THE PROGRESS OF HIMAC AND PARTICLE THERAPY FACILITIES IN JAPAN

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Abstract

More than 1,000 patients have been treated with carbon ions accelerated by a medical synchrotron HIMAC at National Institute of Radiological Sciences, NIRS. Treated patients have tumors on sites of head and neck, lungs, livers, prostates, uteruses, bones and soft tissues, etc. The results of the phase I/II clinical studies, the purposes of which are to confirm the effectiveness of the carbon therapy keeping side effects at extremely low levels, seem excellent, and a part of the clinical studies have advanced in phase II where the optimum way of treatment are studied.

Total of six particle therapy facilities are now in operation or under construction in Japan. Only one of these facilities, NIRS, is designed for carbon or heavier ions. Another one, Hyogo can provides both carbons and protons for the cancer treatments whereas the other four facilities, Kashiwa, Wakasa, Tsukuba and Shizuoka use only protons for the treatment. Brief status of these five facilities is also presented.

1 INTRODUCTION

Based on the long experiences of fast neutron therapy, 1975 - 1993, and proton therapy, 1976 -, with a 90 MeV AVF cyclotron, NIRS has decided to develop heavy ion therapy to treat deeply seated cancers.[1],[2] Excellent clinical results of proton therapy at University of Tsukuba strongly stimulated the start up of the project.

Since the first clinical irradiation on three patients in June 1994 with 290 MeV/u carbon ions, total number of patients treated at HIMAC exceeded 1,000 in this summer. Treated tumors distribute 16% on heads and necks, 15% on lungs, 11% on livers, another 11% on prostates, 8% on bones and soft tissues, 5% on uteruses and 33% on other sites. Most of treated tumors are in advanced stage and cannot be treated with other methods including the surgery. A local control rate (2 year) is better than 70% for most of protocols keeping the side effects at low level, where the local control means that no recurrence is observed within an irradiated volume.

At an early stage of the clinical trials, number of fractional irradiation of carbon beams was typically 18 and the treatment required 6 weeks except for the extra time for diagnostics and treatment planning. The number of fractions, however, has been decreased for some protocols especially of lung and liver without increasing serious side effects. At present, typical number of fractions is as low as 4 and the treatment can be completed within a week for lung and liver cancers. A respiration gated irradiation method with an rf knock out technique works very effectively for these cases. Figure 1 shows a typical example of carbon ion treatment of a liver cancer. In the figure, the cancer is indicated with an arrow.

After accumulating numbers of protocols, the carbon therapy at NIRS will change its phase from a free clinical trial to a charged treatment within a few years.

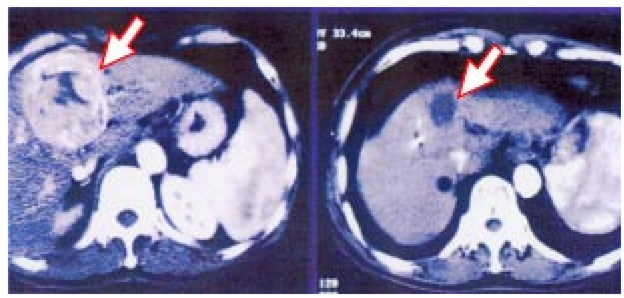

Fig. 1: Typical example of liver cancer treatment. Left and right figures show pre and post treatment, respectively. The position of the cancer is indicated with an arrow.

2 PROGRESS OF HIMAC

The machine time of HIMAC is completely occupied by carbon therapy in day time, but is open for basic experiments of radiation biology, physics, etc. during nights and week ends. Many kinds of ion species are required by these experiments. Our efforts of machine developments are therefore not restricted in improvements of the treatment system.

