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Squamous cell carcinoma and basal cell carcinoma

Background

Surgery and radiotherapy are both highly effective curative treatment modalities for cutaneous squamous cell carcinoma (SCC) and basal cell carcinoma (BCC). The choice of treatment modality is determined by factors including tumour size, location, performance status (PS), age 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 function and cosmetic results can be achieved. Radiotherapy to the lower leg can lead to high risk of radionecrosis and ulceration due to poor vasculature, especially in older patients. Skin radiotherapy can be delivered as external beam or brachytherapy.[1] Brachytherapy is reported to offer favourable cosmesis over external beam in selected patients with SCC and BCC.[2,3] There appears to be a slightly higher local recurrence rate following radiotherapy for SCC compared with BCC.[4–6]

Postoperative radiotherapy for SCC should be considered for high-risk features.[7,8] Elective irradiation of first-echelon lymph nodes can be considered for higher-risk SCC.[8,9]

There are no randomised studies examining dose fractionation; in addition, most historical series report use of multiple dose fractionation schedules.[10] 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.[10,11] Similar doses are used for BCC and SCC, although some suggest higher doses for SCC.[12]

Standard fractionation has long been considered a standard approach to reduce long-term toxicity.[5] A meta-analysis of patients with SCC and BCC showed that hypofractionation has favourable cosmesis and recommended the use of regimens with BED3 of ~100 Gy, such as 50 Gy in 15 fractions, 36.75 Gy in 7 fractions or 35 Gy in 5 fractions, as they result in ‘good’ long-term cosmesis in 80% of patients.[5]

In a large retrospective series of 1,005 predominantly small BCCs and SCCs, single-fraction doses of 18, 20 and 22.5 Gy provided a 5-year local control rate of 90%; the skin necrosis-free rate at 5 years was 84% and skin necrosis occurred more frequently with the 22.5 Gy dose (Level 4).[13,14]

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.[15]

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Recommendations

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 (field size <3 cm) (Grade C)
- 32.5–35 Gy in 4–5 fractions over 1 week (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/or in area of poor radiation tolerance:

- 60 Gy in 30 fractions over 6 weeks (Grade C)

The choice of dose fractionation considers patient factors, tumour and field size.

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.[14]

Squamous cell carcinoma and regional lymph node disease

Background

Surgical management of regional lymph node disease is regarded as the treatment of choice. Retrospective studies have demonstrated an association of higher regional disease control rates with surgery and adjuvant radiotherapy.[7,8]

Several series report multiple factors predictive of regional relapse after surgery, including lymph node ≥3 cm, multiple involved nodes and extracapsular spread.[7,8,16,17]

In the head and neck region, the use of adjuvant radiotherapy has been shown to reduce regional recurrence rates and improve disease-free survival.[18]

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).[18] 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.[8]

Radical radiotherapy can be considered if surgery is inappropriate or declined.

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Recommendations

For adjuvant radiotherapy to nodal regions considered at high risk of relapse after lymphadenectomy:

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

In 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.[14]

