Journal of PharmaSciTech
ISSN: 2231 3788 (Print)
2321 4376 (Online)
Review Article

A Brief Review on Proton Therapy: An Advanced Tool for Cancer Treatment

Saumyakanti Giri*, Falguni Patra

* Department of pharmaceutics, NSHM College of Pharmaceutical Technology, 124 B L Saha Road, Kolkata- 53

Correspondence: rx.saumyakanti.giri@gmail.com (Tel.: +918759818603)

Article Info:
Received: 09.04.2019
Accepted: 16.06.2019
Available online: 01.9.2020

Abstract

The suggestion made in 1946 by Robert R. Wilson that beam of high energy positive charged protons could be used to destroy cancer cells by ionizing them has come long way to become an effective and advanced treatment method for cancer therapy. Conventional radiation therapy damages the deeper tissues and produces unwanted side effects. On the other hand proton therapy is having no such effect on deeper tissue as the protons in the beam have mass and their velocity and tissue penetration can be regulated as opposed to radiations used in conventional therapy. Proton therapy has proven itself to be much safer and efficacious than the conventional radiation method as evident from the reports of clinical studies showing lesser re-occurrence of cancer in case of proton treated patients is much than the conventional radiation treated patients. Presently, this therapy is best applicable for prostate cancer, eye tumour, breast cancer, lungs cancer, brain tumour with ongoing attempts to use in irregular shaped cancer cells and moving cancer cells for an effective treatment with significant long-term benefits.

Keywords: Cancer, Proton, Proton therapy, Prostate cancer, Radiation therapy

Introduction

Proton therapy is one type of particle therapy that uses a beam of protons to damage the cancer cells. There are some significant differences between conventional radiation(x-ray) treatment and proton therapy. The major positive thing about the proton therapy is lesser side effects. In case of conventional radiation therapy healthy tissues may receive a similar dose of radiation like the cancer cells and can be damaged. That is why in case of conventional radiation therapy a less than desired dose is frequently used to reduce damage to healthy tissues and avoid unwanted side effects. The beauty of proton therapy is that, higher doses of radiation can be used to control and manage cancer cells while significantly reducing damage to healthy tissue and vital organs. Another chief advantage of proton therapy over the conventional radio therapy is that the maximum amount of dose is deposited over a narrow range and there is minimal exit dose. This paper explains the theory of proton therapy; benefits of this therapy, specialized equipments used in this therapy and also explore the application of this therapy in different types of cancer.

History

In 1940s Robert Wilson hypothesized that proton beams could be utilized in increasing the radiation doses to tumors while minimizing radiation to adjacent normal tissues.After some initial studies on mice, the Lawrence Berkeley National Laboratory in CA, USA started the world's first proton therapy for humans in 1954. In 1957 Uppsala University in Sweden started using Bragg peaks of proton beams to treat intracranial patients. After that Harvard Cyclotron Laboratory, in collaboration of Massachusetts General Hospital, CA, USA, began intracranial radiation therapy using proton beams in 1961. First hospital based proton therapy program was started in 1990 at Loma Linda University Medical Centre, CA, USA.

Proton therapy

Protons are positively charged subatomic particles which are having massive mass compared with x-rays. In proton therapy, protons can be accelerated in cyclotron or synchrotron to 40%–70% of the speed of light. After entering in to the human body, high-energy protons interact with the body tissues through mostly electromagnetic interaction and sometimes nuclear interaction. The biologic effects of protons and x-rays on cells are similar. Both protons and x-rays cause ionization to the normal cell. This ionization further leads to damage DNA in tumor cells, which may lead to tumor cell death. However, the way protons interact with cells provides advantages compared with x-rays.

A large number of in vitro studies have shown that, proton radiation is approximately 10% more effective than photon radiation in case of killing cancer cells, when the dose of radiation is same in both cases [1]. When protons enter in to the body, they deposit a very low entrance dose. The depth of proton penetration is dependent on kinetic energy of its own and the depth of penetration is directly proportional to the kinetic energy of proton. The protons have minimum exit dose. This physical advantage serves to lower the dose to healthy organs both superficial and deep to the tumor, thus reducing the risk of injury. It also allows administration of a higher dose of radiation to the tumor cells, potentially reducing the recurrence rate. The theoretical benefit of proton radiation is based on the physical distribution of its radiation dose (energy deposited in a unit mass). The rate of energy loss of proton radiation increases when the energy decreases along the depth. As a result, the largest energy loss occurs at the end of a proton's trajectory and almost no radiation dose exists beyond it. This maximum radiation dose is known as Bragg peak [2]. By adjusting the energy of incoming proton beam in the proton accelerator the Bragg peak of a proton beam can be placed right on the tumor to be treated. This causes minimal radiation dose delivered to nearby healthy tissues. In contrast, x-ray (photon) and electron radiation have to deliver extra radiation dose to nearby healthy tissue. Figure 1 shows the depth dose distributions for some typical proton beams and photon beams.

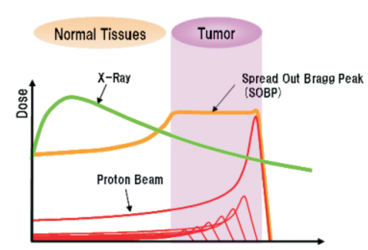

Figure 1: Graphical comparison of X-Ray therapy and Proton therapy

As proton therapy is having superior depth of dose distribution that is why it can save healthy organs around the target and lower the radiation side effects. The overall radiation dose to the patient's body is lower with compare to the conventional radiation therapy. This would lead to a reduction of radiation-induced secondary cancer. The reduced secondary cancer risk is often considered as a major benefit of this therapy especially for paediatric patients. Epidemiology data supporting this claim have started to emerge recently [3].

