of accelerating protons to over 40 MeV. With construction nearly finished, two smaller cyclotrons occupy the shielded rooms; a Japan Steel Works BC1710 and a The Cyclotron Corporation CS-30. The evolution of the cyclotron section is proceeding in concert with the acquisition of two new positron emission tomographs in the Clinical Center Department of Nuclear Medicine. Early results are encouraging that the facility will provide excellent utility and reliability.

HISTORY

During the 1970's, considerable interest was generated by the medical community in many short-lived neutron-deficient radionuclides for diagnostic applications.[1] Their short half-lives, high specific activity and favorable decay characteristics make them particularly attractive for patient studies. Commercial cyclotron facilities located in large population centers offer several radioisotopes of value, but the time required for distribution precludes cost-effective production of high purity radiopharmaceuticals with half-lives less than 3-4 hours. Many positron-emitting radioisotopes of clinical interest have half-lives in the range of 2 minutes to 2 hours. This particular situation encouraged the NIH to consider construction of a cyclotron facility within the Clinical Center. The initial selection of a cyclotron with 45 MeV proton and variable energy capability was influenced by possible neutron therapy applications. The eventual procurement of the two smaller cyclotrons occurred primarily as a result of the original vendor defaulting and experiencing financial difficulties. By this time, interest in Positron Emission Tomography (PET) was the driving force and the determining factor in cyclotron selection. Negotiations were initiated with various vendors and the Japan Steel Works BC1710 with automated targetry was selected. The original vendor then offered a smaller fixed energy (CS-30) cyclotron and the decision to accommodate two machines was made. The specifications for the two machines are in table 1.

Construction of the shielded areas was progressing rapidly and "change orders" were made on site to provide additional conduits, utilities and access ports to allow the smaller BC1710 to occupy the "target room" area. The main cyclotron vault easily accommodated the CS-30 and external beam lines. Both cyclotrons were lowered into the vaults on April 13, 1985. Work progressed on the interior of the facility, but the dusty conditions and lack of airconditioning inhibited progress on the cyclotron installation. The hot cells were installed during two weeks in July. Installation and testing of the JSW cyclotron resumed in September and the cyclotron and targetry was accepted that month. The CS-30 was accepted the following March. Both machines met their advertised specifications easily.

The BC1710 was pressed into service immediately producing $^{18}F_2$ ($^{20}Ne(d,\alpha)^{18}F$, $T_{1/2}$= 110 min.) for the synthesis of ^{18}Fluoro-D-deoxyglucose. Routine production three days per week has yielded over 115 FDG batches of 50-70 mCi without interruption. The demonstrated reliability of the small cyclotron has done much to stimulate the NIH PET program as reflected in over 35 accepted protocols (table 2).

FACILITY DESCRIPTION

The cyclotron facility includes two levels below ground under the NIH Clinical Center. The lowest level, 24 feet (8m) below ground (fig. 1), contains the cyclotron shielded rooms, hot cells, hot chemistry laboratory, radioactive waste storage areas, cyclotron control room, support shops and office areas. The floor above contains two radiochemistry synthesis laboratories, chemistry instrument rooms, mechanical equipment rooms (HVAC) and the cyclotron cooling systems. The ground floor in the Nuclear Medicine Department, above, houses the three positron cameras (specifications in table 3), support computer facilities and radiopharmacy.

A dumbwaiter used to transport supplies and finished products connects the three levels. Delivery of radioactive gasses directly to the camera rooms is planned and a shielded conduit runs from both cyclotron vaults, the hot cells and the synthesis laboratories to each of the three camera rooms. Space has been provided within the dumbwaiter shaft for a pneumatic transfer tube. PET studies are routinely done using $H_2{}^{15}O$ ($T_{1/2}$= 2 min.) allowing for a 35 second transfer time on the dumbwaiter.

Cyclotron Vaults

Originally designed to house a higher energy accellerator, the cyclotron vaults have a shielding wall thickness of 8 feet (2.5 m). Penetrations through the walls are provided for the many power and control cables, target transfer ducts to the hot cells and cyclotron cooling water plumbing. These penetrations are designed to provide radiation flux traps. Located in the vault floor, are storage areas for highly radioactive cyclotron components. They are fitted with cement-filled lids easily removed with a small portable crane. Storage areas for ion sources are located near the machines in the vault walls. The vault doors are rotating plugs weighing 40 tons (36 mtons) supported by two wheels, one of which is electrically driven. The design was economical to fabricate, but suffers from the fact that the door must be rotated through 40 degrees before allowing access. The drive system fitted requires 90 seconds to accomplish this.