2.1 Machine Operation

HIMAC has been operated stably for these several years. The unscheduled shut down was around 1% of total beam on time of about 5,500 hrs., and effects on treatment schedule were at extremely low levels.[3] During fiscal year 2000, needs for the carbon beams exceeded 60% of the total beam time, and Ar, Ne and Fe spent 10%, 5.1% and 4.7% of the beam time, respectively. The heaviest element we could serve was Xe and was used 1.4%. Attempts for acceleration of stable isotopes with relatively small natural abundance were also performed for ^{13}C, ^{15}N, ^{36}Ar and ^{57}Fe, and put into the routine operation for the basic experiments.

2.2 Ion Source Developments

A compact ECR ion source, which uses permanent magnets for generating both of sextupole and mirror fields, has been developed.[4] Detailed beam tests are now underway and the preliminary results show that this type of ion source is promising for a future carbon therapy because of its compactness and its easiness in operation and maintenance. A microwave amplifier for the ECR source is equipped with a travelling wave tube and can change an operation frequency from 9 to 18 GHz. A typical output current of C^{4+} ion exceeds 200 eμA. A photograph of the source is given in Fig. 2.

There is growing need to use heavy metallic ion beams for basic research fields. A few methods have been developed to respond these demands, for examples, a sputtering method with a PIG source for silicon ions, a MIVOC (Metal Ions from VOlatile Compounds) method with a 18 GHz ECR source for iron ions, etc. In addition to these methods, a new technique is developed for a gas supplying system of the ECR source. In the newly developed system, a metallic rod is placed at a high positive potential and gets thermo-electron bombardments emitted from a hot filament surrounding the rod. The metallic gases evaporated from the rod are introduced to the source through existing gas system.

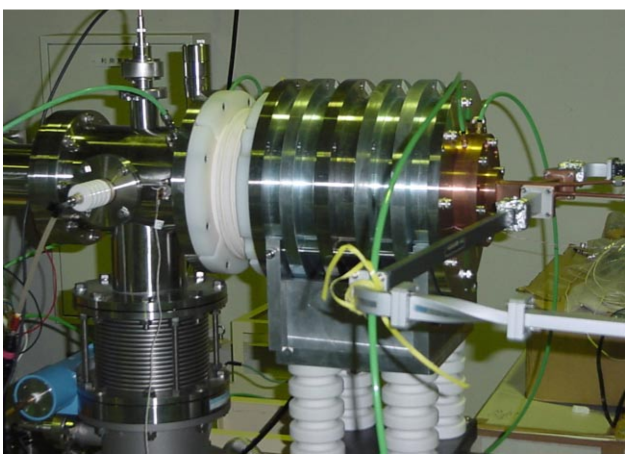

Fig. 2: A compact ECR ion source with permanent magnets. A typical output currents exceeds 200 eμA for C^{4+} ions.

2.3 Treatment with Secondary Beams

A mass and charge analysing system has been developed to separate ^{11}C nuclei from a primary ^{12}C and from other fragmented products of ^{12}C bombardment on a beryllium target.[5] The purified ^{11}C beam will be irradiated on a patient to clarify the range distribution within a patient's body by measuring a pair of annihilation gamma rays of positrons emitted from a ^{11}C nucleus. For a small volume of less than 5×5×5 cm^3, cancer treatment will be possible by applying 3-dimensional spot scanning technique. Preparatory study for clinical application has been extensively underway and detailed reports of this system and test results will be given in another paper of this conference.[6] Only one example of the test results of the spot scanning system is shown in Fig. 3 where characters H, I, M, A and C are drawn with ^{11}C at different target depths.

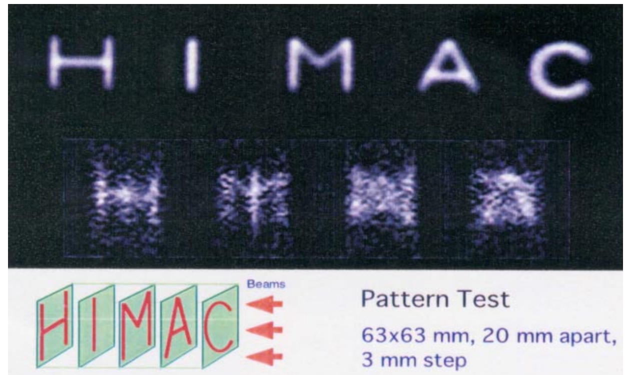

Fig. 3: An example of ^{11}C distribution measurements with a 3D spot scanning system.

