Chapter 2
Equipment and Techniques

2.1 The Big Bang, Hadrons, and the Evolution of Energy

2.1.1 The Big Bang

How did energy and matter evolve immediately after the Big Bang? Approximately 13.7 billion years ago, an explosion called the Big Bang gave birth to the universe (Fig. 2.1), with the universe expanding and cooling. The Big Bang corresponds to the quantum epoch. The probable history of the universe was divided didactically into two eras: the era of radiation and the era of matter. The radiation era initially experienced the differentiation of quarks, forming the epoch of grand unification (10^{-34} s). The electroweak epoch (asymmetry) and the formation of nucleons (10^{-10} s) with quark confinement followed, forming protons and neutrons and experiencing the disappearance of anti-quarks.

At the end of this era of radiation, we entered the era of matter, relating to the formation of the nucleus (180 s) with decoupling matter-radiation, succeeded by forming atoms (300,000 years), and the universe became transparent. Finally, stars were formed (1 billion years) with the first supernova. Here, the formation of heavy atoms, protogalaxies, and black holes occurred. Approximately 13.7 billion years later is the present time, with the spiral galaxy and solar system, etc. [1]. Thus, after just 10^{-10} s from the Big Bang, protons were already formed.

For more information about the physics of the Big Bang related to hadron therapy, the reader is referred to the book *Particle Accelerators: From Big Bang to Physics Hadron Therapy* by Amaldi [2].

It is worth noting that only 5 % of the matter in the universe is visible matter (which is subject to the standard model). The rest is dark matter (20 %) and dark energy (75 %) [1], which does not apply this model (see Fig. 2.2). Our knowledge of the universe is minimal, but the advantage that the universe has over man—being immense and eternal—is not known to it because the universe does not think (as the French philosopher Pascal said).

M. d'Ávila Nunes, *Protontherapy Versus Carbon Ion Therapy*,
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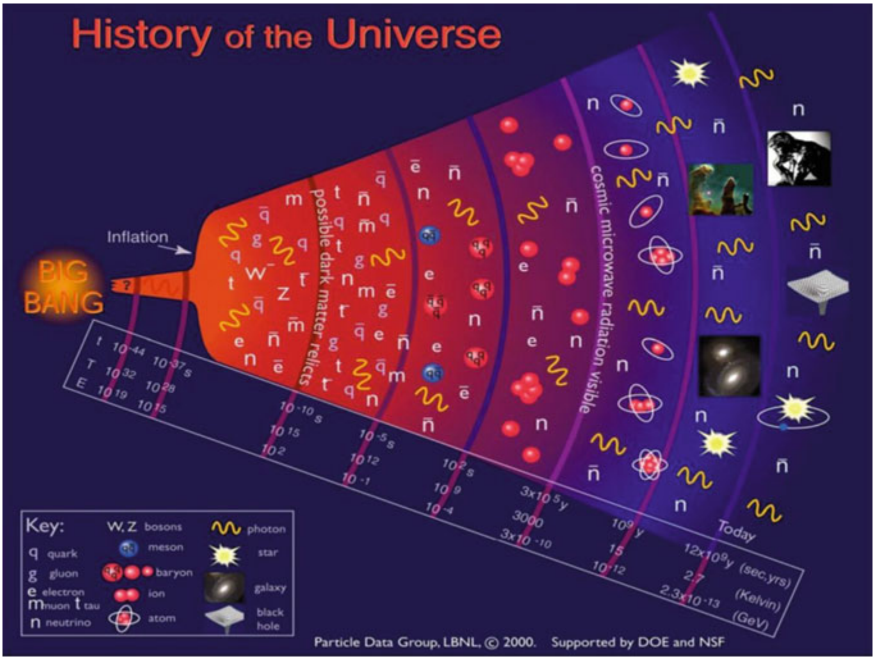

Fig. 2.1 Brief history of the universe. *Courtesy* Wikimedia Commons, [3]

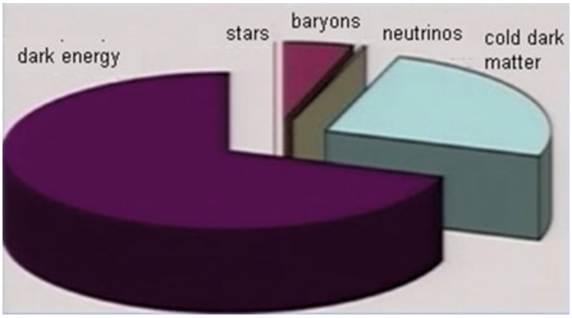

Fig. 2.2 Composition of the observable universe. Reproduced from [1]

2.1.2 Hadrons

The hadrons known to date are protons, neutrons, and a meson (pions). Pions are the most common types of particles in a particle collision and may be considered mild proton mass to approximately 15 % of that of the proton. There are two kinds of hadrons, classified according to their spins: baryons (half spin) and mesons (integer spin). Thus, the hadrons [1] are baryons (proton [p], neutron [n]) and mesons (pion π^+, π^- and π^o)

Hadrons penetrate deeper than electrons and photons but not as deeply as muons and neutrinos. In general hadron therapy, it is considered as hadrons protons, neutrons, pions, ions (alpha, C, N). The hadrons are highly interactive particles experiencing strong force. Hadron therapy (HT) is radiation therapy that uses hadrons. The strength of HT lies in the physical and radiobiological properties unique to these particles; they can penetrate tissues with limited diffusion and deposit maximum energy just before stopping (Bragg peak). This allows a precisely defined region to be specifically irradiated. HT allows access to a more controlled distance than conventional radiotherapy; however, the patient cannot move during application so that the radiation does not harm healthy tissue. Thus, with the use of hadrons, the tumor can be irradiated with less damage to healthy tissue compared with X-ray [4, 5].

2.1.3 Evolution of Energy

When working with particle accelerators, smaller distances are tested for higher energy accelerated particles. In 1930, testing values for a distance of 10^{-11} m required about 100 keV. Twenty years later, approximately 100 MeV was reached with testing distances of 10^{-14} m. In 1970, 100 GeV was reached and distances up to 10^{-17} m could be tested; in 1990, 10^{-18} m was reached with energy of 1 TeV. Currently, 10 TeV in the large hadron collider (LHC) has reached 10^{-19} m. How much we will we be able to reach in the coming years as accelerators grow in size, complexity, and cost?

Figure 2.3 shows a sharp increase in power over time: an order of magnitude for every 6–10 years. Each generation replaces the previous for increasingly high energy. It is important to note that energy is not the only interesting parameter: consider also the intensity and size of the beam.

Protontherapy uses accelerators with energy around 200–250 MeV/u, whereas carbon ion therapy uses 400–450 MeV/u with a current of 0.1 nA [1]. Circular accelerators, such as the Cyclotron and Synchrotron, are the most frequently used. The Cyclinac (which is a combination between a linac and Cyclotron accelerator) and the Laser and dielectric wall accelerators (DWA) are in development; if successful, they will reduce the cost, size, and complexity of current accelerators. The largest particle accelerator in the world, the LHC, has a biomedical facility for advanced research and education, called Low Energy Ionizing Ring (LEIR; http://medicalphysicsweb.org/cws/article/opinion/56295) to study basic physical and radiobiology, carbon ion fragmentation, dosimetry, and test instrumentation.

All circular accelerators use a linear accelerator), which, by means of electrical fields generated by radiofrequency (RF) cavities accelerate particles, and the bending trajectory, and the focusing, made by magnets. For the LHC to preserve proton beams in a path of 27 km, the magnetic fields require constant adjustment to compensate for the beam energy increases. The magnetic fields are on the order of

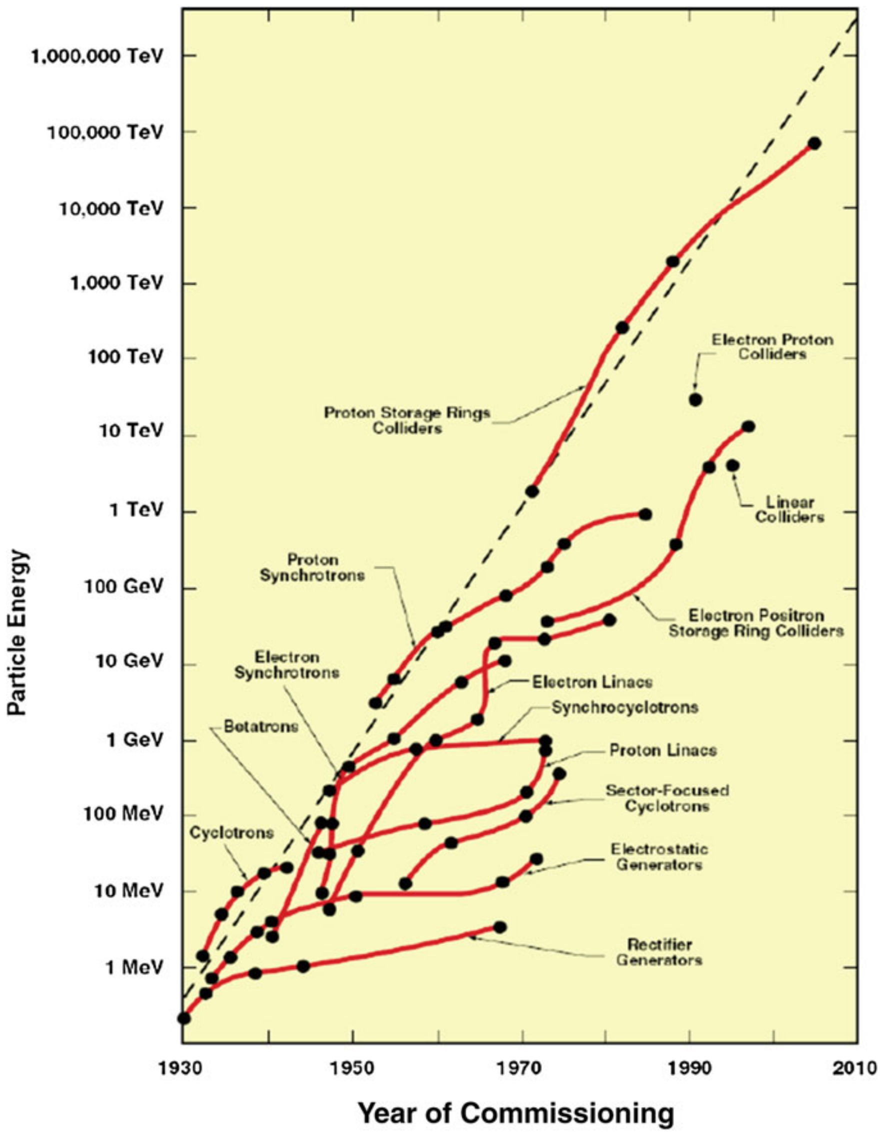

Fig. 2.3 A Livingston plot showing the evolution of accelerator laboratory energy from 1930 until 2005 [6]. The energy of colliders is plotted in terms of the laboratory energy of particles colliding with a proton at rest to reach the same center of mass energy. *Courtesy* Prof. Dr. Wolfgang Kurt Hermann "Pief" Panofsky

8.3 T—in other words, 170,000 times stronger than the earth's magnetic field. A field of this value requires a current of approximately 11,800 A. The 1232 magnets consume an electric current that could fill the needs of a small town with 150,000 houses!

