Radiation Therapy in Pediatric Oncology: Balancing Treatment Efficacy and Long-Term Risks

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ABSTRACT

Radiation therapy is a crucial component of pediatric oncology treatment; however, its use in children poses unique challenges. This review article explores the complex balance between treatment efficacy and long-term risks associated with radiation therapy in pediatric patients. While radiation therapy is a cornerstone of pediatric cancer treatment, its application requires meticulous consideration because of the heightened sensitivity of children to the long-term effects of radiation. Drawing on case studies and expert insights, it is essential for healthcare providers to be fully aware of the treatment and its management to deal with the long-term effects on the developing body. Additionally, the importance of personalized treatment plans, ongoing monitoring, and research to minimize risks and optimize outcomes for pediatric patients undergoing radiation therapy is discussed in this review.

Key words: Radiation exposure, pediatric cancer, health risks, prevention

INTRODUCTION

It is widely recognized that children exhibit greater sensitivity to radiation compared to adults, primarily due to their higher rates of cell division. Furthermore, children have a longer potential lifespan following radiation exposure, which increases the likelihood of radiation-induced cancer development. Consequently, children may face elevated stochastic risks from ionizing radiation exposure, even at doses equivalent to those received by adults. Studies have shown that the lifetime attributable risks for overall cancer incidence and mortality in 10-year-old children (both male and female) are approximately 5.29 and 3.16 times higher, respectively, than those of 70-year-old adults. These risks are even more pronounced in younger children.[1]

The increased vulnerability stems from several factors such as cellular sensitivity, longer life span organ development, cumulative exposure etc.[2]While radiation can be life-saving, the potential harm it causes to healthy tissues is a major concern, especially for pediatric patients. The challenge is to balance the need to effectively treat cancer while reducing the lifelong impact of radiation exposure on a child's health and development.

PEDIATRIC CANCER

Pediatric cancer encompasses a range of malignancies affecting children under 18 years of age. Common types include leukemias, brain tumors, lymphomas, and bone tumors.[3]The symptoms of pediatric cancer can vary depending on the type and location of the tumor, but may include pain, fatigue, nausea, and neurological issues. Children with cancer often experience multiple symptoms simultaneously, which can significantly impact on the quality of their lives and ability to function.[4] Interestingly, while pediatric cancers are relatively rare, they remain a leading cause of death in children.[5]

However, advancements in treatment have dramatically improved survival rates, with overall survival now reaching around 90% .[6]This progress is largely due to increasingly aggressive multimodal therapies delivered within clinical research trials.[7] Treatment approaches for pediatric cancer typically involve a combination of chemotherapy, radiation therapy, and surgery, tailored to the specific type and stage of cancer, as well as the child's age and overall condition.[8] Additionally, newer therapies such as immunotherapy and targeted therapies are showing promise, although they may come with their own set of side effects, particularly affecting the central nervous system[9]. Importantly, pediatric cancer treatment requires a multidisciplinary approach, integrating medical interventions with psychological support and symptom management strategies to address the complex needs of young patients and their families.

RADIATION THERAPY

Radiation therapy is a cancer treatment that uses high-energy rays to kill cancer cells. The rays damage the DNA strands of the target cells, either directly by hitting the DNA strand or indirectly by interacting with a water molecule to produce a hydroxyl radical that impacts the DNA.[12] This process is mediated by oxygen-derived free radicals.

Research has shown that exposure to high levels of ionizing radiation can increase cancer risk. Recent studies suggest that even low radiation doses may contribute to cancer development. Common imaging techniques, such as CT scans, PET scans, and bone scans, involve significant radiation exposure. Children with cancer, especially those with solid tumors, frequently undergo multiple imaging studies during diagnosis, treatment, and follow-up, resulting in repeated low-dose radiation exposure. The radiation exposure from these imaging studies may be sufficient to elevate the lifetime cancer risk for these children.[13]

Radiation therapy is a crucial method for treating malignant neoplasms, offering high efficacy in cancer treatment.[14] It is commonly used to alleviate pain associated with bone metastases and can be applied for both systemic and local effects in patients with bone and soft tissue tumors .[15]The treatment has curative or palliative potential in approximately half of all incident solid tumors and offers organ and function preservation in most cases.[16] Despite its effectiveness, radiation therapy can lead to various complications in both the early and late periods. These complications can affect multiple systems, including the bone system, lungs, myocardium, gastrointestinal tract, genitourinary system, and hematopoiesis system.[17] Interestingly, the symptoms of late complications are often nonspecific and similar to those of somatic diseases, making diagnosis challenging for general practitioners and therapists.