References

1. Veness MJ, Delishaj D, Barnes EA, Bezugly A, Rembielak A. Current role of radiotherapy in non-melanoma skin cancer. *Clin Oncol (R Coll Radiol)* 2019; **31**(11): 749–758. doi:10.1016/j.clon.2019.08.004.
2. Zaorsky NG, Lee CT, Zhang E, Galloway TJ. Skin cancer brachytherapy vs external beam radiation therapy (SCRiBE) meta-analysis. *Radiother Oncol* 2018; **126**(3): 386–393. doi:10.1016/j.radonc.2017.12.029.
3. Guinot JL, Rembielak A, Perez-Calatayud J *et al*. GEC-ESTRO ACROP recommendations in skin brachytherapy. *Radiother Oncol* 2018; **126**(3): 377–385. doi:10.1016/j.radonc.2018.01.013.
4. Lovett RD, Perez CA, Shapiro SJ, Garcia DM. External irradiation of epithelial skin cancer. *Int J Radiat Oncol Biol Phys* 1990; **19**(2): 235–242.
5. Zaorsky NG, Lee CT, Zhang E, Keith SW, Galloway TJ. Hypofractionated radiation therapy for basal and squamous cell skin cancer: a meta-analysis. *Radiother Oncol* 2017; **125**(1): 13–20. doi:10.1016/j.radonc.2017.08.011.
6. Gunaratne DA, Veness MJ. Efficacy of hypofractionated radiotherapy in patients with non-melanoma skin cancer: results of a systematic review. *J Med Imaging Radiat Oncol* 2018; **62**(3): 401–411. doi:10.1111/1754-9485.12718.
7. Keohane SG, Botting J, Budny PG *et al*. British Association of Dermatologists guidelines for the management of people with cutaneous squamous cell carcinoma 2020 [published correction appears in *Br J Dermatol* 2021 Sep; **185**(3): 686] [published correction appears in *Br J Dermatol* 2022 Mar; **186**(3): 596–597]. *Br J Dermatol* 2021; **184**(3): 401–414. doi:10.1111/bjd.19621.
8. Likhacheva A, Awan M, Barker CA *et al*. Definitive and postoperative radiation therapy for basal and squamous cell cancers of the skin: executive summary of an American Society for Radiation Oncology clinical practice guideline. *Pract Radiat Oncol* 2020; **10**(1): 8–20. doi:10.1016/j.prro.2019.10.014.
9. Wray J, Amdur RJ, Morris CG, Werning J, Mendenhall WM. Efficacy of elective nodal irradiation in skin squamous cell carcinoma of the face, ears, and scalp. *Radiat Oncol* 2015; **10**: 199. doi:10.1186/s13014-015-0509-2.

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10. Cho M, Gordon L, Rembielak A, Woo TC. Utility of radiotherapy for treatment of basal cell carcinoma: a review. *Br J Dermatol* 2014; **171**(5): 968–973.
11. McPartlin AJ, Slevin NJ, Sykes AJ, Rembielak A. Radiotherapy treatment of non-melanoma skin cancer: a survey of current UK practice and commentary. *Br J Radiol* 2014; **87**(1043): 20140501.
12. Locke J, Karimpour S, Young G, Lockett MA, Perez CA. Radiotherapy for epithelial skin cancer. *Int J Radiat Oncol Biol Phys* 2001; **51**(3): 748–755.
13. Chan S, Dhadda AS, Swindell R. Single fraction radiotherapy for small superficial carcinoma of the skin. *Clin Oncol (R Coll Radiol)* 2007; **19**(4): 256–259.
14. www.cebm.ox.ac.uk/resources/levels-of-evidence/oxford-centre-for-evidence-based-medicine-levels-of-evidence-march-2009 (last accessed 28/11/2023).
15. Herskind C, Ma L, Liu, Q *et al*. Biology of high single doses of IORT: RBE, 5 R's, and other biological aspects. *Radiat Oncol* 2017; **12**(24). doi:10.1186/s13014-016-0750-3.
16. Veness MJ, Porceddu S, Palme CE, Morgan GJ. Cutaneous head and neck squamous cell carcinoma metastatic to parotid and cervical lymph nodes. *Head Neck* 2007; **29**(7): 621–631.
17. Porceddu SV, Veness MJ, Guminski A. Nonmelanoma cutaneous head and neck cancer and merkel cell carcinoma: current concepts, advances, and controversies. *J Clin Oncol* 2015; **33**(29): 3338–3345.
18. Veness MJ, Morgan GJ, Palme CE, Gebski V. Surgery and adjuvant radiotherapy in patients with cutaneous head and neck squamous cell carcinoma metastatic to lymph nodes: combined treatment should be considered best practice. *Laryngoscope* 2005; **115**(5): 870–875.

