# **REVIEW ON HI ACCELERATOR FOR HADRONTHERAPY**

K. Noda

National Institute of Radiological Sciences, Chiba, 263-8555 Japan

## Abstract

Heavy-ion beams have attractive growing interest for cancer treatment owing to their high dose localization at the Bragg peak as well as high biological effect there. Recently, therefore, heavy-ion cancer treatments have been successfully carried out at various facilities and several construction projects for the facility of the heavyion therapy have also been progressing in the world, based on the development of accelerator technologies.

# **INTRODUCTION**

Heavy-ion beams are very suitable for treatment of deeply seated tumours, because of the excellent physical dose localization and a high LET characteristic around the Bragg peak, which was supported by the prospective results of heavy-ion research work at LBNL [1]. The National Institute of Radiological Sciences (NIRS) decided to carry out heavy-ion therapy based on the 20 years experience of radiotherapy with protons and neutrons. The HIMAC project [2] had been progressed since 1984, as one of the major projects of "Comprehensive 10 years Strategy for Cancer Control" promoted by Japanese government. The HIMAC facility was completed in October 1993 as the world's first heavy-ion accelerator dedicated to medical use. Since June 21, 1994, at NIRS, more than 4,500 patients have been treated, and the clinical efficiency of carbon-ion radiotherapy has been demonstrated for various diseases. With stimulating results of the HIMAC treatment, therefore, various facilities in the world have carried out the heavy-ion cancer therapy, and several projects have also been progressing. This report reviews the heavy-ion accelerator facility for the cancer therapy and the related development of accelerator and beam-delivery technologies.

## **PROGRESS OF HIMAC**

We have continuously developed the accelerator and beam-delivery technologies for the cancer therapy and the related research fields.

## Development of Beam-Delivery Method

## Respiration-gated irradiation

Damage to normal tissues around tumour was inevitable in treatment of a tumour moving along with respiration of a patient. A respiration-gated irradiation system with the broad-beam method [3], therefore, which can respond quickly to irregular respiration, was developed. In this system, the irradiation-gate signal is generated only when target is at the design position and the synchrotron can extract a beam. The beam is delivered by the RF-KO extraction method [4], according to the gate signal. This method has been applied to liver, lung and uterus cancers since February 1996. Fig. 1 shows the view of irradiation gated with respiration.



Figure 1: The view of irradiation gated with respiration using the horizontal irradiation port.

# Layer-stacking Irradiation

In a conventional broad-beam method, the fixed SOBP (Spread-Out Bragg Peak) produced by a ridge filter results in undesirable dosage to the normal tissue in front of target, because the width of an actual target varies within the irradiation field. In order to suppress the undesirable dosage, thus, the layer-stacking irradiation method was proposed [5] and experimentally verified [6,7], which has been routinely utilized.

This method is to conform a variable SOBP to a target volume by controlling dynamically the conventional beam-modifying devices. The target volume is longitudinally divided into slices, and the small SOBP with several mm in WEL, which is produced by a single ridge filter, is longitudinally scanned over the target volume in a stepwise manner. Changing an aperture of the MLC (Multi Leaf Collimator) dynamically, on the other hand, a lateral dose distribution of each slice is conformed according to a cross-sectional shape of each slice.

# Development of Accelerator Technology

# RF-KO Slow-Extraction Method

We developed the RF-KO slow extraction method for a respiration-gated irradiation system. The RF-KO method has a huge ripple of kHz order in time structure of the extracted beam (spill) due to the coherency in its extraction mechanism. However, the huge spill ripple has never disturbed the dose distribution in the beamwobbling method, while it disturbs in the beam-scanning method, because the disturbance magnitude depends on the difference between the ripple and wobbling frequencies. Thus we developed the dual FM method and separated function methods [8] in order to significantly suppress the spill ripple. Furthermore, we have also developed the method to suppress a fluctuation of Hz order in the time structure by optimizing AM function of the RF-KO system [9].

