HIMAC AND MEDICAL ACCELERATOR PROJECTS IN JAPAN

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Abstract

A heavy ion synchrotron complex, HIMAC, has stably worked during these four years for cancer therapy at National Institute of Radiological Sciences (NIRS). A number of patients treated with carbon beams from HIMAC has exceeded 300 in the last autumn. Interim observations of the treated patients show the excellent performance of the heavy ion therapy. Besides carbon ions for clinical treatments, various ion species are also accelerated and provided for the basic experiments scheduled during nights and the weekends. Major efforts of the accelerator group of NIRS are directed toward the improvements of the beam performance of the accelerator complex, and some results are described here: Time sharing acceleration of the injector, Heavy ion treatment gated with the respiration of the patients, RI beam production for the confirmation of the irradiation volume *etc*. Triggered by the success at NIRS, several facilities for particle therapy have been proposed in Japan. Outline of these projects is also described.

1. INTRODUCTION

Since 1975, fast neutron therapy has been performed at NIRS to treat malignant human tumors. It has long been known that a fast neutron beam gives strong damage on tumor cells comparing with conventional radiations such as X-rays. Instead of the further developments of the fast neutron therapy, NIRS has adopted heavy ion therapy because of excellent dose localization of heavy ion beams. An RBE (Relative Biological Effectiveness) value of carbon ions is almost the same as that of fast neutrons. A heavy ion accelerator complex, HIMAC, has been developed at NIRS for this purpose[1],[2].

The maximum energy of HIMAC is designed to be 800 MeV/u for light ions with q/A = 1/2 so that silicon ions can reach 30 cm deep in a human body. In the facility, there are three treatment rooms, one of which has both vertical and horizontal beam lines. The other two treatment rooms are equipped with a vertical and a horizontal beam lines, respectively.

The first clinical irradiation was carried out in June 1994 with 290 MeV/u carbon ions for three patients who have been afflicted with cancers in the head or the neck. Radiation damage on the inside surface of the mouth seems very small, whereas the tumor cells are perfectly destroyed. At present, clinical trials include treatments of cancers in the head or neck, the lungs, the central nerve system, the liver, the uterus, the prostate *etc*. A number of treated patients is increasing year after year and reaches 159 in FY1997. Total number of the patients amounted to 389 at the end of FY1997. The interim following up of the treated patients suggest promising results of the heavy ion therapy even for the adeno-carcinomas.

2. ADVANCES IN HIMAC

The HIMAC accelerator has worked very well during these four years. Operation time of the accelerator has exceeded 5,000 hrs. throughout this fiscal year. More than 2,800 hrs. were used for carbon therapy and 3,200 hrs. were for basic experiments, where machine time was estimated as a sum of those with the injector and two synchrotron rings. Unscheduled shut down was 28 hrs. for the injector and 23 hrs. for the synchrotron rings.

In order to get a high efficiency of the accelerator usage, there are three treatment rooms in the HIMAC facility. Beam switching time from one treatment room to the next room is required to be less than 5 minuets. The reproducibility of the beam position should be better than ±2.5 mm at the target position of the isocenter. Such precise beam positioning is realized with a special sequence in the switching magnet excitation. The beam switching process must be completed without introducing heavy ion beams into the treatment rooms. An energy change of the synchrotron is also required once in a day to select the optimum residual range for different patients. It takes about 20 min. except for the checking procedures of the residual range and the dose uniformity within the given irradiation field.

Besides the daily efforts to improve the reliability and stability of the accelerator system, further improvements of beam performances are also required. Brief review of the recent developments of the HIMAC accelerator is given in the following subsections.

2.1. Ion Source Developments

There have been two types of ion sources working at HIMAC: a hot cathode PIG source and a 10 GHz ECR source. Four fold carbon ions from the ECR source are used to the clinical trials and metallic ions of Si^{5+} are produced by the PIG source with a sputtering method.