Considering the LHC complex as a whole, the power consumption would be about 120 million watts of electrical power during peak demand [7]. The stored energy totals 11 billion joules—the amount of energy stored in 2.5 tons of TNT, spread over the 27 km. Each bending magnet of the trajectory of the protons is 14 m long and weighs 35 tons. The system temperature is maintained at −271 °C, requiring 10,800 tons of liquid nitrogen, followed by 120 tons of liquid helium (the cooling process takes a month and a half). The cables are made of an alloy of superconducting niobium-titanium. The length of the filaments used in bending magnets is equivalent to five times the distance from Earth to the sun and back, with plenty for any round trip around the moon (Don Lincoln). Thus, we can say that we have entered a golden age with new discoveries in all areas of human knowledge—physics, astronomy, chemistry, mathematics, computer simulation, industry, and others—through the creation of the LHC and the injection of $10 billion from participating nations in its construction.

Only with international integrated cooperation was it possible to build the LHC. With the additional experiments to be performed at the LHC, we believe that the importance may not be learning about elementary particles but to bring a deeper understanding of the fundamental questions about the universe. Finally, hadronic therapy will eventually move through physical and biophysical research; with the use of the LEIR of the European Organization for Nuclear Research (CERN), researchers will embrace new therapeutic approaches to save lives and cancer will be destroyed.

2.2 The Cyclotron, Ernest Orlando Lawrence, and Equations

The cyclotron was invented in 1932 by Ernest Lawrence. It accelerated protons with a fixed frequency of up to 1.25 MeV, allowing nuclear transmutation [8, 9]. Lawrence received the Nobel Prize 7 years later. The University of Berkeley recognized the potential of this new machine and built a 5-m-long cyclotron that accelerated protons to an energy of 20 MeV. Figure 2.4 shows two current cyclotrons and a schematic drawing in which the magnetic field imposes a circular path on the particles. The oscillating electric field (RF) is responsible for particle acceleration; the final trajectory is a spiral.

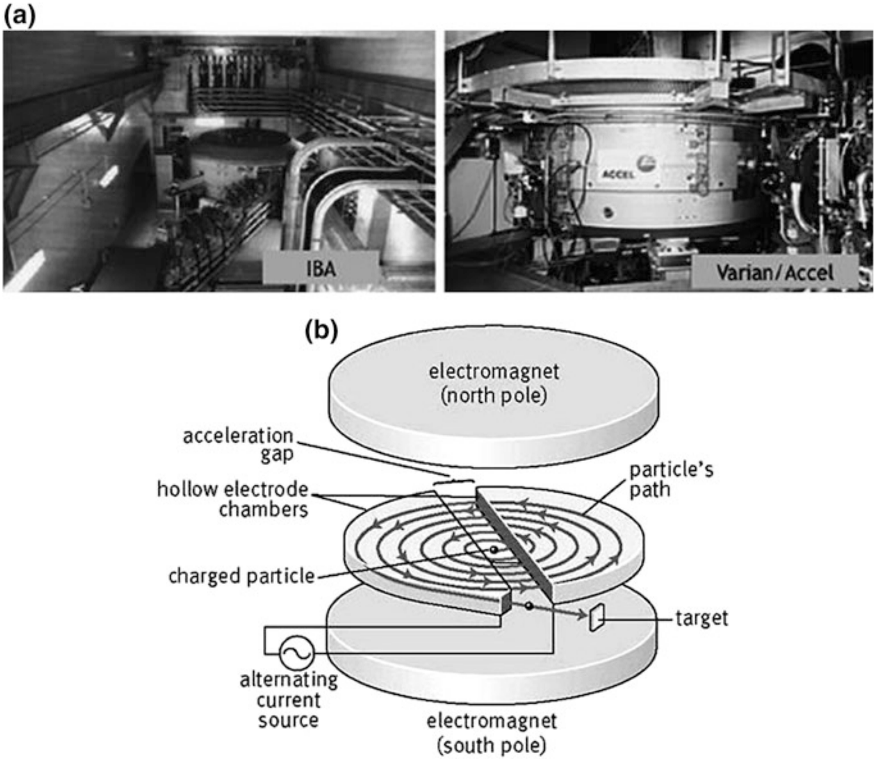

Fig. 2.4 **a** Commercial cyclotrons (Ion Beam Applications variants and the Varian Accelerator). **b** Schematic drawing of a cyclotron. Reproduced from [10]

2.2.1 Motion of Particles: Equations

The force acting on a particle, with velocity v in a magnetic field B, has the following characteristics. The direction is perpendicular to the plane (v, B); this can be represented by the lefthand rule where the thumb, index, and middle fingers are mutually perpendicular (90°). The thumb indicates the direction of the force, the index finger is the vector magnetic field, and the middle finger is the speed. The magnitude of the magnetic force that acts on the particle is given by $f = qv\,B\sin\phi$, where f is the magnetic force, q is the particle charge in Coulombs, and ϕ is the angle between the vectors B and v (this angle can vary from 0 to 180°). This is explained in more detail in Fig. 2.5.

Furthermore, when observing the particles from a proton–proton collision, for example, it can be concluded that particles of lower energy bend more and higher energy particles bend less because the magnetic field can bend the path of a particle. Because the magnetic force depends on the active particle charge, the trajectory can curve in either direction. If v is perpendicular to B, the equality decreases to $F = qvB$. However, Newton's equation gives the expression for the force F = mass

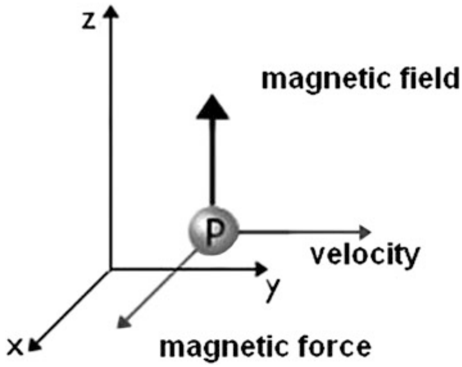

Fig. 2.5 Magnetic field vectors, velocity, and magnetic force acting on a proton [1]

(m) × acceleration (a), which means that to find the necessary replacements, the following equations are used for the speed and radius:

$$v = qBr/m \text{ and } r = mv/qB$$

Because we know v, we can calculate the acceleration as $a = v^2/r$. Substituting the value of v in the equation, the acceleration is obtained. Because the radiated power is given by $P\alpha\ (q^2\ a^2/c^2)$—that is, $P\alpha\ (qB/m)^4\ r^2$, it can be concluded that a smaller mass has greater radiated power, which causes the withdrawal of the beam particle. Thus, the electron radiates more power than the proton.

2.2.2 Calculating the Frequency of the Cyclotron

Calculation of the frequency of the cyclotron is very straightforward. The total turn is equal to $2\pi r$ in a path of radius r. If t is defined as the time spent in the half turn, $v = \pi r/t$, then $t = \pi r/v$. However, because $v = qBr\ /m$, then $t = \pi m\ /qB$. Thus, the time spent on the course is the same for all orbits, independent of the radius. Because the period of one complete turn (T) is twice that spent in the half turn $T = 2t$, then $T = 2\pi m/qB$. Because the frequency (ν) is the inverse of the period, we have $\nu = 1/T$, and thus $\nu = qB\ /2\pi m$. The angular frequency becomes $\omega = 2\pi v$, then $\omega = qB/m$.

This is the frequency value obtained from the RF source to produce the acceleration of a charged particle q and mass m, which are subjected to the magnetic field B. It can be concluded that the cyclotron frequency is directly proportional to B and inversely proportional to the ratio m/q. Thus, the particle with the lowest m/q ratio produces a spiral with more full turns (higher frequency), provided that the field remains constant.

A video on the cyclotron can be viewed at http://www.youtube.com/watch?v=cNnNM2ZqIsc.

If a cyclotron (200 MeV) were as small and inexpensive as the 5–20 MeV linacs used in conventional radiotherapy, then more than 90 % of patients could be treated with a proton beam. The accelerators used today are large and expensive, costing around 20 million Euros for a proton accelerator and 40 million Euros for a carbon ion beam facility. The installation of gantries would add another 10–12 million Euros to the cost. The gantry used at the Heidelberg Ion-Beam Therapy Center (HIT) weighs 670 tons and consumes 400 kW of power. Considering the LHC complex as a whole, the power consumption would be approximately 120 million watts of electrical power at peak demand. The stored energy is 11 billion joules (1). In the future, it is possible that gantries will be built using superconducting magnets. The current situation regarding size and costs is expected to change in the future. The Belgian company Ion Beam Applications (IBA) already offers a superconducting cyclotron with a 6 m diameter, which accelerates carbon ions up to 400 MeV/u. The TERA Foundation introduced and developed a new type of accelerator, the cyclinac [11], to accelerate protons and carbon ions, with a time of only 1 ms required to vary the energy of the beam, compared with the 20–50 ms needed by a cyclotron and the 1 s needed by a synchrotron.