2.4 Electron Beam Cooling

In order to realize high quality and high intensity beams, an electron cooling system has been installed in HIMAC[7]. The electron energy can be varied from 3 to 30 keV and the corresponding ion energies are 5.5 and 55 MeV/u, respectively. The maximum electron current is expected to be 1.2 A, and an electron beam size is designed to be 100 mm at the cooling section of 1 m long.

A photograph of the electron cooler installed in HIMAC is shown in Fig. 4. In the figure an electron gun can be seen at left and an electron catcher at right.

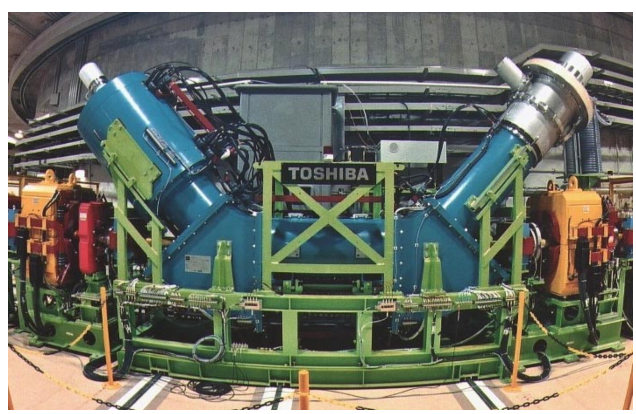

Fig. 4: An electron cooling apparatus installed in the HIMAC synchrotron ring. An electron gun is seen at left and an electron catcher at right.

An example of the transverse cooling at the injection energy of 6 MeV/u is given in Fig. 5. A 30 mm wide (FWHM) multiturn injected Ar beam is cooled by 200 mA and 3.4 keV electron beam, and the width is reduced to 1.8 mm after 3.5 sec. The beam profiles are measured with a non destructive multi channel plate monitor.

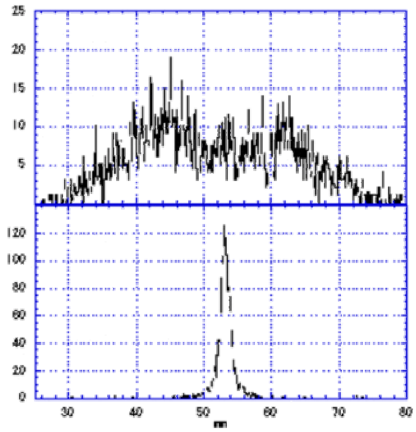

Fig. 5: Typical transverse beam profiles for 6 MeV/u Ar ions: just after the multiturn injection (top) and 3.5 sec after beginning of electron cooling (bottom).

3 DEVELOPMNTAL STUDIES

Major activity of our group is concentrated on the developments of a small sized therapy system aiming to spread the carbon therapy in the whole country.

3.1 Design and Construction of Small Ring

A small ring has been proposed and designed to establish an electron cooling technique for the bunch shortening and for a cooling stacking to increase beam intensities. A circumference of the ring is 24 m and the maximum field strength of the bending magnets is 1.4 T. A magnetic rigidity can be changed from 0.13 to 1.54 Tm, and covers an energy range of 0.2–28 MeV/u for ions with q/A = 1/2. A bunch length of the circulating beam is expected to be around 10 ns after longitudinal cooling and bunch rotation. A fast beam extraction method is adopted for the ring. Some accelerator components for the compact carbon therapy facility will be developed with this small ring.

