ACCELERATOR DEVELOPMENTS FOR CANCER THERAPY

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Abstract

Japanese accelerator developments in heavy-ion cancer therapy can trace its history back to the R&D studies of NUMATRON project, which was proposed for nuclear physics research in the mid 1980s. As a direct extension of these studies, the world's first dedicated heavy-ion synchrotron, Heavy Ion Medical Accelerator in Chiba, HIMAC, was constructed in the beginning of the 1990s. Systematic clinical studies with carbon beams show excellent results even for radio-resistive cancers such as sarcomas on bones and soft tissues. Based on the success of HIMAC, a newly designed carbon therapy facility has been constructed at Gunma University and will open up a new era of the carbon therapy.

INTRODUCTION

There are a variety of accelerators used in cancer therapy, such as electron linacs in conventional photon therapy, PET cyclotrons, and synchrotrons and cyclotrons in charged-particle therapy. In this paper, I will restrict to the accelerators mainly used in carbon therapy in Japan.

In the early stage of this field, the basic research on cancer therapy had been performed using high-energy cyclotrons constructed for nuclear physics research. RIKEN has been one of the most active laboratories of this field.

In 1979, the first proton treatment was initiated at NIRS with 70 MeV cyclotrons for eye melanoma. Four years later, proton therapy for deeply seated cancers was initiated with KEK-booster synchrotron by a Tsukuba University Group. In 1994, carbon therapy was initiated with HIMAC at National Institute of Radiological Sciences, NIRS. The success of the cancer treatment with HIMAC stimulated radiation therapeutists, and many particle therapy facilities have been constructed in Japan. Now we have seven working therapy facilities in Japan, whereas we had only 30 therapy facilities working in the world at the end of last year. Seven of the 30 facilities are located in Japan, and five of the seven Japanese facilities are using protons for the therapy, one is using carbon ions, and the last one at Hyogo Prefecture can provide both protons and carbons.

A new carbon therapy facility was put into operation in March 2010 at Gunma University, three more proton facilities are now under construction, and two more carbon facilities are now in detailed design stage; so, we will have a total of 13 particle therapy facilities in Japan by the end of the fiscal year 2015. The rapid increase in the number of facilities is mainly due to the excellent dose localization of the particle beams. Figure 1 shows the depth-dose curves for various radiations in water. The dose distribution of X-ray shows a broad peak near the surface, and then it exponentially decreases. The carbon ions, on the other hand, make a very sharp peak called the Bragg peak at the end of their paths. Protons form a similar Bragg peak having a rather broad width due to the multiple Coulomb scattering with atoms in water.

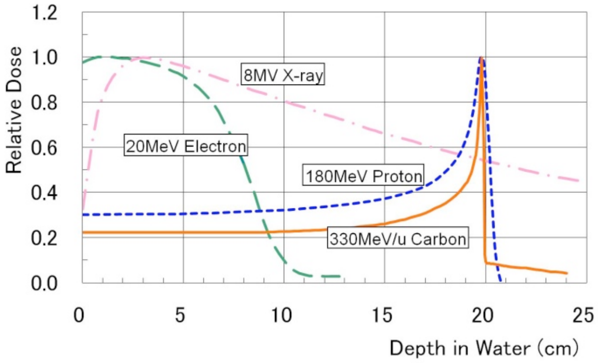


Figure 1: Dose distribution of various radiations.

In transverse directions, the boundary of the irradiated particle beam becomes obscure at the end of its trajectory mainly due to multiple scattering. Since the effects of multiple scattering are more serious for lighter ions, the boundary of the irradiated area is clearer for carbon ions than for protons. The dose distribution of carbon ions will be much better than that of protons both in the axial and transverse directions.

In order to realize a carbon therapy facility having the excellent characters described above, researches on heavy ion accelerators have been carried out in Japan. In this paper, a brief history of accelerator developments in cancer therapy is described.

NUMATRON PROJECT

The NUMATRON project[1] is the origin of Japanese developmental studies on heavy-ion synchrotrons for cancer treatment. NUMATRON is the abbreviation for the NUclear MAtter TRON and was proposed to study the characteristics of high-temperature and high-density nuclear matter in the middle of the 1970s. The basic researches on cancer treatments with high-energy heavy ions were also included in the project. The design and the R&D studies on the accelerator had been performed by the Institute for Nuclear Study, University of Tokyo, since 1976.