2.3 The Proton Synchrotron, E.M. McMillan and V. Veskler

Conceptually, the principle of the synchrotron was published in a Russian newspaper by Vladimir Veksler; however, it was built by Edwin McMillan in 1945 (Fig. 2.6). The first proton synchrotron was designed by Sir Mark Oliphant, Australian physicist, and built in 1952 [12]. In particle physics, the synchrotron is an accelerator of cyclic particles in which the electric field is responsible for the acceleration of the particles and the magnetic field is responsible for the change of direction of the particles; both fields are synchronized with a beam of particles. The magnetic field is increased to keep the charged particles in a constant radius orbit as they reach higher speeds. Because the radius is constant, the “dees” used in the cyclotron are not needed and the particle moves in an annular chamber vacuum in a ring-shaped magnet. One or more resonant cavities are used to accelerate particles. An RF is applied into the cavity so that the particles are attracted when they approach and repelled when they leave it (Fig. 2.7).

The orbit of a synchrotron is not a circle; rather, straight sections are added by the RF cavities, injection, and extraction, etc. Usually, the pre-accelerated beam is a linac (or small synchrotron, prior to injection). The curvature of beam radius does not match the machine radius.

An interesting comparison was proposed by Don Lincoln in his book *The Quantum Frontier* [7], which facilitates an understanding of the functioning of a proton synchrotron. The principle governing this accelerator is the same as that governing a tetherball (i.e., a ball attached to one end of a rope, with the other end

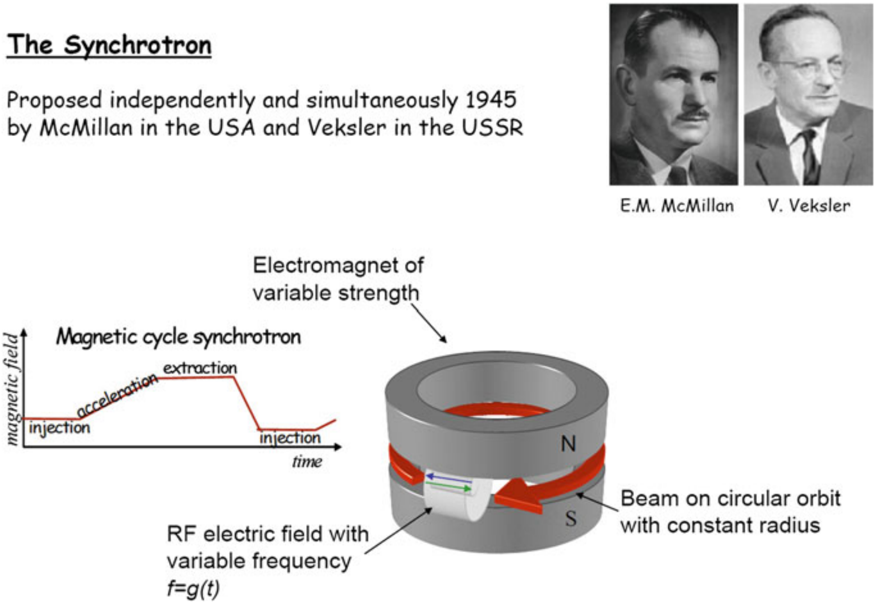

Fig. 2.6 The Synchrotron. *Courtesy* Prof. Dr. Hans-H. Braun

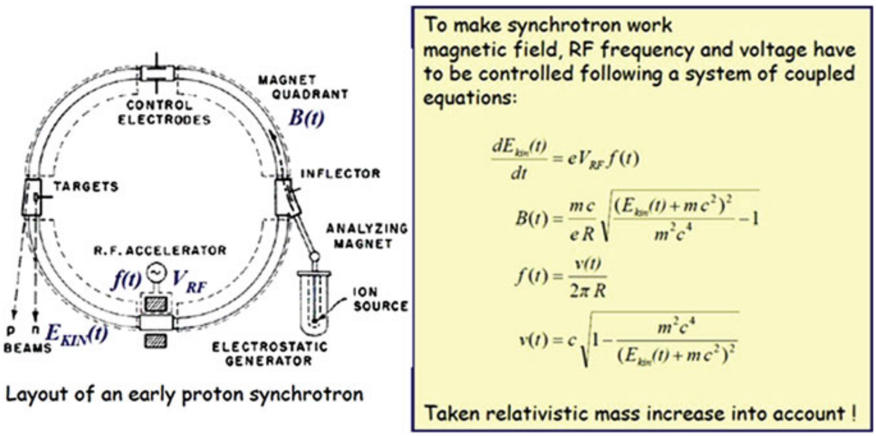

Fig. 2.7 Layout of an early proton synchrotron and a system of coupled equations. A synchrotron can be built for very high energies. For proton beams, limits are given by achievable magnetic field and size. *Courtesy* Prof. Dr. Hans-H. Braun

attached to the top of a tall pole that is anchored deep in the ground). A person hits the tetherball and the rope ensures that the ball travels in a circular path. Once the ball makes a full circle, it is hit again. The ball goes faster and makes another circuit. If the rope is attached to the top of the pole, it does not wrap itself around the pole; in principle, the ball can be made to travel very rapidly by synchronizing both its orbit and the person hitting it (hence the derivation of the name synchrotron). In a proton synchrotron, the electric field “hits” the proton and accelerates it. However, the counterpart of the rope in the tetherball analogy is not provided by electric fields, but rather by magnetic fields. Particles are accelerated by an electric field over a short distance and are then guided by magnetic fields in a circular path back to the electric field region for another round of acceleration.

The synchrotron was based on the cyclotron with a time-dependent magnetic guide, which was synchronized to a particle beam with increasing kinetic energy. The difference between the cyclotron and synchrotron is that the latter uses the principle of phase stability, maintaining the synchronism between the applied electric field and the frequency of revolution of the particle. Beam focusing and acceleration can be separated into different components using the curvature of the synchrotron beam. Thus, radiofrequency cavities are used for acceleration, the magnetic dipoles for particle deflection, and quadrupole/sextupole magnets for focusing the beam particles. The magnetic field maintains the orbit instead of accelerating the particles, and hence the magnetic field lines are only necessary in the region defined by the orbit.

The synchrotron facility consists of the following components (Fig. 2.8):

(1) The ion source accelerator: This is where ion beams composed of positively charged atoms are produced. For protons, hydrogen gas is used. For carbon ions, dioxide is used.
(2) A two-stage linear accelerator: Ions are accelerated in structures at high frequency up to 10 % of the speed of light.
(3) The synchrotron: Six 60° magnets bend the ions into a circular path. After a million orbits, ions are accelerated to 75 % of the speed of light.
(4) The treatment room beam lines: Magnets guide and focus the beam of ions in vacuum tubes.
(5) The treatment room: The beam enters the treatment room through a window. The patient is positioned on a treatment table that is adjusted accurately by a computer-controlled robot.
(6) Position control: Using a digital X-ray machine, images are obtained before irradiation. The computer software compares the images obtained with those used in treatment planning and precisely adjusts the position of the patient.
(7) The gantry: The rotation system enables the beam to be directed toward the patient at an optimized angle. The gantry weighs about 670 tons—600 tons of which can be rotated with submillimeter accuracy.
(8) The treatment room in the gantry: This is where the beam exits the gantry (beam line). Two rotation systems and digital X-rays are used to optimize the position of the patient guided by the images taken before irradiation.

The combination of magnetic field “guides”, time dependency, and the principle of strong focus enables the design and operation of modern large-scale accelerators as colliders and even synchrotron light sources, such as at the Brazilian Synchrotron Light Laboratory in Campinas, São Paulo. The power limit could be increased by

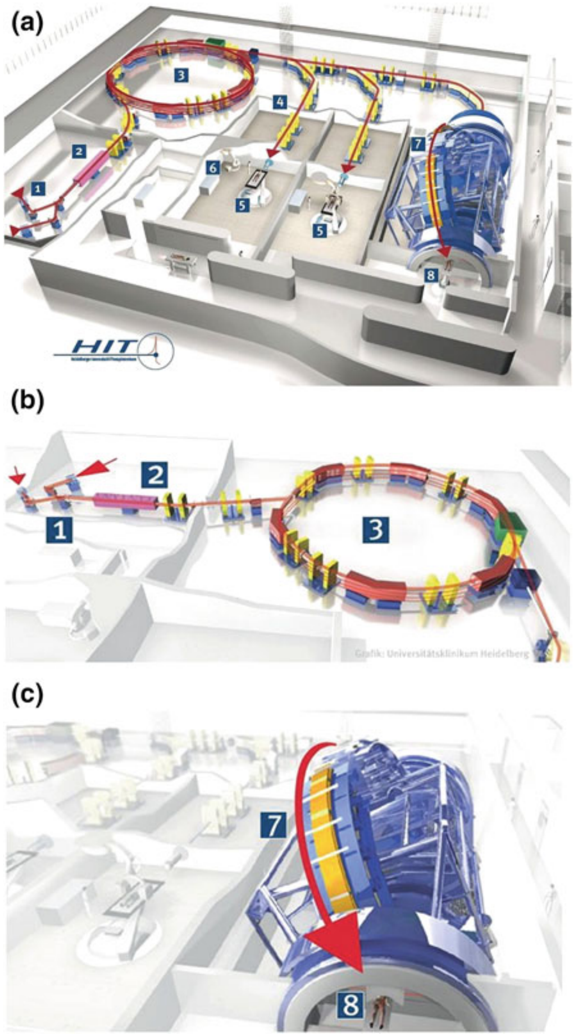

Fig. 2.8 **a** Synchrotron at the HIT in Heidelberg. **b** Schematic of the synchrotron at the HIT. **c** Schematic drawing of the HIT gantry. *Courtesy* Annette Tuffs, Head of Corporate Communications/Press Office, Heidelberg University Hospital

using superconducting magnets, which are not limited by magnetic saturation. Electron and positron accelerators may be limited by the emission of synchrotron radiation, resulting in a partial loss of kinetic energy of the particle beam. Therefore, the energy of electron and positron accelerators is limited by the loss of this radiation, which does not happen with proton or ion accelerators. The energy of these accelerators is limited by the strength of the magnets and the cost.