NIH CYCLOTRON BEAM SPECIFICATIONS

THE CYCLOTRON CORPORATION CS-30

Particle	Energy (mev)	Res (%)	Emittance (mm-mr) Vert, Horiz	I int. (μa)	Iext. (μa)
P	26.53	0.85	8.6, 21.8	200	60
D	14.8	0.64	9.1, 11.8	300	100
He-3	38.13	0.35	10.0, 24.0	135	60
He-4	29.58	0.36	13.3, 30.0	90	40

JAPAN STEEL WORKS BC-1710

Particle	Energy (mev)	Res (%)	Emittance (mm-mr) Vert, Horiz	I int. (μa)	Iext. (μa)
P	17.5	0.34	15., 32.	---	50
D	9.8	0.71		---	50

Table 1.

NIH CYCLOTRON FACILITY B-3 LEVEL

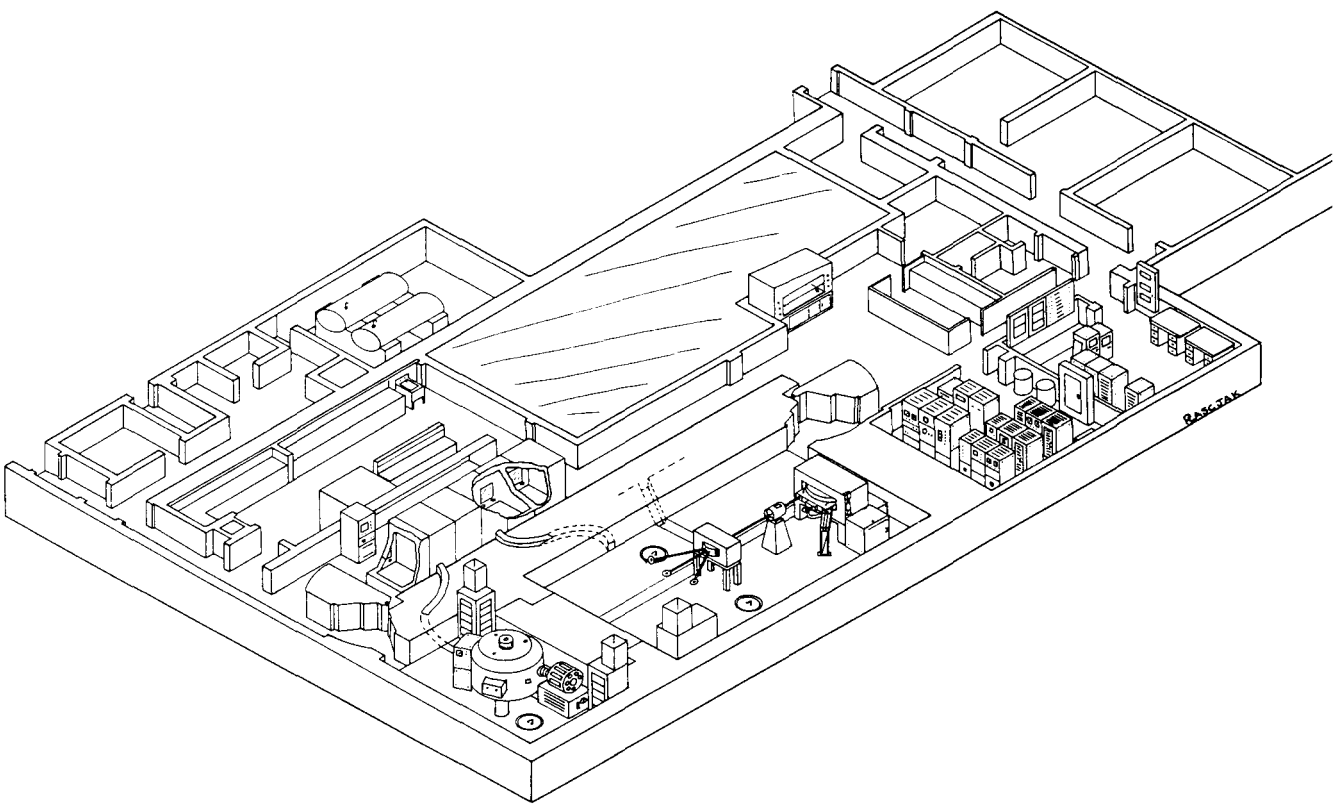

Fig. 1.