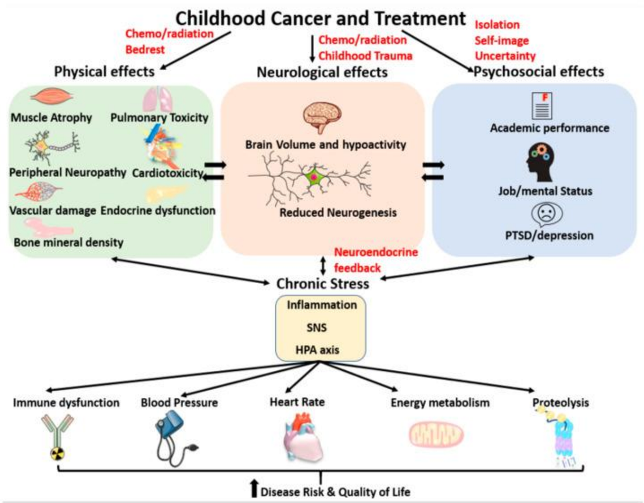

Figure 1: The above representation depicts the complex relationships between pediatric cancer, its treatment, and the resulting physical, neurological, and psychosocial impacts that contribute to long-term stress.

The diagram shows a two-way connection among physical, neurological, and psychosocial effects, as well as between chronic stress and impairment in these systems. It also highlights the significant health consequences of prolonged stress, which can increase disease susceptibility and diminish overall life quality.[27]

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The incidence of major complications is estimated at about 12%, but this figure may be underestimated due to the long delay between radiation therapy and the diagnosis of some adverse events.[18]

The long-term risk of cancer development in children exposed to radiation is the second cancers. The sources highlight that child treated with radiation therapy, a key component of cancer treatment, face an elevated risk of developing second cancers later in life[20]. This increased risk is attributed to the DNA-damaging effects of radiation and the prolonged lifespan of children, which allows more time for radiation-induced cancers to emerge.[2] The risk of developing second cancers is generally dose-dependent, meaning higher radiation doses are associated with a greater risk.[12] This observation suggests that minimizing radiation doses during treatment is crucial to reducing the risk of future malignancies. This risk extends to various cancer types, potentially including a type different from the one initially treated. To determine the likelihood of a specific cancer recurring in a child who has undergone radiotherapy, additional factors must be considered, including certain cancers that are inherently more prone to recurrence than others. The stage of cancer at the time of diagnosis significantly impacts the risk of recurrence. Some children may have a genetic predisposition to certain cancers, making them more susceptible to recurrence. It is essential to consult with an oncologist to obtain personalized information about the risk of cancer recurrence and appropriate follow-up care for a child who has received radiotherapy.

Radiation therapy remains an essential component in cancer treatment, but it is crucial to consider and manage its potential side effects. Recent progress in molecular pathology and normal-tissue radiobiology has improved the understanding of late normal-tissue effects, shifting focus towards damage recognition and tissue remodeling. This has stimulated research into new pharmacological strategies for preventing or reducing side effects. Additionally, the role of nurses in predicting and managing side effects of radiation is becoming increasingly important, thereby emphasizing the need for comprehensive patient care and follow-up.[19]

MITIGATION

Radiation exposure in children with cancer is a significant concern due to their increased susceptibility to radiation-induced late effects. Different types of External Beam Radiation Therapy (EBRT) Techniques and associated advantages and disadvantages are summarized in table 1.

Table: 1 Advantages and Disadvantages of EBRT

S. No.	External Beam Radiation Therapy (EBRT) Technology	Types of Cancer Treated	Advantages	Disadvantages
1.	3 dimensional conformal radiotherapy (3DCRT)	Brain tumors, breast cancer, gastrointestinal (GI) cancer, lung cancer and gynecologic malignancies.	Improve short-term response rate, reduce mouth dryness and parotid gland injury, and promote the prognosis of patients with nasopharyngeal carcinoma.	Shows higher gastrointestinal toxicities in patients with endometrial cancers. Difficult to perform correct quality procedures, positioning, imaging, contouring, dosimetry, follow-up, and dose delivery
2.	Intensity modulated radiotherapy (IMRT)	Head and neck, prostate, breast, lung, brain, gynecologic, and GI cancers.	Provides high conformity and high precision.	IMRT is prone to geometrical errors, due to higher dose conformity indices.
3.	Volumetric modulated arc therapy (VMAT)	Head and neck, non-small cell lung cancer (NSCLC), prostate, gastrointestinal, gynecological, thoracic, central nervous system, and breast tumors	Provides a full 360° of beam directions with the entire dose volume delivered in a single rotation VMAT treatment shows a lower risk of OAR irradiation and has better homogeneity compared to IMRT. Significant role in uncomfortable immobilization.	Increase in the low dose radiation to the surrounding tissues and organs, with a greater chance of having secondary malignancies.
4.	Image guided radiotherapy (IGRT)	Prostate, lung and head and neck cancers	Significant reduction in set-up margins resulting in reduced toxicities in sites with demonstrable, quantifiable, and correctable inter- and/ or intra- fraction motion	Uncertainties in target volume delineation, image quality, longer acquisition times, high intra-fractional errors, and extra-dose delivery during daily imaging
5.	Stereotactic body radiation therapy (SBRT)	Prostate, head and neck, spinal, renal, oligo metastases, and pancreatic	Provides high doses of radiation to the tumor and has low risk of postoperative risk and death.	Post treatment side-effects.
6.	Particle therapy Proton Neutron Carbon	Stage II–III NSCLC, prostate carcinoma, chordoma and hepatocellular carcinoma etc.	Particle radiation has a higher biological effectiveness and is very effective in radio-resistant cancers.	The production of particle radiation therapy is much more expensive than the production of photons, and has more logistical requirements
7.	Photodynamic therapy (PDT)	Esophageal, non-small cell lung cancer and Barrett's esophagus patients	PDT specifically accumulates into tumors and uses intense non-thermal visible light source.	Success of PDT is limited by uptake and localization of the photosensitizer, the method of light delivery, spatio-temporal organization and location of tumors, singlet and triplet quantum yields, and associated side-effects