A beam-spill control system has been developed [10], based on the improvement of the time structure in the spill as mentioned above. The core part of this system requires the following functions: 1) calculation and output of AM signal according to request-signals from a irradiation system, 2) real-time processing with a time resolution less than 1ms, and 3) feed-forward and feedback controls to realize the extracted intensity as requested. This system allows us to control dynamically the beam intensity almost as required, as shown in Fig. 2.



Figure 2: Time structure of extracted beam obtained by the spill control system. Spill time structure (green) can be modulated by request signal (yellow).

#### Control of Beam Profile and Position

In order to deliver the beam with the desired profile and positions at a target through a beam-transport line, it has been essential to match the beam-optical parameters with those at an extraction channel of the ring. For the optical matching, thus, we developed an accurate prediction method of the optical parameters at the extraction channel through an outgoing-separatrix estimated by a rod-monitor measurement [11]. As a result of the experiment, it was verified that the predicted beam-optical parameters was in good agreement with the measured ones.

#### Intensity Upgrade

In order to increase the delivered beam intensity, the optical-parameter matching in the vertical direction was carried out in a flat-base of the synchrotron-operation cycle. As a result, the vertical emittance was decreased to 15 from 33  $\pi$ ·mm·mrad before matching. Increasing the beam intensity in the ring, we observed a large beam loss due to the space-charge effect. Since the vertical tune of 3.13 is close to an integer resonance due to the incoherent tune-shift under high ion density after bunching, we changed it to 3.23. Even in this tune,

however, the 3rd-order coupling resonance (Qx + 2Qy = 10) caused a large beam loss. We thus tested the resonance correction by using four sextupoles. After the correction, the beam lifetime was increased by more than 5 times under (Qx,Qy) = (3.74,3.23). An un-tuned RF-cavity, further, having a Co-based amorphous core, has been developed so as to make multi-harmonics operation possible for reducing the longitudinal space-charge effect [12]. By the multi-harmonics operation, the beam intensity was increased by 40% [13]. As a result of studies mentioned above, more than  $2 \times 10^{10}$  carbon ions can be delivered to the iso-center with one operation cycle of the ring.

#### New Treatment-Facility Project

# *New 3D Scanning for Both Moving and Fixed Targets*

For further development of the HIMAC treatment, we have developed a 3-D scanning method for a moving target as well as a fixed one. As a feasible solution, we found the respiration phase controlled rescanning (PCR) [14]. In the PCR method, the rescanning completes the irradiation on one slice during one gated period. Since the movement of the target is close to "zero" on average, thus, we can obtain the uniform dose distribution even under the irradiation on the moving target. The PCR method has required mainly two technologies:1) Intensity-modulation technique for a constant irradiation time on each slice having a different cross section, and 2) Fast-scanning technique for completing several-times rescanning within a tolerable irradiation time [14].

#### Design of new treatment facility

Based on the development of the PCR method, the new treatment facility has been designed and being constructed, as shown in Fig. 3. The facility is connected with the upper synchrotron of HIMAC. In the treatment hall, placed underground of the facility, three treatment rooms are prepared in order to treat more than the present number of patients at the existing HIMAC treatment. Two of the treatment rooms are equipped with both horizontal and vertical fixed beam-delivery systems, and the other one is equipped with a rotating gantry. Two treatment-simulation rooms are also equipped for obtaining CT-image for a treatment planning and for patient positioning as a rehearsal. Furthermore, there are six rooms devoted for patient preparation before irradiation.

In the new treatment facility, the maximum ion energy is designed to be 430 MeV/n in the fixed beam-delivery system in order to obtain the residual range of around 30 cm in a <sup>12</sup>C beam and more than that 22 cm in an <sup>16</sup>O beam. The maximum lateral-field and SOBP sizes are 25 cm  $\times$  25 cm and 15 cm, respectively, so as to cover almost all treatment needs with the HIMAC [15]. On the other hand, the rotating gantry system has a maximum energy of 400 MeV/n, a maximum lateral-field of 15 cm  $\times$  15 cm and a maximum SOBP size of 15 cm, in order to downsize the rotating-gantry size and weight.



