20.
Oligometastases

Background

The oligometastatic state can be defined as 1–3 isolated metastatic sites, typically occurring more than six months after successful treatment of primary disease.[1] In colorectal cancer (in addition to sarcoma and other sites), surgical treatment of oligometastatic disease (most frequently liver metastases) is associated with prolonged overall survival.[2] Multiple single-arm studies have shown that stereotactic radiotherapy is effective and well tolerated in the oligometastatic setting, across multiple histologies and anatomical sites. Thus, it may be deployed as an alternative to surgery or where surgery is not possible.

There is no randomised data, and no established consensus for dose fractionation in radiotherapy for oligometastatic disease. Recommendations have been derived from systematic reviews of non-randomised studies (prospective and retrospective [Level 3a]), along with expert consensus from the Comissioning through Evaluation (CtE) Service Specification (Level 5).[3,4] For all sites, it is recommended that the critical organ dose constraints agreed by the UK Stereotactive Ablative Radiotherapy (SABR) consortium should be followed.[5]

It is not possible to discuss dose fractionation without discussing treatment technique. The majority of evidence comes from stereotactic body radiotherapy (SBRT or stereotactic ablative radiotherapy [SABR]). Developments in radiotherapy technology have allowed the safe delivery with high-precision of an ablative dose in five or fewer fractions. Patients have been treated using dedicated stereotactic systems (such as Cyberknife) and using conventional gantry-based systems with stereotactic capability. The optimal system for delivery is unknown, but image guidance, either with implanted fiducials and/or soft tissue tomography, is essential. Dose fractionation recommendations are, however, independent of the stereotactic platform used.

Oligometastases: bone (including spine) and lymph nodes

In this setting, treatment can expect to achieve a local control around of 80% and progression-free survival (PFS) of approximately 20% at 2–3 years.[1] Doses delivering a biologically equivalent dose (BED) at 2 Gray (Gy) per fraction (EQD2) >100 Gy, and those tumours ≤3 centimetres (cm) have best outcomes. Treatment is, in general, well tolerated with myelopathy rates for spinal treatments being less than 1% in most series.[6,7]

Contouring for spinal treatment should be based on the expert consensus guidelines by Cox et al (Level 5).[4,8]

Recommendations

Initial treatment:

18–24 Gy single dose (Grade C)
30–45 Gy in 3 fractions over 1 week (10–15 Gy per fraction given on alternate days) (Grade C)

Retreatment

Pelvis: 30 Gy in 5 fractions over 2 weeks, given on alternate days (Grade C)
Spine: 20–30 Gy in 2–5 fractions over 1–2 weeks, given on alternate days (Grade C)

The types of evidence and the grading of recommendations used within this review are based on those proposed by the Oxford Centre for Evidence-based Medicine.[4]

In this setting, it is vital to take into account the dose previously received by critical organs. As far as possible, cumulative doses to critical organs should be calculated and, allowing for recovery, tolerances described in the UK SABR consensus document should not be exceeded, if necessary modifying prescription doses to the planning target volume (PTV).[5]

In the specific case of remaining spinal cord tolerance, the method described by Sahgal is recommended.[7] Following this, the maximum cumulative dose to the thecal sac (similar to cord planning organ at risk volume [PRV]), at a minimum of six months after initial irradiation, should not exceed a BED of 140 Gy ($\alpha\beta$=2 Gy). For other organs, there is no consensus on recovery of tolerance following radiation and clinical judgment, along with the available literature, should be used.[9]

Oligometastases: lung

Lung oligometastases present a similar clinical problem to early-stage primary lung cancer, for which stereotactic treatment is a standard of care.[10] Specifically for patients with oligometastases, an EQD2 >100 Gy is associated with approximately 90% local control at 1–2 years.[10,11] Although Timmerman *et al* found a significant increase in toxicity when treating central lung tumours, other series have found no increase in toxicity when treating with more than three fractions.[12–15] These current recommendations are consistent with the CtE Service Specification.[3]

Recommendations

48–54 Gy in 3 fractions over 1 week given on alternate days (Grade C)

Peripheral lung oligometastases in contact with chest wall or where three fraction constraints cannot be met:

55–60 Gy in 5 fractions over 2 weeks given on alternate days (Grade C)

Lung oligometastases in the central lung/mediastinum:

60 Gy in 8 fractions over 1 week given on alternate days (Level 4)

The types of evidence and the grading of recommendations used within this review are based on those proposed by the Oxford Centre for Evidence-based Medicine.[4]

Oligometastases: liver

The use of surgery and radiofrequency ablation to treat liver oligometastases is well established. For colorectal liver tumours under 6 centimetres (cm) in diameter, local control above 90% at one year can be achieved with stereotactic doses of at least 48 Gy in three fractions.[16] This analysis included patients who were heavily pre-treated with systemic therapy. Further reviews have indicated this dose is effective in other tumour types, with grade 3–4 toxicity of 1–10% (Level 3a).[4,17,18]

Recommendations

45–50 Gy in 3 fractions over 1 week, given on alternate days (Grade C)

For larger PTV volumes or where dose constraints cannot be met with a three-fraction approach:

50–60 Gy in 5 fractions over 2 weeks (Grade C)

The types of evidence and the grading of recommendations used within this review are based on those proposed by the Oxford Centre for Evidence-based Medicine.[4]

Oligometastases: adrenal

Due to a rich sinusoidal blood supply, adrenal metastases are frequently observed in patients with melanoma, breast, lung, kidney and gastrointestinal tumours. Based on observations of enhanced survival in patients undergoing adrenalectomy for oligometastatic disease, stereotactic radiotherapy has also been been used. Local control rates vary from 55% to 90% with doses ranging from 16 Gy in four fractions to 50 Gy in ten fractions (Level 4).[4,19,20]

Recommendation

30–36 Gy in 3 fractions over 1 week (Grade C)

The types of evidence and the grading of recommendations used within this review are based on those proposed by the Oxford Centre for Evidence-based Medicine.[4]

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