Development of Accelerators for Medical Applications at SAMEER

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Dr. Tanuja Dixit is working on accelerator related R&D at SAMEER since 1997. She also took up advanced studies at High Energy Accelerator Research Organization (KEK), Japan and obtained her Ph.D. in 2008. She played a crucial role in establishing the 6 MeV linac technology for cancer therapy. Her area of expertise is electron gun and target design. At present, she is working towards the development of 30 MeV linac for radio-isotope generation and the design of a novel compact Hadron Therapy machine capable of delivering any ion as well as fast dose delivery.

Dr. Abhay Deshpande is working on accelerator related R&D at SAMEER since 1997. He pursued higher studies at High Energy Accelerator Research Organization (KEK), Japan and was awarded Ph.D. in 2010 for the work done on RF photocathode gun. His main area of expertise is design of linear accelerators, RF injector and high gradient structures. Along with colleagues and collaborators he is working on novel accelerators for Cancer Therapy including the proposed All Ion Accelerator.

Shri. R. Krishnan is Head of Medical Electronics Division at SAMEER for past 16 years. He joined SAMEER at TIFR Campus in 1986. The focus of his work has been establishment of linac technology for medical and industrial applications. Under his leadership, the group has established 6 MeV Linac based radiotherapy and also the Kharghar facility for linac batch fabrication.

Abstract

Medical accelerators R&D is being carried out at SAMEER for a long time. The technology for 6 MeV Radiotherapy machine is well established and thousands of patients are treated at various hospitals, where these machines are installed. Based on the 6 MeV experience, R&D for higher energy and dual-mode medical linac was taken up and the key technologies involved were successfully demonstrated. Thereafter, electron beam of even higher energy of 30 MeV is targeted for radioisotope production, mainly ^{99m}Tc, for medical applications. The experience of medical accelerators has enabled us to take up the challenge of designing and developing a Hadron Therapy machine, based on all ion accelerator technology developed at KEK, Japan. Presently, only proton and carbon ion therapy machines are commercially available in the world. We propose to develop a hadron therapy machine capable of giving He, C, N, O, Ar ions, which are desired by the medical community. The key features of the machine are described here and a global comparison with current developments in hadron therapy is presented.

Introduction

Radiation therapy (RT) or radiotherapy is one of the effective treatments for cancer and is used for the treatment of various types of cancers for more than a century. The high energy X-rays or gamma rays from accelerators or radioactive sources are used to treat the deep-seated tumours by altering the growth and division of cancerous cells. After the discovery of X-rays in 1895 by W. C. Roentgen and of radium by Marie Curie in 1898, the application of radiation for treatment of cancer was possible. Many advancements took place during early 1910 till 1950s. This era was termed as the Orthovoltage era, where maximum energy achieved was in the range of few tens of kilovolts to hundreds of kilovolts. With the discovery of high-power RF sources during the second world war, compact high energy **lin**ear **ac**celerators (linac) were developed for industrial as well as medical purposes [1,2]. Subsequently, linacs delivering megavolt electron beams were developed, which provided deep penetrating X-rays. One of the problems with gamma-radiation is that the depth dose curve of photons has a large exit dose. On the other hand, protons and heavy ions provide a very sharp Bragg peak. The effectiveness of the Bragg peak in providing dose at an accurate location was well known to the medical community. Therefore, heavy ion therapy or hadron therapy trials began much earlier using research accelerators. Unfortunately, research facilities for the heavy ion accelerator require huge infrastructure and running costs. Hence, research and development for commercially viable and easy to use hospital-based machines have been in great demand. For proton therapy, cyclotrons proved to be the best option considering compactness, dose requirement for treatment and easy handling. For Carbon ion therapy, synchrotron is the present choice.

