

**EPTN consensus-based guideline for the
tolerance dose per fraction of
organs at risk in the brain**

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Fractions	Dose constraint EQD2	Tolerance dose (physical dose, depending on number of fractions)																																						α/β [Gy]	Toxicity
		15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40														
Organ at risk																																									
Brain [3-7]	$V_{60Gy} < 3cc$																																							2	symptomatic brain necrosis
		46.8	48.0	49.1	50.1	51.1	52.1	53.0	53.9	54.8	55.6	56.4	57.2	57.9	58.6	59.3	60.0	60.7	61.3	61.9	62.5	63.1	63.7	64.2	64.8	65.3	65.8														
Brainstem [8-17]	Interior $D_{0.03cc} \leq 54Gy$ Surface $D_{0.03cc} \leq 60 Gy$																																							2	Permanente craniale neuropathie of necrosis
		43.9	44.9	45.9	46.9	47.8	48.7	49.5	50.4	51.1	51.9	52.6	53.3	54.0	54.7	55.3	55.9	56.5	57.1	57.6	58.2	58.7	59.2	59.8	60.2	60.7	61.2														
		46.8	48.0	49.1	50.1	51.1	52.1	53.0	53.9	54.8	55.6	56.4	57.2	57.9	58.6	59.3	60.0	60.7	61.3	61.9	62.5	63.1	63.7	64.2	64.8	65.3	65.8														
Chiasm & Optic nerve [18-25]	$D_{0.03cc} \leq 55 Gy$																																							2	Optic neuropathy
		44.4	45.4	46.5	47.5	48.4	49.3	50.1	51.0	51.8	52.5	53.3	54.0	54.7	55.3	56.0	56.6	57.2	57.8	58.4	58.9	59.5	60.0	60.5	61.0	61.5	62.0														
Cornea [26,27]	$D_{0.03cc} \leq 50 Gy$																																							3	Erosion/ulceration
		42.7	43.6	44.5	45.3	46.1	46.8	47.5	48.2	48.8	49.4	50.0	50.6	51.1	51.6	52.1	52.6	53.1	53.5	53.9	54.4	54.8	55.2	55.5	55.9	56.3	56.6														
Lens [28,29]	$D_{0.03cc} \leq 10 Gy$																																							1	Cataract
		15.0	15.3	15.6	15.9	16.2	16.5	16.7	16.9	17.2	17.4	17.6	17.8	18.0	18.2	18.4	18.5	18.7	18.9	19.0	19.2	19.3	19.5	19.6	19.7	19.9	20.0														
Retina [18,26,30,31]	$D_{0.03cc} \leq 45 Gy$																																							3	Loss of vision
		39.8	40.6	41.4	42.1	42.8	43.5	44.1	44.7	45.3	45.8	46.4	46.9	47.3	47.8	48.2	48.7	49.1	49.5	49.9	50.2	50.6	51.0	51.3	51.6	51.9	52.2														
Skin [32]	$D_{0.03cc} \leq 25 Gy$																																							2	Permanent alopecia
		26.5	27.1	27.6	28.1	28.5	29.0	29.4	29.8	30.2	30.6	30.9	31.2	31.6	31.9	32.2	32.4	32.7	33.0	33.2	33.5	33.7	34.0	34.2	34.4	34.6	34.8														

References:

1. Hoffmann AL, Nahum AE. Fractionation in normal tissues: the (α/β) eff concept can account for dose heterogeneity and volume effects. *Phys Med Biol* 2013;58:6897–914. doi:10.1088/0031-9155/58/19/6897.
2. Perko Z, Bortfeld TR, Hong TS, Wolfgang J, Unkelbach J. Derivation of mean dose tolerances for new fractionation schemes and treatment modalities. *Phys Med Biol* 2017. doi:10.1088/1361-6560/aa9836.
3. Mayo C, Yorke E, Merchant TE. Radiation associated brainstem injury. *Int J Radiat Oncol Biol Phys* 2010;76:S36–41. doi:10.1016/j.ijrobp.2009.08.078.
