STATUS OF THE TOHOKU UNIVERSITY MULTIPURPOSE CYCLOTRON

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The Tohoku University cyclotron of K = 50 MeV has been used as a multipurpose one for seven years since July 1979. The research fields of the users of the cyclotron are numerous, i.e., nuclear physics, physics, engineering, chemistry, radioisotope production and labeling, basic medicine and biology, clinical medicine, and so on. The facilities and typical researches corresponding to these fields are presented as well as the performance and operation of the cyclotron.

Introduction -- CYRIC Cyclotron

The cyclotron of CYRIC (CYclotron and RadioIsotope Center) has been used by the scientists of Tohoku University from various research fields for the last seven years since July 1979. From April 1983 clinical researches, i.e., medical researches applying short-lived radioisotopes to patients and volunteers have been also conducted. In this report we emphasize the facilities related with and the uses of the cyclotron; the details of the cyclotron itself and its performance have been described elsewhere.[1]

The CYRIC cyclotron, Model 680, having an extraction radius of 680 mm is a medium-sized machine in the series of cyclotrons manufactured by CGR-meV and Sumitomo Heavy Industries. The beam performance is shown in Table I. In ordinary operations light ions beams of $\leq$20 μA extracted current have been used actually.

A compact PIG type heavy-ion source was developed and has been used for acceleration of heavy ions as shown in Table I.[2]

A very convenient emittance scanner of the cyclotron beams on the basis of a slit and an array of detectors controlled by micro-processors was constructed and has been used routinely for adjusting beams before transportation down the beam lines; a beam contour in the horizontal or vertical phase space can be displayed within a minute.[1]

Table I. Beam performance of CYRIC cyclotron

Particle	Energy (MeV)[a]	Maximum beam current (μA)[b]
p	3-40	15-100
d	5-25	15- 60
^{3}He	7-65	12- 60
α	10-50	30- 50
$^{12}C^{4,5+}$	65, 105	0.6, 0.03
$^{13}C^{4+}$	60	1.0
$^{14}N^{4,5,6+}$	56, 84, 120	5.0, 2.5, 0.17
$^{16}O^{5,6+}$	75, 115	1.0, 0.1
$^{20}Ne^{5+}$	50	$\leq$5.5

a Protons of energy up to 42 MeV and alphas up to 52 MeV have been accelerated with a weaker beam current.

b Extracted current for light ions, and internal current at R = 650 mm for heavy ions, both in charge μA.

Recently, the residual radioactivity in and around the cyclotron is becoming more and more serious, although the radiation level inside the cyclotron can be reduced by a factor of ∿20 by shielding the magnetic channel with 5 cm-thick lead blocks at the time of maintenance of the interior of the cyclotron. Also activation of the deflectors is rather a serious problem because insulation break down has recently become frequent. Therefore, replacement of the magnetic channel and parts of the deflectors is in progress.

Most of the beam lines are evacuated with turbo pumps of the oridnary type. Recently, turbo pumps of magnetic levitation type have become available. Replacement of the present turbo pumps with the latter type is being tried.