In the synchrotron, particle injection is pre-accelerated using a linac, microtron, or even another synchrotron, because synchrotrons are unable to accelerate particles from zero kinetic energy. The Tevatron at Fermilab was the largest collider in the world in 2008. It accelerated protons and antiprotons to 1 TeV and then collided them. The LHC has seven times this energy; accordingly, the proton–proton collisions occur at about 14 TeV. The LHC also accelerates heavy ions (such as lead) up to an energy of 1.15 PeV [13].

2.4 Hybrid Systems: C400 from IBA and New Synchrotron from Brookhaven National Laboratory

The C400 from Ion Beam Applications (IBA, Belgium), is being developed in partnership with the Joint Institute for Nuclear Research (JINR, Dubna, Russia). It is a cyclotron with superconducting coils that can produce 400 MeV energy, allowing the acceleration of protons and carbon ions. This cyclotron follows the current trend in the development of systems for providing protontherapy and carbon ion therapy in the same equipment—that is, hybrid systems. However, despite the IBA having developed a compact gantry for ProteusOne, it does not have a similar system for the C400. The C400, shown in Figs. 2.9 and 2.10, has a diameter of 6.3 m; its estimated main parameters are provided in Table 2.1.

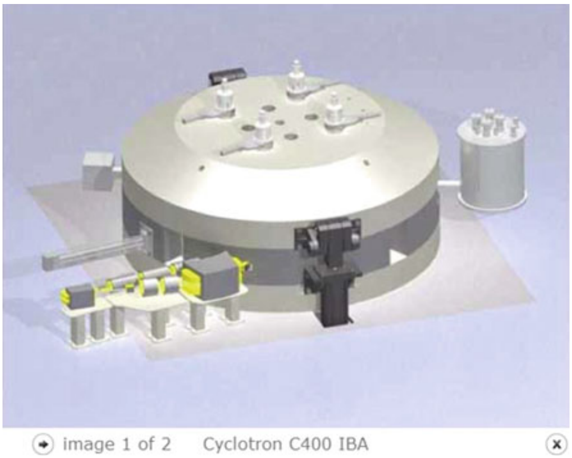

Fig. 2.9 Cyclotron C400 IBA. *Courtesy* IBA

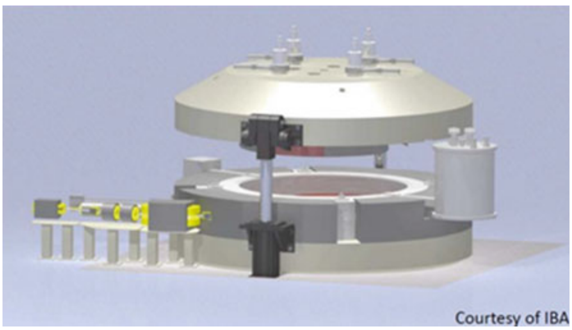

Fig. 2.10 Cyclotron C400 IBA, about 6.3 m in diameter with superconducting coils. *Courtesy* IBA

Table 2.1 Estimated parameters of the C400 cyclotron in the pre-study phase

General properties	
Accelerated particles	H_2^-, $^4He^{2-}(\alpha)$, $(^6Li^{3+})$, $(^{10}B^{2-})$, $^{12}C^{6-}$
Injection energy	25 keV/Z
Final energy of ions, protons	400 MeV/u
	265 MeV/u
Extraction efficiency	~70 % (by deflector)
Number of turns	~2000
Magnetic system	
Total weight	700 t
Outer diameter	6.6 m
Height	3.4 m
Pole radius	1.87 m
Valley depth	0.6 m
Bending limit	K = 1600
Hill field	4.5 T
Valley field	2.45 T
RF system	
Number of cavities	2
Operating frequency	75 MHz, 4th harmonic
Radial dimension	1.87 m
Vertical dimension	1.16 m
dw voltage	
Center	80 kV
Extraction	160 kV

From [33]. *Courtesy* IBA

In January 2014 at the 5th Asian Forum for Accelerators and Detectors in Melbourne, Australia, the synchrotron Ion Rapid Cycling Synchrotron Medical (iRCMS) was presented (Fig. 2.11). The iRCMS was developed at Brookhaven National Laboratory through a cooperative research and development agreement with Best Medical International. The iRCMS will be used in future cancer therapy, working with protons and carbon ions. It was designed and optimized to provide maximum energy of 400 MeV/u and a frequency of 15 Hz for carbon ion therapy, effecting treatment at a maximum depth of 27 cm.

The iRCMS offers an advanced scanning spot with quick energy modulation, facilitating the release of beams with unprecedented accuracy. Its display is 12 m wide by 23 m length, and it uses one linac to inject protons and carbon ions to a kinetic energy of 8 MeV/u. Table 2.2 provides a comparison of several beam accelerators.

Because the iRCMS cycle is about 100 times faster than other “slow-cycling” synchrotrons, the number of protons accelerated per cycle can be as much as 100

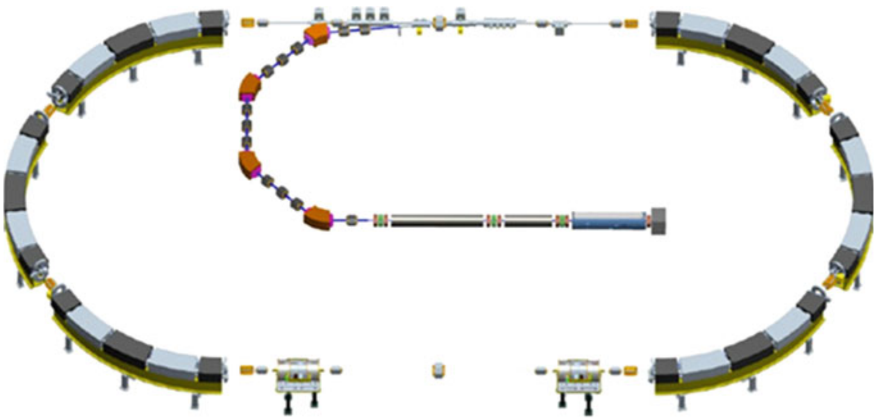

Fig. 2.11 Schematic diagram of the footprint of the medical synchrotron. The *rectangles* along the 180° arcs of 5 m radius are combined function magnets. The length of each of the straight sections is 12 m. The *bottom* straight section is dedicated to the RF acceleration system, and the *top* one is for the beam injection and extraction systems. The pre-accelerator that injects protons or C^{5+} ion bunches at 8 MeV/u is located in the area enclosed by the racetrack. Reproduced from: [14]

Table 2.2 Properties of the beam of various accelerators

Accelerator	The beam is always present?	The energy is electronically adjusted?	Which is the approx. time (in ms) to vary E_{max}?
Cyclotron	Yes	No	100
Synchrotron	No	Yes	1000
Linac	Yes	Yes	1

Reproduced from: [14]

times smaller for a fixed treatment time. This leads to five main advantages: faster energy change, less beams per cycle, efficient beam extraction, better control of delivered dose, and a smaller magnet size. Because less beams are used in the accelerator at any given time, it is far less likely that a worst-case incident would occur, in which excess beam is suddenly and inadvertently delivered to the patient. Low beam intensities also avoid the ravages of space charge effects, which at best cause the beam size to increase with intensity, and at worst put a hard limit on the intensity of the beam. Low beam intensities (per cycle) also allow the beam to be extracted from the synchrotron in a single turn of the accelerator, at an energy that can be easily modified from one cycle to the next [14].

Figure 2.12 provides a comparison of intrinsic spot width to protons ($\sim$206 MeV/u) and carbon ions ($\sim$400 MeV/u). Under these conditions, the minimum voxel volume would be 715 mm^3 for protons and 13.8 mm^3 for carbon ions, at a depth range up to 27 cm. Therefore, carbon ions are 52 times more accurate than protons.

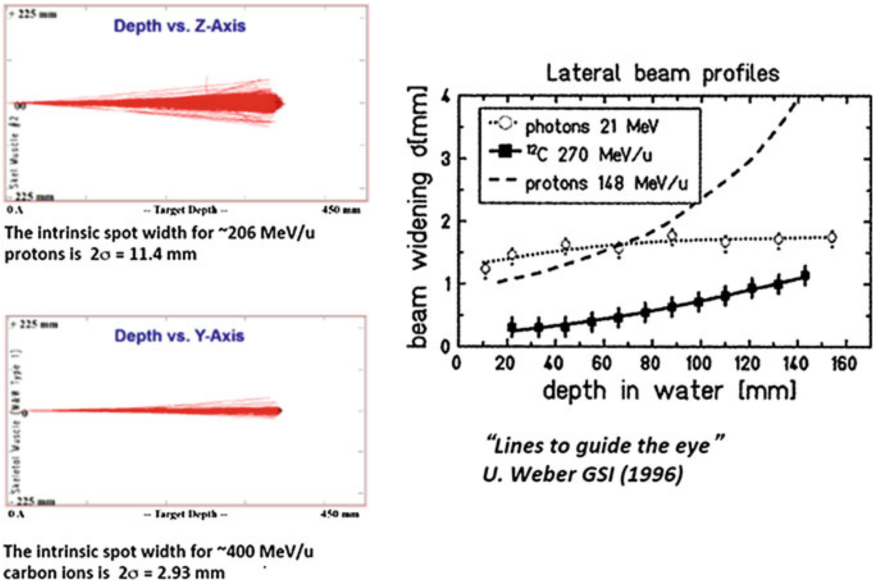

Fig. 2.12 Comparison of intrinsic spot width for protons and carbon ions. Reproduced from [14]

The beams of particles extracted from the synchrotron iRCMS are initially so small that the size of the final spot in the end of its range is just the intrinsic width given by the inevitable multiple scattering. The width of the intrinsic spot to protons at 206 MeV/u (at 270 mm depth) is 11.4 mm. The minimum value of the voxel volume is 715 mm^3. The intrinsic width of the spot for carbon ions at 400 MeV/u (at 270 mm depth) is 2.93 mm. The minimum value of the voxel volume is only 13.8 mm^3. Thus, carbon ions are 52 times more accurate than protons.

