## ABSTRACT

Neuro Oncol. 2022 Jun 7:noac126. doi: 10.1093/neuonc/noac126. Online ahead of print.

Long-term outcomes and late toxicity of adult medulloblastoma treated with combined modality therapy: a contemporary single-institution experience.

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BACKGROUND: Medulloblastoma (MB) is a rare central nervous system malignancy of adults, with limited contemporary studies to define treatment guidelines and expected late toxicity.

METHODS: A single-center, retrospective study was conducted of patients age ≥18-years from 1997-2019 with MB and who were treated with postoperative radiotherapy. Late toxicity was defined as a minimum of 18-months from diagnosis. Overall survival (OS) and progression-free survival (PFS) were characterized using Kaplan-Meier and Cox regression analyses.

RESULTS: Fifty-nine patients met criteria, with median age of 25-years (range 18-62y) and median follow-up of 6.5-years (range 0.7-23.1y). At diagnosis, 68% were standard-risk, 88% Chang M0, and 22% with anaplastic histology. Gross total resection was achieved in 75%; median craniospinal irradiation dose was 30.6Gy(relative biological effectiveness [RBE]), median total dose was 54.0Gy(RBE), 80% received proton radiotherapy; 81% received chemotherapy. 5-year PFS and OS were 86.5% and 95.8%, respectively; 10-year PFS and OS were 83.9% and 90.7%, respectively. Anaplastic histology was associated with worse PFS (p=0.04). Among eight recurrences, 25% presented after 5-years. Most common grade  $\geq$ 2 late toxicities were anxiety/depressive symptoms (30%), motor dysfunction (25%), and ototoxicity (22%). Higher posterior fossa radiation dose was associated with increased risk of late toxicity, including worse cognitive dysfunction (p = 0.05).

CONCLUSIONS: Adults with MB have favorable survival outcomes, but late failures and toxicity are not uncommon. Better understanding of prognostic factors, possibly from molecular subtyping, may help to define more personalized treatments for patients with high risk of recurrence and long-term treatment sequelae.

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DOI: 10.1093/neuonc/noac126 PMID: 35671386