IN-HOUSE CYCLOTRON AND RADIOISOTOPES PRODUCTION SYSTEM

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Summary

We developed the in-house cyclotron which can deliver 18MeV protons and 10MeV deuterons, and radioisotopes production system such as carbon-11, nitrogen-13, oxygen-15 and fluorine-18. This system has the following features;

1. Reliable and stabilized functions.
2. Easy operation and maintenance.
3. Economically profitable machine.
4. Compactness.
5. Securing the production yield radioisotopes capacity.
6. Flexibility in adaptation of shielding.

Using this system, carbon-11-labelled N-methyl spiperone was synthesized from carbon-11 CO2 in 30min, with a radiochemical yield of 80%.

This in-house cyclotron and radiosiotopes production system has been under operation at Kyoto University Hospital and Chiba University Hospital.

Introduction

Recently, the method to use the short-lived positron emitting radioisotopes in clinical diagnosis has been rapidly developed. To use the short-lived radioisotopes means to decrease the amount of the patient's exposure to the radiation. Radionuclides as C-11, N-13 and O-15 are the isotopes of the essential elements constituting the body. Thus these nuclides are suitable to measure the metabolic functions in the body quantitatively from outside. The half-lives of these radionuclides are so short that the cyclotron and radioisotopes production system have to be installed in the hospital and hundled by small number of operators.

For this purpose, we developed the in-house cyclotron and radioisotopes production system.[1-4]

Characteristics of in-house cyclotron

The cyclotron (model-370) can accelerate 18MeV protons and 10MeV deuterons. These values are sufficient to produce enough yield of radioisotopes listed in table 1.

Electromagnet

The electromagnet is of a frame-type structure to facilitate the maintenance of the inside of vacuum box and the compact housing layout. Main probe, ion source and other attachments are installed in open spaces in front and in the rear, with no attachment on each side for space saving.

Radiofrequency system

The radiofrequency system is the original single 180° dee associated with a compact resonant cavity oscillating at two frequencies ; one for the fundamental mode of operation (proton), the other for the third harmonic operation (deuteron). The single 180° dee system has been adopted to simplify the RF system, to ease the maintenance and operation and to stabilize particle acceleration.

Ion source

Vertical housing space is minimized and a horizontal insertion system is adopted to ease filament replacement. The positions of ion source and puller need not be changed when shifting the mode of acceleration because of the optimal design in the center region.

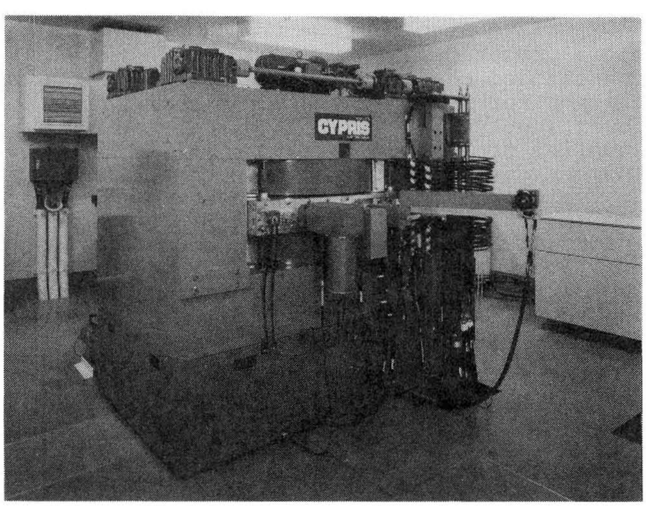
Table 1 : Radioisotopes produced by in-house cyclotron

Nuclide	Half-life (min)	Nuclear reaction
C-11	20.4	$^{14}N(p,\alpha)^{11}C$
N-13	10.0	$^{16}O(p,\alpha)^{13}N$
O-15	2.0	$^{14}N(d,n)^{15}O$
F-18	109.8	$^{18}O(p,n)^{18}F$ $^{20}Ne(d,\alpha)^{18}F$

The specifications of the cyclotron are summarized in table 2.

Table 2 : Specifications of cyclotron

Beam	
Particles	protons, deuterons
Energy (MeV)	18 , 10
Maximum extracted beam current (μA)	100
Electromagnet	
Number of sectors	4
Weight (tons)	17
Pole diameter (mm)	880
Extraction radius (mm)	370
Maximum magnetic field (KG)	17.8
Number of trim coils	4
Number of harmonic coils	4
Size (m)	1.9(L)x1.1(W)x1.2(H)
Radiofrequency	
Number of dee	1
Dee angle (°)	180
Maximum dee voltage (KV)	40
Power tube (KW)	25
Harmonic number	1 (p) 3 (d)
Frequency (MHz)	25 (p) 40 (d)
Ion source	
Type	Livingstone-Jones
Location	internal horizontally introduced
Extraction	
Type	electrostatic deflector
Maximum field (KV/cm)	100
Angular span (°)	75
Gradient corrector	1 pair
Vacuum system	
Oil diffusion pump (l/s)	1300



Picture of in-house cyclotron

Characteristics of radioisotopes production system

Figure 1 shows the radioisotopes production system configration.

