ABSTRACT

Int J Radiat Oncol Biol Phys. 2021 Mar 1;109(3):726-735. doi: 10.1016/j.ijrobp.2020.09.049. Epub 2020 Nov 23. A Multi-institutional Comparative Analysis of Proton and Photon Therapy-Induced Hematologic Toxicity in Patients With Medulloblastoma. Liu KX(1), Ioakeim-Ioannidou M(2), Susko MS(3), Rao AD(4), Yeap BY(5), Snijders AM(6), Ladra MM(4), Vogel J(4), Zaslowe-Dude C(1), Marcus KJ(1), Yock TI(7), Grassberger C(7), Braunstein SE(3), Haas-Kogan DA(1), Terezakis SA(8), MacDonald SM(9). Author information: (1)Department of Radiation Oncology, Brigham and Women's Hospital, Dana-Farber Cancer Institute, Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts. (2) Department of Radiation Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts; Department of Radiation and Molecular Radiation Sciences, Sidney Kimmel Comprehensive Cancer Center Johns Hopkins School of Medicine, Baltimore, Maryland. (3)Department of Radiation Oncology, University of California San Francisco, San Francisco, California. (4)Department of Radiation and Molecular Radiation Sciences, Sidney Kimmel Comprehensive Cancer Center Johns Hopkins School of Medicine, Baltimore, Maryland. (5)Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts. (6)Biological Systems and Engineering Division, Lawrence Berkeley National Laboratory, Berkeley, California. (7)Department of Radiation Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts. (8)Department of Radiation and Molecular Radiation Sciences, Sidney Kimmel Comprehensive Cancer Center Johns Hopkins School of Medicine, Baltimore, Maryland; Department of Radiation Oncology, University of Minnesota Medical School, Minneapolis, Minnesota. (9)Department of Radiation Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts. Electronic address: smacdonald@partners.org. PURPOSE: This multi-institutional retrospective study sought to examine the hematologic effects of craniospinal irradiation (CSI) in pediatric patients with medulloblastoma using proton or photon therapy. METHODS AND MATERIALS: Clinical and treatment characteristics were recorded for 97 pediatric patients with medulloblastoma who received CSI without concurrent chemotherapy or with concurrent single-agent vincristine from 2000 to 2017. Groups of 60 and 37 patients underwent treatment with proton-based and photon-based therapy, respectively. Overall survival was determined by Kaplan-Meier curves with log-rank test. Comparisons of blood counts at each timepoint were conducted using multiple t tests with Bonferroni corrections.

Univariate and multivariate analyses of time to grade  $\geq 3$  hematologic toxicity were performed with Cox regression analyses.

RESULTS: Median age of patients receiving proton and photon CSI was 7.5 years

(range, 3.5-22.7 years) and 9.9 years (range, 3.6-19.5 years), respectively. Most patients had a diagnosis of standard risk medulloblastoma, with 86.7% and 89.2% for the proton and photon cohorts, respectively. Median total dose to involved field or whole posterior fossa was 54.0 Gy/Gy relative biological effectiveness (RBE) and median CSI dose was 23.4 Gy/Gy(RBE) (range, 18-36 Gy/Gy[RBE]) for both cohorts. Counts were significantly higher in the proton cohort compared with the photon cohort in weeks 3 to 6 of radiation therapy (RT). Although white blood cell counts did not differ between the 2 cohorts, patients receiving proton RT had significantly higher lymphocyte counts throughout the RT course. Similar results were observed when excluding patients who received vertebral body sparing proton RT or limiting to those receiving 23.4 Gy. Only photon therapy was associated with decreased time to grade  $\geq 3$ hematologic toxicity on univariate and multivariable analyses. No difference in overall survival was observed, and lymphopenia did not predict survival. CONCLUSIONS: Patients who receive CSI using proton therapy experience significantly decreased hematologic toxicity compared with those receiving photon therapy.

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