

Supplementary Materials

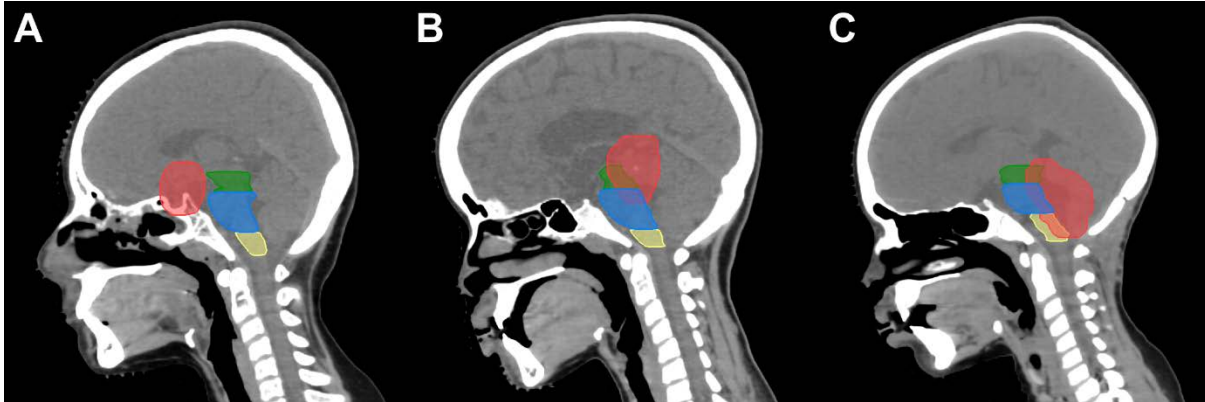


Figure E1 Three patients diagnosed with craniopharyngioma (A), low-grade glioma (B) and ependymoma (C). Delineated: Midbrain (green), pons (blue), medulla oblongata (yellow) and PTV (red). *Abbreviation:* PTV = planning target volume.

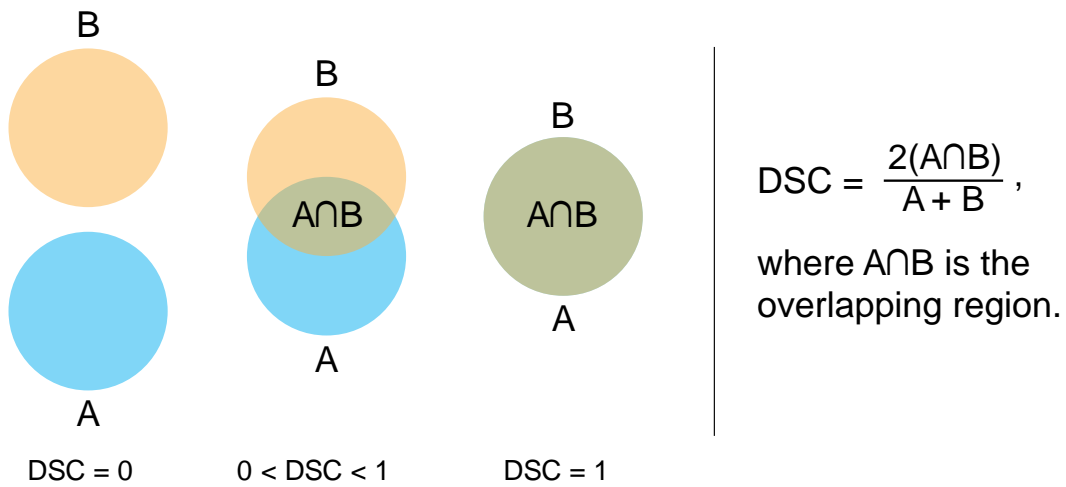


Figure E2 Illustration of the Dice similarity coefficient (DSC).