Melanoma

Background

Melanoma has high repair capacity; this is evidenced by per fraction cell kill seen in *in vitro* cell lines irradiated with 2 Gy fractions.[1,2] Despite the high repair capacity, radiotherapy has an established role in certain circumstances and modest hypofractionation beyond 2.5 Gy per fraction may be advantageous, although randomised data defining the most effective dose fractionation schedule is lacking.

The primary treatment for cutaneous melanoma is complete local excision followed by adjuvant systemic therapy in those at high risk of cancer recurrence. Adjuvant radiotherapy 48 Gy in 20 daily fractions over 4 weeks delivered to the lymph node basin after lymphadenectomy reduces risk of relapse in the lymph node basin when compared with surveillance (21% versus 36%, p=0.023). Adjuvant radiotherapy delivered to the lymph node basin has no impact on relapse-free or overall survival.[3] An alternative hypofractionated schedule of 30 Gy in 5 fractions over 2.5 weeks is reported retrospectively from a single centre with high rates of locoregional control (94%) and low rates of late Grade 2 toxicity (10%).[4] The data for mucosal melanoma in the postoperative setting mirror the above, with adjuvant radiotherapy impacting upon local control (HR 0.51 [95% CI 0.35–0.76], p=0.155) but not impacting on risk of distant metastasis (HR 2.26 [95% CI 1.01–5.05], p=0.006).[5]

Adjuvant radiotherapy delivered to the lymph node basin in high-risk melanoma is associated with 20% risk of high-grade toxicity and is therefore not considered as the standard of care; this is because improvements in local control do not translate to improvements in the rate of distant metastatic spread or overall survival.[3]

Definitive radiotherapy for melanoma has a role where the primary disease is unresectable. Small case series in mucosal melanomas report 50% 3-year local control with hypofractionated regimens, an example being 50 Gy in 15 daily fractions over 3 weeks.[6,7]

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Desmoplastic melanoma is a rare melanoma subtype predominantly developing in sun-exposed sites and is associated with perineural spread with an increased risk of local recurrence.[8,9] Adjuvant radiotherapy 48 Gy in 20 daily fractions over 4 weeks improves local control (HR 0.48 [95% CI 0.27–0.87], p=0.02) in instances where the pathological resection margins were less than 8 mm.[8–10] There is no benefit from adjuvant radiotherapy where resection margins are 8 mm or greater.[10]

Lentigo maligna is an *in situ* melanoma developing in regions of sun-damaged skin characterised by atypical melanocytes involving the dermo-epidermal junction. Lentigo maligna can progress to lentigo maligna melanoma in up to 50% of cases. The gold standard approach is surgical resection with a 5 mm margin with Mohs' surgery considered for selected anatomical sites. Non-surgical approaches include topical therapies and radiotherapy; both non-surgical approaches have advantages in this often older patient population where the primary lesion can be ill defined and where extensive surgical resection and reconstruction has added morbidity. Systematic review reports 5% recurrence rate of lentigo maligna at 3 years following definitive radiotherapy.[11] Reported schedules extend from 35 Gy in 5 fractions over 5 weeks to 54 Gy in 27 fractions over 5.5 weeks. The RADICAL trial (NCT02394132) evaluating 2-year local recurrence in those treated with non-surgical therapies has completed recruitment and is in follow-up.[12]

20–30% of patients with advanced melanoma develop brain metastases within the first year of diagnosis.[13] Historical data report that whole-brain radiotherapy (WBRT) improves neurological symptoms in 76%, with 31% reporting complete symptom response.[14] Despite this, the median overall survival of the cohort was short at 10 and 14 weeks.[14]

Modern systemic therapies offer high overall response rate within the brain; most of the systemic therapies can be combined or sequenced alongside stereotactic radiosurgery or stereotactic radiotherapy (see chapter on 'Brain metastases'). WBRT should now not be routinely offered to patients with brain metastases. The sequencing of stereotactic radiosurgery and stereotactic radiotherapy alongside systemic therapy is being explored in clinical trials.