Figure 3: Schematic view of the new treatment facility.

A rotating gantry employs also the PCR method [16] in order to increase significantly treatment accuracy for a tumour located close to a critical organ through the multi-field optimization method [17]. Further, the rotating gantry can reduce considerably patient stress due to the face-downward attitude while the patient is positioned. It is important for the gantry design to avoid any change of the beam size depending on the rotation angle. Thus, we will adapt a compensation method of the asymmetric phase-space distribution [18]. This method is based on multiple scattering by a thin foil placed at the position with the optimum beam-optical parameters in the BT line. Further, the final dipole magnet is divided into 30° and 60° magnets, and two scanners are placed between the two dipole magnets in order to extend the effective length from the scanners to the iso-center. The total weight of the rotating-gantry system is around 350 tons.

# HEAVY ION FACILITY IN THE WORLD FOR CANCER TREATMENT

#### Asia

# Hyogo Ion Beam Medical Center

This facility has treated 2,339 patients to October 2008 from May 2001, with both proton and carbon beams. A utilization ratio of proton and carbon are 82% and 18%, respectively. An accelerator complex consists of two ECR ion sources, an injector linac cascade (RFQ and Alvarez linacs) and a separated function synchrotron, which was designed based on the HIMAC one. Output energy is variable and the maximum values are 230 MeV and 320 MeV/n for protons and carbon ions, respectively. A residual range in water is 30 cm for protons and 20 cm for carbons. There are two rotating gantries for protons, and three treatment rooms are prepared for carbons; a horizontal, a vertical and a 45° beam lines for each room.

# Gunma University Heavy Ion Medical Center

For the purpose of widespread-use of carbon-ion radiotherapy in Japan, the NIRS designed a standard type of carbon-ion radiotherapy system [15] so as to reduce the construction cost. Based on the design study, the Gunma University has been constructing the standardtype facility since 2006 and the first patient will be treated in FY2009. This facility consists of an ECR ion source, an RFO and an APF-IH linac, a synchrotron ring, three treatment rooms and one experimental room for basic researches. In this facility, a  $C^{4+}$  beam, which is generated by the compact 10 GHz ERC source, is accelerated to 4 MeV/n through the injector linac cascade. After fully stripped, the  $C^{6+}$  beam is injected to the synchrotron by the multi-turn injection scheme and is accelerated to 400 MeV/n at maximum. All the magnets in the beam transport lines are made of laminated steel in order to change the beam line quickly within one minute. The beam-delivery system employs a spiral beamwobbling method [19] for forming a uniform lateral dose distribution with a relatively thin scatterer. The facility size is downsized to be one-third of the HIMAC facility. An image view of the Gunma-University facility with installed equipments is shown in Fig. 4.



Figure 4: An image view of Gunma facility with installed equipments.

# Institute of Modern Physics in China

The Institute of Modern Physics (IMP) in China, using a carbon beam with 100 MeV/n from a tandem of heavyion cyclotrons (SFC and SSC) [20], has already treated 103 patients with superficially-placed tumours since Nov. 2006. As a good result of these treatments, the treatment of deeply-seated tumour started successfully since March 2009, with a carbon beam having 400 MeV/n from CSR (Cooling Storage Ring). A C<sup>4+</sup> beam with 7 MeV/n from the cyclotron is injected to CSR [20] by the charge-exchange injection method. After being stacked by the cool-stacking method, the beam is accelerated to a desired energy. The CSR can accelerate a C<sup>6+</sup> beam to 1000 MeV/n at maximum and deliver to the beam intensity of  $2\times10^9$  pps at maximum.