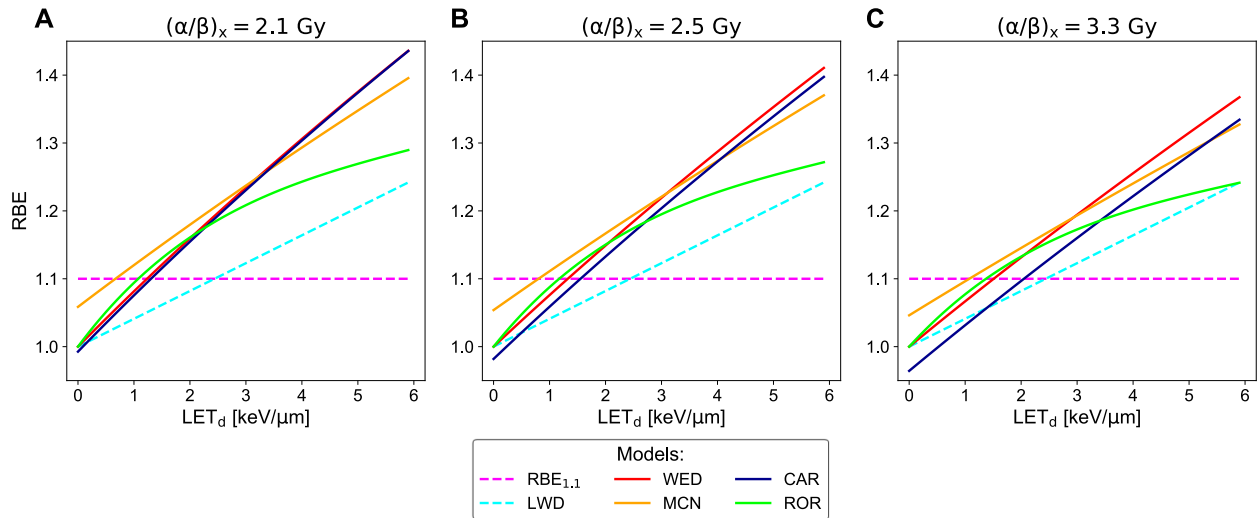


Figure E3 LET_d dependencies for the phenomenological models at a physical dose of 1.55 Gy (median physical fraction dose in the midbrain for the glioma patient), $(\alpha/\beta)_x = 2.1, 2.5$ and 3.3 Gy. LWD RBE and RBE_{1.1} ($(\alpha/\beta)_x$ independent) are shown for reference. *Abbreviations:* LET_d = dose-averaged linear energy transfer; RBE = relative biological effectiveness, WED = Wedenberg; CAR = Carabe; MCN = McNamara; ROR = Rørvik; LWD = LET-weighted dose.

