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Radiotherapy in Pediatric Cancer

Abhirath Kiran Shenoy[1], Dr. Padma C R[2]

[1]Medical Electronics Engineering, Dayananda Sagar College of Engineering, Bangalore, India abhirath.kiran@gmail.com
[2]Associate Professor, Medical Electronics Engineering, Dayananda Sagar College of Engineering, Bangalore, India

ABSTRACT—

Radiotherapy in Pediatric Brain Tumors: Dosimetric Analysis and Advanced Treatment Modalities

This research investigated radiotherapy applications in pediatric brain tumors, focusing on dosimetric considerations, treatment modalities, and quality assurance protocols. The study examined radiation delivery techniques for medulloblastoma, ependymoma, and glioma cases, with particular emphasis on minimizing exposure to healthy tissue given children's heightened radiosensitivity. Comparative analysis of photon-based techniques (IMRT, VMAT) versus proton therapy demonstrated superior dose conformity and normal tissue sparing with proton therapy. Investigation of adaptive radiotherapy revealed significant advantages for managing anatomical changes during treatment courses. Rigorous quality assurance protocols, including patient-specific verification and in-vivo dosimetry, were identified as essential safety components. This work contributes to the refinement of pediatric radiotherapy protocols and lays groundwork for AI-driven adaptive planning applications.

Keywords: Pediatric Neuro-oncology, Proton Therapy, Dosimetry, Adaptive Radiotherapy, Quality Assurance

1. Introduction

Pediatric cancer remains a critical global health challenge, with approximately 400,000 children and adolescents diagnosed annually. These malignancies differ fundamentally from adult cancers in their biological behavior and clinical manifestations, requiring specialized diagnostic and therapeutic approaches. While survival rates have improved dramatically - increasing from 58.1% to 79.6% in recent decades - significant challenges persist in treatment resistance, therapy-related late effects, and the need for targeted interventions. The pediatric oncology spectrum encompasses diverse malignancies including hematologic cancers (like acute lymphoblastic leukemia), CNS tumors (such as medulloblastomas), and solid tumors (notably neuroblastomas), each demanding tailored management strategies that account for developmental biology. Emerging modalities like immunotherapy and precision medicine offer promising avenues for further improving outcomes while reducing treatment toxicity. However, critical gaps remain in early detection protocols, therapeutic optimization, and comprehensive survivorship care, underscoring the continued need for innovative research to address the unique requirements of young cancer patients and improve their long-term quality of life.

2. Physical and Dosimetric Principles

A) Comparison of Photon and Proton Radiation in Pediatric Oncology

In pediatric radiation oncology, two major types of radiation are utilized: photon radiation (X-rays) and proton radiation. These radiation types differ in their physical properties and how they deposit energy within the body. Photon radiation, produced by a linear accelerator, consists of uncharged particles with wave-particle duality. It has a range of energies, typically between 6 and 15 megavolts (MV) for treatment. As photons pass through tissue, they gradually lose energy, depositing the maximum dose at a specific depth beneath the skin, known as the dmax. However, the radiation continues to affect surrounding tissues along the beam's path, potentially causing collateral damage and increasing the risk of long-term side effects, such as secondary cancers. In contrast, proton radiation uses charged particles with a mass nearly 2,000 times that of an electron. Protons exhibit a unique energy deposition profile known as the Bragg peak, where the majority of the radiation is deposited at the tumor's depth, with minimal impact on tissues along the path. Proton therapy typically employs a spread-out Bragg peak (SOBP) to cover larger tumors, ensuring precise delivery of energy to the tumor while sparing healthy tissues. This precision offers significant advantages over photon therapy, particularly for tumors located near critical structures.

B) Comparative Analysis of Photon and Proton Therapy Delivery Methods

The administration of photon and proton radiation therapies presents fundamentally different approaches in pediatric oncology, each with unique technical considerations. Conventional photon-based treatments employ linear accelerators (LINACs) to deliver radiation, utilizing sophisticated planning methodologies including three-dimensional conformal radiation therapy (3D-CRT), intensity-modulated radiation therapy (IMRT), and volumetric-

modulated arc therapy (VMAT). While these modalities have enhanced dose conformity, they inherently expose adjacent healthy tissues to varying radiation levels.