Figure 2 indicates a layout of the NUMATRON accelerator complex; it has a big injector linac, a storage ring to accumulate low-intensity heavy ion beams, and a synchrotron ring to accelerate heavy ions up to a relativistic energy of 670 MeV/u. A variety of R&D studies were performed on the injector linacs, accumulator ring, and other components of the accelerator complex.

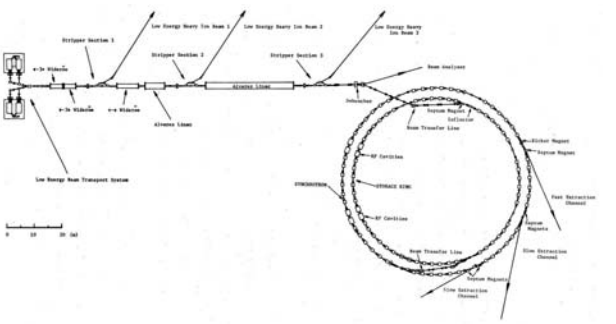


Figure 2: NUMATRON was designed to accelerate heavy ions such as Uranium ions up to 670 MeV/u.

In the R&D studies, a Test Accumulation Ring for Numatron, TARN[2] was constructed to study the technical feasibility of the accumulator ring. The injector was an existing sector-focused cyclotron used in studies of nuclear physics. The vacuum pressure of the ring is required to be better than 10^{-11} Torr. To increase the circulating beam intensity, we adopted the multi-turn-injection plus RF-stacking method as an injection scheme. For further acceleration, we introduced a stochastic cooling system for momentum cooling. A photograph of TARN is shown in Fig. 3.

Figure 3: Test accumulation ring for NUMATRON, TARN.

We have another round of studies for injector developments. Figure 4 shows the world's first heavy-ion RFQ linac, Lithium Ion Test Linac, LITL[3] constructed in 1982. This linac adopted a single-loop coupler for high-power coupling, and after LITL, this coupling system has become the standard for the RFQ linac. And then, we constructed the world's longest RFQ linac, TALL, whose vane length is 7.2 m. We introduced inductive block tuners to tune the gap voltage distribution along the beam axis. The LITL[4] is shown on the right-hand side of Fig. 4, and TALL is on the left.

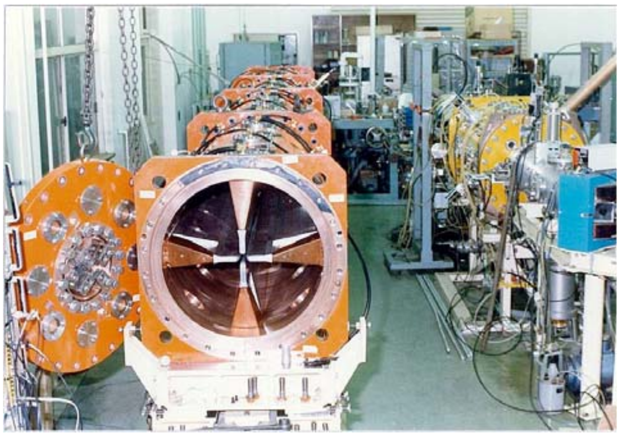


Figure 4: World's first heavy-ion RFQ linac LITL on the right and world's longest RFQ linac TALL on the left.

In 1985, we constructed a synchrotron, TARN2, which accelerates protons up to 1 GeV, as the final R&D studies of the NUMATRON project. The mean radius of the synchrotron ring is 12 m, and the vacuum is also better than 10^{-11} Torr. A layout of TARN2 is given in Fig. 5.