## Other projects in Asia

China has several projects of the heavy-ion therapy, except for the IMP. One of them is the Shanghai project,

which will construct the Siemens machine as described in the later section. The EMIT (Energy Modulation Ion Therapy) facility, which has rapid cycle proton and carbon synchrotron rings, was designed by IHEP group. Taiwan also has a plan to construct the standard-type carbon facility in Japan, collaborating with the NIRS.

In Japan, the Saga and Kanagawa projects were approved by their prefectural governments and they started the conceptual design based on the standard-type carbon-therapy facility.

#### Europe

In Europe, the EULIMA (European Light Ion Medical Accelerator) project was started in 1987 by the European Commission and proposed carbon-ion radiotherapy with the different 400 MeV/n accelerators: a superconducting cyclotron and a synchrotron ring [21]. Unfortunately, this project has never been realized. The GSI pilot project has begun in 1993 and carries out fixed target treatments since 1997. The GSI pilot project brought the construction of the HIT (Heidelberg Ion Therapy) facility. On the other hand, the PIMMS (Proton and Ion Medical Machine Study) project was also started in 1996. Based on the modified PIMMS design by the PMMS/TERA project, the construction of the CNAO (Centro Nazionale di Adroterapia Oncologica) facility is being constructed since 2003.

### **GSI/HIT Project**

Since 1997, the GSI has successfully carried out the cancer treatments of around 400 patients with a <sup>12</sup>C beam from SIS with applying the intensity controlled rasterscanning method. Based on the developments and experiences of the GSI, the HIT facility, which is a hospital based light ion accelerator facility for the clinic in Heidelberg, has been proposed and been being constructed [22]. In the HIT project at the present, almost all beam commissioning has been successfully completed, and the first patient will be treated this autumn.

The HIT facility consists of two ECR ion sources, a RFQ and IH linac cascade, a synchrotron ring and two treatment rooms with a horizontal beam-delivery system and one rotating gantry. Light ions (p, He, C, O) generated by ECR sources are accelerated to 7 MeV/n by the RFQ and IH linac cascade and are injected to the synchrotron. The ions slowly extracted by the RF-KO method are delivered to each treatment room. The residual range of  $C^{6+}$  ions is designed to be 30 cm at maximum, which corresponds to 430 MeV/n. The main characteristics of this facility are the application of the raster-scanning method with active variation on intensity,

energy and beam-size both in two treatment rooms and in the rotating gantry. The facility layout is schematically shown in Fig. 5.



Figure 5: Layout of the HIT facility.

The developed technologies have been transferred to Siemens. Siemens has carried out a cost-reduction program, while keeping its performance, and has constructed the complete therapy unit in both Marburg and Keil Universities, Germany. Further, Siemens has already made a contract with the Shanghai project. In these projects, 45° beam line is employed, instead of a rotating gantry.

## **CNAO** Project

The Italian hadron-therapy centre CNAO is presently under construction in Pavia, Italy. The CNAO project will be devoted to the treatment of deeply-seated tumours with proton and carbon beams and to clinical and radiobiological research [23]. The CNAO accelerator is designed based on the modified PIMMS. The facility consists of two ECR ion sources, a 7 MeV/n injector linac cascade designed by GSI and a 400 MeV/n synchrotron ring. The CNAO synchrotron consists of two symmetric achromatic arcs connected by two dispersion free straights and has a circumference of approximately 78 m. The maximum energy of the ions is 400 MeV/u. The extraction scheme employs both the acceleration-driven and RF-KO methods under the thirdorder slow extraction condition. In the final phase the CNAO project will have 5 treatment rooms (3 rooms with fixed beams and 2 rooms with gantries) and one experimental room. In the first phase, three treatment rooms will be equipped with 4 fixed beams, three horizontal and one vertical line. As a beam-delivery method, the CNAO will employ the active scanning that has been developed at GSI. At present, the commissioning of the injector part has been carried out. A schematically view of the CNAO facility is shown in Fig. 6.



Figure 6: Schematic view of CNAO facility.