2.4.1 Summary

Best Medical International and Brookhaven National Laboratory are jointly developing a rapid-cycle proton/carbon synchrotron that enables advanced features, including a unique combination of advanced spot scanning with rapid energy modulation and elimination of the neutron contamination associated with patient-specific hardware. This technology has many advantages, including the following:

1. Intrinsically small beam emittances facilitating beam delivery with unprecedented precision
2. Small beam sizes, small magnets, and light gantries
3. Highly efficient, single-turn extraction
4. Efficient extraction, less charge per bunch, and less shielding
5. Flexibility in the choice of protons or carbon, future beam delivery modalities.

2.5 Gantry Specifications: Compact Gantry

The gantry is an extremely useful, essential piece of equipment (Figs. 2.13, 2.14, 2.15 and 2.16). If a conventional room was used instead of a gantry, the radiation would have to be provided in horizontal, vertical, or inclined beams, which prevents proper treatment, including for tumors in children.

Companies selling equipment for protontherapy and carbon ion therapy offer gantries that allow irradiation at any angle. Only horizontal irradiation is used in the treatment of cancer in the eye or head and neck. For the torso, it is possible to note a change both in dimensions as the position changes (e.g., due to breathing), thus necessitating the technique of "gating." It also uses the vertical irradiation. Robotic systems to keep the patient in different positions are being developed.

Fig. 2.13 The Heidelberg carbon-ion gantry (18 m × 7 m, 600 ton). *Courtesy* Thomas Haberer/Heidelberg Ion Beam Therapy Centre. *Courtesy* Prof. Dr. Thomas Haberer, Head of HIT and MIT

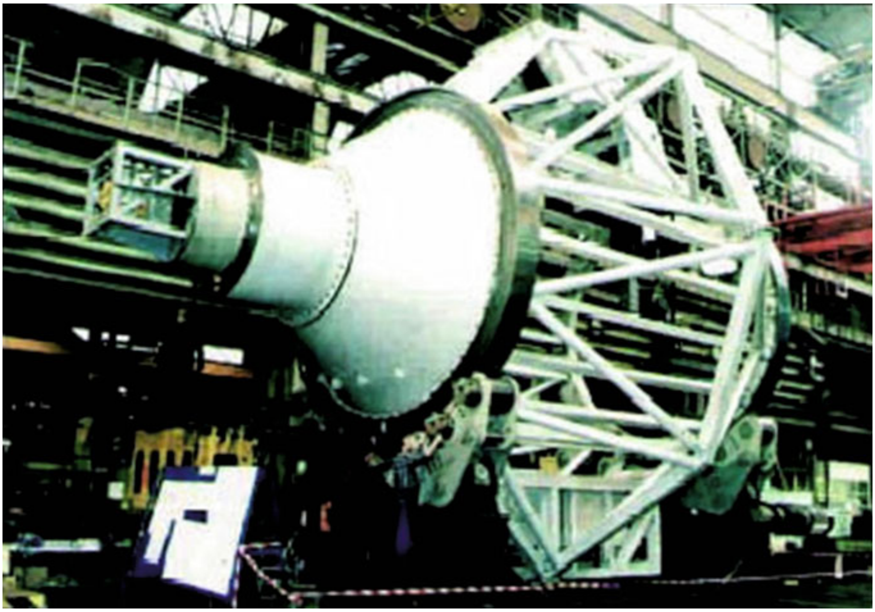

Fig. 2.14 IBA proton gantry (diameter > 6 m, weight ∼ 100 tons, proton beam displacement from isocenter <1 mm). *Courtesy* IBA

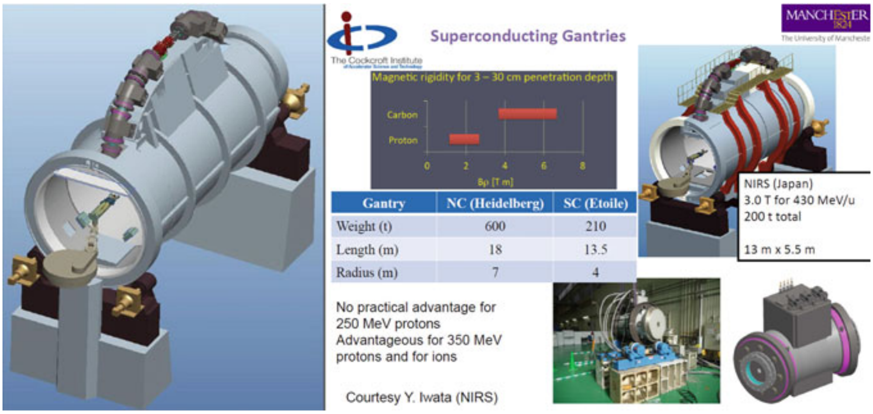

Fig. 2.15 Three-dimensional image of the NIRS superconducting rotating gantry for heavy-ion therapy (dimension 13 m × 5.5 m, weight 200 tons, 3.0 T for 430 MeV/u). *Courtesy* Prof. Dr. Y. Iwata, National Institute of Radiological Sciences (NIRS)

A hadron therapy center typically has 4–5 rooms. Researchers are working hard to create more affordable systems for the acceleration of protons and carbon ions. The IBA has adopted a more compact gantry system with a lower price, coupled to

Fig. 2.16 The gantry mechanism and final dipole of Gantry 2 at the Paul Scherrer Institute. The upstream design enables parallel scanning, which thereby simplifies treatment planning and gives an infinite SAD, which assists in skin sparing but necessitates a rather large 45-ton final dipole to give sufficient aperture to deliver the desired treatment field size. *Courtesy* Prof. Tony Lomax/PSI

ProteusONE, and approved by the U.S. Food and Drug Administration (FDA), which facilitates its acquisition.

To further obtain precise dose distributions, an isocentric superconducting rotating-gantry for carbon therapy was developed [15]. This rotating gantry is designed to transport carbon ions of 430 MeV/u to an isocenter with irradiation angles of more than ±180°. It is further capable of performing the fast raster-scanning irradiation.

2.6 Obtaining Particles (Protons, Neutrons) and Heavy Ions for Hadron Therapy

This section explains how to prepare protons, neutrons, and heavy ions for use in hadron therapy.

2.6.1 How Are Protons Obtained?

Protons are produced by applying an arc discharge of hydrogen gas into a source called a duoplasmatron. The electron is released from the hydrogen atom, leaving the positive nucleus, a proton, floating freely in the resulting plasma. By applying a strong electric field, the protons are extracted from the plasma surface and are sent on their way as a stream of positive particles. Currents of up to 300 mA can be obtained.

The protons interact with matter in three distinct ways:

1. They slow down through collisions with atomic electrons and finally stop.
2. They are deflected by collisions with atomic nuclei causing scattering.
3. Collisions with a nucleus yield secondary particles in motion. This is called nuclear interaction.

The first two conditions occur via electromagnetic interaction between the charge of the proton and the charge of the electrons or the atomic nucleus. There are mathematical theories for the first two conditions. Nuclear interactions are known to be infrequent and function according to a set of models. Even though computer programs are used to solve these problems, which are accurate to within seconds, predicting the dose for a patient is very complex and time-consuming.

2.6.2 How Are Neutrons Obtained?

Neutrons can be obtained by accelerating deuterons with an energy of 48.5 MeV onto a beryllium target. The deuterons are accelerated using a superconducting cyclotron. Generally, neutrons can be obtained by accelerating protons or deuterium and colliding them with a beryllium or lithium target, provoking reactions of the type 9Be (p, n) 9B, 7Li (p, n) 7Be, 3H (2H, n), and 4He (where p = proton, 2H = deuterium, n = neutron, Be = beryllium, B = boron, and 4He = helium-4).

James Chadwick discovered the neutron in 1932 using alpha particles (from radioactive polonium), with which he bombarded a blade of beryllium. He noted that uncharged particles left the beryllium bulwark. He placed in its path a paraffin bulwark from which the protons were discharged after bombardment by particles without being charged. The neutron was discovered! Its mass was determined in a way that was very similar to the proton because the impact removed protons from paraffin. The discovery of the neutron triggered a considerable increase in knowledge regarding nuclear structure. Additionally, in 1932, Werner Heisenberg realized that the nuclei of atoms were composed of protons and neutrons. He described the quantum mechanics involved and received the Nobel Prize in Physics in 1932. James Chadwick also received the Nobel Prize in 1935 for his discovery of the neutron. After the discovery of the neutron, Robert Stone began clinical trials with fast neutrons (radiation therapy) at the Lawrence Laboratory in Berkeley, CA, USA.

