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CLINICAL INVESTIGATION **Brain**

RADIATION DOSE TO THE LENS DURING CRANIOSPINAL IRRADIATION—AN IMPROVEMENT IN PROTON RADIOTHERAPY TECHNIQUE

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Purpose: To evaluate the effect of angle modification of cranial field proton beam therapy on the radiation dose delivered to the lens during craniospinal irradiation (CSI).
Methods and Materials: Thirty-nine patients with central nervous system tumors who received CSI with a posterior fossa boost were analyzed for the radiation dose to the lens. Thirteen patients received cranial field treatment using standard opposed-lateral proton beams, and 26 patients received treatment with angled posterior-oblique proton beams. The lens dose in a test case also was evaluated by comparing conventional X-rays with the two proton beam planning methods by using a CMS/Xio three-dimensional planning system.
Results: Substantial lens dose sparing was realized with the angling of the cranial proton beams 15°–20° to the posterior. In the 39 treated patients who were analyzed (median age, 7 years), average dose delivered to the lens was decreased by approximately 50% by angling of the proton beams, with the average maximum dose decreasing from 74% to 40% of the prescribed dose ($p < 0.0001$). Significant lens sparing was seen in patients 10 years and younger (median age, 6 years; $p < 0.0001$), whereas an insignificant decrease was seen in older patients (median age, 16 years; $p = 0.14$). With the opposed-lateral technique (median age, 6 years), the lens dose increased significantly with decreasing age ($p = 0.002$), whereas there was no effect of age on lens dose in the angled beam–treated group (median age, 8.5 years; $p = 0.73$).
Conclusion: The present study clearly shows an advantage in sparing of the lens dose by angling the beams used during proton beam CSI. This effect is most pronounced in patients 10 years and younger because of anatomic effects of sinus development. © 2008 Elsevier Inc.

Medulloblastoma, Craniospinal irradiation, Proton beam therapy, Radiation-induced cataract.

INTRODUCTION

Medulloblastoma is the most common malignant brain tumor of childhood. Treatment requires a combined-modality approach of surgery, radiotherapy, and chemotherapy. Radiotherapy entails treatment of the entire craniospinal axis with a boost to the posterior fossa or tumor bed and other gross disease. Long-term disease-free survival rates are greater than 60% in high-risk patients and 80% in low-risk patients, making the late morbidities of radiotherapy a significant issue in the treatment of patients with medulloblastoma and a major priority for further improvements in radiotherapy (1–3).

The fundamental technique used in conventional photon radiotherapy is opposed lateral fields irradiating the cranium and upper cervical spinal cord, matching one or two posterior spinal fields to cover the entire spinal subarachnoid space (4). In younger children, the cribiform plate dips low between the eyes, and the radiation oncologist must take great care to include this area in the radiation port. Failure to adequately cover the cribiform plate results in recurrence at this subfrontal lobe site (5–9). Such coverage usually necessitates that the eyes and lens receive significant unwanted direct or scatter dose in these patients.

The eye has several tissues that are variably affected by radiation therapy. Most of the eye is relatively unaffected by dose levels typically used in craniospinal irradiation (CSI), with the lacrimal glands, eyelids, conjunctiva, iris, and retina experiencing adverse effects only after doses greater than 45 Gy (10). However, the lens of the eye is particularly sensitive to low-dose irradiation. When the lens is irradiated, the germinal zone of the epithelium on the equator of the lens is damaged, causing a radiation-induced cataract (11).

Merriam and Focht (12) first reported the dose–response relationship of radiation-induced cataracts in 1958. For single doses of radiation, clinically significant opacities were seen

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after doses in excess of 4–5 Gy. With fractionated irradiation, a 60% frequency of cataracts was seen after 7.5–9.5 Gy, whereas 100% was seen after 11.5 Gy. Another study suggested a threshold dose of 20 Gy for damage to the lens (13). The time to the appearance of abnormality varied from 6 months to 35 years, with evidence to suggest that the latent time became shorter as the dose was increased (11). Deeg *et al.* (14) reported that 80% of patients had lens effects after a single dose of total-body irradiation of 10 Gy, but only 19% after fractionated regimens to 12–15 Gy. In one report, instantaneous dose rate correlated with the risk of developing a cataract, with dose rates of 9 cGy/min or greater corresponding to an increased risk factor (15). If a radiation-induced cataract causes visual impairment, it may be surgically removed, with final visual acuity depending on the health of the remaining ocular structures (16). Although the precise doses leading to radiation-induced cataract formation vary from study to study, the evidence points to a definite threshold of several Gray for the induction of lens opacification and a dose- and fraction-related response above the threshold.