NIH PET STUDY PROTOCOLS

81-N-131	Movement Disorders
81-N-98	Tardive Dyskinesia/Muscularum Deformans
80-N-36	Cerebral Gliomas
80-N-58	Epilepsy
80-N-89	Alzheimer/Huntington Disease
82-N-51	ALS
80-AG-26	Normal Aging
81-AG-10	Organic Dementia/Alzheimer's Type
81-AG-10A	Downs Syndrome
80-AG-26A	Autism
83-N-58	Lennox/Gestaut
82-A-73	Thyroid Hormone Effect
81-AG-10B	Arecholine: Alzheimer's
81-AG-10C	Hypertension in Aging
82-AG-86A	Apamorphine-Aging
83-H-36	Sickle Cell
83-AG-156	Non-afflicted Alzheimer's Relative
83-CH-107	Hypogonadal, Anorectic
81-AG-10D	Creutzfeldt-Jacob Disease
84-AA-81	Alchohol Induced Dementia & Normals
84-AG-6	Mental Retardation Syndrome
84-N-115	Effect of Antiepileptic
84-M-114	Dr. Cohen/Schizophrenic, Affective Disorders, Neuropsychiatric Disorders
85-M-3	Dr. Cohen/Normals
84-N-77	Stimulation Produced Analgesia
85-C-11	Tumor Response to Radiation Therapy
85-N-14	Barbiturate Anesthesia
85-N-13	Intracarotid Cisplatinum
85-N-38	Involuntary Motor Disorders
85-N-39	Human Voluntary Movement
85-CC-83	Reactor 18-FDG Controls
84-AG-142	Obsessive-Compulsive Disorder
85-M-99	Effect of Scopolamine on Neuropsychiatric Patients and controls
85-N-125	Familial Alzheimer (NINCDS)
85-AG-139	Evaluation of Swallowing in Multi-Infarct Dementia

Table 2.

NIH POSITRON TOMOGRAPH CHARACTERISTICS

	Neuro-PET	Scanditronix PC-1024	Posicam 6.5
Planes: Detector	4	4	6+5=11
Image	7	7	21
Detector Mtl.	BGO	BGO/GSO	BGO
Detector (in plane)	8.5x20	6x20	9x20
Detector (per plane)	128	256	120
(total)	512	1024	1320
Field (plane cm)	25	26	55
of view (axial mm)	89	100	116.5
In-Plane Res.(mm)	6-7.5	5	6.3
Axial Res.(mm)	12	10-11	11-20
Computer	D G Eclipse S/250	VAX 11/750	VAX 11/750
Reconstruction Time/Slice (sec)	50	60-120	40

These systems are currently under evaluation and all values should be regarded as approximate and subject to minor change.

Table 3.

Hot Cells

The hot cells were provided by Von Gahlen Nederland B.V. of Didam, Holland. They were installed against shielding walls to minimize space requirements and allow direct connection to target transport ducts. Radioactive gas lines from cyclotron targets and shielded conduits to the positron camera rooms are routed to the rear and top of the cells. The front shielding of the individual cells is supported on driven screws and allows the fronts to be lowered permitting convenient access to the inside for installing apparatus.

Radiation Protection and Safety Systems

Radiation level monitoring is provided by simple area monitors and a centrally operated system which monitors air-conditioning ducts from the cyclotron vaults and exhaust ducts from the hot cells and numerous fume hoods. The common exhaust duct from the facility is sampled continuously for radioactive gasses, particulates and halogens. Because many of the cyclotron targets are gasses, precautions have been taken to minimize their release in the event of leakage or input window failure. Both vaults are equipped with large high efficiency charcoal filters through which vault air is recirculated when the plug doors are closed. A small amount of air is exhausted to maintain vault pressure slightly negative with respect to outside areas. Opening the plug door allows normal intake and exhaust operation.