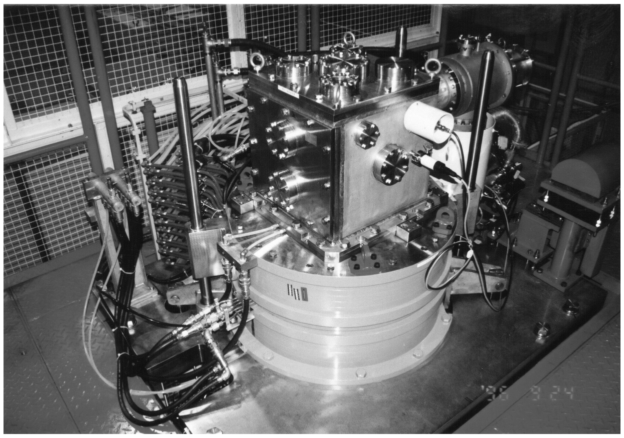

Fig. 1: A photograph of NIRS 18 GHz ECR source.

The third source, 18 GHz ECR source, has been developed to provide heavier ions such as Fe, Kr and Xe[3]. A photograph of the 18 GHz ECR source is given in Fig.1. Between a plasma chamber and an extraction electrode, a high voltage of 56 kV is applied at maximum to reduce unwanted space charge effects in the extraction region.

In the preliminary beam tests with an after glow mode, intensities of Kr^{13+} and Kr^{14+} are obtained around 40 eμA. Iron ions of Fe^{9+} are obtained about 30eμA with $Fe(C_5H_5)_2$ vapor. An extracted intensity of iron beam from the HIMAC synchrotron exceeds 10^8 pps and is well acceptable for biophysical users.

2.2. Time Sharing Acceleration of Injector

In nights and weekends, the machine time of HIMAC is open for basic experiments of physics, biology *etc*. Such user's requirements for ion species, however, tend to conflict with each other and often reduce efficiency of the usage of our two ring synchrotron system. The two rings of the HIMAC synchrotron has been operated with different flat top energies under a restriction of the same ion species at a time. By replacing transport magnets of the injector, however, it has become possible to provide three different ion species with two synchrotron rings and the injector itself (to a medium energy experimental room) in a time sharing mode[4]. The pulse length of each beam line is variable from 1μs to 1ms with an electrostatic buncher.

A set of non-destructive beam monitors (capacitive pick-ups) is installed to realize on-line monitoring beam intensities. A control system of beam monitors has been also modified to distinguish the signals with selected trigger signal for each ion source. The time sharing acceleration mode of the injector will be in use in the next machine time series starting at April.

2.3. Respiration Gated Carbon Therapy

When the liver or the lung are treated, the movement of the tumor position due to the patient's respiration cannot be negligibly small during relatively long irradiation time of several minuets. The distance of the movements is estimated to be as large as a few cm with CT diagnostic images. In the conventional radiotherapy, an irradiation area is determined in a way that the selected area include the whole excursion of the tumor. Therapeutical irradiation, however, may give unwanted effects on the normal cells within the irradiation area.

The position change of the organs occurs mainly in the inspiration period and is small and slow in the relatively long expiration period. This fact suggests that irradiation area can be reduced appreciably without serious increase of the treatment time if one can synchronize the therapeutical irradiation with the patient's respiration[5].

2.3.1. Respiration Signals of a Patient

In order to realize such a new irradiation method, an LED is set on a surface of plastics for patient fixture. A position sensitive detector on a fixed arm is used to detect the movement of the LED. An example of output signals of the respiration detection system is shown as a line (b) of Fig. 2 together with a current pattern of the ring magnet of line (a). A gate signal to permit the beam extraction is then generated during the time when the respiration signal is small comparing with a given fixed level. An example of the gate signal is given as line (c)