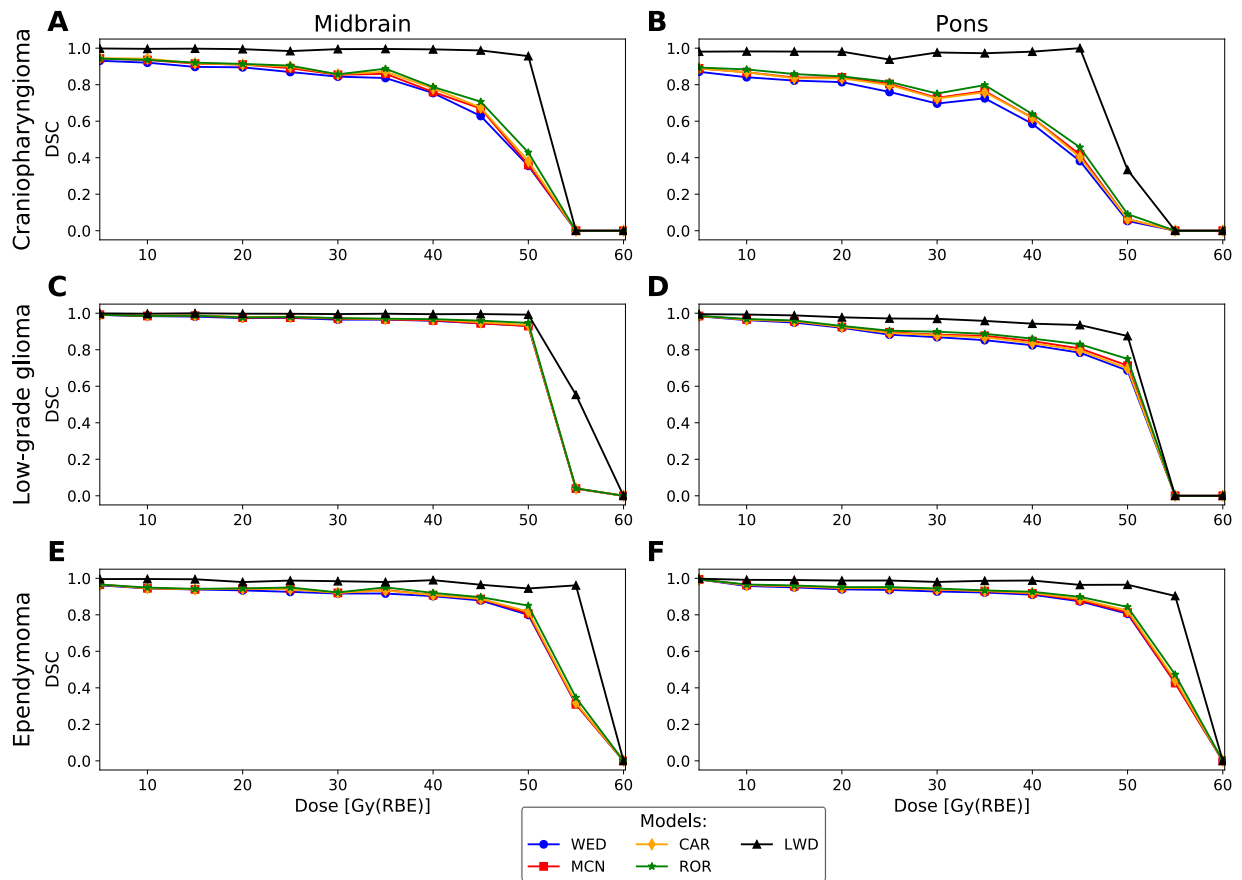


Figure E4 Dice similarity coefficients for every 5 Gy(RBE) isodose step in the midbrain and pons for the three patients. $(\alpha/\beta)_x = 2.1$ Gy was used for the phenomenological RBE models. *Abbreviations:* RBE = relative biological effectiveness; DSC = Dice similarity coefficient; WED = Wedenberg; CAR = Carabe; MCN = McNamara; ROR = Rørvik; LWD = LET-weighted dose.