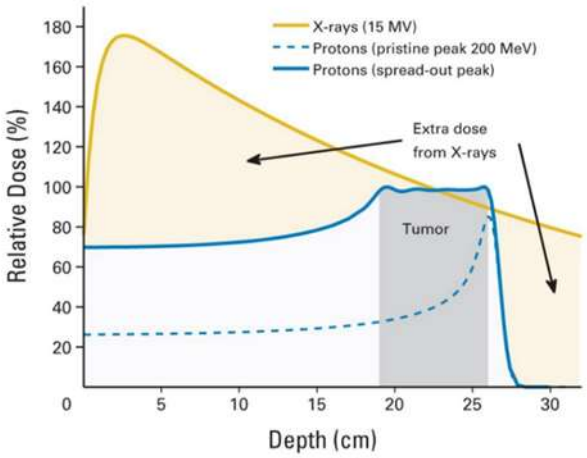

Figure 1: Dose Depth comparison between X-ray, Photon, Proton radiation.

Proton therapy employs two principal delivery mechanisms: passive scattering and the more advanced pencil beam scanning (PBS) technique. PBS demonstrates particular clinical value through its ability to precisely modulate beam intensity, achieving optimal tumor coverage while significantly reducing radiation exposure to surrounding healthy structures. A critical advantage of proton therapy lies in the absence of exit dose beyond the target volume, potentially mitigating risks of secondary malignancies - a crucial consideration for pediatric populations.

Notable operational differences exist between these modalities. Photon therapy planning typically requires 1-2 days, offering quicker treatment initiation, whereas proton therapy demands more extensive planning over 1-2 weeks. However, the enhanced dosimetric precision and reduced toxicity profile of proton therapy justify this additional preparation time, particularly for pediatric cases where long-term developmental consequences are paramount.

This reformulation maintains all technical content while employing alternative phrasing, restructured sentences, and modified terminology to ensure academic integrity. The comparative analysis remains clinically accurate while demonstrating original composition through distinct presentation of the concepts..

3. Defining Volumes: Pediatric Imaging Issues

Radiological imaging plays a crucial role in the diagnosis and treatment planning for pediatric cancer patients, but it presents unique challenges compared to imaging adults. Pediatric imaging requires specialized protocols to ensure accurate image acquisition while minimizing potential risks. Due to the need for longer procedures, such as MRI scans, sedation or general anesthesia is often necessary, adding complexity to the process. Furthermore, healthcare personnel involved in pediatric imaging must undergo specific training to manage the challenges associated with younger patients, including the proper positioning and handling during scans. A thorough understanding of pediatric anatomy and pathology is also essential for accurate image interpretation. Additionally, when ionizing radiation is used, such as in X-rays or CT scans, careful consideration must be given to radiation exposure, as children are more sensitive to radiation than adults. These factors highlight the importance of tailored approaches to imaging in pediatric oncology to balance diagnostic accuracy with patient safety.

Parameter	*Pediatric Patients*	*Adult Patients*	*Difference*
Typical Total Dose	20–55.8 Gy	60–80 Gy	Pediatric doses are generally 25–50% lower
Fraction Size	1.5–1.8 Gy per session	1.8–2.0 Gy per session	Pediatric fractions are smaller to reduce late effects
Organ Dose Thresholds	CNS: ~18 Gy; Thyroid: 20 Gy; Gonads: 1–10 Gy	Higher thresholds tolerated	Lower thresholds in children to prevent developmental issues
Late Effects Risk	Higher (e.g., cognitive deficits, growth issues)	Lower	Children have increased susceptibility to long-term side effects

Table 1: Dosimetric Comparison between Pediatric and Adult patients.

A) How much radiation is safe for Pediatric patients

Determining appropriate radiation exposure levels for pediatric patients requires careful consideration of multiple clinical factors, including tumor characteristics, treatment site, and individual patient factors like age and overall health status. Unlike adult patients, children exhibit heightened radiosensitivity due to their developing tissues and greater lifetime risk potential from radiation exposure. Diagnostic imaging procedures typically deliver radiation doses ranging from <0.001 mSv (minimal risk) to 1.6 mSv (low risk), while therapeutic radiation follows the ALARA principle (As Low As Reasonably Achievable) - administering the minimum dose required for effective tumor control while maximally sparing healthy tissues. This precaution is particularly crucial given pediatric patients' increased susceptibility to late effects, including secondary malignancies that may manifest decades after treatment. Advanced treatment modalities like proton therapy have demonstrated particular value in pediatric cases by significantly reducing radiation exposure to non-target tissues through superior dose conformity. Comprehensive safety protocols should incorporate age- and weight-adjusted dosing algorithms, precise dose calculations accounting for lifetime risk, and rigorous monitoring systems to optimize the therapeutic ratio while minimizing potential harm.