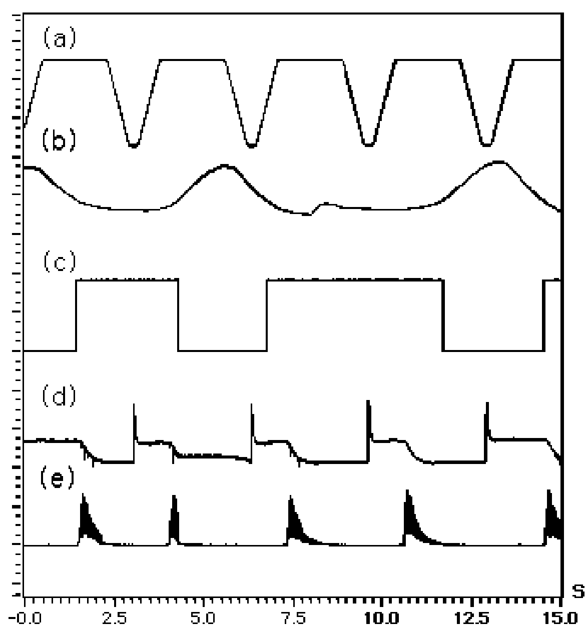

Fig. 2: An example of a set of signals for the respiration gated treatment. (a) Current pattern of the synchrotron ring magnets. A repetition rate of the synchrotron is usually chosen to be 1/3 Hz. (b) Respiration signal of the patient. (c) Gate signal for permission of the beam extraction. (d) Beam signal circulating in the synchrotron ring. Accelerated beams are waiting for the gate signal and unused beams are decelerated to the injection energy as shown in the second pulse. (e) Extracted beam signal.

in Fig. 2. Lower two lines in the figure indicate circulating beam current in the synchrotron ring, and extracted beam signals. Examples of improved penumbra are measured for a moving phantom with the system described above and shown in Fig. 3. Before the actual treatment, a discrimination level of the respiration signal is checked with the gated CT images.

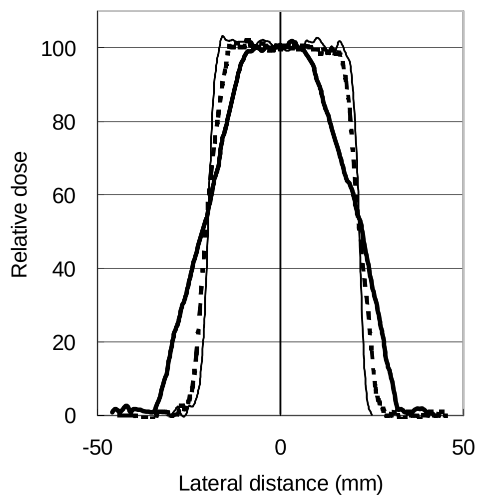

Fig. 3: Examples of improvements of penumbra with the respiration gated treatment. Thin solid line shows relative dose distribution for a fixed phantom. Thick solid and broken lines indicate un-gated and gated irradiation for a moving phantom, respectively. A stroke of the moving phantom is chosen to be ±22 mm.

2.3.2. *Beam Extraction with Rf-knockout Method*

Other important developments in the respiration gated carbon therapy consist of a newly developed beam extraction system[6] and deceleration of unused beams[7]. Fast and stable response of the beam extraction is an essential point of this scheme, and realized by adopting an rf-knockout method. In the method, a set of parallel plate electrodes is installed in the ring, and gives horizontal kick to the circulating beams with an rf voltage resonanced with the horizontal betatron tune. A frequency modulation and an amplitude modulation of the rf signal are very much effective to improve an extraction efficiency. A response time from a trigger signal to the beam extraction is measured as short as 1 ms. An extraction efficiency exceeds 80% in daily operation.

2.3.3. *Deceleration of Residual Ions*

When the patient's expiration is not well synchronized with the flat top of the synchrotron magnets, only a part of the circulating ions are extracted. In such a case, deceleration of residual circulating ions is very much effective in reducing residual activities of the ring. A pattern memory in a rf control system of the HIMAC synchrotron has been modified for this purpose. The improved control system works well and a deceleration efficiency of higher than 80% is achieved in daily operation.