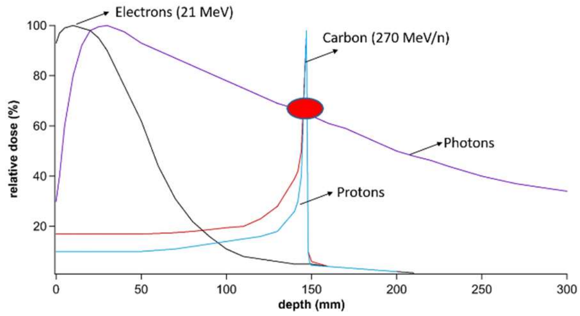

Figure 1: *Dose deposition curve*

It is important to know the accurate dose deposition profile to understand the various irradiation options available. Figure 1 shows the dose deposition profile of various particles as a function of depth in water. The red circle in the figure depicts the target volume (the tumour) which needs to be treated (irradiated). Electrons do not penetrate deep and lose most of their energy near the surface. Thus, a very low dose is given to the target volume. Therefore, electrons are useful for treating superficial tumours like skin cancer. High energy photons or X-rays deposit maximum dose at a certain depth depending on their energy and gradually lose this energy. A deep-seated tumour can be treated using high energy X-rays, but a significantly large dose is also delivered to the depth beyond the tumour. Proton and carbon ions deposit the dose at the desired location and a very small tail dose is delivered to the depth beyond it. Therefore, these ions are more suitable for cancers near critical organs like spinal cord, eye, brain or lungs. It is also very effective when treating paediatric cancers because of fewer side effects leading to a better life later. This advantage has given a boost to hadron therapy in recent years, when the acceleration of protons and carbon ions became feasible with easy-to-use accelerators in a hospital environment.

It is predicted that by 2020 there will be 1.6 million cancer patients in India and by 2040, the numbers will increase to 2 million [3]. The number of radiotherapy machines per million of the population is approximately 5 for western countries. This number reduces to 1 machine per million population for developing nations and for African countries the number falls to less than 1 [4]. There are 7345 radiation therapy centres worldwide with 14133 equipments, out of which 11945 are electron linacs. Others are radioisotope-based ^{60}Co therapy units. About 82 % of the worldwide radiotherapy machines deliver 6 MeV energy and are used to treat most types of cancers. Share of higher energy linacs providing both photons and electrons is 64 %. Over 104 installations are particle therapy accelerators, which provide hadron beams for patient treatment. The number of hadron machines is steadily increasing with the advancement of heavy ion therapy accelerators technology in the world.

Background of SAMEER

SAMEER, an offshoot of the Special Microwave Products Unit (SMPU) of Tata Institute of Fundamental Research (TIFR), was established in the year 1984 as an autonomous research and development laboratory under the Department of Electronics. Currently, it is an autonomous institution under MeitY (Ministry of Electronics and Information Technology) The main mission of SAMEER is to achieve excellence in application-oriented research in the areas of RF/Microwave/ Millimeter-wave Technology and Electromagnetics. SAMEER has 5 centres with head office at Mumbai and more details can be found at https://www.sameer.gov.in. At the Medical Electronics Division of SAMEER, R&D for a 4 MeV energy electron linac for cancer therapy was taken up in the late 1980s. An “S” band side coupled linear accelerator operating at $\pi/2$ mode was developed for electron acceleration. The linac was integrated with other subsystems in collaboration with CSIO and PGIMER and commissioned at PGI, Chandigarh in the year 1991. The machine was called Jeevan Jyoti-I and is shown in Figure 2 [5].