The cyclotron safety system consists of interlocks on the cyclotron R.F. systems, inspection switches within the vaults and remotely actuated shunt-trip breakers on the power panels serving the cyclotrons and the control room. A "single key" system is used to control access to the vaults and operation of the cyclotrons. Operation is only permitted after inspection station buttons within the vault are pressed and the door closing sequence completed. The same key used to permit door operations must then be used in the control room to complete the interlock chain on the appropriate cyclotron. Annunciators are provided to indicate door closing, magnet on, ion source on and r.f. on. Emergency buttons for actuating the shunt trip breakers are located in the cyclotron vaults, power supply room and the control room. Additionally, numerous annunciators in the control room indicate facility door status, HVAC operation, fire and halon system alarms and radiation levels.

FACILITY OPERATIONS

The current mission of the cyclotron facility is to develop and produce radiochemicals and radiopharmaceuticals in support of the Clinical Center Department of Nuclear Medicine. This is being achieved through the cooperative efforts of a staff with a wide range of expertise, and programs in cyclotron target development, radiochemical labeling and organic synthesis, and chemical production process development.

Target Development

Advantages of having two cyclotrons include reliability of support through redundancy of critical equipment and the ability to develop new target systems without compromising radioisotope delivery schedules.

The JSW BC1710 was purchased complete with targetry and processing equipment which allowed production of required radioisotopes soon after installation. The range of available radioisotopes has been adequate to support the patient studies and new positron camera evaluation currently in progress in the clinical center. As the new cameras are commissioned and the patient load increases, it will become necessary to increase the quantity and variety of cyclotron facility products. The need for $H_2{}^{15}O$ was recently satisfied by a simple modification to existing hardware and software.[2] The ^{15}O target effluent was allowed to mix with $5\%H_2/N_2$ (another target source gas) and combusted at a controlled rate to yield readily usable (up to 500mCi) amounts of $H_2{}^{15}O$. Fabrication of a powder

JSW BC1710 CYCLOTRON TARGET SYSTEM CHARACTERISTICS

Reaction	Compound	Target Mtl.	Irradiation (min.) X Beam Current(μA)	Yield EOB (mCi)
$^{20}Ne(d,\alpha)^{18}F$	$^{18}F_2$	^{20}Ne gas	110 x 40	600
$^{18}O(p,n)^{18}F$	$H^{18}F$	$H_2{}^{18}O$ 90%	110 x 8	400
$^{14}N(p,\alpha)^{11}C$	^{11}CO	$^{14}N_2$ gas	20 x 50	1600
"	$^{11}CO_2$	"	20 x 50	2300
$^{14}N(d,n)^{15}O$	$^{15}O_2$	2% O_2+N_2 gas	2 x 50	1500
"	$H_2{}^{15}O$	"	12 x 20	500
"	$C^{15}O$	"	2 x 50	700
"	$C^{15}O_2$	2.5% CO_2+N_2	2 x 50	1300
$^{16}O(p,\alpha)^{13}N$	$^{13}NO_x$sol	H_2O	10 x 30	500
$^{12}C(d,n)^{13}N$	$^{13}N_2$	CO_2	10 x 50	150

Table 4.

target system employing expendable target cups is nearing completion and will be installed on the BC1710.

The TCC CS-30 cyclotron was provided with a simple internal target/beam probe system and an external beam transport system with seven ports and three extended lines for target stations. Current work includes fabrication and installation of gas targets and a isolation foil cooling system. This cyclotron will be fitted with targets capable of producing critical radisotopes to insure clinical center support when the BC1710 is not available. Targets required for new products and chemical synthesis research will be developed on the CS-30 maximizing availability for research efforts.

Interest has been shown for utilization of the facility by several local government and academic groups as a specific resource. As the facility nears completion and modifications and renovations are made to adapt it to its present purpose, it is becoming apparent that we have built a very useful tool and valuable NIH resource.

References

1. M. Ter-Pogossian, H. N. Wagner, Jr.,"A new look at the cyclotron for making short-lived isotopes", Nucleonics, (Oct.,1966)

2. R. Finn et al, "Modification and Integration of JSW gas targets at the National Institutes of Health", Nuclear Instruments and Methods, to be published (Apr.,1987)