Equipments

Recently cyclotrons or synchrotrons are used to accelerate the protons to therapeutic energies. Commercial production of cyclotrons or synchrotrons for clinical purposes started in 1990. The major production companies are Ion Beam Applications (IBA, Louvain-la-Neuve, Belgium), Hitachi, Toshiba, Mitsubishi, and Sumitomo (Japan). Cyclotrons and synchrotrons both are particle accelerators. It uses powerful magnetic fields to speed up protons. The cyclotron uses constantly applied magnetic and electric fields to move the protons in spiral, while the synchrotron increases the strength of the magnetic field to match the change in particle energy [4].

Applications in different types of cancer

Brain cancer

The main benefits of this proton therapy for adults in meningioma, low-grade glioma, craniopharyngioma, pituitary adenoma, chordoma/ chondrosarcoma, and paranasal sinus tumors. And in case of paediatric patients, it is also well documented5. These cancers are often close to critical or complex organ structures and therefore surgery should be avoided. Postoperative proton therapy reduces the local recurrence and complications compared with photon radiation therapy [5].

Prostate cancer

In 2010 there were 217,000 estimated new cases of prostate cancer in USA, the most common malignancy (excluding skin cancer) in males [6]. Though IMRT produces excellent local control rates and genitourinary and gastrointestinal toxicity but it is manageable in most patients with low rates of long-term dysfunction. Therefore, the bar is set high for a new technique such as proton beam therapy (PBT) to deliver either improved tumor control or reduced toxicity over IMRT.

Paediatric cancer

Proton therapy is expected to benefit paediatric patients in general if they receive radiation therapy for cancer treatment. Due to the lowered dose to healthy tissues and secondary cancer risk, the impact to cognitive and endocrine functions should be lower, compared with photon radiation. Although published results are still rare, reports from ongoing investigations have shown promising results [7].

Medulloblastoma

Proton Beam Therapy is also used in case of medulloblastoma [8]. To treat medulloblastoma, we need to deliver the radiation to the entire brain and the entire spine. Generally Photon radiation spreads to the other parts of the patient's body to achieve the therapeutic goal inside the brain and spine. On the contrary, proton beams enter the patient's body posteriorly and deliver radiation dose to the spine only using the Bragg peaks; radiation dose to thoracic, abdominal, and pelvic organs that are behind the Bragg peaks are close to zero. Several data have shown that proton therapy reduces acute toxicity for adult medulloblastoma patients [9] and the secondary cancer risk in paediatric medulloblastoma patients is reduced by 90% [10].

Recent developments

There is a newer approach for proton therapy called as pencil beam. This method uses a narrow single-proton beam with a diameter near about 5 mm. The main pencil beam's characteristic is to use multiples pulses of small proton beam that hits defined planned spots within the target tissue. It starts in the deepest layer of the body and deposits dose, layer by layer, until the whole target volume is covered. Pedroni et al. estimated that a typical tumor can have from 1,000 to 2,000 spots that can be distributed in up to 24 layers for a single pencil beam treatment [11].

Conclusion

In conclusion we can say that, technically PBT is more superior to the conventional radiation therapy because the former is more target-specific in nature and have fewer side effects. Yet due to high cost it is not so much popular among patients. Apart from some technical and financial obstruction regarding this method, it is one of the best alternatives of conventional radiation therapy for the treatment of cancer.

Acknowledgement

The authors are grateful to NSHM College of Pharmaceutical Technology for providing the facilities to conduct this study.

Conflict of interest

The authors declare that they have no competing interest.

References

[1] Paganetti H, Niemierko A, Ancukiewicz M. Relative biological effectiveness (RBE) values for proton beam therapy. Int J Radiat Oncol Biol Phys 2002; 53(2):407-21.

[2] Raju MR. Proton radiobiology, radiosurgery and radiotherapy. Int J Radiat Biol 1995; 67(3): 237-59.

[3] Chung CS, Yock TI, Nelson K, Xu Y, Keating NL, Tarbell NJ. Incidence of second malignancies among patients treated with proton versus photon radiation. Int J Radiat Oncol Biol Phys 2013; 87(1):46-52.

[4] Wieszczycka W, Scharf WH. Proton radiotherapy accelerators.Singapore: World Scientific Publishing Co. Pte. Ltd.; 2001;203-17.

[5] Foote RL, Stafford SL, Petersen IA. The clinical case for proton beam therapy. Radiat Oncol 2012; 7:174.

[6] Jemal A, Siegel R, Ward E. Cancer statistics, 2008. CA Cancer J Clin 2008; 58:71-96.

[7] Jimenez RB, Sethi R, Depauw N. Proton radiation therapy for pediatric medulloblastoma and supratentorial primitive neuroectodermal tumors: outcomes for very young children treated with upfront chemotherapy. Int J Radiat Oncol Biol Phys 2013;87(1):120-26.

[8] National Association of Proton Therapy, http://www.proton-therapy.org/howit.htm . Accessed on 15/05/18

[9] Brown AP, Barney CL, Grosshans DR, et al. Proton beam craniospinal irradiation reduces acute toxicity for adults with medulloblastoma. Int J Radiat Oncol Biol Phys 2013;86(2):277-84.

[10] Miralbell R, Lomax A, Cella L, Schneider U. Potential reduction of the incidence of radiation-induced second cancers by using proton beams in the treatment of pediatric tumors. Int J Radiat Oncol Biol Phys 2002; 54(3):824-29.

[11] Pedroni E, Scheib S, Böhringer T, Coray A, Grossmann M. Experimental characterization and physical modellingof the dose distribution of scanned proton pencil beams. Phys Med Biol 2005; 50(3):541-61.