Figure 2: *Jeevan Jyoti: India's First indigenous Radiotherapy machine*

Table 1: *Medical machine parameters.*

Parameter	Single Energy	Dual Energy
Particles	Photons only	Photons and Electrons
Photon Energy	6 MV	6 & 15 MV Photons
Electron Energy	–	6, 9, 12, 15 & 18 MeV
Dose rate	300 rads/min at 1 m	500 rads/min at 1 m
Field size	0×0 to 35×35 cm with sharp corners	0×0 to 35×35 cm with sharp corners
Flatness	± 3 % at average dose of 80 %	± 3 % at average dose of 80 %
Iso-center height	134 cm	130 cm

Later under the Jai Vigyan (JV) initiative of the Government of India, six radiotherapy units were developed and commissioned in hospitals. JV machines, called Siddhartha, cumulatively treated more than 1.5 lakh patients at various centres till date. Treatment is ongoing at IIHNO, Indore and ACF Hospital, Amravati. The specifications of the Siddhartha Radiation Oncology machine are given in Table 1.

Linac for radiotherapy & isotope production

Linac is the source of electrons as well as X-rays. A schematic of a linac and the associated subsystems is shown in the block diagram in Figure 3.

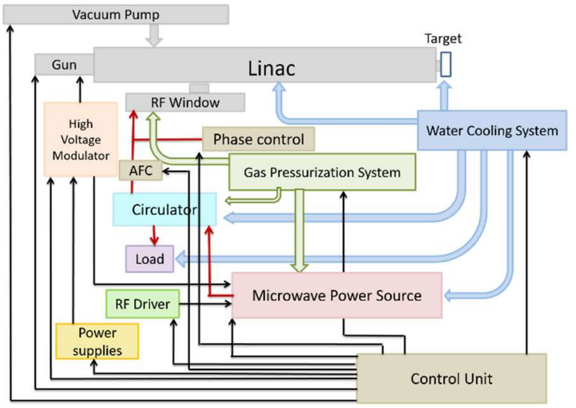

Figure 3: *Block diagram of a linac-based system*

Electrons are generated in the electron gun, where a cathode filament is heated by a low voltage AC supply. A voltage of ~20 kV is provided across the electron gun from a high voltage modulator, which provides initial acceleration to inject the electrons in the linac. The linac is made of RF cavities that generate high electric fields to accelerate electrons. RF power is provided to the linac from a microwave power source such as a Magnetron or Klystron depending on the energy. Generally, Magnetrons are used in low energy systems ($E < 6$ MeV) and Klystrons are used in systems delivering high energy ($E > 15$ MeV). Highly energetic electrons then impinge on the target made of high Z material to produce X-rays due to bremsstrahlung. SAMEER's 6 MeV linac is an S-band, bi-periodic structure, operating at $\pi/2$ mode at 2.998 GHz frequency as shown in Figure 4.

Figure 4: *6 MeV linac*

Electrons are produced in a Pierce type electron gun consisting of a dispenser cathode with emission current density of 1 A/cm^2. The focussed pulsed beam is injected with an energy of 20 keV from the gun.

The dominant mode responsible for the acceleration in the RF cavities is TM_{010}. The linac consists of a buncher and accelerating sections. The buncher section cavities are shorter in length and help in forming bunches of electrons with small relativistic β. Electrons become relativistic at $E \sim 1$ MeV and thereafter β remains nearly constant. At 2.998 GHz frequency, the wavelength (λ) is 10 cm and the length of the accelerating cavities is fixed accordingly. The accelerating structure is powered in pulsed mode with microwaves of 2.6 MW. The acceleration gradient achieved is 30 MV/m. Therefore, in accelerating structure length of 30 cm, 6 MeV energy gain is achieved. Electrons exiting from linac are bombarded onto a tungsten target to produce bremsstrahlung X-rays. The generated X-ray spectrum is continuous in nature, with maximum energy equal to the energy of electrons. Ultra-high vacuum is maintained inside the linac to minimize scattering of the electrons.

The high-power microwave side from RF source to the entrance of linac needs a proper insulating gas such as sulphur hexafluoride (SF_6) to avoid breakdown issues. Hence to separate the high pressure SF_6 region from the ultra-high vacuum side of linac, an RF window made of ceramic was designed and inserted. The RF window is designed in such way that it transmits microwaves across it without significant loss, while maintaining high pressure on one side and vacuum on the other side. Water cooling is provided to the entire structure to remove the heat dissipated in the cavities. During operation, with the insertion of RF power, residual outgassing takes place. Therefore, a small sputter ion pump with 8 L/sec capacity is provided. The pump also acts as an indicator of the vacuum level inside the linac.