To mitigate this risk, various strategies have been implemented in pediatric oncology. Intra operative radiotherapy (IORT) has shown promise in limiting radiation exposure to normal tissues, potentially reducing toxicity compared to conventional external beam radiotherapy.[21] Advanced treatment techniques, including better dose delivery to target areas while minimizing exposure to nearby organs at risk, have led to improved outcomes and reduced treatment-related toxicities.[22] Interestingly, while oncologists recognize the importance of radiation dose reduction, there is a lack of awareness about specific techniques used in their institutions. However, the majority support long-term imaging surveillance despite the absence of national guidelines. This highlights the need for better communication and education among healthcare providers regarding radiation exposure management. Several approaches have been developed to mitigate radiation exposure in pediatric oncology patients. These include the use of low-dose CT imaging for specific patient populations,[23]implementation of dose reduction techniques in radiography systems,[24] and the adoption of radiation-limiting measures during catheterization procedures.[25]

Some new technologies in radiation therapy that can reduce the risk of acute and late organ dysfunction and toxicity, specifically for tumors in the thoracic cavity[1] which include techniques like Deep Inspiration Breath-Hold (DIBH) which involves delivering radiation only during one phase of breathing (deep inspiration), allowing for less exposure to normal tissues.[2]

Conformal radiation therapy and proton-beam therapy are two other newer techniques that may be associated with fewer long-term adverse effects than traditional radiation therapy. Conformal radiation therapy uses advanced imaging techniques to shape the radiation beams to the tumor, thus minimizing exposure to surrounding healthy tissue. Proton-beam therapy uses a beam of protons instead of X-rays. Protons deposit their energy more precisely in the tumor, reducing damage to nearby healthy tissue. More research on childhood cancer survivors is needed to establish long-term risks and to evaluate the impact of newer radiation techniques.[12]

Additionally, strategies to improve children's experience during radiation therapy, such as video-based distraction therapy and augmented reality, may help reduce the need for anesthesia and potentially decrease overall radiation exposure.[26] Continued efforts in research, education, and implementation of these strategies are crucial to optimize the balance between effective treatment and minimizing radiation-related risks in pediatric cancer patients.

CONCLUSION

Radiation exposure in children with cancer can have serious consequences for their health and well-being. It is important for parents and caregivers to be aware of the risks and take steps to protect their children from unnecessary radiation exposure. One way to do this is to carefully review the treatment plans suggested by their doctor and ask questions about any radiation therapy that may be recommended. Another way is to advocate for alternative treatments that do not involve radiation, such as chemotherapy or immunotherapy. Additionally, it is important to ensure that children receive proper nutrition and hydration to help their bodies better tolerate the effects of radiation therapy. Finally, it is essential to follow the doctor's orders carefully and ensure that the child attends all scheduled appointments to ensure the best possible outcome. Certainly, here are some ideas and tips on radiation exposure in children with cancer based on the reviewed papers: Personalized treatment plans are crucial. Each child's needs are unique and medical history must be considered when determining the appropriate radiation dosage and treatment plan. Collaboration between healthcare professionals is essential. Pediatric oncologists, radiation oncologists, and other healthcare professionals must work together to ensure that the child receives the best possible care. Regular monitoring and follow-up appointments are important for the children who undergo radiation therapy to assess their progress and detect any potential side effects. Psychological support is vital as children with cancer and their families may experience significant emotional stress and anxiety. Providing them with psychological support and counseling can help them cope with the challenges of radiation therapy. Parents and caregivers of children with cancer should be informed about the benefits and risks of radiation therapy and be involved in the decision-making process. Continuous improvements in medical technology and treatment options should be explored to minimize the risk of radiation exposure in children with cancer. Education and awareness campaigns are necessary as educating the public about the importance of radiation safety and the risks associated with radiation exposure can help prevent unnecessary exposure and promote better health outcomes for children with cancer. Overall, radiation therapy can be an effective treatment for children with cancer, but it requires careful planning and monitoring to minimize the risk of radiation exposure and ensure the best possible outcomes.

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