Facilities of CYRIC

Figure 1 shows the plan view of CYRIC which is

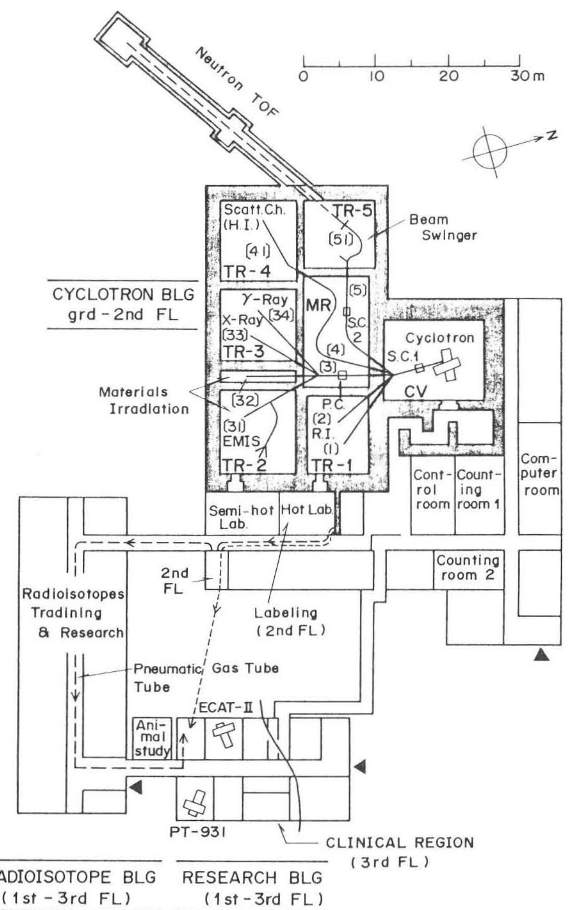

Fig. 1. Facilities of Cyclotron and Radioisotope Center.

composed of CYCLOTRON BUILDING consisting of the cyclotron vault as well as TR's (target rooms), hot and semi-hot laboratories and offices, RADIOISOTOPE BUILDING for researches using radioisotopes of short as well as long halflives and for training of safehandling of radioisotopes, and RESEARCH BUILDING used for life sciences as well as a library and a machine shop. In the latter building a branch clinic *appears whenever* clinical researches are conducted in order for these researches to be performed under the medical legislations.

Facilities connected with the cyclotron

RI production The two beam lines [1] and [2] are used for radioisotopes production with solid/liquid and gas targets, respectively (TR-1 of Fig. 1). At beam line [1] a solid target can be remotely handled with a robot. At beam line [2] one of the seven targets and a beam viewer is remotely selectable. The irradiated gas is transferred through a thin pipe to the labeling room or directly to the clinic.

On-line isotope separator The beam line [31] (TR-2) is equipped with an electromagnetic on-line isotope separator. Recently, the ion source of the separator has been replaced with the ion-guide device for on-line separation of refractory isotopes.[3] The target-rotor was used also at this beam line.[4]

Materials irradiation At the ends of beam lines [31] and [32] are stations for materials irradiation for radiation damage studies.

X-ray and in-beam spectroscopy In TR-3 there are two beam lines [33] and [34], the former for x-ray measurements with Si detectors as well as a crystal diffraction spectrometer and the latter for in-beam nuclear spectroscopy with Ge and a mini-orange spectrometers.[5] The beam line [34] is equipped with a high-field electromagnet for magnetic moment measurements. This magnet is equipped with a pair of active magnetic channels for correcting the beam bending.[6]

Scattering chamber A one-meter diam. scattering chamber (TR-4) together with Si detectors has been used for heavy-ions scattering experiments.

Neutron time-of-flight TR-5 together with a long flight path houses a high-resolution time-of-flight facility for nuclear reaction studies with neutron detection; a swinger magnet changes the incident angle of charged particles.[7]

Beam choppers We have two kinds of cyclotron-beam choppers, two S-type (sinusoidal voltage) choppers in cyclotron vault and in MR (magnet room), and one P-type (pulse voltage) chopper in MR.[8] These choppers have been extensively used in TOF, in-beam spectroscopy and in the study of short-lived nuclei.

Other facilities

Automated synthesizers Seven sets of devices of automated synthesis of radiopharmaceuticals have been developed and are in use in Hot Laboratory and rooms upstairs.[9] They routinely yield gaseous labeled compounds such as ^{11}CO, $^{11}CO_2$, $^{15}O_2$ (more exactly ^{15}OO), $C^{15}O_2$, $^{13}N_2$, $^{13}NH_3$ and ^{11}C-methyl iodide which are used for the study of blood flow and oxigen consumption in the brain, as well as liquid ones, i.e., ^{11}C-fatty acids and *false sugars* such as ^{11}C-glucose, ^{18}F-FDG (^{18}F-labeled fluoro-deoxy-glucose), ^{18}F-FDGal, ^{18}F-FDFuc and ^{18}F-FdUr for tumor diagnosis from sugar and nucleatide metabolisms.