2.6.3 How Are Heavy Ions Obtained?

Heavy ions are atomic nuclei that have lost their electrons and are heavier than protons (hydrogen nuclei). A variety of ions are used, such as helium, carbon, and oxygen nuclei. Heavy ions are three times more effective than protons and helium ions. In the human body, heavy ions can be targeted with millimeter precision and are therefore superior to protons in the treatment of certain tumors. As is well known, ions are charged atoms. Thus, to obtain ions, atoms must necessarily lose their negatively charged electrons. For this purpose, carbon dioxide gas flowing within an ionic chamber is used. Free electrons in the gas are accelerated using magnetic fields and microwaves. Traveling through the ionic chamber, the electrons impact the molecules of carbon dioxide. After a collision, the molecules dissociate, and four of the six electrons in the carbon atom are separated. Electric fields are then employed to extract the carbon ions from the chamber. A special magnet transports them in a vacuum in a steady flow. This flow is converted into a pulsating flow with a frequency of 217 million pulses per second. The beam is collimated and the ions are accelerated. Subsequently, electromagnetic fields accelerate the ions to more than 10 % of the speed of light. Leaving the accelerator through a sheet of carbon, the carbon atoms lose their last two electrons, so that only nuclei with six positive charges remain.

2.7 Other Techniques in Development: Cyclinac, Laser, Dielectric Wall Accelerator

2.7.1 Cyclinac

The name *cyclinac* is a combination of cyclotron and linac. The cyclinac consists of a linac with a high frequency and a fast cycle that increases the energy of the particles previously accelerated by a cyclotron. The cyclinac can easily accelerate currents of the order of 2 nA, which are required for proton beam therapy (carbon ions), producing optimized ion beams for the irradiation of solid tumors using the most modern techniques [11]. The accelerators used for protontherapy are cyclotrons that are 4–5 m in diameter and synchrotrons of 6–8 m diameter. For carbon ion therapy, only synchrotrons of 20–25 m diameter are employed. Recently, large superconducting cyclotrons have been built for carbon ion acceleration.

Cyclinacs are excellent accelerators for hadron therapy because of the following characteristics: they work with frequencies of 300 Hz, allowing efficient tumor mapping; they have a low power consumption of 800 W (reducing costs); they rapidly modulate the active energy (1 ms) that is essential for studying organs in motion; and finally, they have steep acceleration gradients and have a reduced size (a cyclotron weighs 190 tons and a linac is 24 m long). The compact cyclotron used for the first particle acceleration to 120 MeV/u is smaller than the more widely used

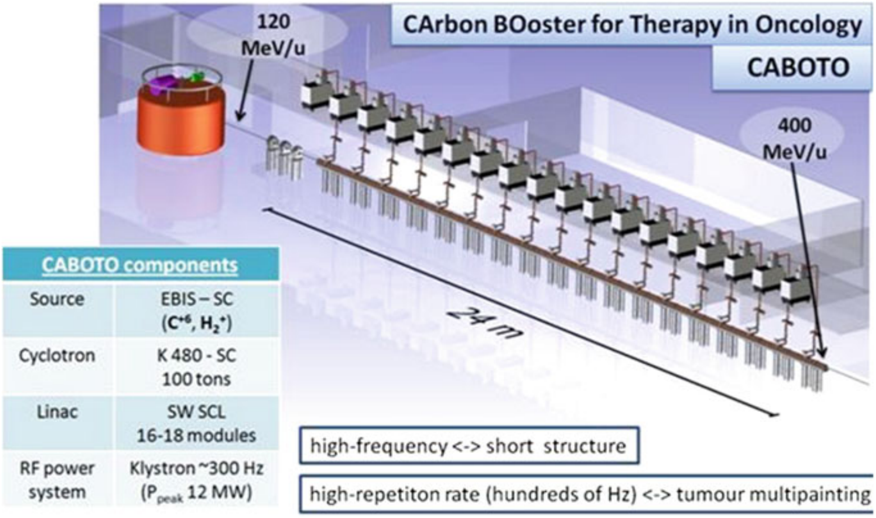

Fig. 2.17 The TERA Foundation's proposed cyclinac [11]. *Courtesy* Prof. Dr. Ugo Amaldi, President of Tera Foundation

cyclotron for protontherapy (e.g., IBA C235). Figure 2.17 shows the cyclinac (CABOTO) machine proposed by the TERA Foundation.

2.7.2 Use of Lasers in Hadron Therapy

Improvements in heavy ion therapy can be achieved using less expensive acceleration technologies. For potential use in therapy, the laser pulses need to accelerate protons to energies of ≤150 MeV and carbon ions to an energy of 350 MeV. Working with proton beams and focusing them is costly and difficult. Eccentric and isocentric equipment is used to transport proton beams from the final section of the accelerator to the target tumor. These structures are made of heavy magnets used to deflect the beam; they weigh 100–200 tons and have a diameter of 4–10 m. All of this equipment can generate costs of up to 150 million Euros.

Petawatt class lasers are not necessarily much smaller than the conventional accelerators used for hadron acceleration. The targets used to generate protons are only a few centimeters in size. Therefore, the target is positioned close to the patient, using small mirrors to transport the laser instead of heavy and expensive magnets. This makes the equipment much lighter, smaller, and less expensive. The laser beam can be sent to different treatment rooms using mirrors. In addition, the safety system for the laser is simple and inexpensive, and damage to the eyes of the doctor and the patient is prevented. An additional advantage is that the laser accelerator does not require radioprotection with thick concrete walls. The repetition rate of lasers will soon be increased to kilohertz levels, and petawatt lasers with diode-pumps (used in Germany) and fiber lasers will have power and repetition rates >100 Hz.

In 2002, Fourkal et al. [17] showed that, under conditions of optimal interaction, protons can be accelerated to relativistic energies of 300 MeV using petawatt lasers. The protons are accelerated by means of the Coulomb force, which arises from charge separation induced by high-intensity lasers. The proton energy and phase spatial distribution obtained from the particle simulations in cells are used to calculate the dose distribution using the GEometry ANd Tracking (GEANT) Monte Carlo simulation code. Because of the wide range of energy and the angular spectrum of protons, compact particle selection and beam collimation is necessary to generate small polyenergetic beams of protons for modulated-intensity protontherapy.

Intense and collimated proton beams produced by a high-intensity laser pulse interacting with plasma were first developed for protontherapy of malignancies by Bulanov et al. [16]. The fast proton beam was produced by directing a laser at the target, which generated accelerated proton beams of high quality. A simple comparison between the traditional accelerators and laser accelerators shows the superior qualities of the laser.

2.7.3 How Are Protons Accelerated with a Laser?

It is possible to accelerate protons by means of a violent acceleration of electrons in the laser field that draws protons behind them on the posterior surface of the target (Fig. 2.18). This creates a continuous proton spectrum. Computations have shown that by using two appropriately shaped targets, a scattering energy of 3 % can be achieved.

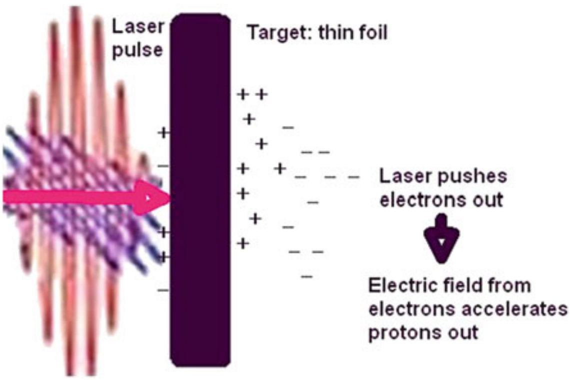

Fig. 2.18 Schematic drawing of a powerful laser blast onto a thin solid blade doped with hydrogen. Reproduced from [10]

In Fig. 2.18, a powerful laser pulse is shown acting violently on a target constituted by a thin blade doped with hydrogen atoms [18]. The laser accelerates electrons off the posterior region of the target, creating an electric field that favors the output of protons from the target. In the future, it is hoped that laser pulses with intensities in the range of 1018–1020 W/cm^2 and pulse durations of 30–50 fs will be possible [19]; this will allow a facility for treatment with protons (single facility) to be constructed based on illumination of a thin target.

Some companies are working to reduce the size and cost of high-power lasers, and there are several projects focused on improving beam quality. It is possible that the cyclotron will eventually become obsolete and will be replaced by more compact laser systems. Many years of dedicated research are needed to achieve this goal; for now, it is not considered to be economically advantageous.

Dielectric wall accelerators (DWA) are a type of induction accelerator. A traveling high-gradient field is created by switching high voltages on electrodes that are sandwiched between high-gradient insulators. This is the operating principle of the DWA. The accelerator tube is made of fused silica (250 μm thick), which is a pure transparent quartz and acts as an insulator. This method maximizes the electric field through the use of new insulators in the accelerator structures. However, with normal insulators, the maximum electric field strength is limited by the formation of sparks, which arise because the electrons repeatedly bombard the surface, creating an avalanche of electrons. Thus, to obtain a strong field accelerator, the formation of sparks must be presented by shortening the time during which the field is present. To decrease the insulation, the conventional high-voltage pulse of 1,000–1 ns leads to an increase in the surface cracking field of 5–20 MV/m. A new dielectric insulating configuration has enabled this limit to be increased to 100 MV/m. This high-gradient insulator (HGI) is constructed using a row of floating conductors sandwiched between sheets of insulators. Thus, a DWA can be made by forming rings of HGI-material and additional conductive sheets at frequent intervals along the stack. Each of these blades is connected to a high-voltage circuit with a switch. When these switches are closed, an electric field is produced in the inner side of the HGI ring. By successive closures of the switches along the stack, the region of the strong electric field is changed along the stack, and protons traveling in phase with the wave will be accelerated through these rings. This arrangement accelerates protons to 200 MeV in a system that is 2 m in diameter (Fig. 2.19).