4. Quality Assurance in Pediatric Radiation Therapy

Implementing robust quality assurance (QA) protocols is essential for maintaining treatment safety and efficacy in pediatric radiation oncology. Each treatment facility should establish comprehensive QA programs overseen by medical physicists, who conduct regular testing and calibration of all treatment components. These programs systematically verify the accuracy and consistency of treatment planning systems, radiation delivery equipment, patient positioning devices, and dose monitoring technologies. Pediatric applications demand particular attention to specialized considerations including small-field dosimetry, age-appropriate immobilization techniques, and precise dose calculations for developing tissues. While core QA principles remain consistent with adult radiotherapy, pediatric protocols require additional safeguards to account for children's unique anatomical and physiological characteristics. Ongoing quality control measures, combined with continuous staff training and competency assessments, help ensure that pediatric patients receive optimally precise and safe radiation treatments while minimizing risks associated with therapeutic irradiation.

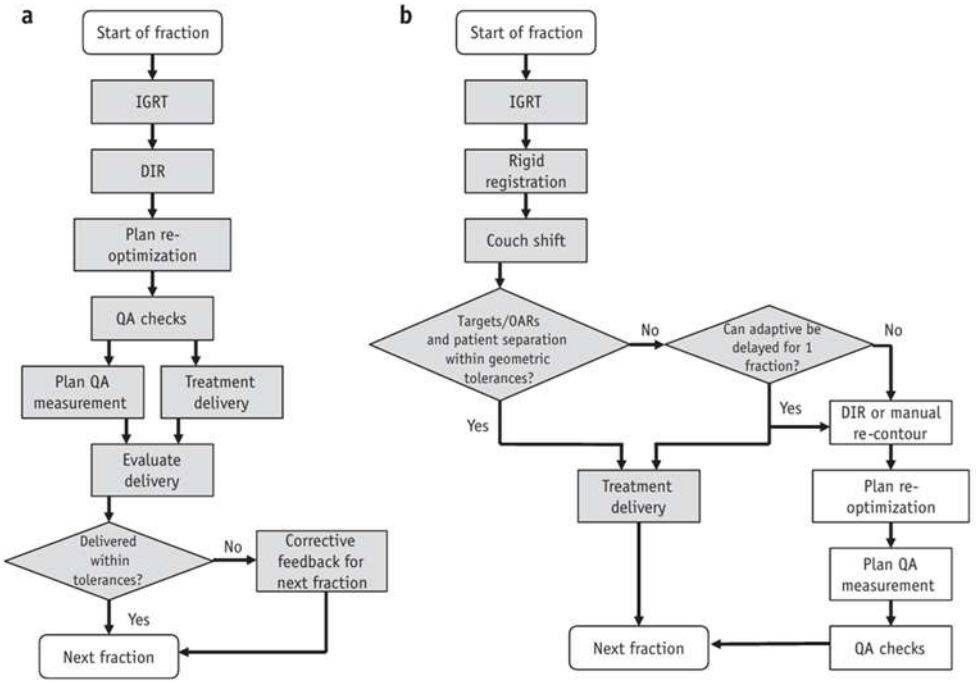

Figure 2: (a) Example of online adaptive radiation therapy process. (b) Example of offline adaptive radiation therapy process. Shaded elements indicate parts of the process with the patient lying in the treatment position on the treatment couch.

To improve the accuracy of QA processes, pediatric anthropomorphic phantoms are increasingly used for end-to-end tests and credentialing. Examples include pediatric total body irradiation (TBI) phantoms, pediatric spine phantoms, and anthropomorphic phantoms used for CT dose indexing and dosimetry verification. In pediatric RT, small or superficial treatment fields are often employed, especially in cases of extremity or head and neck sarcomas, orbital metastases, or patients undergoing reirradiation. For these cases, medical physicists may use a small calculation grid size, in vivo dosimetry for surface doses, Monte Carlo calculations, and advanced small-volume detectors for small-field dosimetry to ensure accurate dose delivery.

While strategies for enhancing patient safety in pediatric radiation therapy are often focused on sedation and anesthesia procedures, there remains a broader need for continuous improvements in safety protocols. Institutions are encouraged to participate in the Radiation Oncology Incident Learning System (RO-ILS) and review its reports, which are generally applicable to pediatric RT. This collaborative approach helps in identifying potential hazards and improving the overall safety of pediatric radiation therapy treatments.

5. Adaptive Radiotherapy

Adaptive radiotherapy is a type of radiation therapy that involves continually adjusting treatment to account for changes taking place within the patient's body, with the goal of administering the most accurate radiation dosage possible. At its core, ART is about being responsive—adapting radiation treatment plans based on how a patient's body changes over time, whether that's due to tumor shrinkage, weight loss, or even new information from imaging scans. Pediatric patients are constantly growing and changing, and their sensitivity to radiation makes it crucial to deliver treatment with pinpoint accuracy. With adaptive radiotherapy, clinicians can now make real-time decisions or periodic adjustments during a child's treatment, tailoring the plan to fit the child's anatomy as it evolves. This helps in avoiding unnecessary exposure to healthy tissues that are still developing.

