Optimizing the radiation therapy dose prescription for pediatric medulloblastoma: Minimizing the life years lost attributable to failure to control the disease and late complication risk.

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Abstract

Background. A mathematical framework is presented for simultaneously quantifying and evaluating the trade-off between tumor control and late complications for risk-based radiation therapy (RT) decision-support. To demonstrate this, we estimate life years lost (LYL) attributable to tumor recurrence, late cardiac toxicity and secondary cancers for standard-risk pediatric medulloblastoma (MB) patients and compare the effect of dose re-distribution on a common scale. Methods. Total LYL were derived, based on the LYL attributable to radiation-induced late complications and the LYL from not controlling the primary disease. We compared the estimated LYL for three different treatments in 10 patients: 1) standard 3D conformal RT; 2) proton therapy; 3) risk-adaptive photon treatment lowering the dose to part of the craniospinal (CS) target volume situated close to critical risk organs.

Results. Late toxicity is important, with 0.75 LYL (95% CI 0.60-7.2 years) for standard uniform 24 Gy CS irradiation. However, recurrence risk dominates the total LYL with 14.2 years (95% CI 13.4-16.6 years). Compared to standard treatment, a risk-adapted strategy prescribing 12 Gy to the spinal volume encompassing the 1st-10th thoracic vertebrae (Th1-Th10), and 36 Gy to the remaining CS volume, estimated a LYL reduction of 0.90 years (95% CI -0.18-2.41 years). Proton therapy with 36 Gy to the whole CS volume was associated with significantly fewer LYL compared to the risk-adapted photon strategies, with a mean LYL difference of 0.50 years (95% CI 0.25-2.60 years).

Conclusions. Optimization of RT prescription strategies considering both late complications and the risk of recurrence, an all-cause mortality dose painting approach, was demonstrated. The risk-adapted techniques compared favorably to the standard, and although in this context, the gain is small compared to estimated uncertainty, this study demonstrates a framework for all-cause mortality risk estimation, rather than evaluates direct clinical applicability of risk-adapted strategies.

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