Abstract

The carbon-ion radiotherapy (RT) with HIMAC has been conducted since 1994, and the accumulated number of patients treated exceeded 7,500 in July 2013. On the basis of the HIMAC experience, NIRS developed a compact carbon-ion RT facility in order to boost the carbon-ion RT in Japan, and a pilot facility of this work was constructed and conducted at the Gunma University. Toward the further development of the HIMAC treatment, further, NIRS has developed the new treatment technologies such as a fast 3D rescanning with a pencil beam and a compact rotating gantry, which will boost the heavy-ion RT in the world.

INTRODUCTION

Heavy-ion beams are very suitable for deeply-seated cancer treatment not only due to their high dose localization around the Bragg peak, but also due to the high biological effect in this region. NIRS, therefore, decided to construct HIMAC [1]. The HIMAC facility was completed in October 1993 as the world’s first heavy-ion accelerator facility dedicated to medical use. The HIMAC treatment chose a carbon-ion, based on the fast-neutron RT experience at NIRS and has employed a single beam-wobbling method as a beam-delivery method because it is robust toward beam errors and offers easy dose management. NIRS has conducted the HIMAC treatment since 1994. The protocols were significantly increased after the respiratory-gated irradiation method was developed for the moving-tumor treatment. As a result of the accumulated numbers of protocols, in 2003, the Japanese government approved the carbon-ion radiotherapy with HIMAC as a highly advanced medical technology. Therefore, NIRS proposed a standard carbon-ion RT facility in Japan [2] in order to boost applications of carbon-ion RT, with emphasis being place on a downsized version so as to reduce cost. The design study and R&D works for the proposed facility had been carried out during two years since 2004. The fruits of this work were realized in the Gunma University, which has been conducted since 2010.

NIRS, further, has been engaged in a “new treatment research project” [3] since April 2006 for the further development of HIMAC treatments. One of most important purposes in this project is to realize an “adaptive cancer radiotherapy”, which can accurately treat tumors even with changing size and shape during a treatment period. A 3D scanning method with a pencil beam has been well known to be very suitable for the adaptive cancer RT. Since both the static and moving tumors should be treated in NIRS-HIMAC, a fast 3D rescanning with the gated irradiation [4] was proposed to move toward the goal of adaptive cancer RT. On the basis of this technology, the new treatment research facility was constructed. The facility, which is connected with the existing HIMAC accelerator complex, has three treatment rooms: two rooms equipped with both horizontal and vertical beam delivery systems, while one room with a rotating gantry. As the first stage, one of the treatment rooms has been opened for the pencil-beam 3D scanning since May 2011, utilizing an energy degrader for slice change. As the second stage, the second room has been also operated since September 2012. In this stage, the hybrid energy scanning with eleven energy steps of the synchrotron has been applied toward more accurately treatment. Owing to opening the new treatment rooms, the annual treatment number was considerably increased, as shown in Fig. 1, although the annual treatment number in 2011 was reduced because of the big earthquake effect. The respiratory-gated 3D rescanning with the pencil-beam is scheduled in 2013 for the moving-tumor treatment. As the third stage, a compact heavy-ion rotating gantry, which will be installed in the third room, has been developed with the superconducting technology toward the completion after two years, in order to realize the intensity modulated carbon-ion RT (IMCT) combined with the pencil-beam 3D scanning for the more accurate and shorter-course treatment.

The recent progress of HIMAC for the heavy-ion cancer RT is reported.

Fig. 1: Annual treatment number with HIMAC from June 1994 to March 2013.
PROGRESS OF BROAD-BEAM THEOD

The carbon-ion RT has required a 3D uniform field with several% of the uniformity on a tumour, while dosage in normal tissue as low as possible. For the purpose, the beam-delivery methods have been developed as well as the accelerator technology. The HIMAC beam-delivery system has employed a single beam-wobbling with ridge filter method, which is one of the broad beam methods, in order to deliver its dose safely and reliably. The broad-beam method in HIMAC has been progressed in order to improve the irradiation accuracy: they are the respiratory-gated irradiation and layer stacking methods.