4. Lawrence YR, Li XA, el Naqa I, Hahn CA, Marks LB, Merchant TE, et al. Radiation Dose–Volume Effects in the Brain. *Int J Radiat Oncol* 2010;76:S20–7. doi:10.1016/j.ijrobp.2009.02.091.
5. Su S-F, Huang Y, Xiao W, Huang S-M, Han F, Xie C, et al. Clinical and dosimetric characteristics of temporal lobe injury following intensity modulated radiotherapy of 885 nasopharyngeal carcinoma. *Radiother Oncol* 2012;104:312–6. doi:10.1016/j.radonc.2012.06.012.
6. Zhou X, Ou X, Xu T, Wang X, Shen C, Ding J, et al. Effect of Dosimetric Factors on Occurrence and Volume of Temporal Lobe Necrosis Following Intensity Modulated Radiation Therapy for Nasopharyngeal Carcinoma: A Case-Control Study. *Int J Radiat Oncol* 2014;90:261–9. doi:10.1016/j.ijrobp.2014.05.036.
7. McDonald MW, Linton OR, Calley CSJ. Dose–Volume Relationships Associated With Temporal Lobe Radiation Necrosis After Skull Base Proton Beam Therapy. *Int J Radiat Oncol* 2015;91:261–7. doi:10.1016/j.ijrobp.2014.10.011.
8. Flickinger JC, Lunsford LD, Singer J, Cano ER, Deutsch M. Megavoltage external beam irradiation of craniopharyngiomas: analysis of tumor control and morbidity. *Int J Radiat Oncol Biol Phys* 1990;19:117–22.
9. Guimas V, Thariat J, Graff-Cailleau P, Boisselier P, Pointreau Y, Pommier P, et al. [Intensity modulated radiotherapy for head and neck cancer, dose constraint for normal tissue: Cochlea vestibular apparatus and brainstem]. *Cancer Radiother* 2016;20:475–83. doi:10.1016/j.canrad.2016.07.077.
10. Jian JJ-M, Cheng SH, Tsai SY-C, Yen K-CL, Chu N-M, Chan K-Y, et al. Improvement of local control of T3 and T4 nasopharyngeal carcinoma by hyperfractionated radiotherapy and concomitant chemotherapy. *Int J Radiat Oncol Biol Phys* 2002;53:344–52.
11. Uy NW, Woo SY, Teh BS, Mai WY, Carpenter LS, Chiu JK, et al. Intensity-modulated radiation therapy (IMRT) 910 for meningioma. *Int J Radiat Oncol Biol Phys* 2002;53:1265–70.
12. Schoenfeld GO, Amdur RJ, Morris CG, Li JG, Hinerman RW, Mendenhall WM. Patterns of Failure and Toxicity after Intensity-Modulated Radiotherapy for Head and Neck Cancer. *Int J Radiat Oncol* 2008;71:377–85. doi:10.1016/j.ijrobp.2007.10.010.
13. Zheng Y, Han F, Xiao W, Xiang Y, Lu L, Deng X, et al. Analysis of late toxicity in nasopharyngeal carcinoma patients treated with intensity modulated radiation therapy. *Radiat Oncol* 2015;10:17. doi:10.1186/s13014-014-0326-z.
14. Weber DC, Malyapa R, Albertini F, Bolsi A, Kliebsch U, Walser M, et al. Long term outcomes of patients with skull-base low-grade chondrosarcoma and chordoma patients treated with pencil beam scanning proton therapy. *Radiother Oncol* 2016;120:169–74. doi:10.1016/j.radonc.2016.05.011.
15. Nishimura H, Ogino T, Kawashima M, Nihel K, Arahira S, Onozawa M, et al. Proton-Beam Therapy for Olfactory Neuroblastoma. *Int J Radiat Oncol* 2007;68:758–62. doi:10.1016/j.ijrobp.2006.12.071.