The progress in treating medulloblastoma and reducing the doses to nontarget structures has been significant. In particular, clear advantages of protons over photons in sparing normal structures was reported previously (17). However, doses delivered to the lens during proton beam therapy were not reported in previous studies. The same beam alignments described (opposed lateral fields for cranial irradiation and posterior spinal fields) are used for proton beam therapy for patients with medulloblastoma and other brain tumors at risk of subarachnoid dissemination. The use of opposed lateral fields potentially makes lens sparing a difficult challenge for the treatment of patients with medulloblastoma, especially younger patients. To minimize the risk of cataract development, this report investigates modifications in the radiation delivery technique that can lead to sparing of this critical structure, as well as compares proton doses to the lens with traditional X-ray doses.

METHODS AND MATERIALS

This investigation compares the dose delivered to the lens for three methods of treating the craniospinal axis by using a test case for comparison. In addition, two methods are compared further by evaluating doses delivered to 39 consecutively treated patients at the Francis H. Burr Proton Therapy Center of Massachusetts General Hospital with a craniospinal proton beam irradiation protocol.

Test case

A 5-year-old boy with medulloblastoma to be treated with proton CSI was sedated and immobilized prone in a commercially available (Medtec, Orange City, IA) CSI immobilization device. He then underwent scanning in our standard planning system using 3.75-mm increments from the top of the head through the lower sacrum. Images were transferred to the treatment planning system (CMS/Xio), and the target and nontarget structures within the treated area were outlined. The planned craniospinal axis treatment volume included the entire intracranial volume, as well as the entire circumference of the spinal column, including the transverse and spinal processes extending from the foramen magnum through the completion and lateral extent of the thecal sac as determined from magnetic resonance imaging (18). The entire posterior fossa was also targeted for boost fields. The lenses of the eyes were outlined on the treatment plans for evaluation of absorbed dose using dose–volume histograms.

The following three treatment plans were compared for lens dose in the test case:

(*1*) Standard CSI and posterior fossa boost using opposed-lateral 4-MV X-rays for the cranial irradiation (Fig. 1a) and a single 4-MV posterior field calculated to a depth of 4 cm for the spinal axis. The posterior fossa was boosted with conformal opposed-lateral 6-MV X-rays. Although some centers use a slightly oblique angle when delivering photons to the cranium to avoid divergence of the beams into the lens, it is the standard practice at our institution to use the opposed-lateral technique. With our system, attempting to angle the photon beams created hot spots in the orbits and led to increased radiation dose to the lens (data not shown).

(*2*) Whole-brain irradiation using opposed-lateral proton fields matched to a posterior-anterior proton spine field (Fig. 1b). The posterior fossa subsequently was boosted using three-field conformal protons consisting of right and left posterior obliques and a posterior field. Compensators were specially designed to conform the dose to the target tissue for all fields. The dose was targeted to spare the lens as much as possible without sacrificing coverage of the planned target volume.

(*3*) An identical plan to Plan 2, except that the opposed lateral fields were angled 20° in a posterior direction (Fig. 1c). These angled proton beams, as they are designated in this study, were designed to allow sparing of the lens while still encompassing the entire brain, including the cribriform plate, in the targeted area. For both Plans 2 and 3, the end of the spread-out Bragg peak for the proton doses was at the skin surface or beyond.

Details of the photon and proton beam techniques for CSI were reported earlier (17). Briefly, all plans used a three-level 1-cm moving matchline technique abutting at the anterior cord surface. In all cases, 1.8 Gy was planned for the daily fractionation. Total CSI dose was 23.4 Gy, and total dose delivered to the posterior fossa was 54 Gy. Margining for each plan included a 3-mm setup error and an appropriate penumbra. The planned target volume was defined as the clinical target volume plus 3-mm in all three cases.

Comparison of "lateral" and "angled" proton doses in 39 patients

In addition to analyzing the test case, the delivered dose to the lens of the eye was measured for 39 patients treated with proton beam CSI at the Burr Center. Patient characteristics, including patient age, tumor diagnosis, radiation dose, and proton beam alignment, are listed in Table 1. The first consecutive 13 patients during a 2-year period were treated with the traditional opposed lateral fields for the cranial irradiation, as described in Plan 2 (termed Lateral in Table 1), and the next 26 patients treated during the following 2 years were treated using the modified angled proton beam fields as described in Plan 3 (termed Angled in Table 1). In both groups, minimizing lens dose without sacrificing target volume coverage was a factor in planning the irradiation. Dose–volume histograms for the doses received by the lenses were analyzed for each patient, and the variation in lens dose was assessed, along with comparison

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