2.4. *Radio-Active Beams*

It is desirable to know the precise dose distribution around the tumor in performing high precision particle therapy. This can be done, in principle, by measuring residual activities in a patient with a PET (Positron Emission Computer Tomography) or a gamma camera just after the clinical irradiation. This procedure is known as an auto-activation method and may be effective for the treatment of tumors in a head. Resolution of the measured dose distribution, however, tends to be very low because of small amount of the induced activities. This situation is dramatically improved when radio active isotopes are used as therapeutical beams. A secondary beam course in HIMAC is developed for this purpose[8]. A layout and a photograph of the beam course are shown in Fig. 4 and Fig.5, respectively.

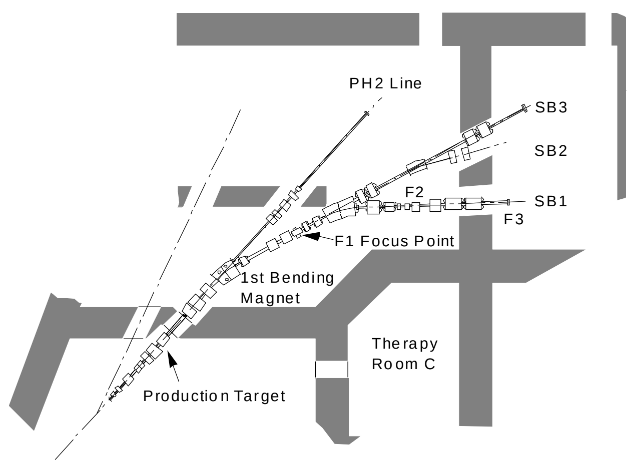

Fig. 4: A layout of the secondary beam line.

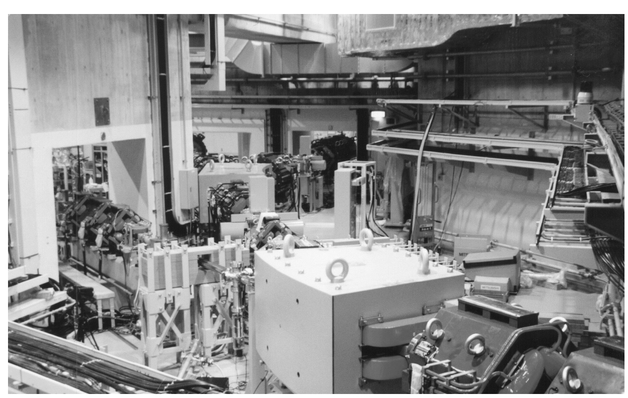

Fig.5: A photograph of the secondary beam line.

Main course of SB1 consists of a production target, a pair of bending magnets and eleven quadrupole magnets, and satisfies the double achromatic condition at F2.

Major part of the secondary beam line has been finished and beam tests are now under way with 400 MeV ^{12}C as a primary beam. The production rate and purity of ^{11}C are estimated with 51 mm thick beryllium target to be 0.2% and 97%, respectively. Preliminary tests of automatic tuning of the bending magnets were also done and a tuning time of about 40 min. was obtained without reducing the production rate and the purity.

A new position detection system has been developed to realize a high spatial resolution in measuring the distribution of ^{11}C in a human body. The system consists of a pair of NaI(Tl) scintillators equipped with photo-multiplier arrays and detects annihilation gamma pairs. By averaging the output signal of each photo-multiplier, a spatial resolution is expected to be better than 1 mm.

3. FUTURE EXTENSIONS

A therapeutical irradiation system with the secondary beam has the first priority among our new projects. In the new beam course, a spot scanning technique will be applied to realize high-efficiency treatment with very low beam loss. The construction of the system will be completed in 1999.

In addition to the various improvements of the accelerator components, we have some new plans to be developed: An intense synchrotron light source for medical use[9] and a small synchrotron with an electron cooler. The synchrotron light source will be dedicated to the medical purposes of a subtraction angiography, a mono-energetic X-ray CT, a X-ray microscope *etc* and the details are presented in another paper to this conference[9].