16. Noël G, Feuvret L, Calugaru V, Dhermain F, Mammari H, Haie-Médér C, et al. Chordomas of the base of the skull and upper cervical spine. One hundred patients irradiated by a 3D conformal technique combining photon and proton beams. *Acta Oncol (Madr)* 2005;44:700–8. doi:10.1080/02841860500326257.
17. Debus J, Hug EB, Liebsch NJ, O'Farrell D, Finkelstein D, Efid J, et al. Brainstem tolerance to conformal radiotherapy of skull base tumors. *Int J Radiat Oncol Biol Phys* 1997;39:967–75.
18. Archer DB, Amoaku WMK, Gardiner TA. Radiation retinopathy—Clinical, histopathological, ultrastructural and experimental correlations. *Eye* 1991;5:239–51. doi:10.1038/eye.1991.39.
19. McClellan RL, el Gammal T, Kline LB. Early bilateral radiation-induced optic neuropathy with follow-up MRI. *Neuroradiology* 1995;37:131–3.
20. Jiang GL, Tucker SL, Guttentberger R, Peters LJ, Morrison WH, Garden AS, et al. Radiation-induced injury to the visual pathway. *Radiother Oncol* 1994;30:17–25.
21. Goldsmith BJ, Rosenthal SA, Wara WM, Larson DA. Optic neuropathy after irradiation of meningioma. *Radiology* 1992;185:71–6. doi:10.1148/radiology.185.1.1523337.
22. Martel MK, Sandler HM, Cornblath WT, Marsh LH, Hazuka MB, Roa WH, et al. Dose-volume complication analysis for visual pathway structures of patients with advanced paranasal sinus tumors. *Int J Radiat Oncol Biol Phys* 1997;38:273–84.
23. Flickinger JC, Lunsford LD, Singer J, Cano ER, Deutsch M. Megavoltage external beam irradiation of craniopharyngiomas: analysis of tumor control and morbidity. *Int J Radiat Oncol Biol Phys* 1990;19:117–22.
24. Hoppe BS, Stegman LD, Zelefsky MJ, Rosenzweig KE, Wolden SL, Patel SG, et al. Treatment of nasal cavity and paranasal sinus cancer with modern radiotherapy techniques in the postoperative setting—the MSKCC experience. *Int J Radiat Oncol* 2007;67:691–702. doi:10.1016/j.ijrobp.2006.09.023.
25. Mackley HB, Reddy CA, Lee S-Y, Harnisch GA, Mayberg MR, Hamrahian AH, et al. Intensity-modulated radiotherapy for pituitary adenomas: the preliminary report of the Cleveland Clinic experience. *Int J Radiat Oncol Biol Phys* 2007;67:232–9. doi:10.1016/j.ijrobp.2006.08.039.
26. Cancer Institute N. Common Terminology Criteria for Adverse Events (CTCAE) Common Terminology Criteria for Adverse Events v4.0 (CTCAE) 2009.
27. Barabino S, Raghavan A, Loeffler J, Dana R. Radiotherapy-induced ocular surface disease. *Cornea* 2005;24:909–14.
28. Merriam GR, Worgul B V, Worgul B V. Experimental radiation cataract—its clinical relevance. *Bull N Y Acad Med* 1983;59:372–92.
29. Henk JM, Whitelocke RA, Warrington AP, Bessell EM. Radiation dose to the lens and cataract formation. *Int J Radiat Oncol Biol Phys* 1993;25:815–20.
30. Brown GC, Shields JA, Sanborn 705 G, Augsburger JJ, Savino PJ, Schatz NJ. Radiation retinopathy. *Ophthalmology* 1982;89:1494–501.
31. Parsons JT, Bova FJ, Fitzgerald CR, Mendenhall WM, Million RR. Radiation retinopathy after external-beam irradiation: analysis of time-dose factors. *Int J Radiat Oncol Biol Phys* 1994;30:765–73.
32. Stram DO, Mizuno S. Analysis of the DS86 atomic bomb radiation dosimetry methods using data on severe epilation. *Radiat Res* 1989;117:93–113.