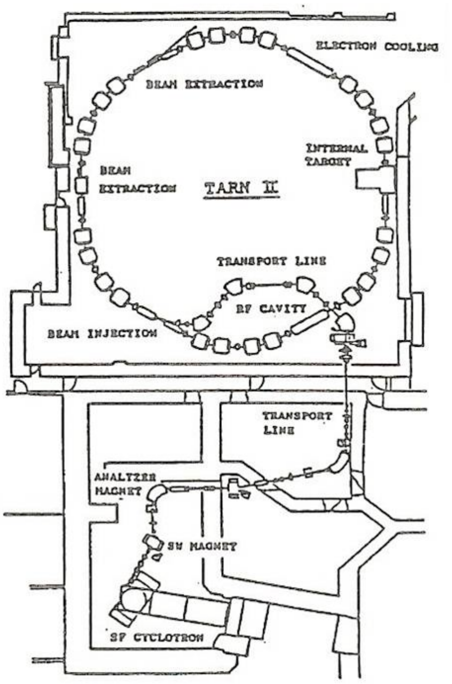


Figure 5: Layout of the TARN2 synchrotron.

The TARN2 synchrotron was designed to accelerate heavy ions, and we need an RF acceleration cavity having a very wide frequency range of 0.6 to 7.5 MHz. As the extraction method, we adopted an RF knockout method; this is very powerful in switching the beam on and beam off within a very short time of around 1 ms. We adopted an electron cooling system to reduce the momentum spread of the circulating beams. In Fig. 6, a ferrite-loaded RF cavity having a wide frequency range is shown. A photograph of the NUMATRON accelerator group members is given in Fig. 7.

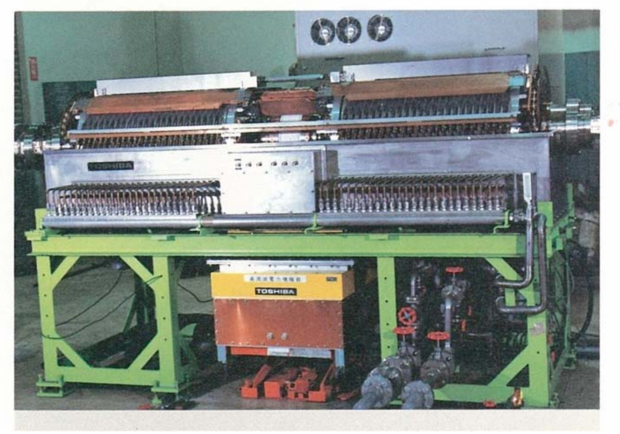


Figure 6: RF cavity with a wide frequency range of 0.6 to 7.5 MHz.

Figure 7: NUMATRON accelerator group members.

MEDICAL SYNCHROTRON HIMAC

On the basis of the R&D studies on the NUMATRON accelerator, a heavy-ion medical synchrotron, HIMETRON, has been proposed by the INS group. In 1985, National Institute of Radiological Sciences, NIRS, started the conceptual design study of Heavy Ion Medical Accelerator in Chiba, HIMAC[5], in collaboration with INS. NIRS organized a study group for this purpose including the INS group and the four private companies, Mitsubishi Electric, Hitachi, Toshiba, and Sumitomo Heavy Industries. The construction of the HIMAC was started in 1988 and was completed in 1993.

A layout of HIMAC is given in Fig. 8. The accelerator consists of three different types of ion sources, an RFQ linac with 7 m length, a 25-m-long Alvarez type linac, a pair of synchrotron rings, and a beam transport system. We have three treatment rooms having a horizontal beam port, a vertical beam port, and both horizontal and vertical beam ports to a single iso-center. HIMAC can accelerate ions ranging from protons to xenon ions. The maximum energy is designed to be 800 MeV/u for light ions with a charge-to-mass ratio greater than 1/2. The maximum range in water is designed to be 30 cm for silicon ions.

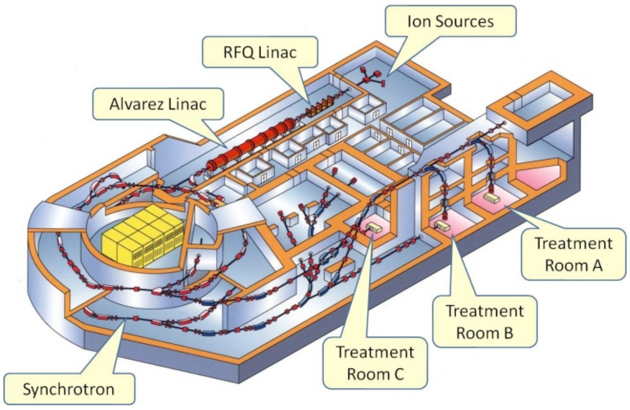


Figure 8: A layout of HIMAC.

