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PROTON BEAM THERAPY IN PEDIATRICS : A REVIEW

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ABSTRACT

Pediatric cancer, including leukemia and brain tumors, is increasingly diagnosed, with about 400,000 cases annually. Conventional radiation therapy, while effective, can lead to long-term side effects, including secondary cancers. This review paper aims at discussing what proton beam therapy (PBT) has to offer for children suffering from cancer looking at its advantages and disadvantages. Literature on PBT and conventional radiotherapy was reviewed to compare treatment efficacy and side effects. PBT allows precise tumor targeting while minimizing damage to surrounding healthy tissue, resulting in fewer long-term effects. Studies show higher conformity indexes for PBT, reducing risks of growth disorders and cognitive impairment. Proton beam therapy shows significant promise for improving pediatric cancer treatment outcomes and quality of life. However, high costs and limited long-term data hinder its broader adoption, necessitating further research to optimize its use.

Keywords: *Proton therapy, Pediatrik, Radiotherapy*

INTRODUCTION

Cancer is an abnormal cell growth disorder caused by genetic or epigenetic changes in somatic cells. The uncontrolled growth of these abnormal cells ultimately leads to damage in the body and can spread to other parts of the body (metastasis) (1,2). The incidence of cancer is increasing year by year, with an estimated 420 million new cases expected annually by 2025 based on global demographic characteristics (1). Approximately 400.000 children and adolescents aged 0-19 are diagnosed with cancer each year (3). Acute leukemia, brain tumors, lymphoma, bone and soft tissue sarcomas, and germ cell tumors are among the most common cancers in children. Typical "embryonal" tumors (such as neuroblastoma, kidney tumors, and retinoblastoma) are primarily found in younger children, while cancers in adolescents include more epithelial tumors (like thyroid carcinoma) and melanoma (4).

Pediatric cancer is difficult to detect early because it often presents with nonspecific signs and symptoms. Radiation therapy is an integral part of cancer treatment in children (5). There are several established treatment modalities commonly used for cancer therapy, such as radiation therapy and systemic therapies, including chemotherapy and surgery (6). In the early history of pediatric cancer treatment, surgical resection and radiation therapy were the primary treatment modalities (7). In the multidisciplinary approach to treating cancer in children, adolescents, and young adults, radiation therapy plays a crucial role as a local treatment. However, it can also be closely associated with long-term side effects, including secondary cancers (8).

Proton therapy has emerged as a preferred radiation therapy modality for certain types of cancer due to the physical properties of protons that deliver lower doses to surrounding normal tissue, thereby reducing acute and long-term side effects (9). Proton beam therapy (PBT) effectively enables the delivery of high radiation doses to tumor cells while minimizing or completely avoiding doses to normal cells which is an ideal therapeutic modality for treating malignant diseases, especially for organs at risk (OAR) with lower toxicity (10). The use of PBT tends to reduce the risk of growth and development disorders, endocrine dysfunction, fertility reduction, and second cancers in children, owing to its characteristic dose distribution with reduced dose and volume to normal organs while maintaining effectiveness against tumors (8).

MATERIAL & METHODS

In order to execute a systematic review of the literature, which is focused solely on proton beam treatment for pediatric cancers, we adhered to a particular methodology. Initially, we went through various resources for relevant studies recently done like PubMed and Scopus limiting ourselves to papers published within ten years back. Important search criteria were “proton therapy”, “paediatric cancer” and “radiation therapy.”

Data extracted includes treatment efficacy, adverse effects and proton therapy’s relative biological effectiveness in comparison with typical x-ray cancer care procedures for kids. Our intention is to track the trajectory as well as voids in popular knowledge regarding the idea of proton Beam Therapy (PBT) for children’s malignancies, underlining both its possible benefits – if properly applied – versus constraints. This systemized method was aimed to provide a clear picture of how PBT can enhance treatment while minimizing adverse effects in young patients.

RESULT & DISCUSSION

Pediatric Cancer

Cancer is a leading cause of death in both adults and children. The incidence of cancer in children is relatively lower then adults, highlighting that cancer is a genetic disease caused by the accumulation and selection of uncorrected mutations over time. However, considering children with cancer merely as a result of random "bad luck" does not fully explain the underlying etiology, which differs from that seen in adults (11). Essentially, pediatric cancer is distinct from tumors in adults because it arises from deviations in normal developmental processes, rather than developing in response to environmental DNA damage over decades, as is common in adult malignancies (12).

Pediatric cancer causes many significant impact not only in children but also in their families, and it has become one of the most frequent causes of mortality in children all over the word (13). The incidence of cancer in children who are less than 5 years weighs less than 1% in mortality among this group. In contrast to usual contagious conditions, management of c cancer in children signifies the need for collaboration among various experts, enhanced provision of resources, adequate facilities, and sufficient diagnostic resources (14).

Childhood cancer could be viewed as different from adult cancer with effective management due to both chemotherapy and radiation are associated with severe effects and treatment might come late (13). In the last few decades, progressive realization is that childhood cancer survivors develop health problems secondary to prior therapies that should be expected to include virtually every organ or body system (15). As the population of children with the diagnosis of cancer, survives the population and grows older, the long-term consequences of surviving childhood cancer are becoming apparent. Thus, the requirement for enhanced medications formulated for children is justified; however, designed therapies remain underutilized because few cancer medications have been approved for only children (11).