Positron tomographs in use and in development Radiopharmaceuticals are transported via a thin tube, when they are gases, or a pneumatic system, when they are liquids, to the clinical region of RESEARCH BUILDING, where they are given to subject patients or animals for examination by a positron emission tomograph (PET) ECAT-II from EG & G ORTEC having a spatial resolution of 12 mm.[10] This PET has been extensively used for the past five years; more than 500 patients and volunteers have been examined for clinical diagnosis and researches.

Table II. Distribution of beam time among research fields (%)[a]

Fiscal year	79[b]	80	81	82	83	84	85	86[c]	79/82[d]	83/86[d]	Total	Average[e] b.t. (hr)
Nuclear physics	45.8	53.1	52.7	56.8	58.0	56.1	55.1	53.4	52.7	56.0	54.3	22.1
Physics except nucl. phys.	14.2	12.1	11.4	9.1	7.7	11.7	8.0	6.1	11.4	8.8	10.2	17.4
Engineering	8.4	15.4	9.4	9.2	8.2	7.3	12.4	10.4	10.8	9.5	10.1	10.4
Chemistry	5.6	4.8	5.1	5.4	3.9	2.0	2.5	3.4	5.2	2.9	4.0	3.2
RI production & Labeling	0.0	2.0	6.2	6.1	5.7	4.9	4.4	5.5	4.0	5.0	4.5	1.4
Basic medicine & Biology	8.5	6.5	7.2	7.8	5.0	3.8	4.5	7.4	7.4	4.8	6.1	1.5
Clinical medicine	---	---	---	---	8.4	10.0	9.7	11.5	---	9.6	4.8	1.6
Machine maintenance/dev.	17.3	6.1	8.0	5.5	3.0	4.3	3.4	2.5	8.4	3.4	5.9	6.6
Total beam time (hr)	1827	2787	3065	2858	2860	2963	3208	1387	10537	10418	20955	6.0
Machine failure[f] (hr)	39	49	66	69	36	55	2	14	223	107	330	---

a The number does not include the time of preparing the beam, and one day corresponds to 16 to 23 hr depending on the cases; mostly, however, one day corresponds to 22 hr.
b From the middle of June, 1979.
c Until the middle of September, 1986.
d Sub totals for fiscal years for 79 to 82 and 83 to 86. Note that the clinical researches newly started at the beginning of April, 1983.
e Average duration of a single beam time in hr.
f Sum of scheduled time of acceleration which was not performed due to the failure of cyclotron or beam transport; it does not add to the total beam time directly above.

Recently, a second generation PET, model PT-931 from CTI (Computer Technology and Imaging, Inc.), has been installed; it has a wide axial field of view (55 cm), multislices (4 rings and 7 slices), and a superior spatial resolution (5 mm).[11] These performances have been achieved by the use of numerous BGO crystals (2048).

A completely new generation PET using the TOF technique is under construction (model PT-711) by collaboration of CYRIC and CTI.[12] By using TOF information the S/N ratio of PET imaging will be greatly improved, enabling to detect a low level of radioactivity density distribution and hence a cancer in an early stage.

Application of the Cyclotron

Schedule of operation and beam statics

Schedule of operation One year is divided into 4 beam-time periods, each consisting of 8 weeks of beam times for allocation by a research program committee, intervened by 2 weeks of maintenance and additional beam times and approximately 2 weeks of no cyclotron operation. The proposed research subjects are examined and beam times allotted once for every period. The number of cumulative beam-time periods is 30 up to the present with the cumulative number of subjects more than 2000 already. During a week of acceleration the cyclotron is run from Tuesday morning till Saturday morning except holidays.

Beam statistics Since 1979 the cyclotron beam have been utilized in research fields which have been more or less stable for the first 4 years. The situation changed, however, by the start of the clinical researches from the beginning of April, 1983.

We classify these fields into; 1) Nuclear physics, 2) Physics except nuclear physics (atomic, molecular and solid-state physics etc.), 3) Engineering, 4) Chemistry, 5) developmental researches of Radioisotopes (RI) production and Labeling for use in life sciences including supply to non-clinical researches, 6) Basic medicine and Biology, and 7) Clinical medicine. The statistics of beam time distributions among these items are shown in Table II.