After successful demonstration of patient treatment at various locations, it was decided to enhance the technology for dual photon energies 6 and 15 MeV from the same linac, along with multiple electron energies from 6 to 18 MeV for the treatment. The energy is varied by introducing a plunger in the coupling cavity in the acceleration section shown in Figure 5.

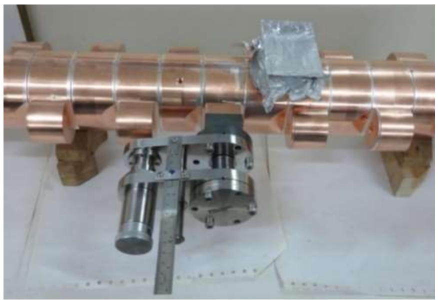

Figure 5: *Energy variation mechanism*

When plunger is inserted in the cavity, it detunes the cavity and RF power is no longer coupled to the adjacent cavity, thus providing only a section of length for the acceleration of electrons. The prototype of this novel dual-energy linac is already developed and tested at SAMEER [6]. This linac, with the possibility of multiple energies together with provision for both photons and electrons at the same location, will meet varied requirements of oncologists.

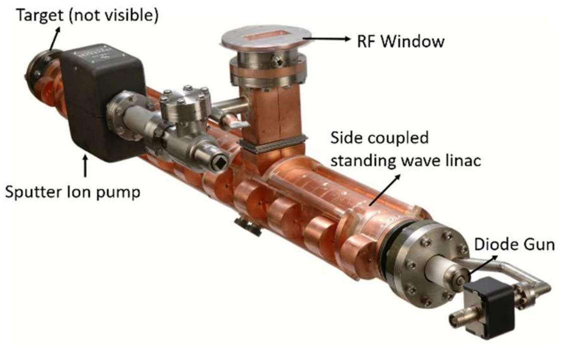

Figure 6: *15 MeV linac*

As a next application, a 15 MeV linac design, shown in Figure 6, is underway for the production of SPECT scan radioisotope ^{99m}Tc from ^{99}Mo. Usually, ^{99m}Tc is eluted from ^{99}Mo which comes from the reactor. In our proposal, the electron beam from 30 MeV, 5-10 kW linear accelerator will be used to produce high energy X-rays. These X-rays strike the target of enriched ^{100}Mo discs, knocking away a neutron to create ^{99}Mo with a half-life of 66.02 h, which decays to ^{99m}Tc [7]. The 140 keV gamma ray emitted by ^{99m}Tc is useful for imaging purpose in medical tests. As per the standard data reaction cross-section of (γ, n) peaks at photon energy of 14 -15 MeV up to 0.15 b. The 30 MeV electron linac is expected to produce sufficient photon flux of high energies in this range. The layout of the proposed radioisotope production setup is shown in Figure 7.