Use of the DWA would circumvent some of the problems associated with conventional accelerators, such as their expense and enormous size; the DWA costs US $20 million and is much smaller than the accelerators used in the medical field. However, the DWA currently requires several improvements because of the high energies involved, including improvement of the high-gradient insulators. As compared with other proton accelerators, the DWA is apparently the only accelerator for which the power, intensity, and beam spot size can be varied pulse by pulse. The cyclotron only allows variation of the intensity under these conditions and the synchrotron allows variation of the energy and intensity, but not the spot size. The DWA allows variation of all these factors, pulse by pulse. Another advantage of this small linac is that it would be possible to mount it on a

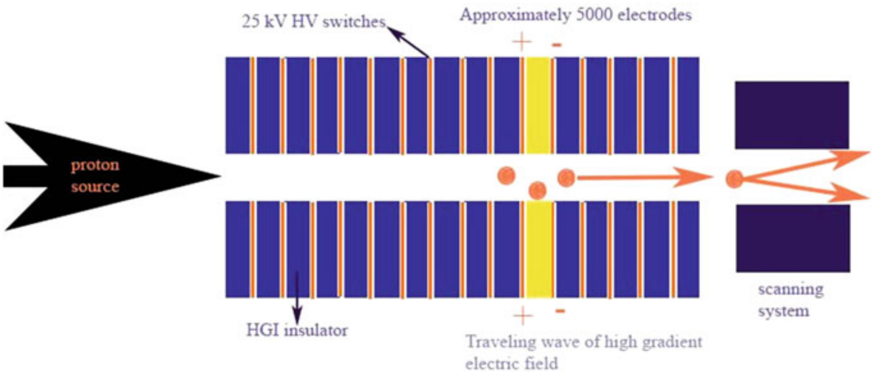

Fig. 2.19 Operating principle of the dielectric wall accelerator. Reproduced from: [10]

tomotherapy system. The Compact Particle Acceleration Corporation (CPAC) is developing a very flexible compact system for protontherapy based on the DWA that is much smaller and more powerful than conventional accelerators. The idea of a compact proton accelerator comes from a team led by George Caporaso of the Livermore Beam Research Program at the Physical and Life Sciences Directorate. Their HGI is built with layers made of metal, such as stainless steel, alternating with layers of insulating plastic, such as polystyrene.

An induction accelerator formed by a set of HGIs can maintain extreme voltages. A particle injector starts the action, and the transmission lines made of dielectric materials and embedded conductors produce the electric field that drives the particles along the tube. The transmission lines are called Blumleins (named after British inventor Alan Blumlein). A laser supplies power to switches in the Blumleins through a distribution system consisting of optical fibers. The small, solid-state silicon carbide optical switches open and close at high speeds to control the high voltage that reaches each Blumlein, increasing the energy of the particles as they traverse the tube. The opening and closing of each switch creates a virtual traveling wave that pushes the energized particles along the tube (Fig. 2.20).

This advance in size and power is due to three inventions: (1) the high-gradient insulator, which allows a substantial increase in voltage-holding capacity; (2) the optical switches, which can handle high-power loads at high speeds in a very compact size; and (3) the dielectric materials with embedded nanoparticles, which facilitate the transmission and isolation of extremely high voltages (Fig. 2.21).

Thus, the CPAC estimates that it will be able to create a system for protontherapy that is accessible to all cancer treatment centers and their patients. The DWA can be used to accelerate electrons, protons, or any ion, but more time is required before a clinical system can be established. Figure 2.22 shows a representation of the DWA.

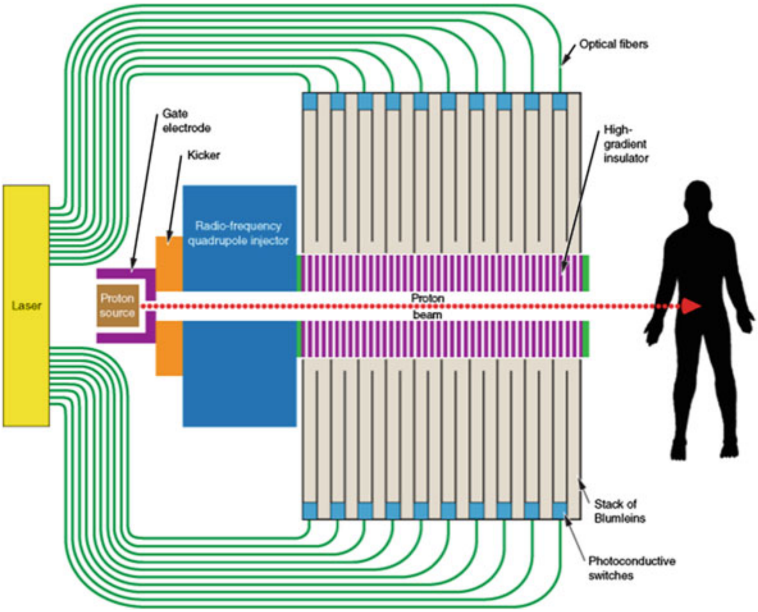

Fig. 2.20 Diagrammatic representation of the flow of protons in the dielectric wall accelerator from their source to the patient. Protons are sent to the interior of a "kicker" that injects them in pulses into a radiofrequency quadrupole, which compresses them into small bunches. Switches along the accelerator open and close at high speeds to control the voltage and increase the energy of the particles. Careful control of the switch mechanism creates a beam pulse with the velocity, shape, amplitude and length required for a given patient. Reproduced from [10]

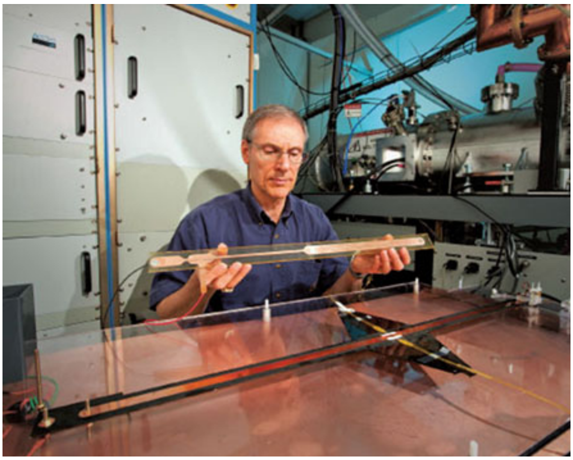

Fig. 2.21 George J. Caporaso examines the Compact Particle Acceleration Corporation's (CPAC's) newest Blumlein design. Tests at the CPAC are combined with computer simulations at Livermore Laboratory to produce a practical design. *Courtesy* George J. Caporaso

Fig. 2.22 An artist's rendition of the DWA in its fully developed form. *Courtesy* Dr. Anthony Zografos, Chief Operating Officer, Compact Particle Acceleration Corporation

2.8 Phantoms

The Timepix detector [20] is a system capable of recording the traits of characteristic particle shapes, including their energy deposited in the detector. The data recorded for each event allow estimation of the particle type, energy, and direction of flight. Opalka et al. conducted experiments for the detection and characterization of secondary radiation beams generated by primary therapeutic tissue equivalent material (water). The measurements were made in a water phantom irradiated by carbon ions in the Heidelberg Ion-Beam Therapy Center. Figures 2.23 and 2.24 show the pixel detector Timepix and the assembly for measures in a phantom water tank.

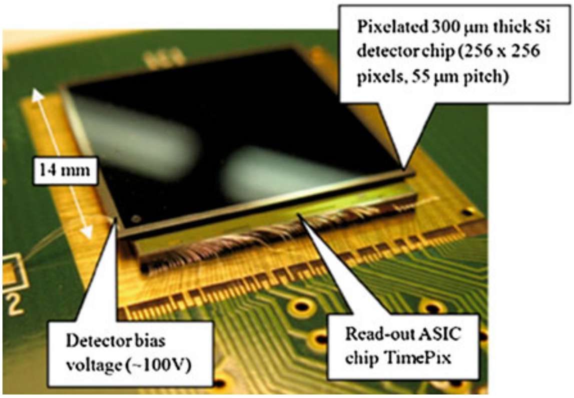

Fig. 2.23 The pixel detector Timepix. The device consists of two chips connected by a bump-bonding technique. The *upper chip* is a semiconductor sensor (usually silicon). The *bottom chip* is an ASIC readout containing a 256 × 256 matrix of preamplifier comparators and counters. *Courtesy* Prof. Dr. Lukas Opalka

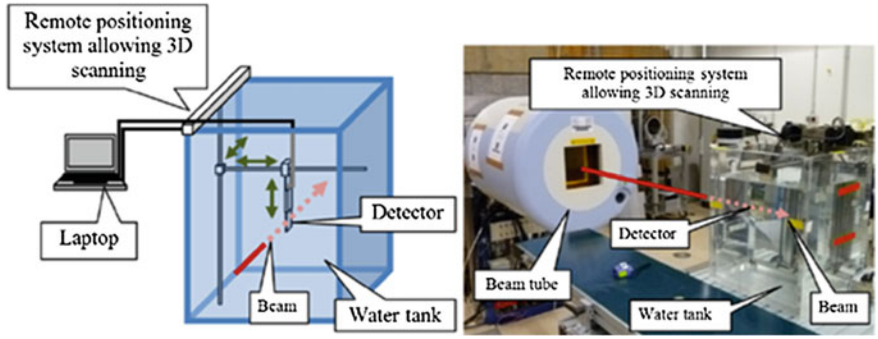

Fig. 2.24 Setup for measurements in the water tank phantom. The Timepix device and the readout interface were immersed in water inside using a waterproof rubber sleeve and mounted onto a three-dimensional positioning system. The beam axis is marked by the *red arrow*. *Courtesy* Prof. Dr. Lukas Opalka

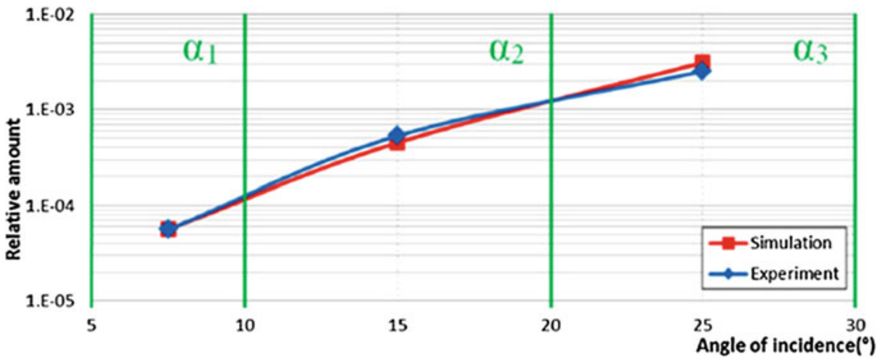

Fig. 2.25 A comparison of the measured number of secondary protons identified by Timepix and the prediction by Monte Carlo simulation at three angular intervals. *Courtesy* Prof. Dr. Lukas Opalka

It is also possible to achieve with this mount using a Monte Carlo simulation. Figure 2.25 shows a comparison between the number of secondary protons and the prediction by Monte Carlo simulation, which are in excellent agreement.