Radiotherapy for palliation of symptomatic melanoma metastases outside brain is effective, yielding complete and partial pain response in 9–25% and 35–75% of instances.[15–17] Standard palliative schedules such as 20 Gy in 5 fractions over 7 days or 8 Gy in 1 fraction are feasible for those whose PS precludes longer fractionated schedules.

Large case series report total dose greater than 30 Gy to be associated with improved palliative outcomes.[17] The choice of dose and fractionation in the palliative setting should be tailored to the needs of each patient.

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Recommendations

Adjuvant radiotherapy to the lymph node basin improves local control but is not considered as the standard of care for high-risk melanoma:

- 48 Gy in 20 fractions over 4 weeks (Grade A)
- 50–60 Gy in 25–30 fractions over 5–6 weeks (Grade C)

Definitive radiotherapy to primary unresectable disease:

- 50 Gy in 15 fractions over 3 weeks (Grade C)

Desmoplastic melanoma:

- 48 Gy in 20 fractions over 4 weeks (Grade C)

Palliative radiotherapy:

- 30 Gy in 10 fractions over 2 weeks (Grade C)
- 20 Gy in 5 fractions over 1 week (Grade B)
- 8 Gy in 1 fraction over 1 day (Grade B)

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.[18]

References

1. Dewey DL. The radiosensitivity of melanoma cells in culture. *Br J Radiol* 1971; **44**(526): 816–17.
2. Barranco SC, Romsdahl MM, Humphrey RM. The radiation response of human malignant melanoma cells grown *in vitro*. *Cancer Res* 1971; **31**(6): 830–3.
3. Burmeister BH, Henderson MA, Ainslie J *et al*. Adjuvant radiotherapy versus observation alone for patients at risk of lymph-node field relapse after therapeutic lymphadenectomy for melanoma: 6 year follow-up. *Lancet Oncol* 2015; **16**(9): 1049–1060.
4. Ballo MT, Bonnen MD, Garden AS *et al*. Adjuvant irradiation for cervical lymph node metastases from melanoma. *Cancer* 2003; **97**(7): 1789–1796.
5. Li W, Yu Y, Wang H, Yan A, Jiang X. Evaluation of the prognostic impact of postoperative adjuvant radiotherapy on head and neck mucosal melanoma: a meta-analysis. *BMC Cancer* 2015; **15**: 758.
6. Gilligan D, Slevin NJ. Radical radiotherapy for 28 cases of mucosal melanoma in the nasal cavity and sinuses. *Br J Radiol* 1991; **64**(768): 1147–50.
7. Wada H, Nemoto K, Ogawa Y *et al*. A multi-institutional retrospective analysis of external radiotherapy for mucosal melanoma of the head and neck in Northern Japan. IJROBP 2004; **59**(2): 495–500.
8. Strom T, Caudell JJ, Han D *et al*. Radiotherapy influences local control in patients with desmoplastic melanoma. *Cancer* 2014; **120**(9): 1369–1378.
9. Guadagnolo BA, Prieto V, Weber R, Ross MI, Zagars GK. The role of adjuvant radiotherapy in the local management of desmoplastic melanoma. *Cancer* 2014; **120**(9): 1361–1368.
10. Varey AHR, Goumas C, Hong AM *et al*. Neutrotropic melanoma: an analysis of the clinicopathological features, management strategies and survival outcomes for 671 patients treated at a tertiary referral centre. *Mod Pathol* 2017; **30**: 1538–50.