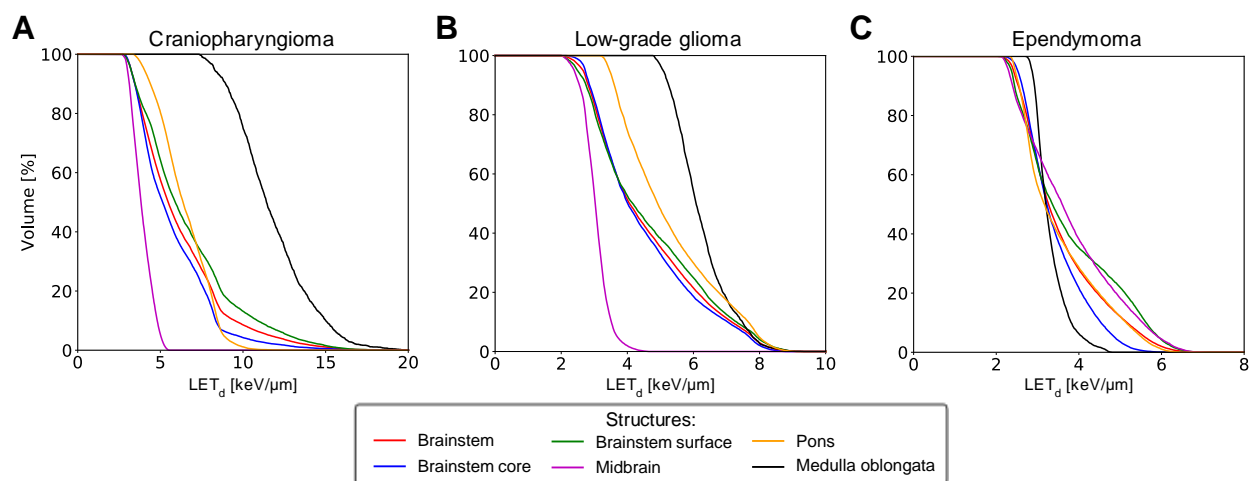


Figure E5 LET_d volume histograms for all structures within the three patients. *Abbreviation:* LET_d = dose-averaged linear energy transfer.

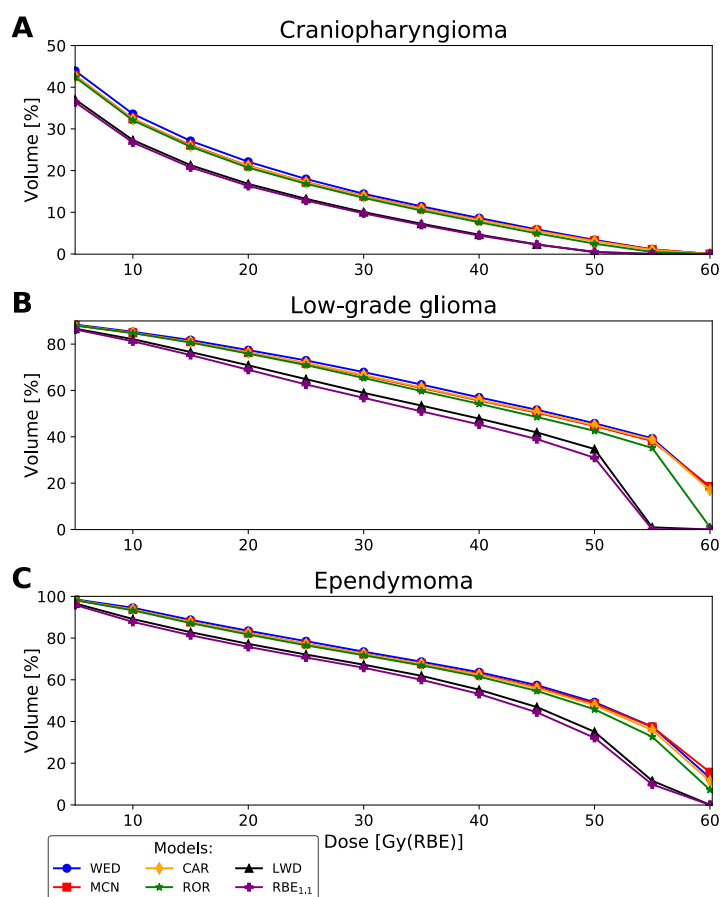


Figure E6 Volume metrics for every 5 Gy(RBE) isodose step in the brainstem for the three patients. $(\alpha/\beta)_x = 2.1$ Gy was used for the phenomenological RBE models. *Abbreviations:* RBE = relative biological effectiveness; DSC = Dice similarity coefficient; WED = Wedenberg; CAR = Carabe; MCN = McNamara; ROR = Rørvik; LWD = LET-weighted dose.

Table E1 Structures with the highest and lowest increase in median biological dose between the WED model and RBE_{1.1}, in addition to the increase in median biological dose to the full brainstem

Patient	Highest biological dose increase [Gy(RBE)] (structure)	Lowest biological dose increase [Gy(RBE)] (structure)	Biological dose increase in the full brainstem [Gy(RBE)]
Craniopharyngioma	3.5 (midbrain)	0.0 (medulla oblongata)	1.5
Ependymoma	8.3 (midbrain)	7.2 (pons)	7.7
Glioma	12.4 (pons)	0.2 (medulla oblongata)	10.5

Abbreviations: RBE = relative biological effectiveness; WED = Wedenberg.