ASK THE EXPERTS

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When should proton radiation therapy be used to treat brain tumors?

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(MA, USA). He also served as Director of the Brain Tumor Center at Brigham and Women's Hospital, Dana-Farber Cancer Institute and Children's Hospital from 1988 to 1996. He was recruited to the Massachusetts General Hospital (MA, USA) in 1996 as Director of the Northeast Proton Therapy Center. He served as the Andreas Soriano Professor and is currently the Herman and Joan Suit Professor of Radiation Oncology, Harvard Medical School and Chairman of the Department of Radiation Oncology since 2000. Loeffler is an authority on the treatment of benign and malignant brain tumors. He is an author of over 210 peer-reviewed publications, 180 book chapters and review articles, and co-editor of nine textbooks in the fields of radiation oncology and neuro-oncology. He has served as the principal investigator on a large program project grant from the National Cancer Institute concerning proton therapy. He has served on numerous journal editorial boards in the field of oncology. Loeffler is a Fellow of the American College of Radiology and the American Society of Radiation Oncology and is a Member of the Institute of Medicine of the National Academy of Sciences.

Q What diagnostic work-up is required before initiating radiation treatment for brain tumors?

Diagnostic evaluation for patients with brain tumors includes MRI in essentially all patients. For newly diagnosed patients with presumed primary brain tumors, pathology is required to tailor the volumes and doses of radiation. For patients with certain presumed benign tumors, particularly of the cranial base (e.g., cavernous sinus meningioma), radiation is often delivered without a definitive diagnosis. For patients undergoing proton radiation,

CT scanning is also required to determine tissue density for dose distribution consideration.

Q What are the toxicity risks for patients treated with radiation therapy?

Toxicity is dependent on dose, volume, location of the brain irradiated, age of the patient and any comorbidities the patient has at the time of treatment, such as multiple sclerosis or uncontrolled hypertension or diabetes. The toxicities potentially include white matter injury with subsequent neurocognitive decline,

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neuroendocrine deficits, vascular injury, treatment-associated neurovascular formation, as well as a low probability of radiation-associated secondary tumors.

Q What are the benefits of proton radiation therapy compared with photon-based intensity-modulated radiation therapy?

The benefits of proton radiation therapy are the reduction of integral dose – the volume and amount of radiation delivered outside the defined target volume. This will reduce the probability of complications, as well as allow for higher doses to be delivered safely in certain tumor histologies.

Q What tumor types can be treated most effectively with proton radiation therapy?

We typically chose patients with curative tumors with photon radiation for proton therapy. Since these patients often have projected normal life expectancies, reduction of integral dose should reduce the risks of late effects discussed above. This includes pediatric brain tumors such as medulloblastoma, germ cell tumors, craniopharyngioma, retinoblastoma, optic pathway glioma, localized ependymoma and pilocytic astrocytomas. In adults, we offer proton radiation for patients with benign tumors such as meningioma, schwannoma and pituitary adenoma. We also have a lot of experience with proton therapy for patients with malignant cranial base tumors such as chordoma and chondrosarcoma. We have completed a Phase II trial, and have begun a second study for adults with low-grade gliomas.

Q How is proton radiation therapy planned for an individual patient?

The same diagnostic studies are used as with photon therapy. Higher reproducible immobilization techniques are used for all patients, and many of our patients have stereotactic fiducial markers placed in the outer table of the skull. The planning process is significantly longer for proton patients since apertures and compensators have to be manufactured for every field used in a patient's treatment.

Q How do you verify the dose distribution in proton therapy?

In proton therapy, the verification of the distal edge of the beam is of utmost importance. This can be influenced by different tissues with various densities, such as bone versus soft tissue versus air-containing sinuses in the path of the various beams used for clinical treatment. Because of these uncertainties, conservative treatment plans (treatment volume expansion) are often used, which reduce the primary dosimetric advantage of protons. We have studied changes in post-treatment MRI and PET to document these uncertainties in patients. These imaging technologies represent an exciting chance to observe proton dose distribution *in vivo*. For instance, vertebral bone marrow undergoes fatty replacement after exposure to ionizing radiation that can be visualized on T₁-weighted MRI. A clear, well-delineated post-treatment line of fatty replacement can be seen a few months after therapy. In our studies, the MRI observations have correlated nicely with the proton range prediction from our planning calculations. Positron emitters are activated by proton beams used in therapy. Thus, PET images can be used for dose verification. Using an in-room PET scanner immediately after treatment allows for the detection of shorter-lived isotopes, such as O¹⁵ and N¹³, minimizing isotope washout and avoiding patient repositioning errors. Our results in phantom models and clinical cases suggest the potential of this technology to predict expected activity with great accuracy.

Q What factors affect patient outcome?

Intrinsic radiocurability of the tumor is probably the most important factor. Localized versus disseminated tumor characteristics are also critical as to whether a tumor can be controlled with either proton or photon therapy.

Q What follow-up is required for patients undergoing proton radiation therapy?

The same as with photon patients, with regular follow-up diagnostic studies and physical examinations.

Financial & competing interests disclosure

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