

Supplementary material for Indelicato DJ, et al. Incidence and dosimetric parameters of pediatric brainstem toxicity following proton therapy. Acta Oncol 2014;53:1298–304.

Supplementary Table I. Patient, tumor, preradiotherapy, and radiotherapy characteristics (N = 313).

| Characteristics | Value |
|---|--|
| <i>Patient and tumor characteristics</i> | |
| Age | |
| Median patient age | 5.9 y (range 0.5–17.9 y) |
| < 5 y at time of radiotherapy | 130 pts |
| Sex | |
| Male | 168 pts |
| Female | 145 pts |
| Race | |
| White | 214 pts |
| Black | 41 pts |
| Hispanic | 27 pts |
| Asian | 4 pts |
| Histologies | |
| Ependymoma | 73 pts |
| Craniopharyngioma | 68 pts |
| Low-grade glioma | 66 pts |
| Medulloblastoma/primitive neuroectodermal tumor | 38 pts |
| Parameningeal rhabdomyosarcoma | 13 pts |
| Other | 305 pts |
| Site | |
| Supratentorial | 164 pts |
| Posterior fossa | 114 pts |
| Skull base | 35 pts |
| <i>Preradiotherapy treatment details</i> | |
| Operations prior to RT | |
| 1 | 213 pts |
| 2 | 76 pts |
| > 2 | 18 pts |
| Treatment based on radiographic characteristics alone, without biopsy | 6 pts |
| Gross total or near total resection ¹ | 109 pts |
| History of hydrocephalus | |
| Extended or permanent shunting to manage hydrocephalus | 182 pts |
| 73 pts | |
| Disease-specific chemotherapy | |
| Intrathecal or high-dose intravenous methotrexate | 155 pts |
| 48 pts | |
| <i>RT treatment details</i> | |
| Posterior fossa tumor site | 114 pts |
| Anesthesia during RT ² | 173 pts |
| Mean brainstem volume | 21.1 cm ³ ± 4.9 cm ³ (range 8.1–36.9 cm ³) |
| Median time between diagnosis and RT | 4.6 mo (range 0.6–92.9) |
| Median time between last surgery and RT | 3.2 mo (range 0.6–81.7) |
| Median prescribed radiation dose | 54 CGE (range 48.6–75.6 CGE) |
| Dose per fraction | |
| 1.8 CGE daily | 561 pts |
| 1.2 CGE fractions twice daily | 2 pts |
| Median duration of RT | 44 days (range 38–65) |
| Combined proton and photon RT | 31 (9.9%) pts |

CGE, Cobalt Gray equivalent; mo, months; pt, patient; RT, radiotherapy; y, years.

¹At the time of radiotherapy; ²Inhalational sevoflourane and intravenous propofol.

Supplementary Table II. Modern literature review of central nervous system toxicity (limited to series > 40 patients).

| Study | N | Incidence of symptomatic CNS radiation toxicity | Incidence of fatal CNS radiation toxicity | Notes |
|----------------------------|------|---|---|---|
| Shaw 2002 [17] | 203* | 2.5–5%, 2-y actuarial incidence | 2% | Prescription dose 50.4 vs. 64.8 Gy Higher dose increases risk |
| Fouladi 2004 [19] | 134 | 2.2%, 1-y cumulative incidence | NR | Prescription dose 55.8 Gy Overall 17.5% incidence of white matter lesions at 2 years |
| Ruben 2006 [18] | 426* | 13.3%, 3-y actuarial | NR | Prescription dose 45–60 Gy Chemotherapy increases risk |
| Spreafico 2008 [21] | 49 | 18.5%, 3-y crude rate | 2% | Prescription dose 50–60 Gy Patients received high-dose chemotherapy and transplant |
| Merchant 2009 [20] | 153 | 2.5%, 7-y cumulative incidence | 1.3% | Prescription dose 54–59.4 Gy |
| Merchant 2010 [12] | 68 | 7%, crude rate of ‘progressive neurologic deficits’ related to brainstem toxicity in 2-year survivors | 1.4% | Prescription dose 54–59.4 Gy Surgical morbidity, volume, and extent of tumor may be risk factors |
| Murphy 2012 [23] | 196 | 4.4%, 5-y cumulative incidence | 0.5% | Infratentorial tumors Prescription dose 55.8 Gy |
| Murphy 2012 [23] | 236 | 3.7%, 5-y cumulative incidence | 0.4% | Infratentorial tumors Prescription dose 55.8 Gy |
| Indelicato (current study) | 313 | 3.8%, 2-y cumulative incidence | 0.3% | Brainstem dose \geq 50.4 Gy Only series including proton therapy |

CNS, central nervous system; NR, not reported.

*Included adult patients.