Proton therapy for paediatric medulloblastoma

Radiation oncology has changed greatly in recent decades, driven mainly by technical advances in treatment planning and delivery. Proton radiation therapy is a further advance; however, it is more expensive than traditional photon therapy and its critics argue that its costs are not justified.

Proton therapy is distinct from traditional photon or x-ray-based therapy since the physical properties of charged particles such as protons enable radiation oncologists to control more precisely the radiation dose, and thus spare healthy tissues outside the target volume. A visual comparison of photon treatment and proton treatment plans will nearly always show that the spread of low-dose radiation is less with proton therapy. This is pertinent for medulloblastoma, the most common malignant paediatric brain tumour, for which the entire brain and spine must be irradiated to minimise the risk of recurrence, and for which late adverse effects can severely affect quality of life. Although visual comparisons of proton and photon radiotherapy are compelling, debate within the radiation oncology community continues as to the clinical benefits of this low-dose, tissue-sparing technique.

Proton therapy has been in clinical use for decades; however, until recently, few centres have had access to it. This lack of availability is largely responsible for the paucity of clinical data supporting the routine use of protons for cancer treatment. In The Lancet Oncology, investigators from the Massachusetts General Hospital, one of the institutions that pioneered proton therapy, present outcomes from a prospective study of proton therapy for childhood medulloblastoma. Given the rarity of this disease, I congratulate the investigators for their careful assessment of disease control and, equally as important, the long-term toxic effects of this treatment.

In addition to having different physical properties, protons and photons also have different biological effectiveness. Some researchers have argued that the biological uncertainties associated with proton therapy could lead to more disease recurrences in patients with medulloblastoma. With 5-year progression-free survival of 85% (95% CI 69–93) for patients with standard-risk disease and 70% (45–85) for those with high to intermediate risk disease, Torunn Yock and colleagues recorded similar disease control to that reported in large cooperative group studies of photon-based treatment. Coupling this finding with a detailed analysis of the patterns of failure, the investigators quell concerns regarding disease recurrence.

In their assessment of late radiation-induced adverse effects, the investigators offer a glimpse of the benefits of the low-dose sparing afforded by proton therapy, yet further improvements are possible. Hearing outcomes, when compared with studies of photons, were slightly improved. With newer delivery techniques for proton therapy, including spot scanning proton therapy for the craniospinal component of treatment, further improvements may be expected, because cochlear doses will be reduced. Treatment of the spine with standard photon therapy exposes anterior structures such as the heart and bowel to substantial exit doses. Proton therapy avoids exit doses to these and other anterior structures. Although not the primary outcome, as predicted, treatment of this group with proton therapy resulted in no cardiac or gastrointestinal sequelae. Conversely, the investigators did report a significant decrease in neurocognitive function, with an average decline in the full-scale intelligence quotient of 1·5 points per year, driven mainly by outcomes for patients younger than 8 years of age at treatment. Practitioners should remind families that they are, out of necessity, treating the entire brain and that this exposure can be associated with cognitive impairment, although again, the results of Yock and colleagues were favourable compared with findings from photon studies. Likewise, pituitary and hypothalamic exposure during the craniospinal component of treatment is likely to induce endocrinopathies and continued follow-up is important to address any deficits that might develop.

The rarity of this disease, in combination with the compelling dosimetric data and clinical results presented by Yock and colleagues, make a randomised trial of photons versus protons for medulloblastoma unlikely. This situation contrasts with more common malignancies in adults, for which randomised trials comparing the two radiation treatments are underway. Unfortunately, in the absence of randomised trials for paediatric patients, US states such as Oregon have gone so far as to say that no child should be treated with protons and that all should be treated with photon...
therapy. If such an approach is widely adopted, survivors of childhood medulloblastoma could unnecessarily experience high rates of cardiovascular disease and other adverse effects.

This study sets a new benchmark for the treatment of paediatric medulloblastoma and alludes to the clinical benefits of advanced radiation therapies. Many researchers in the field have voiced concerns that radiation oncology is becoming stagnant and reluctant to integrate findings from other fields such as cancer genomics into their treatment paradigms. In some sense this might be true, and radiation oncology should embrace change. Medulloblastoma is the poster child disease for integrating genomics and molecular subtyping and it will be increasingly important for radiation oncologists to take these findings into account in the design of new prospective studies. Radiation oncologists should also take measures to prevent cognitive decline in paediatric patients through understanding the underlying biological mechanisms and through clinical experience with adult patients.

By contrast with practitioners in other specialties, I believe that radiation oncologists have always understood that our treatments are associated with the potential for severe adverse effects. I also believe that many in radiation oncology embrace new technology, not simply to have the latest and greatest innovations, but rather to reduce the effect of radiation therapy on patients’ quality of life. Nowhere in oncology is this more important than for paediatric cancers.

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I declare no competing interests.