Figure 9: HIMAC Synchrotron.

For HIMAC, we adopted a PIG-type ion source[6] and a 10 GHz ECR source[7] developed by the NIRS people. With these two different types of ion sources, we can produce heavy ions from protons to argon ions. To accelerate heavier ions, such as iron, krypton, and xenon ions, we added a 18 GHz ECR source. As injector, a conventional four-vane-type RFQ linac and a very big Alvarez-type drift tube linac were adopted. Both linacs are operated at 100 MHz, and the diameter of the drift tube linac exceeds 2 m[8].

In Fig. 9, a part of the synchrotron ring is given. The average diameter of the ring is about 40 m, and a ferrite-loaded RF cavity having exactly the same size and structure of an RF cavity is installed in the ring.

Figure 10 shows the indications for carbon therapy. There are lots of organs treated by carbon ions, for examples, the brain and skull base, head-and-neck region, eye, lung and liver, pancreas, rectum, prostrate and uterus, and bone and soft tissues.

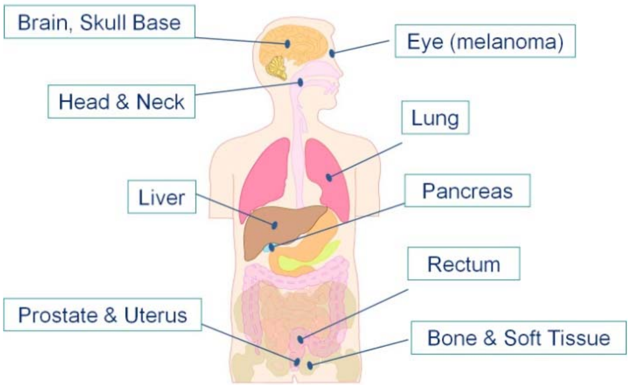


Figure 10: Indications for carbon therapy.

After more than 5,000 clinical experiences at HIMAC, carbon ions show excellent characteristics in cancer therapy: (1) the excellent dose localization reduces the side effects appreciably, (2) we can reduce the number of the fractionation without increasing the side effects and risks of reoccurrence, and (3) carbon therapy is effective for some kind of radio-resistive cancers such as bone and soft-tissue sarcoma.

GUNMA MODEL

Through systematic clinical studies with HIMAC, the carbon ions are recognized to be effective for curing deeply seated human cancers. The high construction and operation costs of facilities, however, are the big obstacles in the wide use of the carbon therapy. So, R&D studies have been carried out at NIRS to obtain a cost-effective design of carbon therapy facility[9]. Gunma University has been collaborating on these R&D studies since 2004.

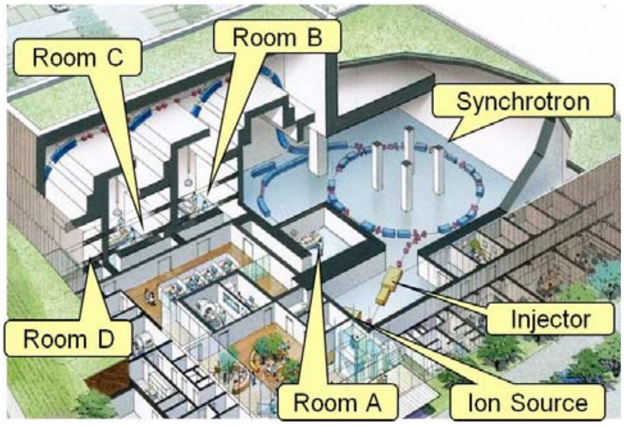
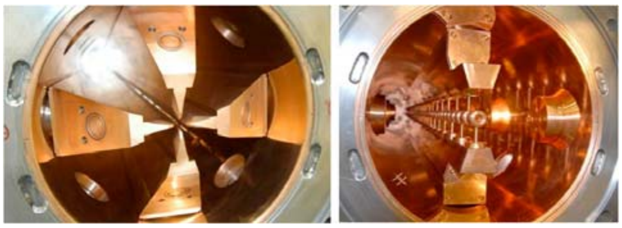


Figure 11: Cut-away view of Gunma University Heavy Ion Medical Center. Rooms A, B, and C are used for cancer treatment and Room D is being prepared for future developments.