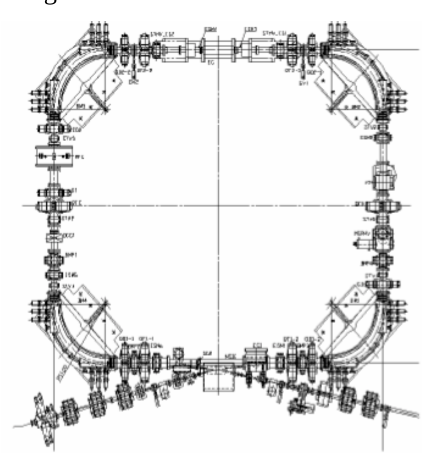

Fig. 6: A layout of a small ring.

3.2 FFAG Accelerator

In order to pursue another scheme from a linac followed by a synchrotron for the carbon therapy, studies have been initiated for a Fixed Frequency Alternating Gradient, FFAG, accelerator. In an FFAG scenario, a very high repetition rate in an order of 100 Hz is possible since the rate is determined only by a possible rf voltage generated at acceleration gaps. Although the extracted beam is a short pulsed beam for the FFAG, the preliminary study shows that such a time structure dose not bring about serious problem in forming uniform irradiation field for the treatment.

Detailed studies have just started up and a small sized model FFAG accelerator will be constructed at NIRS during next five years.

4 OTHER FACILITIES IN JAPAN

Stimulated by remarkable results of the carbon therapy at NIRS, five new particle therapy projects have got started as shown in the table, together with two on going facilities at NIRS. In the following subsections, brief status of these new projects is summarized.

4.1 National Cancer Center Hospital East

A main accelerator of this facility is an AVF cyclotron. The accelerator is operated at a fixed energy of 235 MeV for protons. An energy of protons can be varied with an energy degrader and analyser system installed downstream from an extraction point of the cyclotron. Two rotational gantries and one horizontal beam port are installed in three different treatment rooms. A double scattering method is adopted for one rotational gantry and a wobbler method for another gantry.

The facility was put into operation in 1998 and 77 patients are already treated as clinical trials. Recently an important advance was made in the proton therapy; the proton therapy is approved by the Ministry of Health and Welfare as a routine treatment of cancers and NCC can get an fee for the treatment.

Fig. 7: A 235 MeV fixed energy AVF cyclotron for proton therapy at National Cancer Center Hospital East.

4.2 Hyogo Ion Beam Medical Center

This facility is operated by a local government of Hyogo prefecture and has started clinical trials in May 2001 with protons. Six patients has been treated until middle of July. After completing clinical trials for 30 patients with protons, carbon treatments will start in next year.

An accelerator of this facility is similar to HIMAC and consists of two ECR ion sources, an RFQ linac, a Alvarez linac and a separated function synchrotron. Output energy is variable and the maximum values are 230 MeV and 320 MeV/u for protons and fully stripped carbon ions, respectively. A residual range in water is 30 cm for protons and 20 cm for carbons.

There are two rotational gantries for protons, and three treatment rooms are prepared for carbons; a horizontal, a vertical and a 45 deg. beam lines for each room.

Fig. 8: A synchrotron ring and a part of a high energy beam transport line of Hyogo Ion Beam Medical Center.

4.3 Proton Medical Research Center, University of Tsukuba

Since 1983, University of Tsukuba has accumulated long experiences of proton therapy using a 500 MeV booster synchrotron at KEK. A number of treated patients reaches 700. Because of serious limitations of using the accelerator for physical research, a new medically dedicated facility has been long desired. The construction of the facility and the beam tests have been completed and clinical trials are scheduled in September. Preparatory works for the trials are now extensively underway.

The main accelerator is a compact synchrotron with edge focusing as shown in Fig. 9. The synchrotron has a diamond shape and a circumference of 23 m. Output beam energy is variable in a range 70-250 MeV for protons. The rising and the falling timing of the main magnet current can be triggered by external signals generated from a patient's respiration curve.

Two rotational gantries have been constructed for the cancer treatment and one horizontal beam line for the basic experiments.

Fig. 9: A 250 MeV synchrotron ring at University of Tsukuba. An injection line can be seen on this side and an extraction line is on the other side.

