Nuclear Instruments and Methods in Physics Research A ∎ (∎∎∎∎) ∎∎∎–∎∎∎

Contents lists available at ScienceDirect

Nuclear Instruments and Methods in Physics Research A

journal homepage: www.elsevier.com/locate/nima

Current and future accelerator technologies for charged particle therapy

Hywel Owen [a,b,*], Antony Lomax [c,e], Simon Jolly [d]

[a] School of Physics and Astronomy, University of Manchester, UK
[b] Cockcroft Institute for Accelerator Science and Technology, Daresbury Science and Innovation Campus, Warrington WA4 4AD, UK
[c] Paul Scherrer Institute, Villigen, Switzerland
[d] Department of Physics and Astronomy, University College London, UK
[e] Department of Physics, ETH Zurich, Switzerland

ARTICLE INFO

Keywords:
Accelerator
Radiotherapy
Proton
Cyclotron
Synchrotron
Linac

ABSTRACT

The past few years have seen significant developments both of the technologies available for proton and other charged particle therapies, and of the number and spread of therapy centres. In this review we give an overview of these technology developments, and outline the principal challenges and opportunities we see as important in the next decade. Notable amongst these is the ever-increasing use of superconductivity both in particle sources and for treatment delivery, which is likely to greatly increase the accessibility of charged particle therapy treatments to hospital centres worldwide.

1. Hadron therapy

The development of modern physics and modern medicine have gone hand in hand, and the end of the 19th century heralded not only the birth of the atomic age but also of the field of radiotherapy. Only a few months after the discovery of radioactivity and x-rays [1], high-energy photons were already being used to treat diseases of the skin [2–5] and shortly thereafter to treat cancer [6]. Today, treatment with x-ray photons remains the mainstay of radiotherapy and has become—with surgery and chemotherapy—one of the three pillars of cancer treatment. Modern radiotherapy devices have achieved a remarkable degree of sophistication, and complex techniques such as intensity-modulated radiotherapy (IMRT) are now commonplace in the hospitals of the developed world [7–13].

Whilst treatment with photons is still predominant, already in 1947 Robert Wilson pointed out that heavy charged particles such as protons could have substantial advantages when delivering a therapy dose to a patient [14]. After an initial build-up distance the dose from photons decreases more-or-less exponentially with depth in the patient; a treated region deep in the body thereby incurs an unwanted larger dose proximal (upstream) to that region, and techniques such as IMRT serve to alleviate that problem. Protons in contrast mostly deposit their energy gradually; moreover the rate of energy deposition is roughly inversely proportional to that energy, which gives rise to the characteristic Bragg peak such that most of the initial proton kinetic energy is deposited close to the end of the proton's range. A concentration of the dose deposition gives the potential to irradiate desired regions (such as tumour volumes) whilst sparing as much as possible the surrounding tissue and organs at risk (OARs).

The Bethe-Bloch equation [15–17] describes the behaviour of the energy loss as

$$-\left\langle \frac{dE}{dx} \right\rangle = kz^2 \frac{Z}{A}\frac{1}{\beta^2}\left[\frac{1}{2}\ln\frac{2m_e c^2\beta^2\gamma^2 T_{max}}{I^2} - \beta^2 - \frac{\delta(\beta\gamma)}{2}\right], \quad (1)$$

where Z and A are the atomic number and atomic mass of the absorber, z is the charge of the incident particle, $I \simeq 11.5Z$ eV is the mean ionisation potential, $T_{max} = 2m_e c^2\beta^2\gamma^2/[1+2\gamma m_e/M+(m_e/M)^2]$ is the maximum kinetic energy that may be imparted to an electron in a single collision, $k = 4\pi N_A r_e^2 m_e c^2$, and β and γ are the conventional relativistic factors. $\delta(\beta\gamma)$ is a density correction term [18]. This equation highlights many of the factors influencing the use of heavy charged particles for therapy. Firstly, the depth at which the Bragg peak occurs is set by choosing an appropriate initial energy; as an example, ICRU49 defines that a 230 MeV initial proton energy has a mean range of about 33 cm in water [19,20], a reference material quite close to densities encountered in tissue. Higher-density materials have a greater stopping power, and heavier ions such as $^{12}C^{6+}$ require much greater energies up to 450 MeV/u to obtain the same 33 cm range. Uncertainties in each of these parameters—the value and spread of the initial energies, the composition and density of the material passed through, and the validity of the model used to estimate the

* Corresponding author at: School of Physics and Astronomy, University of Manchester, UK.
E-mail address: hywel.owen@manchester.ac.uk (H. Owen).

http://dx.doi.org/10.1016/j.nima.2015.08.038
0168-9002/

slowing rate—are all important factors in predicting the range of dose deposition mechanisms of the incident particles. Both accurate imaging and accurate estimation of dose deposition are required to obtain the dose advantages that the Bragg peak offers.