Respiratory-gated irradiation method

Damage to normal tissues around tumour was inevitable in treatment of a tumour moving along with a patient’s respiration. Therefore, a respiratory-gated irradiation system with the broad-beam method was developed [5]. In this scheme, an infrared-LED sensor is set on the surface of patient body and its movement is monitored by a position sensitive detector, which results in obtaining a respiratory signal. The beam should be delivered according to the gate signal produced only when the target is in the design position. A key technology, therefore, is a beam-extraction method from synchrotron for this scheme. For the purpose, NIRS developed the RF-KO slow extraction method [6] which can switch the beam on/off within 1 ms respond to respiration. This scheme, as shown in Fig.2, has been successfully applied since 1996.

Layer-stacking irradiation method

In a conventional beam-wobbling 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 developed [7]. A schematic drawing of this method is shown in Fig. 3. This method is to conform a variable SOBP to a target volume by controlling dynamically the conventional beam-modifying devices.

The thin SOBP with several mm in WEL (Water Equivalent Length), which is produced by a single filter, is longitudinally scanned over the target volume in a stepwise manner. The target volume is longitudinally divided into slices, to each of which the small SOBP is conformed using the MLC (Multi Leaf Collimator) and the range shifter, and a variable SOBP coinciding to the target volume is to be formed. This method has been utilized routinely since 2004.

STANDARD CARBON-ION RT FACILITY

For wide spread use of carbon-ion RT in Japan, NIRS designed a standard carbon-ion RT facility, which was a downsized version of the HIMAC facility, in order to reduce the construction cost. NIRS, further, developed the key-technologies for the facility from 2004 and 2005. GHMC (Gunma university Heavy-ion Medical Center), in collaborating with NIRS, had constructed a pilot facility of standard carbon-ion RT facility since 2006, which can be downsized to one-third compared with the HIMAC facility. Treatments with the pilot facility have been successfully carried out since March 2010.

Pilot facility

Considering the clinical statistics accumulated for more than ten years with HIMAC, specifications such as residual range, maximum beam energy and irradiation-field size were determined so as to cover the HIMAC treatments [2].

The maximum residual range was designed to be 25 cm. The residual range depends not only on the beam energy, but also on the forming method of a lateral irradiation field. When the range loss mainly due to scatterer can be suppressed to less than 2.5 cm, carbon ions with energy of 400 MeV/n, corresponding to a 27.5 cm range in water, have a residual range of 25 cm. For the purpose, the spiral beam-wobbling method was developed [8]. The maximum energy, thus, was determined to be 400 MeV/n. On the other hand, the minimum energy was determined to be 140 MeV/n for eye melanoma treatment.

A field diameter of 22 cm and an SOBP of 15 cm can cover almost all types of patient treated with HIMAC. A larger field size of more than 20 cm has been required.
mainly for the treatment of oblong tumors. In such cases, it is important to maintain the field length rather than the diameter. The SOBP size should be changeable from 4 to 15 cm.

The dose rate is required to be 5 GyE/min/l, as same as that at HIMAC. The dose rate corresponds to an intensity of $1.2 \times 10^9$ pps, extracted from the synchrotron by assuming a beam-utilization efficiency of 30% at the beam-delivery system. According to the beam-intensity schedule for the standard facility, the synchrotron requires a $C^{6+}$ intensity of more than 200 e$\mu$A from the injector linac cascade, and the ion source should provide a $C^{4+}$ beam with an intensity of more than 260 e$\mu$A.

An annual treatment number requires to be more than 600 patients for an economical reason. Considering the daily treatment hours of 6, the occupancy time of one treatment of 25 min and annual working days of 240, the annual session number per room is estimated to be around 3400/year. Since the average fraction number is 14 at HIMAC, the annual treatment number per room is estimated to be 250. Finally, it is found that the facility requires three treatment rooms in order to treat more than 600 pts/year. Further, the ratio of the treatment frequency with the horizontal irradiation port (H-port) to that with the vertical one (V-port) is around 5:4. Therefore, the three treatment rooms should be equipped with H-port, V-port and H&V-ports.

The specifications of the standard carbon-ion RT facility in Japan are summarized in Table 1.