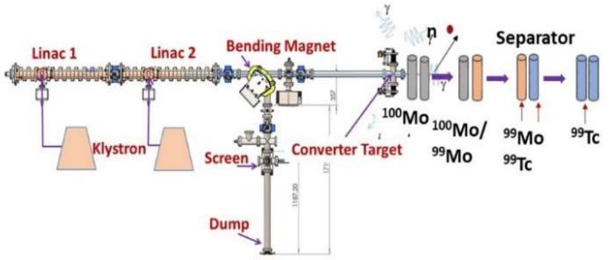

Figure 7: *30 MeV linac based radioisotope setup*

Proposal and design developments for Hadron Therapy Machine

Commercially available proton therapy machines are cyclotrons and synchrotrons from IBA, Hitachi, Sumitomo, Varian etc. In a cyclotron, the strength of the magnetic field and size of the magnet decides the available energy. Presently for cyclotrons the proton output energy is fixed around 250 MeV. Suitable energy degraders are used to vary the energy from 70 to 250 MeV during therapy, leading to large radioactivity near the degrader. In a synchrotron, the particle moves in a fixed path and the magnetic fields are ramped keeping up with the particle energy. In case of a synchrotron, an injector or a pre-accelerator is required to inject the beam in the main ring. Variable energy output can be achieved in a synchrotron by extracting beam at any point during acceleration. The beam transport line is a complex arrangement of magnets for transportation of beam from the extraction ports to the various treatment rooms and the experimental rooms. The gantry is a rotating arm which delivers the beam precisely to the patient from any direction. Normally, gantry for hadron machine is a huge mechanical structure which consumes a major chunk of funds from the facility budget. Linear accelerator option for heavy ion acceleration is becoming viable though the technology is still in the evolving stage. The linear accelerator-based hadron machine footprint will be very large compared to the circular accelerators. For example, 400 MeV/u carbon ions, the linac length required will be around 50 m [8], as compared to 20 m diameter of the synchrotron for similar energy.

In 2015, we proposed the development of carbon ion therapy machine based on a new concept of digital accelerators (DA). DA is basically a fast-cycling synchrotron with special beam handling capability based on induction synchrotron concept [9]. The induction synchrotron is a bunch feedback-based system. When a bunch of particles passes through a bunch monitor, it generates a trigger signal. The trigger signal fires a power supply to energize the induction cell. Induction cell then produces the required voltage for acceleration. Since there is no limit on the repetition of trigger signals, in principle, it is possible to accelerate any ion from very low energy to very high energy. As it is possible to inject particles at nearly 200 kV DC voltage directly into the main ring, the induction synchrotron does not need a separate injector [10,11]. Such an accelerator is also attractive for researchers in various fields. A cost-effective hybrid cancer therapy can be realized using a single DA, from which protons and carbon ions can be provided.

Concept design of the All-Ion Accelerator

A detail design of the *All-Ion Accelerator,* capable of accelerating a variety of ions with A/Q = 2 upto E ~ 400 MeV/A, aimed primarily for medical usage, is being prepared.

For the All-Ion Accelerator, a laser ablation ion source or an ECR ion source (ECRIS) can provide ions for acceleration in the ring. The ion source is embedded onto a 200-300 kV high voltage deck, and hence the ions are ejected into low energy beam transport line with an initial kinetic energy of QeV_{inj}, where Q is the charge state of ions, e is the electronic charge and V_{inj} is the injection voltage (deck voltage). The ring magnets can be designed to operate in a fast cycle mode with 10 Hz frequency. The maximum magnetic field required from bending magnets is ~1.5 T for the specified energy. The beam intensity expected is nearly 10^9 ions/sec. Various preliminary parameters are listed in Table 2.

Table 2: *Machine parameters.*

Parameter	Value
Energy	400 MeV/n for Carbon (*A/Q*=2)
Beam intensity	10^9 ions per second
Ion species	He, C, N, O, Ar
Ion source	Laser ablation ions source or ECRIS
Injection voltage	200-300 kV
Ring	Rapid cycling (10 Hz, B_{max}=1.5 T), Circumference~76 m, Dispersion free straight sections, large flat dispersion region for extraction, separate function
Acceleration	Induction cells using compact switching power supply using SiC-JFET
Vacuum	10^{-8} Pa, outgas free chamber
Extraction	Fast and slow
Injection	Single turn

The induction cell is a key device in the induction acceleration system. The choice of magnetic material, core component of the induction cell, is very important. Due to the high repetition rate, magnetic material with high permeability and low core loss is preferred. Therefore, Finemet®FT-3M is proposed to be used in the induction cell. It is a nano-crystalline alloy with very high relative permeability, $\mu \sim 10^4$.

