16.
Skin cancer

Squamous cell carcinoma and basal cell carcinoma

Background

Surgery and radiotherapy are both highly effective curative treatment modalities for squamous cell carcinoma (SCC) and basal cell carcinoma (BCC). The choice of treatment modality is determined by factors including age, tumour size and functional/cosmetic outcomes. Surgery is generally preferred for younger patients. Primary radiotherapy is often preferred for regions around the lower eyelids, nose and ear, where better functional/cosmetic results can be achieved. Radiotherapy to the lower leg is often avoided in elderly patients due to the risk of radionecrosis. There appears to be a slightly higher local recurrence rate following radiotherapy for SCCs compared with BCCs.[1] Postoperative radiotherapy for SCC can be considered for high-risk features, for example, positive or close margins, perineural invasion, tumour depth >4 millimetres (mm) and poor differentiation.[2] Elective irradiation of first echelon lymph nodes can be considered for higher risk SCC.[3]

There are no randomised studies examining dose-fractionation; in addition, most series report use of multiple dose-fractionation schedules in historical series.[4] As a consequence, there is wide variation in both total dose and dose per fraction in commonly used schedules, with a variety of pragmatic hypofractionated schedules being widely used.[4, 5] Similar doses are used for BCC and SCC, although some suggest higher doses for SCCs.[6] More protracted treatment regimens may provide superior cosmetic results.

A large retrospective study of patients with SCC and BCC showed that schedules of 54 Gray (Gy) in 18 fractions or 44 Gy in ten fractions had similar efficacy with good cosmetic outcomes.[7] A schedule of 34 Gy in five fractions was shown to provide high rates of local control for BCC (five-year recurrence rate of 7%).[8] In a retrospective series employing multiple schedules for BCC and SCC, including 35 Gy in five fractions, no difference in control rates was found between different fractionation schedules.[3] In a large retrospective series of 1,005 predominantly small BCCs/SCCs, single fraction doses of 18, 20 and 22.5 Gy provided a five-year local control rate of 90%; the skin necrosis-free rate at five years was only 84% and necrosis occurred more frequently with the 22.5 Gy dose (Level 4).[9,10]

The relative biological effectiveness of electrons and photons is around 10% less than that for superficial X-rays; treatment with electrons or photons therefore, theoretically, requires a corresponding increase in dose, although this is often not considered in practice.

Recommendations

The choice of dose fractionation takes into account patient factors, tumour and field size. The following schedules are examples of those appropriate for the treatment of skin SCCs and BCCs either definitively or adjuvantly:

Single fraction 18–20 Gy (usually in elderly patients with field size <3 cm) (Grade C)
32.5–35 Gy in 5 fractions over 1 week (usually small lesions <4 cm) (Grade C)
45 Gy in 10 fractions over 2–3 weeks (Grade C)
50 Gy in 15–20 fractions over 3–4 weeks (Grade C)
55 Gy in 20 fractions over 4 weeks (Grade C)

If large area and in area of poor radiation tolerance:

60 Gy in 30 fractions over 6 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.[10]

Squamous cell carcinoma and regional lymph node disease

Background

Surgical management of regional lymph node disease is regarded as the treatment of choice. Relapse rates after therapeutic surgery alone to regional lymph node disease are high.[11] Several series have reported multiple factors predictive of regional relapse after surgery, including lymph node >3 cm, multiple involved nodes, extracapsular spread.[11,12] In the head and neck region, the use of adjuvant radiotherapy has been shown to reduce regional recurrence rates and improve disease free survival.[13] In a large retrospective series, the median dose employed was 60 Gy in 30 fractions with a dose of 50 Gy in 25 fractions to elective at risk regions (Level 4).[10,13] Optimal adjuvant dose fractionation will depend upon the anatomical site. In the head and neck region, doses of up to 66 Gy in 33 fractions can be considered in the presence of extracapsular spread.[14] Radical radiotherapy can be considered if surgery is inappropriate or declined.