Target

To prevent contamination in the target gas during radioisotope production, an independent target box is allocated to each radioisotope. Target change can be done with remote control. A light screwing attaches a target or disconnects it from its holder. Maintenance has become more easily with this procedure.

Radioisotope synthesizers

Table 3 presents the radioisotope synthesizers. Any of these synthesizers can be incorporated in the system selectively at user's option. These have been automated to reduce exposure dose to operational people and withstand continuous operation.

Six types of gases(C-11 CO, C-11 CO2, N-13 N2, O-15 O2, O-15 CO and O-15 CO2) are housed in a single unit as the inorganic gas purifier. All of other synthesizers are unitized so as to be easily housed in the shielded cell. The sizes of these synthesizers are less than 45(L)x48(W)x48(H)cm.

The detailed description of several synthesizers is already reported.[3,4]

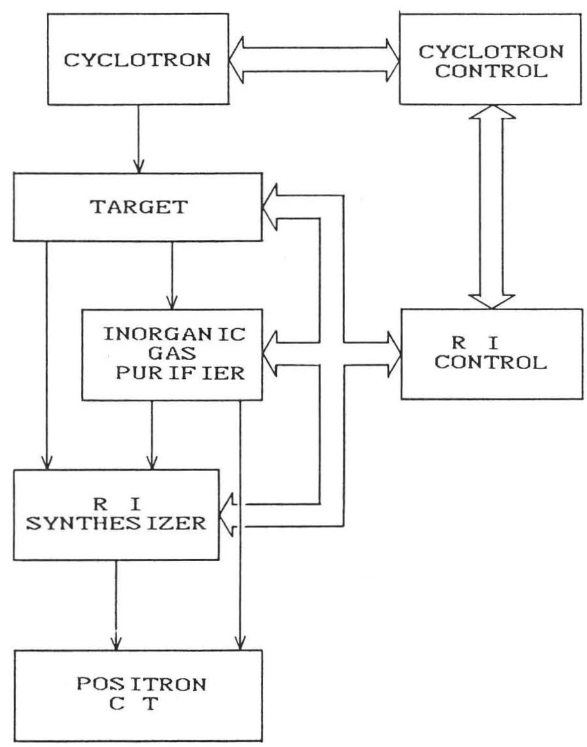


Fig.1 : Radioisotopes production system

N-(C-11)-methyl spiperone

This is a dopamine-receptor antagonist which is useful for positron emission tomography studies of human neurotransmitter receptors.[5,6] The procedures for the synthesis of N-(C-11)-methyl spiperone are shown in Fig 2. C-11 CO2 was produced with the in-house cyclotron by nitrogen gas irradiation with protons. Through the synthesis of C-11 methyl iodide, N-(C-11)-methyl spiperone was synthesized.
For a 20min irradiation with 35μA protons, 500mCi of C-11 methyl iodide was prepared. N-(C-11)-methyl spiperone was synthesized from C-11 CO2 in 30min, with a radiochemical yield of 80%.[7]

Table 3 : Radioisotope synthesizers

Labelled compounds	Use
C-11 CO gas	Local blood flow Pulmonary perfusion
C-11 CO2 gas	Local blood flow
N-13 N2 gas	Ventilatory function
O-15 O2 gas	Oxgen consumption
O-15 CO gas	Local blood flow Pulmonary perfusion
O-15 CO2 gas	Local blood flow
C-11 hydrogen cyanide	Precursor of amino adid, glucose
C-11 methyl iodide	Precursor of various drugs
C-11 glucose	Brain & myocardium imaging Sugar metabolism
C-11 methionine	Brain & pancreas imaging
C-11 methyl spiperone	Receptor study
N-13 ammonia	Brain & heart imaging Precursor of amino acid
O-15 water	Blood flow
F-18 HF aqueous solution	Precursor
F-18 fluoro deoxy glucose	Brain & heart imaging Cancer diagnosis

