E18. CNS metastasis: The role of radiotherapy for brain metastasis and metastatic spinal cord compression

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Brain metastasis

Brain metastases occur in 20–40% of adult cancer patients.[1] Most patients with multiple brain metastases receive whole-brain radiotherapy (WBRT) alone. 30 Gy in 10 fractions over 2 weeks is considered the standard regimen. According to a retrospective study of 416 patients, dose-escalation beyond 30 Gy improved neither survival nor intracerebral control.[2] In another study, the results achieved with 20 Gy in 5 fractions over 1 week (5×4 Gy) were similar to the results after 30 Gy in 10 fractions.[3] At least for patients with a poor expected survival, 5×4 Gy is preferable. Because the risk of radiation related late morbidity such as neuro-cognitive deficits increases with the dose per fraction, 5×4 Gy does not appear optimal for patients with a favourable survival prognosis. These patients appear better treated with 30 Gy in 10 fractions or 40 Gy in 20 fractions.

Patients with a limited number of brain metastases benefit from neurosurgery only if all lesions can be completely removed.[4] The alternative option to neurosurgery is radiosurgery. It is still debated whether WBRT should be administered in addition to neurosurgery or radiosurgery. Additional WBRT does not improve survival but intracerebral control.[5–7] However, both survival and intracerebral control are important endpoints. An intracerebral recurrence (not WBRT) is the major cause of neuro-cognitive dysfunction[8] and must be avoided. In a matched-pair analysis, radiosurgery+WBRT results in significantly better local control than neurosurgery+WBRT, whereas survival was not significantly different.[9] The 1-year local control rates were 87% versus 66%, respectively (p=0.021). Because radiosurgery is a non-invasive procedure, it may be the preferable option for most patients with a limited number of brain metastases. The results of neurosurgery+WBRT may be improved with a radiation boost to the metastatic sites. A matched-pair analysis showed no significant difference between radiosurgery+WBRT and neurosurgery+WBRT+boost for treatment outcomes.[10]

Metastatic spinal cord compression (MSCC)

MSCC occurs in 5–10% of cancer patients.[11] 85–90% of MSCC patients receive RT alone. Most patients have a markedly reduced life expectancy. For these patients, short-course RT (8–20 Gy in $\leqslant$1 week) is preferable to long-course RT (30–40 Gy in 2–4 weeks). Four prospective studies compared different RT schedules for MSCC and did not find a difference in post-treatment functional outcome. A non-randomised prospective study compared two long-course programmes (10×3 Gy versus 20×2 Gy),[12] a randomised trial 2×8 Gy in 8 days and a split-course regimen (3×5 Gy followed by 4-day-rest and 5×3 Gy),[13] another randomised study 1×8 Gy and 2×8 Gy in 8 days,[14] and a multinational non-randomised study compared short-course to long-course RT.[15]

Long-course RT results in better re-calcification than short-course RT.[16] Relevant re-calcification can only be expected several months following RT and is therefore only important for MSCC patients with a favourable survival prognosis. Local control of MSCC is significantly better after long-course RT than after short-course RT.[15] Thus, long-course RT appears the better option for MSCC patients with a favourable survival prognosis, as these patients may live long enough to develop a recurrence of MSCC. Patients with an extraordinarily favourable survival prognosis may be considered for high-precision RT to achieve better sparing of the surrounding normal tissues. Another group of MSCC patients who may benefit from high-precision RT are patients with oligometastatic disease. In a large retrospective study, motor function improved in 40% of patients and remained stable in another 54%.[17] 54% of non-ambulatory patients became ambulatory after RT. Local control at 1 year was 92%.

In most patients developing an in-field recurrence of MSCC after RT, surgery may not be possible nor indicated. Concerns exist about a second RT series to the same spinal area resulting in a high biologically effective dose (BED). Re-irradiation appears safe for a cumulative BED $\leqslant$120 Gy_2, an interval between primary RT and re-irradiation $\geqslant$6 months, and a BED of each RT-course $\leqslant$98 Gy_2.[18] High-precision radiotherapy should be considered if the cumulative BED exceeds 120 Gy_2.

Summary

Patients with multiple brain metastases are generally treated with WBRT alone. Patients with a poor expected

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survival should receive 20 Gy in 5 fractions, and those with a more favourable survival prognosis long-course WBRT. Patients with 1–4 brain metastases appear best treated with radiosurgery+WBRT. RT alone is also the most frequent treatment of MSCC. Patients with an expected survival of $\geqslant$6 months should receive long-course RT. Those with an extraordinarily favourable survival prognosis may benefit from high-precision RT. Patients with an expected survival of <6 months should receive short-course RT.

Conflict of interest statement

None declared.

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