1.1. Clinical treatment requirements

Modern radiotherapy has developed a typical regimen wherein a curative treatment divides application of irradiation to a site into several fractions spaced around a day apart. For example, a prescribed prostate treatment might demand a total treatment dose of 70 Gy to the treatment site (the planning treatment volume, or PTV) administered in 35 fractions of 2 Gy each over 7 weeks. Fractionation benefits from the nonlinear and differing response of diseased and healthy tissues to dose, whilst also spreading the dose over time to treat different phases in each cell's cycle [21,22]. Whilst there is uncertainty as to whether dose administration in very short times ($\ll$1 s) might have a differing biological effect than if spread out over a longer time [23], such differences are likely to be smaller than other uncertainties such as the conversion from dose to response for a particular particle species, energy or tissue type [24–27]. Indeed, the same absorbed dose in Gy gives rise to differing radiobiological effect (RBE) accounted for in planning through a factor. For protons the RBE is presently taken to be 1.1 until there are better systematic measurements; the reference RBE is taken to be 1 for the c.1.3 MeV gamma rays from ^{60}Co decay. Heavier ions and other species such as pions can give rise to a greater RBE due in part to their higher linear energy transfer (LET). However, their higher mass and charge means that substantially higher incident energies are required for the same treatment depths in patients, necessitating larger accelerator equipment; this is discussed later. Another issue with certain species, such as pions, antiprotons and ^{12}C ions, is that the sharp distal fall of dose beyond the Bragg peak may be somewhat spoilt by other processes such as annihilation or fragmentation; this effect must be balanced against the RBE advantages for some tumour sites. For example ^{12}C might have an RBE as much as 3.5 depending upon the cell type and end point studied, and carbon-ion therapy is indicated in particular for some radioresistant tumours [22,28–31]. The use of heavy ions such as carbon may allow fewer fractions to be utilised; consideration of the differing biological effects is described for example in Tsujii et al. [32]. The relative merits of using protons or carbon ions for radiotherapy is the subject of some debate at present [33–35].

To determine the requirements of the accelerator one must also consider the total volume of the PTV into which the dose must be administered; the larger the volume, the larger the number of particles that must be delivered. A typical volume useful for specifying accelerators is to assume a litre-sized PTV some depth within the patient. If the depth range of the PTV is, say, 10–20 cm then it may be covered by varying the incident proton energy such that the Bragg peaks for each energy occur at different depths. This is the concept of the spread-out Bragg peak (SOBP), and may be achieved either by interposing a suitable varying-thickness modulator wheel [36], or by adjusting the proton energy in discrete steps by some other means; the latter method forms part of the burgeoning method of spot scanning which is replacing the previous passive spreading methods as a means of efficiently covering the PTV. To cover this canonical 10–20 cm depth in water requires proton energies from about 112–166 MeV, and 1 Gy of dose in this litre volume requires around 90 billion protons (90 Gp) of 22 pJ average energy, or about 16 nC of charge [37]. Appropriate intensity weighting of the different-energy spots allows a homogenous dose to be obtained within the PTV; this technique is known as Intensity-Modulated Proton Therapy (IMPT). It should be noted that it typically takes some minutes to adequately settle and position a patient so that an accurate treatment may be administered, and so from the point of view of patient throughput it is adequate to deliver that 1 Gy in about a minute. A very high proton fluence might allow tumours to be treated without correcting for patient motion, but this would be quite difficult owing to the requirement to monitor fluctuations in the delivery of those protons. Delivering 1 Gy in a minute translates to a required average proton current of less than 1 nA, a rather modest value compared to other applications of such particle accelerators; somewhat lower currents are required e.g. for therapy with carbon ions. Proton and carbon-ion treatments already benefit from motion compensation methods using techniques such as beam gating [38,39].

As well as the current and energy requirements one must also consider the requirements on the transverse beam size and energy spread. As any heavy charged species such as a proton traverses a solid material, it scatters and loses energy with some statistical fluctuations. The primary ionisation energy loss gives rise to a straggling of the range; the Bragg peak has a finite width which to a good approximation is about 1.1% of the range, in other words about 1–2 mm. There is little point therefore in having a very small initial energy spread as it will be smeared out by the straggling, and so 0.4% energy spread is generally adequate. Similarly, multiple coulomb scattering (MCS) will spread the protons out transversely, and again an initial incident spot size of a few millimetres is adequate; this translates to an emittance requirement of around 10 mm-mrad. These beam specifications are readily achieved by conventional accelerator technology as will be seen below [40,37,41].

The final requirement is to be able to vary the direction from which the administered dose is delivered to the patient. In a very limited set of cases the patients themselves may be moved somewhat, but in most treatments the patient is supine and the incident particles must be directed from a variety of angles; this is done primarily to avoid dose to critical structures but also to spread out the proximal (upstream) dose. In this regard the gantries used in charged particle therapy serve a similar purpose to the smaller rotating electron linacs that deliver photons for intensity-modulated radiotherapy (IMRT). The most-used method of achieving a varying field angle is to utilise a so-called isocentric gantry, where the beam is rotated around a stationary patient; this is shown schematically in Fig. 1. Other geometric arrangements are possible, notably the alternative of mounting the accelerator itself upon the gantry, but the isocentric gantry is the method used in most proton treatment rooms today. Whilst a full 360° of rotation means the patient would not have to rotate, recently it has also been proposed to combine a narrower range of gantry rotation angles (say, around 180°) with patient table rotation; the rationale for this is to restrict the floor area required for each treatment room. Gantries may also be used for other ions, but as those species become heavier the magnetic fields required to deflect them increase accordingly. The stiffness of the ion beam is described by its magnetic rigidity $B\rho = p/q$, where the particle momentum p and charge q determine the trade-off between magnetic field B and resultant bending radius ρ. For example, protons of kinetic energy 250 MeV are sufficient to treat adult patients and have a magnetic rigidity of 2.43 Tm; 1.8 T is about the largest field available from a resistive (normal-conducting) magnet, leading to a bending radius of 1.35 m. The only carbon-ion gantry currently in operation is at the Heidelberg Ion Beam Therapy Centre (HIT), where the maximum carbon-ion energy of 425 MeV/u corresponds to a magnetic rigidity of 6.57 Tm; the bend radius in their normal-conducting magnets is thus nearly three times as large (3.65 m), and to make it smaller requires the use of superconducting magnets that may deliver a larger magnetic field.

Please cite this article as: H. Owen, et al., Nuclear Instruments & Methods in Physics Research A (2015), http://dx.doi.org/10.1016/j.nima.2015.08.038