<table>
<thead>
<tr>
<th>Ion Species</th>
<th>Carbon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy</td>
<td>400 – 140 MeV/n</td>
</tr>
<tr>
<td>Range/SOBP/Lateral-Size</td>
<td>250/40-150/220mm</td>
</tr>
<tr>
<td>Max. Dose Rate</td>
<td>5 GyE/min/l</td>
</tr>
<tr>
<td>Beam Intensity</td>
<td>$1.2 \times 10^9$ pps</td>
</tr>
<tr>
<td>Treatment Room</td>
<td>3: H&amp;V, H, V</td>
</tr>
<tr>
<td>Irradiation Method</td>
<td>Gating/Layer Stacking</td>
</tr>
</tbody>
</table>

The pilot facility has an ECR ion source, an RFQ and an APF-IH linac cascade, a synchrotron ring, three treatment rooms and one experimental room for basic research. In this pilot facility, a $C^{4+}$ beam, which is generated by a compact 10-GHz ERC source [9], is accelerated to 4MeV/n through the injector cascade consisted of the RFQ and APF-IH linacs [10]. After the $C^{4+}$ beam is fully stripped by a thin carbon foil, the $C^{6+}$ beam is injected into the synchrotron through the multi-turn injection scheme and is accelerated up to a maximum of 400 MeV/n. All magnets in the beam transport lines are made of laminated steel in order to permit a change in the beam line within one minute. The beam-delivery system employs a spiral beam-wobbling method for forming uniform lateral dose distribution with a relatively thin scatterer.

### Additional projects

Following the pilot facility at GHMC, two additional projects for carbon-ion radiotherapy have been constructed in Japan: The Saga-HIMAT (Saga Heavy Ion Medical Accelerator in Tosu) project and the Kanagawa Prefectural one.

The Saga-HIMAT project [11] has constructed a carbon-ion RT facility since February 2010, based on the GHMC-facility design, and it will be opened in August 2013. Although this facility has three treatment rooms, two of them will be opened with the spiral beam-wobbling method as the first-step operation: the one will be equipped with both the horizontal and vertical beam delivery systems, while the other with both the horizontal and 45-degree beam delivery systems. As the next step, the third room will be opened, using both the horizontal and vertical beam delivery systems with the fast 3D rescanning method developed by NIRS. The bird’s eye view is shown in Fig. 4.

![Fig. 4: Bird's eye view of the Saga-HIMAT](image)

The Kanagawa Prefectural Government has constructed the carbon-ion RT facility as i-ROCK (Ion-beam Radiation Oncology Center in Kanagawa) project in the Kanagawa Prefectural Cancer Center. Although the accelerator system is designed based on the GHMC-facility design, the beam-delivery system has employed the NIRS scanning design as described in the next section. The installation of devices will be started from January 2014, and the first treatment is scheduled in 2015.

### NEW TREATMENT RESEARCH PROJECT

#### New treatment research facility

The technologies developed by the new treatment research project, which has been progressed since 2006, should be finally verified by the clinical study. Therefore NIRS constructed the new treatment research facility, which is connected with the existing HIMAC accelerator. In the treatment hall, placed beneath the facility, three treatment rooms are prepared in order to treat more than...
800 patients per year. Two of them are equipped with fixed beam-delivery systems in both the horizontal and vertical directions while the other one is equipped with a rotating gantry. Two treatment-simulation rooms are also prepared for patient positioning as a rehearsal place, and for observing any changes of target size and shape with x-ray CT during the entire treatment. Furthermore, six rooms are devoted to patient preparation just before irradiation. A bird’s eye view of the new treatment facility with the HIMAC is shown in Fig. 5.

Fig. 5: Bird’s eye view of the existing HIMAC and new treatment research facility

In order to carry out the clinical study in a manner identical to the existing HIMAC treatment, the residual range should require more than 25cm. Thus, the maximum ion energy is designed to be 430MeV/n in the fixed beam-delivery system, corresponding to the residual range of 30cm in a carbon-ion beam and that of 22 cm in an oxygen-ion beam. The maximum lateral-field and SOBP sizes are 22cm × 22cm and 15cm, respectively, in order to cover all treatments with the HIMAC. The rotating gantry system employs a maximum energy of 430MeV/n, a maximum lateral-field of more than 18cm × 18cm and a maximum SOBP size of 15cm.

**Phase-controlled rescanning method**

The project has required a pencil-beam 3D scanning method for a static target, a moving target and/or a target near to critical organs, toward the adaptive cancer therapy. For this purpose, we have proposed phase-controlled rescanning (PCR) with a pencil-beam [4]. In the PCR method, rescanning completes irradiation on one slice during one gated period. Since the movement of the target is close to “zero” on average, we can obtain a uniform dose distribution even under irradiation on the moving target. The PCR method requires mainly two technologies: 1) Intensity modulation technique for a constant irradiation time on each slice having a different cross section and 2) Fast pencil-beam scanning technique for completing several-times rescanning within a tolerable time.