18
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11. Fogarty GB, Hong A, Scolyer RA *et al*. Radiotherapy for lentigo maligna: a literature review and recommendations for treatment. *Br J Dermatol* 2014; **170**(1): 52–8.
12. Kanitakis J. Treatment of lentigo maligna: review. *World Acad Sci J* 2021; **3**(3): 22.
13. Zhang D, Wang Z, Shang D, Yu J, Yuan S. Incidence and prognosis of brain metastases in cutaneous melanoma patients: a population-based study. *Melanoma Res* 2019; **29**: 77–84.
14. Carella RJ, Gelber R, Hendrickson F *et al*. Value of radiation therapy in the management of patients with cerebral metastases from malignant melanoma: Radiation Therapy Oncology Group brain metastases study I and II. *Cancer* 1980; **45**(4): 679–683.
15. Sause WT, Cooper JS, Rush S *et al*. Fraction size in external beam radiation therapy in the treatment of melanoma. *Int J Radiat Oncol Biol Phys* 1991; **20**(3): 429–32.
16. Kirova YM, Chen J, Rabarijaona LI *et al*. Radiotherapy as palliative treatment for metastatic melanoma. *Melanoma Res* 1999; **9**(6): 611–3.
17. Olivier KR, Schild SE, Morris CG, Brown PD, Markovic SN. A higher radiotherapy dose is associated with more durable palliation and longer survival in patients with metastatic melanoma. *Cancer* 2007; **110**(8): 1791–5.
18. www.cebm.ox.ac.uk/resources/levels-of-evidence/oxford-centre-for-evidence-based-medicine-levels-of-evidence-march-2009 (last accessed 28/11/2023).

Merkel cell carcinoma

Background

Merkel cell carcinoma (MCC) is an uncommon but highly aggressive cutaneous neuroendocrine tumour with the highest mortality rate compared with other skin cancers.[1] Advanced aged, immunosuppression, Merkel cell polyomavirus and ultraviolet light exposure are hypothesised to be risk factors.[2–4]

International guidance for stages I–III MCC recommends surgery with a 1–2 cm margin as the primary treatment, with radiotherapy to the tumour bed and draining lymphatics reserved for postoperative high-risk cases, close margins or inoperable disease.[5,6]

MCC is radiosensitive,[7] and this has led to an established role for radiation therapy in primary management, particularly in Australia.[8,9] Due to the rare nature of this tumour, previous studies have largely been limited to case series with relatively small heterogeneous samples, and thus optimal management and dose and fractionation for MCC remains a subject of some debate. There are no randomised controlled trials to assess optimal dose and fractionation.

A large retrospective analysis of 2,735 patients from the National Cancer Database for patients with stages I–III MCC found that adjuvant radiotherapy doses of less than 50 Gy were associated with an increased hazard of death in all stages and anatomical sites (Level 3a).[10]

Radiotherapy in the radical setting can provide clinically meaningful outcomes with locoregional control rates of 75–85% with radiotherapy doses of 60–66 Gy in conventional 2 Gy fractions (Level 3a).[5,6,11] For T1 MCC, a dose of 57 Gy in 24 fractions is appropriate (Level 5).[12]

Hypofractionation can be considered; a retrospective study of 241 patients demonstrated that 45–50 Gy in 20 fractions and 30–35 Gy in 10 fractions produced no difference in infield or distant recurrence over 2 years compared with conventionally fractioned regimens (Level 3b).[13]

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Recommendations

Primary MCC and/or draining lymph node regions:

Definitive treatment:

- 60–66 Gy in 30–33 fractions over 6–6.5 weeks (Grade C)
- 50–55 Gy in 20–25 fractions over 4–5 weeks (Grade C)
- 45–50 Gy in 20 fractions over 4 weeks (Grade D)
- 30–35 Gy in 10 fractions over 2 weeks (Grade D)

Adjuvant treatment:

- 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.[14]