With such a system, it was possible to show that there are many events occurring beyond the Bragg peak, corresponding to secondary energetic particles, produced in the fragmentation processes as protons, fast neutrons, and gamma rays.

2.8.1 Microdosimetry Measurements

A tissue-equivalent proportional counter (TEPC) is a plastic sphere with a wall thickness of 1.27 mm and an internal diameter of 12.7 mm, which is equivalent to a few microns of a tissue sphere (Figs. 2.26 and 2.27). This device simulates a cell nucleus. The lineal energy is given by $y = \varepsilon/\lambda$, where y is the lineal energy, ε is the energy deposited in the TEPC, and $\lambda = 2/3d$ is the average length. In microdosimetry experiments, the lineal energy is measured using a TECP (Fig. 2.28).

The spheres are created to simulate cell nuclei. They have 1.27-mm-thick plastic walls, an inner radius of 12.7 mm, and are placed in water (phantom). The TEPC can be displaced on the translation table for any point XYZ in three dimensions (spatial). The measurements are performed by the electronics connected to the TEPC. To calculate the absorbed dose of radiation, the following equation can be used:

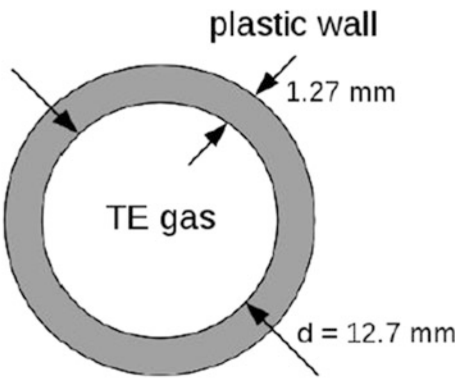

Fig. 2.26 Plastic sphere filled with gas at low pressure. TE = tissue equivalent. Reproduced from [10]

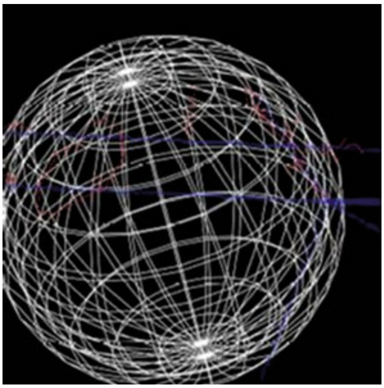

Fig. 2.27 *Sphere* with traces representing nucleons and nuclear fragments (*blue*). Fast electrons are shown in *red*. Reproduced from [10]

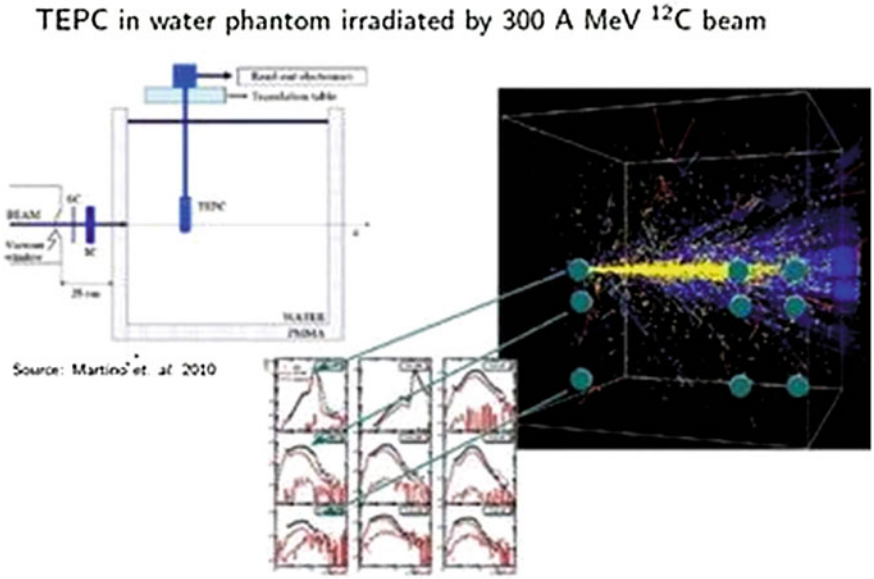

Fig. 2.28 Experimental arrangement used for microdosimetry at Gesellschaft fur Schwerionenforschung. Reproduced from [10]

$$D(\mathrm{Gy}) = \left(0.204/d^2\right)Y_f,$$

where d corresponds to the diameter of the simulated volume (μm), Y_f is given in keV/μm (average value), and D is the dose given in Gray (Gy). This unit is used in physical and not biological measurements.

2.9 Fluka: A Simulation Code

The simulation code FLUKA was originally designed for physics research involving accelerators and detectors. (See [21–26] for links that provide open access to FLUKA.)

Physicists use FLUKA to precisely predict electromagnetic and nuclear interactions in matter. For example, at CERN it is used to study beam-machine interactions and radiation damage. NASA has used it to analyze the radiation exposure of astronauts [27]. FLUKA is now used in state-of-the art therapy involving ion beam facilities, such as the HIT in Germany, to support treatment planning for cancer patients undergoing radiation therapy.

FLUKA used employed to generate large amounts of data and provide access to commercial software for treatment planning. It is also used for recalculating and

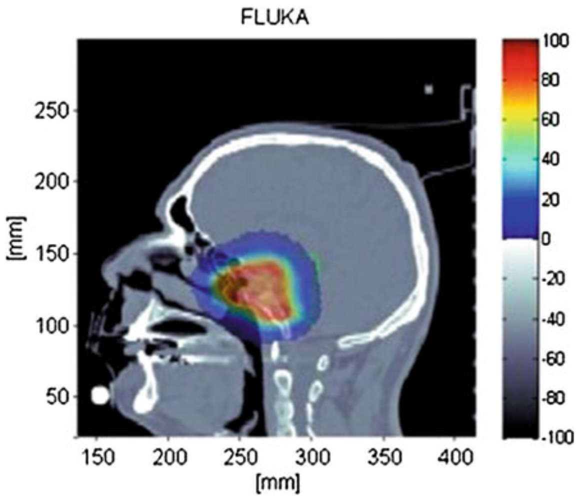

Fig. 2.29 Use of FLUKA to calculate the radiation dose distribution in a patient. The *color bar* shows the normalized values of the dose. *Courtesy* of Andrea Mairani (CNAO, Pavia, Italy)

verifying treatment plans. Till Böhlen, a researcher at the CERN Partner Project, is developing FLUKA for ion beam therapy. According to Böhlen, FLUKA is a valuable tool to accurately compute treatment doses, which is particularly useful in critical treatment care situations (e.g., the patient has a metal implant in the target area of intervention).

Future developments will include the development of improved FLUKA physical models for new ions, such as oxygen and helium, with a view to possible use in hadron therapy. The code is also widely used to simulate the secondary radiation that is produced during treatment when patient tissues interact with the beam. Secondary radiation is being studied as a very powerful tool to perform in vivo monitoring during treatment (Fig. 2.29).

In addition to FLUKA, GATE and GEANT4 software should be mentioned [28, 29]. GEANT4 has been used in applications involving particle physics, nuclear physics, accelerator design, space engineering, and medical physics. It was created by physicists and software engineers using object-oriented technology and is implemented in the C++ programming language. GEANT4 is a code used to simulate the passage of particles through matter, encompassing geometry, physical models and tips, which are very useful in electromagnetic, optical, and hadronic processes. It covers an energy range from 250 eV to TeV. GEANT4 has been widely used in simulations for hadron therapy.

A literature search to check the comparative effectiveness of FLUKA indicates that it is still difficult to give any recommendation. The problem should first be studied in more detail [30–32]. CERN comprehensively supports the development and use of FLUKA. It is also used at the Centro Nazionale di Adroterapia Oncologica, Pavia, Italy, where CERN researchers, mainly Entervision fellows, seek experimental data for their theses.

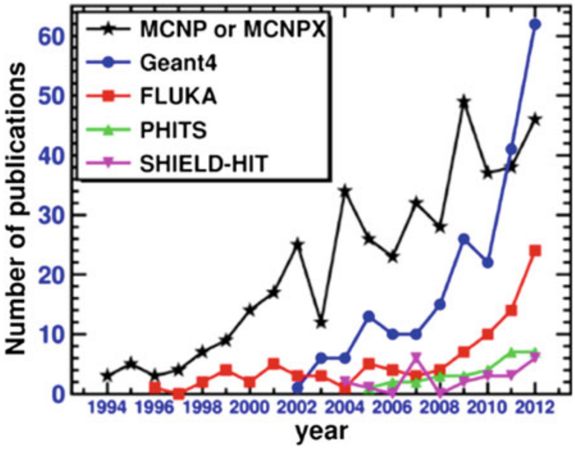

Fig. 2.30 Annual number of publications related to hadron therapy, where respective Monte Carlo codes/tools were used. *Source* Web of Science database (Thomson Reuters), October 2013. *Courtesy* Prof. Dr. Angela Bracco, NuPECC Chair

Figure 2.30 shows the number of publications related to hadron therapy by year, where different codes/tools in the Monte Carlo simulation are used. As shown, GEANT4 is predominately used today. However, FLUKA's flexibility and satisfactory agreement with dosimetry data and production of nuclear fragments indicate that the code is a valuable for supporting a wide variety of applications for proton and carbon ion therapy.

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