1) **Intensity modulation**

We have developed a spill control system [12] in order to deliver the beam with intensity modulation, based on the improvement of the RF-KO slow extraction method. The core part of this system requires the following functions: (1) calculation and output of an AM signal according to request-signals from an 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.

2) **Fast 3D scanning**

For the fast pencil-beam 3D scanning, three key-technologies were developed as follows: (a) new treatment planning for raster scanning, (b) extended flattop operation of the synchrotron, and (c) high-speed scanning magnet.

1) **New treatment planning [13]**

Raster-scanning has been employed, instead of spot scanning, in order to save the beam-off period during spot-position movement. In the raster scanning method, on the other hand, it is inevitably necessary to deliver an extra-dose to the position between the spot-positions. It should be noted that the extra-dose is proportional to the delivered intensity. Owing to the high reproducibility and uniformities in the time structure of the extracted beam through the spill control system, we can predict the extra-dose and incorporate its contribution to the treatment planning. Consequently, we can increase the beam intensity, which results in the shorter irradiation time.

2) **Extended FT operation**

Owing to a high beam-utilization efficiency of around 100% in the scanning method and to an intensity upgrade to $2 \times 10^{10}$ carbon-ions, we can complete the single-fractional irradiation of almost all treatment procedures in a single-operation cycle of the synchrotron. This single-cycle operation, which can be realized by using a clock-stop technique in the flattop period, can increase the treatment efficiency especially for the respiratory-gated irradiation. Thus we have proposed the extended flattop operation of the synchrotron. In this operation mode, the stability of the beam was tested, and it was verified that the position- and profile-stability were less than ±0.5mm at the iso-center in more than 100 s of the extended flattop operation. This extended flattop operation can shorten the irradiation time by a factor of 2.

3) **High-speed scanning magnet**

The scanning speed is designed to be 100mm/ms and 50mm/ms in the horizontal and vertical directions, respectively, which are faster by around one order than that in the conventional one. In order to increase the scanning speed, we designed a scanning magnet having slits in both ends of the magnetic poles, according to thermal analysis, including an eddy-current loss and a hysteresis loss. The power supply of the scanning magnet was designed for fast scanning, and this consists of two
stage circuits; the first stage for voltage forcing by IGBT switching elements and the second stage for the flat-top-current control by FET switching ones. As a result of the test, the temperature rise was measured to be around 30 degrees maximum, which is consistent with our thermal analysis.

Experimental study

A test irradiation port for the fast raster-scanning experiment was designed and constructed in order to verify the design goal, which is the same configuration as the fixed beam-delivery system adapted to the new treatment research facility. Using this test port, it was verified for the proposed technologies to give the physical dose distribution for both the static and moving targets [14,15] and the survival curve of HSG cell line, as designed.

Clinical study

After the pre-clinical study using the beam-delivery system in the new treatment research facility constructed, the clinical study has been conducted since May 2011. In the first year, one of treatment rooms in the new facility opened for 11 patients from May to July 2011. In this stage, the irradiation areas of all patients were verified by PET imaging with the auto-activation method. After preparing the second room, as the second stage, 121 patients were treated in a half day operation of two rooms from September 2012 to March 2013. In this stage, we applied the hybrid energy scan for slice change. In this scheme, eleven-step energies are changed by the synchrotron itself [16], while smaller change of beam energy by thin energy absorbers.

In the fall or the winter 2013, the respiratory-gated irradiation with the pencil-beam 3D scanning is scheduled for the moving-tumor treatment.

Future plan

As the third stage, a compact heavy-ion rotating gantry [17], which will be installed in the third room, has been developed with the superconducting technology toward the completion after two years, in order to realize the intensity modulated carbon-ion RT (IMCT) combining with the pencil-beam 3D scanning for the more accurate and shorter-course treatment. A design key is to use combined-function superconducting magnets, thus allowing us to design a compact rotating gantry. Having optimized the layout of the gantry as well as the beam optics, the length and radius of the gantry should become approximately 13 and 5.5 m, respectively, which are comparable to those for proton gantries. This rotating gantry has ten superconducting magnets. In 2012, two of them were completed. Both the mechanical movement and excitation-level change tests were already carried out. The experimental results are in good agreement with the expected ones. At present, the field measurement has been being carried out. Within two years, this rotating gantry will be completed and will be initiated the clinical study after pre-clinical study.

Fig. 5: Image view of the rotating gantry.

REFERENCES