The small synchrotron will accelerate or decelerate the output beams of the HIMAC injector to an energy range from 1 to 50 MeV/u for ions with q/A=1/2. The ring has a double bend achromatic structure and a circumference of about 25m. An electron energy required for the electron cooling ranges from 3 to 15 keV and a cooling time is estimated to be about 200 ms. With the cooler, a cooling stacking will be tried to increase the injected beam intensity. The cooler will also be used to shorten the bunch length of the circulating beams to less than 10 ns. Only a fast extraction scheme will be adopted for the ring. The construction of the small synchrotron is a part of R&D studies of HIMAC improvements including the connection of two synchrotron rings with new beam line.

4. NEW PROJECTS IN JAPAN

There are about 20 facilities in the world, where charged particle therapy is now going on, and more than 24,000 patients have been treated with charged particles including pions, protons and heavier ions[10]. In Japan, NIRS and PMRC (University of Tsukuba) have been only facilities of charged particle treatments. Numbers of treated patients are about 100 with 70 MeV protons from the NIRS cyclotron, 550 with 500 MeV protons from the KEK booster synchrotron and 390 with 290, 350 and 400 MeV/u carbons from HIMAC, respectively.

Stimulated with the success at these facilities, several plans are approved or in construction stage: National Cancer Center, Hyogo Hadoron Therapy Center, Wakasa Bay Energy Research Center, Shizuoka Cancer Center and University of Tsukuba (new plan). Almost all of these facilities, except for Wakasa, are aiming to perform proton therapy in a hospital environment. Status of each facility is given in the table and the details are described in reference 11.

National Cancer Center at Kashiwa, Chiba has almost completed the mechanical construction and will start the first clinical treatment soon. In the facility, a 235 MeV proton beam (30 cm residual range in water) has been successfully extracted from a cyclotron and transported to the target positions through the gantries.

Hyogo Hadoron Therapy Center is now under construction and will provide 230 MeV proton beams through two rotational gantries and one horizontally fixed beam line. The 320 MeV/u carbon beams (15 cm in water) will also be accelerated and transported to the treatment rooms through a fixed horizontal and a fixed 45 deg. beam lines. The first clinical treatment with protons is scheduled in 2001. Starting time of the carbon therapy depends strongly on the clinical results at NIRS.

In a plan of Tsukuba, high proton energy of 270 MeV is adopted to perform proton radiography. Respiration triggered (not gated) operation and pulse to pulse change in the flat top energy will be tried with a newly constructed synchrotron.

A 200 MeV proton synchrotron at Wakasa is now under construction and will be a multi-purpose accelerator. The medical applications are considered to be one of the most important purposes. An accelerator building will be completed in this autumn and the first beam will be obtained in FY1999.

Shizuoka Cancer Center project have been funded but still in a design stage. The construction of the Cancer Center will start at Mishima during FY1998 and the fist treatment will be performed in FY 2001.

5. CONCLUDING REMARKS

Most of clinical trials at NIRS are still in a stage of phase I/II studies, where side effects of the carbon therapy are mainly checked with strict protocols. Tentative results of the trials, however, show that the carbon therapy is very much promising in treatments of deeply-seated human cancers. With increased numbers of patients, part of protocol studies will be pushed up to routine treatments.

Efforts toward the high precision irradiation are required to make full use of characteristics of carbon beams. Secondary beam treatments will match with this purpose. In the proper treatments with the secondary beams, two rings system of the HIMAC synchrotron will work effectively.

6. ACKNOWLEGMENTS

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Table: Ongoing charged particle therapy in Japan

Place	Machine	Max. energy	1st patient	Major facility	Status
NCC	Cyclotron	p: 235 MeV	1998	2 gantries, 1 horiz.	1st beam obtained
Hyogo	Synchrotron	p: 230 MeV, C: 320 MeV/u	2001	2 gantries, 1 horiz. 1 horiz., 1 45 deg.	under construction
Tsukuba	Synchrotron	p: 270 MeV	2001	2 gantries, 1 research	construction started
Wakasa	Synchrotron	p: 200 MeV	2001	1 horiz.	under construction
Shizuoka	Synchrotron	p: 230 MeV	2002	2 gantries, 1 horiz.	funded