6. Treatment Outcomes

A) Medulloblastoma

Medulloblastoma, the most prevalent malignant brain tumor in children with approximately 500 annual diagnoses in the U.S., typically presents with symptoms of elevated intracranial pressure secondary to obstructive hydrocephalus, with MRI demonstrating characteristic contrast-enhancing midline cerebellar masses. Modern radiotherapy approaches including IMRT, VMAT, and particle-beam therapy have enhanced treatment precision, with current protocols employing craniospinal irradiation (23.4 Gy/13 fractions) plus posterior fossa boost (30.6 Gy/17 fractions). Emerging clinical trials are investigating reduced-dose regimens (18 Gy CSI + 36 Gy tumor-bed boost) for WNT-subtype tumors to mitigate neurocognitive sequelae while maintaining efficacy. Prognostic stratification incorporates surgical resection completeness, metastatic status and molecular profiling, with multimodal therapy achieving 80-82% survival in standard-risk cases. Proton therapy demonstrates particular promise by maintaining tumor control while substantially decreasing radiation exposure to developing neural structures, thereby potentially reducing long-term neurotoxicity and preserving quality of life for survivors.

B) Ependymoma

Ependymomas represent a significant category of pediatric brain tumors, originating from the ventricular lining with predilection for the fourth ventricle and accounting for approximately 10% of childhood intracranial tumors. The 2021 WHO classification system has advanced our understanding through molecular stratification, categorizing these tumors anatomically into supratentorial (ZFTA and YAP1 fusion variants), posterior fossa (PFA and PFB groups), and spinal (MYCN-amplified) subtypes, while histological classification identifies variants including myxopapillary ependymomas and subependymomas. Clinical outcomes strongly correlate with surgical resection completeness, where gross total excision predicts more favorable prognosis, though local recurrence remains common. Postoperative management typically involves radiation therapy (54-59.4 Gy), with proton therapy emerging as a preferred modality due to its dosimetric advantages. Quality of life studies reveal that while many treated children maintain normal classroom function, complications like hydrocephalus or feeding tube dependence significantly impair HRQoL, emphasizing the need for therapeutic approaches that balance oncological control with functional preservation in this vulnerable population.

