4.4 Central nervous system (CNS) malignancy

Radiotherapy fractionation in the CNS

4.4.1 Two important considerations underpin decision-making in radiation neuro-oncology. Firstly, the results of treatment vary widely and, secondly, the brain and spinal cord are susceptible to late radiation damage which is strongly dependent on radiation dose-per-fraction. Although there is an extensive (predominantly older) literature on CNS radiation damage, it is still difficult to give precise tolerance limits.\(^1\)–\(^6\) Quoted threshold doses are 35 Gy in 10 fractions, 60 Gy in 35 fractions or 76 Gy in 60 fractions. Patients with a life expectancy of more than 12–18 months are rarely treated with doses-per-fraction greater than 2 Gy. In effect, the fractionation of radical radiotherapy for CNS tumours is based almost entirely upon avoidance of late radiation damage. The tolerance of the brainstem (50 Gy in 25 fractions) and optic chiasma (55 Gy in 30 fractions) may impose a lower dose limit and necessitate changes in planning. There is considerable uniformity of practice in the UK\(^7\) (level 4) and a systematic overview of clinical trials is recently available.\(^8\)

High-grade glioma

4.4.2 Retrospective analyses\(^9\) and one randomised trial\(^10\) have demonstrated a dose–response relationship for high-grade glioma up to, but not beyond, 60 Gy in 30 fractions.\(^11\) This has led to the adoption of the dose regimen of 60–65 Gy delivered in 1.8–2.0 Gy fractions as standard in the therapy of better prognosis patients with high-grade malignant glioma (level 1+). Further attempts to improve response through hyper-fractionation\(^12\) or accelerated fractionation\(^13\) have failed. The addition of temozolomide to radiotherapy for newly diagnosed glioblastoma has been shown to improve overall and progression-free survival (level 1+, Grade B).\(^14\)

For patients of good performance status being treated for high-grade glioma, a total dose of 60 Gy in 30 daily fractions in 6 weeks is recommended (Grade A).

4.4.3 Treatment is not always appropriate for patients with high-grade glioma and poor performance status but, when it is, hypo-fractionated treatments may be beneficial.\(^15,16\) The most commonly adopted regimen in the UK is 30 Gy in 6 fractions over 2 weeks (level 2+), often delivered by using a parallel pair.

For patients of poor performance status being treated for high-grade glioma, a total dose of 30 Gy in 6 fractions over 2 weeks is acceptable as a palliative treatment (Grade C).

Low-grade glioma

4.4.4 For low-grade glioma two prospective randomised dose comparison trials have demonstrated no difference in outcome between 45 Gy in 25 fractions and 59.4 Gy in 33 fractions\(^17\) and between 50.4 Gy in 28 fractions and 64.8 Gy in 36 fractions.\(^18\) As a result, a standard dose of 45–50.4 Gy in 25–28 fractions of 1.8 Gy is accepted practice in the UK and internationally (level 1++). A dose of 54 Gy in 30 fractions in 6 weeks has been used in a randomised study of the timing of radiotherapy.\(^19\) This provides level 2++ evidence for this regimen.
For patients with low-grade gliomas, a total dose of 45–50.4 Gy in 25–28 daily fractions of 1.8 Gy is recommended (Grade A).

There is evidence to recommend the use of 54 Gy in 30 daily fractions of 1.8 Gy (Grade B).

**Pituitary tumours**

4.4.5 In this context, fractionation is entirely governed by the tolerance of the normal CNS, and there are no randomised studies of fractionation in this area. There is, however, remarkable uniformity of practice using 45 Gy in 25 fractions for small pituitary tumours without suprasellar extension (level 2+). Some centres have used slightly higher doses which might be indicated for tumours with adverse factors (level 4, Grade D). Treatment of the elderly may require particular care.

For small benign pituitary tumours, the dose should usually be no more than 45 Gy in 25 fractions of 1.8 Gy (Grade C).

**References**