As is seen in the table the beam-time fraction for Nuclear physics is nearly constant and is slightly larger than 50 %, and the rest of the beam times are distributed nearly evenly among the rest of the research fields. Clinical medicine starting from 1983 now occupies 12 % of beam time apparently at the cost of Physics (except nucl. phys.), Chemistry, and Basic medicine and Biology, being also supported by the decrease of necessary beam time for Machine maintenance/development.

Table III shows the beam time distribution among accelerated ions, while Fig. 2 shows energy distributions of accelerated light ions. From the table the fraction of proton beam is seen to be nearly constant around 50 %, while that of deuteron has been increasing on the one hand and those of alpha and ^{3}He have been decreasing on the other hand. Increase of deuteron beam is partly due to Clinical researches in producing ^{18}F-FDG and others and partly due to Nuclear physics in TOF experiments by (d,n) reactions. Part of the decrease of alpha beams can be accounted for by acceleration of heavy ions which became noticeable from 1982.

Figure 2 shows that proton beams of lowest energy possible for the CYRIC cyclotron (3 MeV; see Table I) have been actually used to an appreciable extent. Proton beams of 3 to 6 MeV are used mainly for PIXE and inner-shell ionization studies, while those of 15 to 20 MeV are for RI production for life sciences and those of 20 to 42 MeV are for nuclear physics. Deuteron beams of 16 and 18 MeV are used for producing ^{15}O-labeled gases by the ^{14}N(d,n)^{15}O reaction, those of 24 MeV for ^{18}F-labeled false sugars by the ^{20}Ne(d,α)^{18}F reaction, while 25-MeV deuterons are used in Nuclear physics.

Typical research subjects

Typical research subjects using the cyclotron beams are enumerated according to the classification of fields given above.[13]

Nuclear physics 1) Precision measurement of β-decay half-lives of mirror nuclei of fp-shell region using IGISOL (ion-guide isotope separation on-line), 2) Magnetic moments of nuclear isomers by the method of TIPAD (time-integral perturbed angular distribution),[14] 3) Spin-dependent forces between nuclei by double scattering of ^{13}C on ^{12}C,[15] 4) Spin-isospin interaction in nuclei by the (p,n) reaction and nuclear spectroscopy by the (d,n) reaction,[16] etc.

Physics (except nucl. phys.) 1) Atomic inner-shell ionization mechanism by charged-particle impacts,[17,18] 2) Properties of 4f-electrons in rare earth elements from MX-ray emission spectroscopy, 3) Electronic structure and crystal field in Sm_3Se_4 and Sm_3Te_4,[19] etc.

Table III. Distribution of beam time among ions (%)[a]

Fiscal year	79	80	81	82	83	84	85	86	Total
p	46.3	46.9	46.5	49.7	52.2	41.1	47.8	46.1	47.2
d	2.8	16.5	5.7	6.9	9.7	19.3	24.9	24.1	11.7
α	29.0	35.3	31.0	15.8	17.2	14.4	4.6	5.0	19.4
^{3}He	17.1	15.2	11.0	20.1	12.7	13.9	7.5	10.8	13.4
$^{12}C^{4,5+}$	0.8	---	0.7	0.9	---	2.0	6.4	5.3	1.9
$^{13}C^{4+}$	---	---	---	---	---	0.9	8.3	8.7	2.0
$^{14}N^{4,5+}$	4.1	1.0	5.1	6.1	1.9	5.3	0.4	---	3.8
$^{16}O^{5,6+}$	---	---	---	0.3	---	3.0	---	---	0.5
$^{20}Ne^{5,6+}$	---	---	---	0.2	1.2	---	---	---	0.2
Total	1827	2787	3065	2858	2860	2963	3208	1387	20955

a The number does not include the time of preparing the beam, and one day corresponds to 16 to 23 hr depending on the cases; mostly however, one day corresponds to 22 hr.