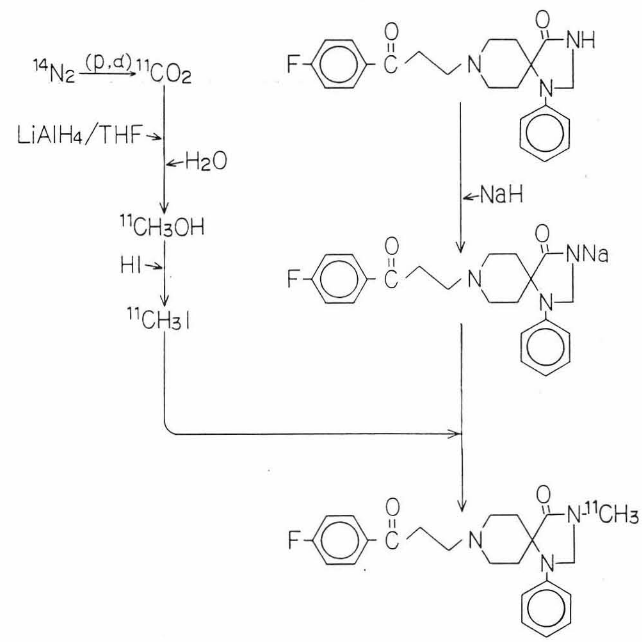


Fig. 2 : N-(C-11)-methyl spiperone synthetic steps

Control system

The control system is divided into for the cyclotron and for the radioisotopes production system as shown in Fig.3. These are connected by the IEEE-488 bus to communicate the irradiation data and by the hard wires to interlock each other.

The cyclotron control

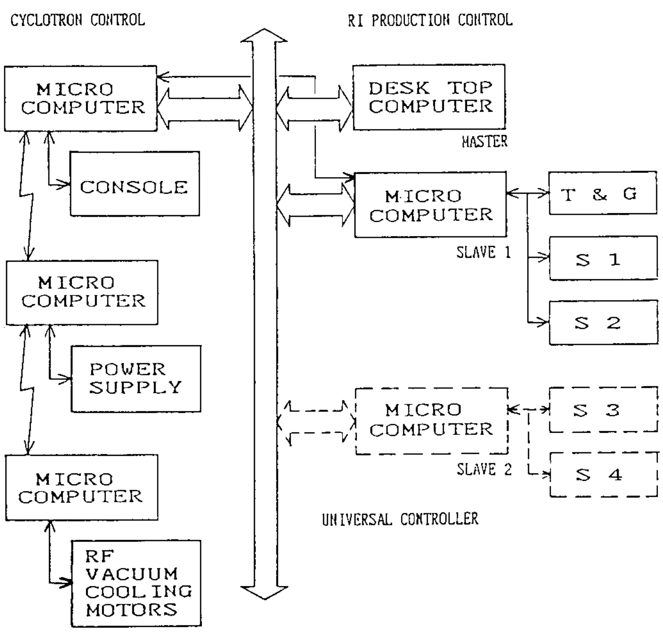
The operation of the cyclotron is fully automatic. All equipments are controlled in a given sequence by pushing some switches. Only five switches are used to accelerate the beams and to irradiate the target.
The necessary parameters and interlocks are displayed with CRT monitor on the console.
This control system is composed of three micro processors(8085). One is in the console and controls the operation panel and the monitor panel, the other one is in the power supply rack and controls the power supplies of ion source, coils and RF. Another one is in the control rack and controls the RF low level, vacuum system, cooling water system, deflector power supply, motors and beam current measurement.
These three are linked by optical fiber cables to improve the interference of noise and decrease the number of hard wires.

The radioisotopes production control

The synthesis of radioisotopes can be fully automated for the easy operation and minimization operators' radioactive exposure. The entire control of the radioisotopes production system is governed by the universal controller.[8]

The universal controller consists of a desk-top type master computer and several number of slave computers (1 to 14 units). As the slave computer has standardized input/output ports, additional synthesizer can be connected to the same one. Two synthesizers can be controlled at a same time by one slave computer.

The synthesis procedures are programmed by BASIC language and memorized in diskette. The improvement of procedures can be performed only by exchange the diskette for the new synthesizers. So extension of the system is very easy.



T&G : Targets and inorganic gas purifier
S * : RI synthesizer
⟷ :Hard wire
:Optical fiber cable
⇔:IEEE-488 bus

Fig.3 : Control system

Conclusion

This system has been under operation at Kyoto University Hospital for more than four years and Chiba University Hospital. Inorganic gases, N-13 ammonia, O-15 water and F-18 fluoro deoxy glucose are in the stage of clinical diagnosis. C-11 methionine and N-(C-11)-methyl spiperone are ready for use. Clinical use of C-11 methionine will start in this autumn.

Furthermore, we will intend to develop new synthesizers and to improve this system in order to keep up with the progress in nuclear medicine.

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