Proton Beam Therapy for Pediatric Malignancies

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Although major advances have been made in radiation techniques, concerns still exist about the treatment-related acute and long-term side effects. This issue is most notable in the pediatric population because of developing organs and tissues combined with longer life expectancies. Proton beam therapy has the advantage of a reduced dose of radiation with less scatter to normal tissue, which may lead to fewer adverse side effects.

At a Glance
- Many pediatric patients with cancer receive radiation therapy.
- Radiation treatments can cause significant acute and long-term side effects.
- Proton beam therapy reduces radiation scatter to normal tissues and may decrease acute and late toxicities.

Proton beam therapy is one of the latest advancements in radiation therapy used to treat cancer. Although initially proposed in 1946, the first patients were treated in 1958 at the Lawrence Berkeley National Laboratory in California (Merchant & Farr, 2014; Mitin & Zietman, 2014). The use of proton beam therapy in clinical practice has been slowly introduced but has gained significant ground with increasing public awareness since 2010 (Mitin & Zietman, 2014). One of the reasons this form of radiation has garnered interest is because of its potential advantages as compared to photon therapy, with specific potential advantages in the pediatric population.

About 12,000 new cases of pediatric cancer occur each year in the United States, and about 3,000 require radiation therapy (Merchant, 2013). Although radiation is an important component of many treatment regimens for pediatric cancers, it is associated with early and late side effects that can be more problematic in children because of their developing organs and tissues (Armstrong, Stovall, & Robison, 2010). The possible benefits of proton beam therapy are the reduction in dose to normal tissues and a reduction in adverse effects of radiation treatment (Merchant, 2013).

Radiation therapy for patients with cancer commonly uses external beam delivery techniques that include photons. This form of ionizing radiation releases energy and delivers radiation doses to the specific areas of a patient’s body. The standard dose of radiation is the Gray (Gy). Photons travel through tissue without stopping, resulting in continuous dosing of radiation beyond the tumor (Merchant & Farr, 2014).

Proton therapy is an external radiotherapy modality that uses protons instead of photons. Protons are positively charged particles that are accelerated by a large, expensive particle accelerator called a cyclotron or synchrotron, available at a limited number of specialized centers (Decker & Wilson, 2012). When a proton beam enters the body, it delivers a constant dose within a few millimeters of the end of the particle range, the so-called Bragg peak (see Figure 1). Beyond the Bragg peak, protons deliver almost no additional exit dose beyond the target. The benefit of this is that the proton beam stops within the patient’s tumor region, and the radiation does not extend to normal tissue beyond the tumor. This allows for radiation absorption to deep tumor targets with less scatter of radiation to normal surrounding tissues and the possible safe escalation of radiation doses to enhance tumor control (Daw & Mahajan, 2013; Swisher-McClure, Hahn, & Bekelman, 2015).

Childhood Cancer

With multimodality therapies for pediatric malignancies, the five-year survival rate exceeds 80%. As many as 60%-90% of survivors of pediatric cancer experience adverse side effects related to the cancer or the treatment received (Geenen et al., 2007). The challenge for the pediatric cancer population with solid tumors undergoing radiation is the large, irregular volume of tumors close to critical structures in the body. In addition, children, when compared to adults, have longer anticipated life spans and an increased sensitivity to the radiation from...
developing organs and tissues, which puts them at greater risk of secondary cancers and late effects of treatment (Daw & Mahajan, 2013). Depending on the location of the tumor in the body and the associated field of radiation, the late effects include deficits in cognition, endocrine function, vascular abnormality, dental anomalies, hypothyroidism, cardiovascular and gastrointestinal toxicity, and secondary malignancies (Armstrong et al., 2010; Geenen et al., 2007; Greenberger et al., 2014; Zhang et al., 2013).

Proton beam therapy has been included as a radiation option in pediatric clinical trials for more than a decade, and the number of patients treated has increased (Merchant, 2013). Guidelines that include proton therapy for pediatric central nervous system, musculoskeletal, and solid tumors have been developed by the Children’s Oncology Group and approved by the National Cancer Institute’s Cancer Therapy Evaluation Program (Merchant, 2013). Biologically, protons have not demonstrated a significant advantage when compared to photons, which leads to similar rates of predicted tumor control, but the physical properties of protons lead to less radiation scatter to normal tissues and a decrease in acute and late toxicities (Rombi, Venmarini, Vinante, Ravanelli, & Amichetti, 2014). However, consensus exists among investigators that proton therapy is well tolerated and may hold therapeutic benefit with certain types of tumors, such as central nervous system tumors, over other forms of radiation therapy (Merchant & Farr, 2014; Merchant et al., 2008).

Challenges

As the cost of health care has increased, the cost and benefits of this new technology continue to be debated. The evidence to support proton beam therapy in terms of outcomes and cost is limited (Moriarty, Borah, Foote, Pulido, & Shah, 2015). Construction of a proton therapy center is costly, ranging from $25 million to more than $200 million, depending on the size of the facility (Swisher-McClure et al., 2015). The costs of treatment are about two to three times greater than photon-based radiation treatments. In addition, because of the cost of constructing a facility, these centers are only available in select locations, adding to the financial burden for patients and their families because receiving proton beam therapy may involve travel, housing, and potential lost wages (Swisher-McClure et al., 2015).

Conclusion

The use of proton beam therapy to treat pediatric malignancies is increasing, with the possible benefit that this modality may improve quality of life for long-term cancer survivors (Palm & Johansson, 2007; Rombi et al., 2014). Longitudinal, comparative clinical trials with long-term follow-up are needed to assess survival outcomes and evaluate for late effects and secondary malignancies of proton beam therapy, as compared to photon therapy. With continued advancement in radiation delivery techniques, the development of smaller and less costly proton beam units could lead to an increase in the development of proton beam treatment centers and a decrease in cost to patients (Mitin & Zietman, 2014).

References


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