The switching power supply is a kind of power modulator. It is capable of generating bipolar rectangular shaped voltage pulses. It works as a full-bridge circuit consisting of four identical switching arms and is energized by a DC power supply at a maximum rating of 2.5 kV at 20 A. The maximum switching frequency is limited due to the heat deposition problem in the switching elements. The maximum repetition rate of 1 MHz is achieved in the switching power supply developed at KEK. The bunch signals are processed in real time in Field Programmable Gate Arrays, FPGAs and Digital Signal Processor, DSPs. They generate the gate trigger signals for the switching power supply to produce pulse voltages. A master signal for the gate trigger signal is first transferred to an optical trigger unit and it is then divided into the necessary number of signals for the switching power supply. The timing of the generation of the voltage pulses in the induction cavity is controlled using feedback from the bunch monitor.

Lattice

The lattice is designed to deliver ions of 400 MeV/A with *A/Q* = 2. The magnetic rigidity, *Bρ,* is defined as

$$B\rho = \left(\frac{A}{Q}\right)\left(\frac{m}{e}\right)\gamma(c\beta) \tag{1}$$

where, *m* is the proton mass, *e* is the electronic charge, *c* is the velocity of light and *βγ* are Lorentz factors of ions. The magnetic rigidity for 400 MeV/A ions is 6.64 T-m. A FODOF lattice as per the required energy of ions is proposed with 76 m circumference, *C* and bending radius of 4.43 m. The lattice, as shown in Figure 8, is based on the PIMMS design studies done at CERN.

The magnets will be ramped in a fast cycle synchrotron mode shown in Figure 9 with a one complete acceleration period of 100 ms. The bunch is injected at the minimum field, B_{min}, calculated using Eq. 2.

$$B_{min} = \frac{1}{\rho c}\sqrt{\left(\frac{A}{Q}\right)\left(\frac{mc^2}{e}\right)V_{inj}} \tag{2}$$

As can be seen, the B_{min} depends on the energy of the injected particles and its mass to charge ratio is 0.027 T for *A/Q* = 2. Before the ramping of the magnet starts, the bunch is captured between the confinement voltages pulses till acceleration starts at time t_0. The acceleration induction cells are located at dispersion free region and extraction devices are located at the large flat dispersion region in the lattice.