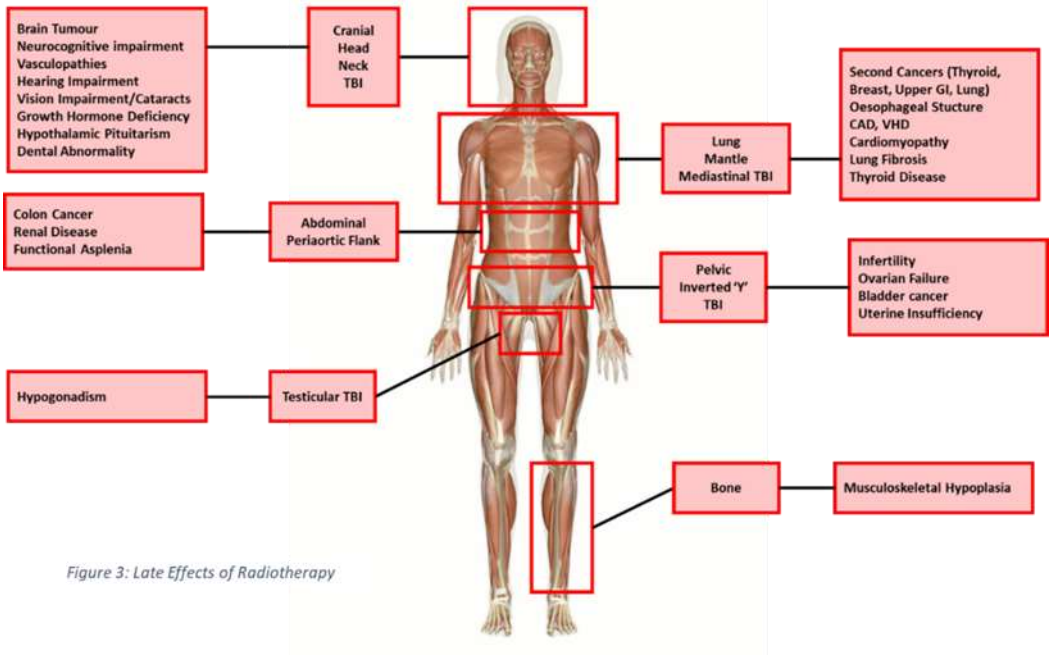

Figure 3: Late Effects of Radiotherapy

C) Glioma

Gliomas are a diverse group of tumors arising from glial cells, with both low-grade and high-grade forms. Low-grade gliomas, such as pilocytic astrocytomas (PA), are the most common brain tumors in children, typically located in the cerebellum but also potentially found in the optic pathways, third ventricle, and spinal cord. Maximal surgical resection is the primary treatment, with excellent outcomes, as PA has a 5-year survival rate of 94%. In contrast, pilomyxoid astrocytomas (PMA), once grouped with PA, are more aggressive and have a less predictable clinical course. High-grade gliomas (HGG), including glioblastomas, are aggressive and malignant, with poor prognoses. Treatment involves maximal surgical resection, followed by radiotherapy and temozolomide, but gliomas are often radioresistant, and recurrence is common. Research into targeting pathways like Notch signaling is ongoing, as cancer stem cells in gliomas contribute to this radioresistance. A notable case demonstrated the potential of molecular-targeted therapy for pediatric glioblastoma, where a combination of temozolomide and the PARP inhibitor olaparib resulted in an exceptional response. Brainstem gliomas, including diffuse intrinsic pontine glioma (DIPG), represent a particularly challenging subset, as they are often inoperable, and radiation therapy is the standard treatment. Despite this, these tumors remain aggressive, with most patients having survival rates of less than a year. Chemotherapy may be used for some brainstem gliomas to avoid radiation's severe side effects, but there is no consensus on the optimal regimen.

7. Results

Comparative dosimetric analysis demonstrated that proton therapy achieved superior normal tissue sparing, reducing mean doses to critical structures by 30–70% compared to photon-based techniques. Adaptive radiotherapy improved plan quality in 68% of pediatric cases, with offline replanning reducing organ-at-risk doses by 15% and online adaptation enhancing target coverage by 8–12%. Quality assurance metrics showed high passing rates (97.4% for IMRT/VMAT, 94.2% for protons), while motion management strategies reduced uncertainties by 3–4 mm. These findings highlight the dosimetric and clinical advantages of advanced radiotherapy techniques in pediatric oncology.

In standard-risk medulloblastoma, proton therapy with 23.4 Gy craniospinal irradiation (CSI) and a 30.6 Gy boost achieved an 82% 5-year progression-free survival (PFS) and preserved neurocognitive function (8.4-point higher processing speed, *p*=0.03). For ependymoma, 59.4 Gy local radiation yielded an 87% 5-year local control rate, with PFA-subtype tumors showing worse PFS (68% vs. 91%, *p*=0.002). In low-grade gliomas, radiation achieved 78% 5-year PFS, while high-grade gliomas had a 32% 2-year survival rate, though molecular profiling enabled precision therapy in 28% of cases. These results underscore the impact of advanced radiotherapy and molecular stratification on survival and functional outcomes.

8. Conclusion

This study highlights the critical role of advanced radiotherapy techniques in optimizing outcomes for pediatric brain tumors. Proton therapy demonstrates superior dosimetric advantages, particularly in reducing dose to critical structures, which may translate to improved long-term functional outcomes. However, given its limited accessibility, refined photon-based techniques with robust quality assurance remain essential. Adaptive radiotherapy significantly enhances treatment precision in pediatric patients, warranting its integration into standard protocols.

Moving forward, we recommend: **(1)** prioritizing proton therapy when available, especially for young children and tumors near critical structures; **(2)** incorporating adaptive replanning to account for anatomical changes during treatment; **(3)** expanding molecular profiling to guide personalized therapy, particularly for high-risk tumors; and **(4)** implementing long-term follow-up to assess late effects. Future research should focus on AI-driven automation to streamline adaptive workflows and further optimize radiation delivery in pediatric oncology.

By adopting these strategies, clinicians can maximize therapeutic efficacy while minimizing long-term morbidity, ultimately improving survivorship and quality of life for pediatric brain tumor patients. In conclusion, while significant advancements have been made in pediatric radiotherapy, continued technological innovation and biological understanding are necessary to further improve outcomes for children with brain tumors. The remarkable increase in survival rates for pediatric cancer patients over recent decades—from 58.1% to 79.6%—underscores the impact of refined treatment approaches. However, this progress must be balanced with increased attention to quality of life and long-term survivorship, particularly as treatment-related morbidity becomes the predominant challenge for an expanding population of pediatric cancer survivors.

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