

Protons: a New Frontier in Optimal Cancer Care

Rahul Sharma

Proton beam therapy is the latest technological advancement and a paradigm shift in the technology-driven medical discipline of radiation oncology. A proton beam is distinct from a photon beam in physical and radiobiological properties but its superiority in clinical efficacy is still a matter of debate (1). Global statistics indicate that approximately 10-15% of patients receiving radiation therapy would benefit from proton therapy. In India, the proton facility is available at Chennai and coming up at TMC, Mumbai and NCI, Jhajjar.

The protons have well defined range of penetration in human body and unlike photons, have no exit dose. The proton beam slows down and deposits a large portion of their energy near the end of their range, thereby creating a central-axis depth dose distribution named as Bragg peak. Dosimetric studies have estimated that proton fields can reduce radiation dose to adjacent normal tissues by 50% as compared to photons (2). These unique physical properties of protons make them desirable for certain clinical situations, especially when organ preservation is a priority. We have the capability to modulate the Bragg peak of protons in energy and time in order to administer a conformal radiation dose with intensity modulation to the target tumor while sparing the surrounding normal tissues. However, protons are more sensitive to organ motion and anatomical changes compared with photons. But image guidance and adaptive radiotherapy techniques have been incorporated to overcome these pitfalls (3).

Besides desirable physics, protons hold the promise of better radiobiology. They usually behave as low Linear Energy Transfer radiation and their relative biologic effectiveness (RBE) is considered as 1.1 at par with those of photons. RBE of protons depends on tissue type, dose, dose rate, energy and depth of penetration. The increased RBE near the end of Bragg peak is as high as 2.05. Oxygen enhancement ratio of protons is like those of photons (2.5-3.0). A study has indicated that protons may be more effective than photons in eliminating cancer stem cells in vitro (4). The clinical superiority of proton therapy over photons is still debatable despite physical and radiobiological advantages. Some studies have shown the possible benefits of proton therapy in the cancers under study; other studies have reported increased toxicity or reduced effectiveness for some

patients (5,6,7). In addition, the cost of proton therapy is prohibitive. The average Medicare reimbursement per course of treatment is approximately \$ 10000 to \$ 20000 greater for proton therapy than for photon based IMRT (8,9). In India, proton therapy costs approximately Rs. 25 lakh per patient. Although proton therapy is Food and Drug Administration approved, insurance coverage policies generally state that proton therapy is unproven as a clinically more effective or less harmful treatment of the cancers. The National Cancer Institute and Patient Centered Outcomes Research Institute are funding seven randomized clinical trials evaluating the benefits and harms of proton therapy for cancers of the breast, lung, prostate, glioblastoma, esophagus, low grade glioma, and liver. Each is open for enrollment and the results are awaited to guide future applications. Current evidence most strongly supports proton therapy in the treatment of pediatric malignancies and sarcomas of the skull base and spine (10).

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From the: Department of Radiotherapy, Govt. Medical College Jammu, J&K India

Correspondence to : Dr. Rahul Sharma, Associate Professor, Radiotherapy, Govt. Medical College Jammu, J&K India