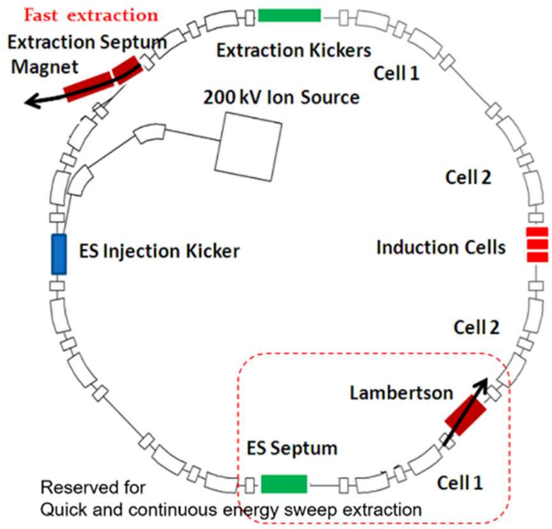

Figure 8: *Schematic of Lattice*

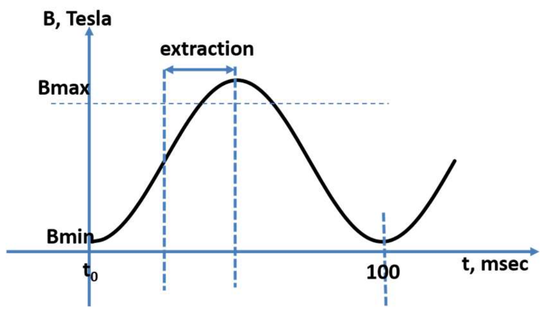

Figure 9: *Acceleration cycle*

Longitudinal scanning

In the proposed All Ion Accelerator when the barrier voltage movement is made non-adiabatic, some of the particles can leak from the barrier bucket. It is possible to extract these particles using a slow extraction method. This gives a continuous energy sweep of the extracted particles and the spilled particle numbers can be controlled by controlling the timing of the barrier voltages. This type of extraction mechanism, which gives continuous energy variation, is being proposed for the first time in a therapy machine [12]. The necessary devices to achieve this type of extraction are being developed. The continuous extraction of particles can be done over a wide time range beginning about ~25 ms after the start of acceleration till the final energy is reached.

This scheme is different from the present synchrotron operation where variable energy is achieved in different acceleration cycle by changing the maximum field of the bending magnets. Therefore, to get Spread Over Bragg Peak (SOBP), a depth is decided for irradiation and then the beam is raster scanned or spot scanned over the area. The longitudinal scanning proposed here is a new way of delivering the particles to the affected area as shown in Figure 10.

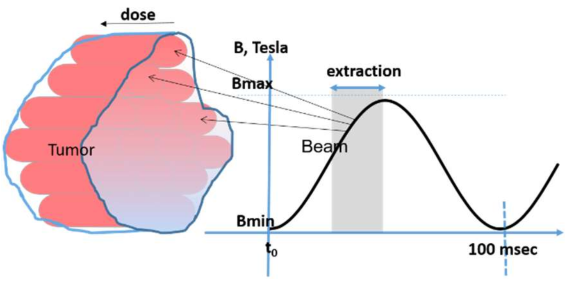

Figure 10: *Longitudinal Scan*

The treatment protocol existing today are based on the beam delivery method of the existing systems, therefore customization is inevitable. It is important to compare All Ion Accelerator with the ongoing research around the world to develop heavy-ion medical machine. The main requirement is to reduce the cost of the machine. As of now Carbon Therapy machine costs ~1000-1200 crore, which is a main deterrent in popularizing heavy ion therapy. Size of the machine is another criterion because of huge infrastructure requirement. Efforts are underway worldwide to overcome these issues. At CERN, with vast experience of designing LHC superconducting magnets, efforts to deploy superconducting magnets with a goal to reduce the footprint of the machine are pursued. The synchrotron design with fast and slow extraction possibility, upgraded injector section and multi-ion delivery beamlines are under design. Three options of a normal conducting synchrotron, superconducting synchrotron and linac based designs are under review as a part of the New Ion Medical Machine Study (NIMMS). The design undertaken by SAMEER-KEK, while similar in desired final features, is simpler as it does not incorporate superconducting magnets, thereby reducing both the cost and complexity. Fast dose delivery due to fast cycling operation, fast extraction, slow extraction with continuous energy variation, intensity control and multi-ion capability are the main features of our design. Most importantly, any ion can be accelerated in the same accelerator, thus giving an edge over any existing designs. Further, the irradiation time of 50 msec and control over ion intensity makes it extremely competitive machine.

Lastly, the gantry is an important integral part of the therapy system. It enables dose to be delivered from any direction to the patient lying on the patient couch. The gantry remains the most expensive component in the entire system consuming almost one-third of the cost compared to the accelerator and research is going on to make it compact as well as cheaper.

Summary

Medical accelerators giving electrons and photons are developed at SAMEER and have been employed for radiotherapy treatment in the country. Recently, design and development of Hadron Therapy machine has been initiated. up. After careful inspection and study of the technologies available in the world and the features offered by current state of art machines, a set of common features are adopted for the next generation Hadron Therapy Proposed by SAMEER. Design of various subsystems are underway and collaboration from various institutes is invited to take up the challenge of making first indigenous hadron therapy machine.

Acknowledgements

The authors would like to express gratitude to KEK collaborators and TMC for constant support.

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