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# Children's outcomes in medulloblastoma proton versus photon craniospinal radiotherapy (CURE): meta-analysis

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## Abstract

**Objective:** To compare the efficacy and toxicity of craniospinal irradiation (CSI) with proton (PBT) versus photon (PHT) therapy in pediatric patients with medulloblastoma, evaluating overall survival (OS), growth hormone deficiency (GHD), hypothyroidism, neurocognitive decline, and ototoxicity.

**Materials and methods:** A systematic review and meta-analysis followed PRISMA and Cochrane guidelines. Retrospective or prospective cohort studies comparing PBT versus PHT-CSI in children (<21 years) with medulloblastoma were included. Outcomes were OS, GHD, hypothyroidism, neurocognitive decline (full-scale IQ), and ototoxicity (grade  $\geq 3$ ). Data from 12 studies were extracted and analyzed using a fixed-effects model, calculating risk ratios (RR) for binary outcomes and standardized mean differences (SMD) for continuous outcomes. Heterogeneity was assessed with Cochran's Q test and I<sup>2</sup> statistic.

**Results:** Ten cohort studies were included (no randomized trials), including 1034 patients (PBT = 537 and PHT = 497). No difference in OS was observed (RR: 0.984; 95 % CI: 0.902-1.073; p = 0.7118; I<sup>2</sup> = 0 %). PBT significantly reduced GHD (RR: 0.379; p < 0.001, NNT = 2), hypothyroidism (RR: 0.256; p < 0.001, NNT = 2), and neurocognitive decline (SMD: 0.708; p = 0.0001, NNT = 5), with no difference in grade  $\geq 3$  ototoxicity (RR: 0.88; p = 0.5704). Grade  $\leq 2$  ototoxicity was increased with PHT (RR: 1.15; p = 0.01, NNT = 15).

**Conclusion:** PBT-CSI provides equivalent survival to PHT-CSI while significantly reducing GHD, hypothyroidism, mild ototoxicity, and neurocognitive toxicities in children with medulloblastoma. These findings support the preferential use of PBT to minimize long-term sequelae, though prospective studies are needed to confirm benefits and assess cost-effectiveness.

**Keywords:** Medulloblastoma; Meta-analysis; Proton therapy; Radiotherapy; Survival.

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