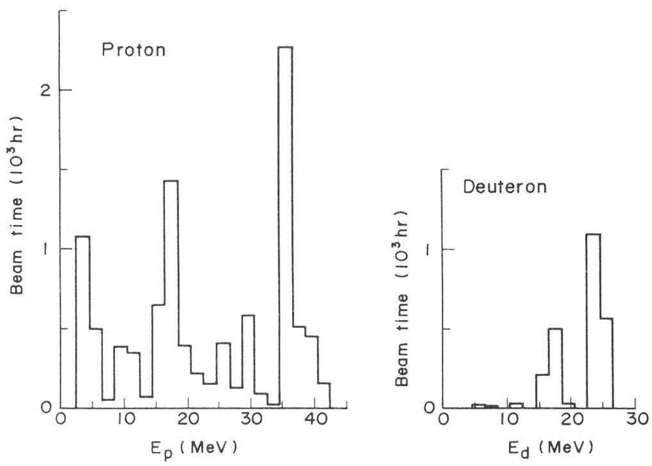

Fig. 2. Distribution of the energy of accelerated light ions.

Engineering 1) Production of focused neutron beam using heavy ion reaction $^1H(^{13}C,n)^{13}N$,[20] 2) Effects of high temperature annealing on the TDPAC (time-differential perturbed angular correlation) spectrum for ^{111}In in Cd crystals, etc.

Chemistry 1) Multielement determination in biological materials by charged-particle activation analysis using the internal standard method, 2) Relation of contact density with Mössbauer isomer shifts for 35.46 keV M1 transition of ^{125}Te,[21] 3) Formation of nucleic base molecules by proton irradiation of formamide, etc.

RI production & Labeling 1) Development of new labeled compounds for tumor diagnosis and brain function studies -- up to the present more than 120 different compounds have been synthesized,[22] 2) Production of ^{18}F by the $^{18}O(p,n)^{18}F$ reaction using an $H_2{}^{18}O$ target, 3) Automated synthesis of ^{11}C-methylspiperone for the study of a dopamine receptor, etc.

Basic medicine & Biology 1) Changes of ^{18}FDG uptake in rat hepatomas by anticancer drugs, 2) Quantification of multi-labeled autoradiography using positron emitters, etc.

Clinical medicine 1) Establishment of the methodology of identification and diagnosis of tumors by PET,[23] 2) Brain metabolism of malignant epilepsy, 3) Cerebral blood circulation and sugar metabolism in Parkinson's disease, etc.

Concluding Remarks

As shown in the last column of Table II the average duration of a single beam time t_{av} differs much from field to field -- from ∿15 hr for physical sciences to ∿1.5 hr for life sciences. Moreover, the clinical researches are to be conducted necessarily during the daytime.

The above situation led to a special formulation of scheduling the beam times, i.e. -- grouping the beam times of a) Basic medicine & Biology plus Chemistry, and b) Clinical medicine, respectively. The value of t_{av} = 22.1 hr for Nuclear physics of Table II is already a result of this formulation; it is much smaller than the value for the cyclotron laboratories dedicated to nuclear physics. Thus the group a) is usually conducted during Tuesday night and that of b) during the daytime of Tuesday and Friday; the rest of the acceleration time of the week is filled by the beam times of the rest of the research fields.

Also in conducting the beam times of life sciences, i.e., a) plus b) above, the change of beam energy is avoided as far as possible, resulting in *quantized* beam energies of 16 and 18 MeV for protons, and 16, 18 and 24 MeV for deuterons; see Fig. 2.

Use of beam energies higher than those used at the dedicated mini-cyclotrons in life sciences also greatly enhances the efficiency of the beams, e.g. -- in producing ^{18}F by the $^{20}Ne(d,\alpha)^{18}F$ reaction use of 24 MeV deuteron energy instead of the necessary 17.5 MeV allows to use a thicker window foil of Al and hence a higher pressure of gas targets (20 atm) with an enhanced production yield.

In this way the CYRIC cyclotron has been utilized very efficiently by the scientists from numerous research fields thanks to their active cooperations, although the number of personnel of CYRIC in charge of the facilities and services is relatively small, i.e., 2 Sc. + 1 En. + 4 Op. for the cyclotron, 2 Sc. + 1 En. + 1 Op. for the beam transport system and other instrumentations, and 4 Sc. + 1 En. + 1 Op. for development and supply of radiopharmaceuticals (Sc. = scientist, En. = engineer and Op. = operator).

Acknowledgement

We acknowledge the cooperations of the staff of CYRIC and the users of Tohoku University.

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