A wide variety of R&D studies include ion source and injector developments. On the basis of these studies, Gunma University had initiated the construction of a new carbon facility at Maebashi in 2007. The facility is the first example of the new cost-effective design in hospital environments. Figure 11 shows a cut-away view of the Gunma-University Heavy-ion Medical Center, GHMC. We have three treatment rooms in the facility, and a fourth irradiation room is being prepared for basic experiments in physics and biological fields. The size of the building is 45×60 m^2, whereas HIMAC building is as large as 65×120 m^2.

(a)



(b) (c)

Figure 12: (a) Injector linacs and ion source. (b) The inside view of the RFQ linac. (c) The inside view of the IH linac.

The ion source is a permanent-magnet-type ECR source[10], and it generates carbon 4+ ions with more than 250 eμA. An injector[11] consists of a four-vane-type RFQ and Interdigital-H-type linear accelerator with Alternating Phase Focusing. Both linacs are operated in 200 MHz and use the RF field both for beam acceleration and beam focusing. Since we do not need any extra focusing elements in the cavities, the injector is very easy to handle and works stably. The output energy of the injector is determined to be 4 MeV/u so that a charge stripping efficiency from carbon 4+ to 6+ exceeds 90% at the end of the IH linac. The maximum surface field is adopted at rather low value of 1.6 Kilpatrick to reduce the risks of sparking problem. A photograph of the injector and the ion source is shown in Fig. 12.

The lattice structure of the synchrotron is conventional FODO-type[12] and the circumference of the ring is 63 m. Fully striped carbon ions are injected into the ring by a multi-turn injection method. The pulse length of the injected beam can be varied by a chopper system in the injector. We can form a circulating hollow beam by tuning the timing and time duration of the pulse length in order to reduce the tune shift caused by space-charge effects at a rather low injection energy of 4 MeV/u. The synchrotron accelerates carbon ions up to an energy ranging from 160 to 400 MeV/u. A slow beam-extraction technique using 1/3 resonance is adopted. The maximum bending field is designed to be 1.5 T. The weight of each bending magnet is about 8 t, and the total weight of the ring magnets is about 150 t. An overview of the synchrotron is given in Fig. 13.

Figure 13: Synchrotron ring with a circumference of 63 m.

We adopted the Wobbler technique to form a wide uniform irradiation field of 15 cm^2, because the requirements for the properties of the extracted beams are not so tight. The details of the beam-shaping technique in the beam delivery system are out of the scope of this paper. In Fig. 14, the inside view of the treatment room B is shown.

Figure 14: Inside view of the treatment room B.

Usually, the therapy accelerator is switched on in the morning and switched off in the evening; so, the start-up time of the therapy accelerator is a very important parameter. Now, we realized 1 h for the start-up time, but we would like to reduce this time to 30 min. The time required for changing synchrotron energy and switching a treatment room to the next should be less than 3 min, and this has already been realized. The reproducibility of the beam intensity and beam position is expected to be better than 10% and 0.5 mm, respectively, without any tuning, and this has also been realized. So, the short scheduled shutdown time is 4 weeks per year in the early stage, and maybe a few years later, we will not need any scheduled shutdown time. This is desired to increase the number of treated patients.

In February 2007, the construction of the Gunma facility was initiated. The building was completed in October 2008. We started the accelerator commissioning in August 2009. In March 2010, we accepted the first patient. From June, we started the charged treatment. The carbon treatment costs about 3 million yen.

New plans for carbon therapy facilities are going on especially in Europe and East Asia. The success of the Gunma facility is expected to open up a new era of charged-particle therapy.

ANOTHER APPLICATION OF HEAVY-ION BEAMS

The ion-beam plant-breeding performed by RIKEN group is another successful application of heavy-ion beams. When heavy ions are irradiated on biomedical cells, the DNA ladder in the nucleus gets damaged by heavy-ion irradiation. When the damage is serious, the biological cells will be killed by the irradiation. But when the damage is not so serious, a part of the characteristics of the cells can be changed. This is an example of such a case: by the irradiation using the heavy-ion beams, the color of flowers can be changed. In Fig. 15, some examples of new colors of flowers in the market are given.

Figure 15: Examples of commercial cultivars produced by ion-beam breeding (data provided by RIKEN).

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