Proton Beam Therapy (PBT)

Proton therapy is a type of radiation treatment for cancer that uses protons instead of X-rays (11). The term "proton" was first proposed by Ernest Rutherford when he reported its existence in 1919 (16). Proton radiation is an emerging therapy for localized cancer that is increasingly sought after by patients (17). Its highly conformal dose distribution compared to photons is a key reason for the use of proton therapy, as it allows for greater sparing of normal tissue while enhancing tumor doses, potentially improving outcomes (18).

The biological effects of proton radiation are believed to be essentially identical to those of photon radiation, where ionization events lead to the formation of free radicals and subsequent DNA damage. However, the relative biological effectiveness (RBE) of protons is estimated to be about 10% higher than that of photons. Therefore, proton doses are described as cobalt gray equivalent (CGE), translated as photon-equivalent doses measured in gray (Gy) (19). Compared to photon therapy, proton therapy spares more critical structures due to its unique physics (17). The physical properties of the proton beam make it ideal for clinical applications, providing clear dosimetric advantages that enhance treatment conformity and reduce doses to surrounding normal tissue. This can yield significant clinical benefits by reducing treatment toxicity while maintaining or improving cure rates (20).

Proton therapy utilizes protons, which are positively charged particles, accelerated to therapeutic energies typically ranging from 70 to 250 MeV. This enables precise targeting of tumors while minimizing damage to surrounding healthy tissue. The depth-dose characteristics of protons are described by the Bragg curve, which shows that protons deposit most of their energy directly at the tumor site, thereby reducing exposure to normal tissue (18).

A major advantage of proton therapy is the Bragg peak phenomenon, where protons release most of their energy at a specific depth within the tissue, allowing maximum doses to be delivered to the tumor while reducing exposure to healthy tissue both in front of and behind the targeted tumor (19). For relatively shallow tumors, unlike the depth-dose curve of photons, which shows an exponential decrease in energy with increasing depth, the Bragg peak allows for a rapid decrease in radiation dose at the end of the range, with sharp lateral dose drop-off and maximum energy deposition at the target area, resulting in nearly no energy deposited in surrounding tissues. Thus, PBT effectively enables high radiation doses to tumor cells while delivering very low or zero doses to normal cells, recognized as an ideal therapeutic modality for treating malignant diseases, especially for OAR with lower toxicity (10).

Despite the potential advantages of proton therapy, controversy surrounding it arises from issues of cost, evidence gaps, marketing practices, and ongoing debates about its appropriate use and value in cancer treatment. To optimize the benefits of proton therapy, there is a need for ongoing efforts to update insurance guidelines, enhance research, and support evidence-based applications (20). Most existing studies on radiation side effects are based on photon therapy, resulting in a knowledge gap regarding the long-term effects of proton therapy. RBE on neutrons, which can be more carcinogenic than photons, adds another layer of complexity due to its significant variability and incomplete understanding in humans (9).

Proton Beam Therapy in Pediatrics

Proton therapy allows for highly precise tumor targeting. Protons can be controlled to release their energy directly at the tumor site, minimizing damage to surrounding healthy tissue. This is particularly beneficial for pediatric patients, as developing organs are more sensitive to radiation exposure and have a higher risk of long-term side effects from conventional radiation therapy (5,9). The conformity index for proton radiotherapy is higher (0.97-0.98) compared to various photon techniques (0.93-0.94). This means that the radiation is more accurately directed at the tumor, minimizing damage to adjacent healthy tissue (21).

Proton therapy is highly beneficial for pediatric patients because their bodies are still developing. Clinical studies have shown that this therapy can limit long-term side effects, especially in cases of pediatric intracranial tumors. This is crucial as children are more sensitive to radiation, and minimizing exposure to non-target organs can help preserve neurocognitive function. Proton therapy can provide significant advantages in minimizing radiation exposure to non-target organs in pediatric patients, potentially reducing long-term side effects associated with radiation therapy. This is especially important in the treatment of pediatric cancer, where preserving the health of healthy tissue is vital for the future well-being of the patient (20).

One significant advantage of proton therapy for children is its ability to reduce late toxicity. Pediatric patients are at higher risk for secondary malignancies and other long-term side effects due to radiation exposure. The precision of proton therapy allows for lower radiation doses to surrounding healthy tissue, thereby reducing this risk. Longitudinal studies on pediatric patients indicate that proton therapy can help maintain cognitive function, as evidenced by the preservation of IQ scores compared to those treated with photon therapy. This is particularly relevant for young patients whose brains are still developing and are more vulnerable to radiation-induced damage (22).

Proton therapy can reduce the risk of long-term side effects related to radiation and the incidence of secondary malignancies compared to conventional photon-based radiotherapy. This is important for maintaining quality of life (QoL) in pediatric patients. The American Society for Radiation Oncology (ASTRO) has recognized the clinical benefits of proton beam therapy (PBT), particularly in cases where photon-based therapy cannot adequately protect surrounding normal tissue. This support is based on medical need and clinical evidence generated through approved trials and registries (23).

CONCLUSION

In summary, one of the most concerning health issues remains cancer, in particular childhood cancer, given its complicated genetic and developmental etiology. Although progress has been made in treatment options like proton beam therapy, which volume of treatment reduces the damaging effects of conventional radiation therapy in children, whose bodies are not yet fully developed, it still presents a problem. The effectiveness of proton therapy is based on accurate and effective delivery of radiotherapy only to tumor-containing areas and protection of organ at risk from being harmed by the therapy, this has the potential of managing childhood cancers and enhancing the quality of life. However, this is not a fully accepted idea because the therapy has cost implications, and long-term data and research on it are limited. More support and studies are required for the proper use of the therapy.

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