Recommendations

For adjuvant radiotherapy to nodal regions considered at high risk o frelapse after theraputic lymphadenectomy:

50–60 Gy in 25–30 fractions over 5–6 weeks (Grade C)

Where there are high pathological risk features in the head and neck region:

66 Gy in 33 fractions over 6.5 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.[10]

Melanoma

Background

The primary treatment for cutaneous melanoma is complete local excision. Adjuvant radiotherapy to the primary site is not usually indicated, other than in rare cases of desmoplastic melanoma, which is a rare subtype associated with perineural spread and increased risk of local failure. Adjuvant radiotherapy to the primary site can be considered for desmoplastic melanoma resected with close margins, perineural invasion or lesions thicker than 4 mm.[14,15]

For patients at high risk of regional recurrence after a therapeutic lymphadenectomy, adjuvant hypofractionated radiotherapy with a dose of 48 Gy in 20 fractions over four weeks has been shown in a Trans Tasmann Radiation Oncology Group (TROG) phase III trial to reduce the risk of regional recurrence, although has no effect on overall survival (Level 1b).[10,16] Hypofractionated schedules have commonly been used for melanoma although no direct comparison with conventional 2 Gy per day fractionation has been performed. The MD Anderson Cancer Centre has reported an alternative hypofractionated schedule of 30 Gy in five fractions (two fractions per week) with high rates of regional control (Level 4).[10,17]

Recommendations

Adjuvant radiotherapy to nodal regions:

48 Gy in 20 fractions over 4 weeks (Grade A)
50–60 Gy in 25–30 fractions over 5–6 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.[10]

Merkel cell carcinoma

Background

Merkel cell cancer is a rare, aggressive, neuroendocrine skin malignancy with a propensity for locoregional and distant recurrence. The primary therapy for Merkel cell carcinoma is surgery. Merkel cell cancer is considered radiosensitive and multiple retrospective series provide evidence that adjuvant postoperative radiotherapy to the primary tumour bed and draining lymphatics provides high rates of locoregional control for higher risk tumours; wide margins are required due to a tendancy for edge recurrences (Level 4).[10,18–20] A prospective cohort study in patients with lymph node positive disease has demonstrated that radiotherapy alone to the regional lymph nodes provides equally high rates of regional control, comparable to surgical outcomes, with no overall survival difference (Level 2b).[10,21] Elective lymph node treatment is not always feasible depending upon the anatomical site of the primary tumour and patient fitness. There are no randomised trials to assess the optimal dose fractionation. Radical radiotherapy can be considered in medically inoperable patients or when the functional/cosmetic deficits due to surgery are considered excessively morbid. Limited data suggest that definitive radiotherapy can be effective. In a series of 43 patients an in-field control rate of 75% was achieved; doses of 50–55 Gy in 20–25 fractions were recommended.[22] In a small series, a dose of 60 Gy was effective in the definitive treatment of the primary lesion, while others have employed doses of up to 70 Gy (Level 4).[10,18,23] In most series, adjuvant doses of >50 Gy are used.[18,19,21] For some patients, such as frail elderly patients, a conventionally fractionated schedule may be considered excessively burdensome and shorter hypofractionated schedules may be considered. Consistent with the radiosensitivity of the disease, lower doses of 20 Gy in five fractions or 30 Gy in ten fractions have been reported to potentially eradicate low volume disease in poor performance status patients (Level 4).[10,22]

Recommendations

Primary and/or draining lymph node regions:

For definitive treatment:

60–66 Gy in 30–33 fractions in 6–6.5 weeks (Grade C)
50–55 Gy in 20–25 fractions in 4–5 weeks (Grade C)
40–45 Gy in 15 fractions over 3 weeks (Grade D)

For adjuvant treatment:

50–60 Gy in 25–30 fractions over 5–6 weeks (Grade C)
40–45 Gy in 15 fractions over 3 weeks (Grade D)

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.[10]

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