#### Other Projects in Europe

The construction of ETOILE [24] has been approved by the French ministries of health and research in May 2006. The basic design of an accelerator system is similar to that of CNAO and the active scanning method will be also employed.

The Med-Austron project [25] has designed a synchrotron based facility for both proton and carbon radiotherapy, based on the modified PIMMS design. The delivered energy of carbon and of proton are variable from 120 to 400 MeV/n and from 60 to 220 MeV, respectively.

ARCHADE project [26] has designed superconducting carbon cyclotron, cooperating with IBA. This cyclotron is designed to deliver 400 MeV/n carbon and 250 MeV proton. 400 MeV/n Carbon beam is extracted through an electrostatic deflector, and 265 MeV proton beam is obtained by a stripping extraction of  $H_2^+$ .

INFN has designed a superconducting cyclotron for both proton and carbon radiotherapy [27]. Acceleration energy is 300 MeV/n. A proton beam with 260 MeV is obtained by  $H_2^+$  stripping method.

#### **SUMMARY**

With stimulating through remarkable results of the carbon therapy with HIMAC, various facilities have carried out the heavy-ion therapy and several projects have also been being progressed. With improving both the beam-delivery and accelerator technologies of HIMAC, on the other hand, the NIRS designed the standard-type carbon therapy facility in Japan, which has been being constructed at Gunma University. The new treatment facility, further, has been designed for further development of the HIMAC treatment, since 2006. The construction of the facility building has been carried out since February 2009, which will be completed at March 2010.

#### REFERENCES

- [1] W. T. Chu et al., Rev. Sci. Instr. 64 (1993) 2055.
- [2] Y. Hirao et al., Nucl. Phys. A538 (1992) 541c.
- [3] S. Minohara et al., Int. J. Rad. Oncol. Bio. Phys. 47, 1097-1103 (2000).
- [4] K. Noda et al., Nucl. Instr. Meth. A 374 (1996) 269.
- [5] T. Kanai et al., Med. Phys. 10, 344 (1983).
- [6] Y. Futami et al., Nucl. Instr. Meth. A 430 (1999) 143.
- [7] T. Kanai et al., Med. Phys. Med. Phys. 33, 2989 (2006).
- [8] K. Noda et al., Nucl. Instr. Meth. A 492 (2002) 253.
- [9] T. Furukawa et al., Nucl. Instr. Meth. A 522 (2004) 196.
- [10] S. Sato et al., Nucl. Instr. Meth. A 574 (2007) 226.
- [11 T. Furukawa et al., Nucl. Instr. Meth. A 515 (2003) 861.
- [12] M. Kanazawa et al., Nucl. Instr. Meth. A566 (2006) 195.
- [13] C. Ohomori et al., Nucl. Instr. Meth. A 547 (2005) 251.
- [14] T. Furukawa et al., Med. Phys. 34, 1085 (2007).
- [15] K. Noda et al., J. Rad. Res., 48 (2007) A43.
- [16] T. Furukawa et al., Nucl Insr. Meth. B 266 (2008) 2186.
- [17] A. Lomax, Phys. Med. Biol. 44:1219 (1999).
- [18] T. Furukawa and K. Noda, Nucl. Instr. Meth. A 565 (2006) 430.
- [19] S. Yonai et al., Med. Phys. 35, 927 (2008).
- [20] Y. J. Yuan et al., Proc. EPAC08, pp.388-390.
- [21] P. Mandrillon et al., EPAC92, pp.179-181.
- [22] H. Eickhoff et al., Proc. EPAC04, pp.290-294.
- [23] S. Rossi, Proc. EPAC06, 2006, pp.3631-3635.
- [24] F. Meot et al., Proc. EPAC02, 2002, pp.2745-2747.
- [25] E. Griesmayer et al., Nucl. Instr. Meth. B 258 (2007)134.
- [26] Y. Jongen et al., Proc. EPAC08, pp.1806-1808.
- [27] M. Maggiore et al., Proc. PAC07, pp.2748-2750.