4.4 Wakasa-Wan Energy Research Center

Wakasa-Wan Energy Research Center is operated by a local government of Fukui prefecture to promote the development of industry in the prefecture. Proton therapy is one of the major purposes of the facility.

An injector is a 5 MV tandem accelerator and delivers 100 μA protons in a DC mode, and 20 mA in a pulse mode for a synchrotron. The separated function type synchrotron has an average diameter of 10 m and accelerates protons to an energy in a range of 80-200 MeV. A photograph of the synchrotron ring is shown in Fig. 10. The beam tests of both accelerators have been completed.

In this summer, construction of clinical beam lines is finished, and the beam tests are scheduled within this year. Clinical trials of the proton therapy are expected to start in early 2002.

Fig. 10: A multi-purpose synchrotron ring at Wakasa-Wan Energy Research Center.

4.5 Shizuoka Cancer Center

A completely new hospital for cancer treatment is funded by a local government of Shizuoka prefecture and now under construction. A proton therapy has been adopted as one of major facilities of the hospital. An accelerator system is very compact and a main accelerator has a diameter of about 6 m by use of the edge focussing.

The beam tests of the accelerator is almost finished at a factory of a maker, and the accelerator will be sent to Shizuoka Cancer Center in this autumn. Clinical trials are expected to start in 2004.

There are three treatment rooms; two rooms are equipped with rotational gantries and the last one is equipped with a horizontal beam line.

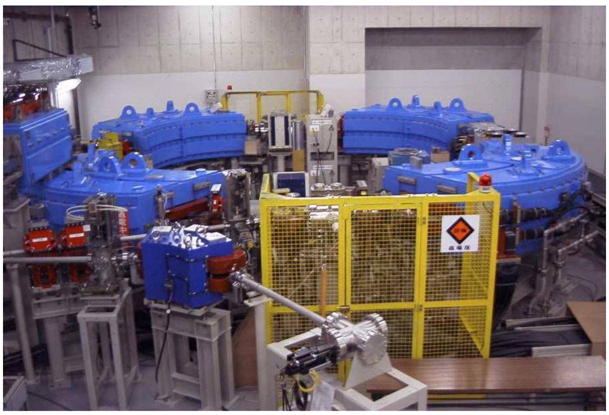

Fig. 11: A synchrotron ring for Shizuoka Cancer Center under final beam tests at an accelerator maker.

5 SAMMARY

In Japan, particle therapy has developed in rather different way from other counties, partly because number of patients of eye melanoma is very small. After the first treatment of eye melanoma with protons at NIRS, major developmental results has been accumulated at University of Tsukuba for deeply seated cancer treatment including respiration synchronized irradiation technique for liver and lung cancers. The treatments were performed using a 500 MeV fast cycling booster synchrotron at KEK. The situation, however, was drastically changed when the carbon therapy was initiated at NIRS. Stimulated with excellent results at HIMAC, five new particle therapy projects were approved mainly by local governments with budgetary support of Science and Technology Agency.

In near future, particle therapy will occupy an important part of routine cancer treatments in Japan. A compact and reliable accelerator system is required to be developed for this purpose.

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Table: Ongoing charged particle therapy in Japan

Place	Machine	Max. energy	1st patient	Major facility	Status
NIRS	Cyclotron	p: 90 MeV	1979	1 Hor.	In operation
NIRS	Synchrotron	C: 400 MeV/u	1994	1 Hor., 1 Vrt., 1 Hor×Vrt	In operation
Kashiwa	Cyclotron	p: 235 MeV	1998	2 Gantries, 1 Hor.	In operation
Hyogo	Synchrotron	p: 230 MeV, C: 320 MeV/u	2001	2 Gantries, 1 Hor. 1 Hor., 1 45 deg.	In operation
Tsukuba	Synchrotron	p: 250 MeV	2001	2 Gantries, 1 Research	Construction completed
Wakasa	Synchrotron	p: 200 MeV	2002	1 Hor., 1 Vrt.	Construction completed
Shizuoka	Synchrotron	p: 230 MeV	2002	2 Gantries, 1 Hor.	Under construction