References

1. Hodgson NC. Merkel cell carcinoma: changing incidence trends. *J Surg Oncol* 2005; **89**(1): 1–4.
2. Agelli M, Clegg LX, Becker JC, Rollison DE. The etiology and epidemiology of Merkel cell carcinoma. *Curr Probl Cancer* 2010; **34**(1): 14–37.
3. Rollison DE, Giuliano AR, Becker JC. New virus associated with Merkel cell carcinoma development. *J Natl Compr Canc Netw* 2010; **8**(8): 874–880.
4. Akaike T, Nghiem P. Scientific and clinical developments in Merkel cell carcinoma: a polyomavirus-driven, often-lethal skin cancer. *J Dermatol Sci* 2022; **105**(1): 2–10.
5. Schmults CD. Merkel cell cancer. Version 1.2021 – 24 March 2022. NCCN guidelines. www.nccn.org/professionals/physician_gls/pdf/mcc.pdf (accessed 09/06/2022).
6. Lebbe C, Becker JC, Grob JJ *et al*. Diagnosis and treatment of Merkel cell carcinoma. European consensus-based interdisciplinary guideline. *Eur J Cancer* 2015; **51**(16): 2396–2403.
7. Leonard JH, Ramsay JR, Kearsley JH, Birrell GW. Radiation sensitivity of Merkel cell carcinoma cell lines. *Int J Radiat Oncol Biol Phys* 1995; **32**(5): 1401–1407.
8. Kok DL, Wang A, Xu W *et al*. The changing paradigm of managing Merkel cell carcinoma in Australia: an expert commentary. *Asia Pac J Clin Oncol* 2020; **16**(6): 312–319.
9. Wang AJ, McCann B, Soon WCL *et al*. Merkel cell carcinoma: a forty-year experience at the Peter MacCallum Cancer Centre. *BMC Cancer* 2023; **23**: 30.
10. Yusef M, Gaskins J, Weston Wall *et al*. Optimal adjuvant radiotherapy dose for stage I, II or III Merkel cell carcinoma: an analysis of the National Cancer Database. *Jpn J Clin Oncol* 2020; **50**(2): 175–184.
11. Gunaratne D, Howle J, Veness M. Definitive radiotherapy for Merkel cell carcinoma confers clinically meaningful in-field locoregional control: a review and analysis of the literature. *J Am Acad Dermatology* 2017; **77**(1).
12. Poulsen M, Rischin D, Walpole E *et al*. High-risk Merkel cell carcinoma of the skin treated with synchronous carboplatin/etoposide and radiation: a Trans-Tasman Radiation Oncology Group study – TROG 96:07. *J Clin Oncol* 2003 1; **21**(23): 4371–6.

18
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13. Liu KX, Milligan MG, Schoenfeld JD *et al*. Characterization of clinical outcomes after shorter course hypofractionated and standard-course radiotherapy for stage I–III curatively-treated Merkel cell carcinoma. *Radiother Oncol* 2022; **173**: 32–40.
14. www.cebm.ox.ac.uk/resources/levels-of-evidence/oxford-centre-for-evidence-based-medicine-levels-of-evidence-march-2009 (last accessed 28/11/2023).

Reirradiation

Background

Reirradiation of the skin can be considered in the radical, adjuvant (following salvage surgery) or palliative settings in instances where the benefits of exposure to further radiotherapy have been discussed within the multidisciplinary team.

Beyond small case series, there are no data to define the approach to skin reirradiation; the risks and benefits of skin reirradiation should be discussed with the patient.

Palliative radiotherapy to the skin

Background

Palliative radiotherapy is an excellent option for patients where there are no viable curative options.

Radiotherapy in this setting aims to reduce local symptoms and prevent disease-related complications such as bleeding or ulceration but can also potentially achieve local control. Palliative treatment should be minimally invasive and of short duration, especially for patients with poor PS or short life expectancy and for those unable to travel for multiple hospital visits.

Several hypofractionated regimes are used in palliative radiotherapy for skin cancer but it is not possible to offer evidence-based guidelines. Commonly used schedules include single exposure of 12–20 Gy for field size <3 cm, 14.8 Gy in 4 fractions twice daily over 2 consecutive days and repeated at 4-weekly intervals for a further 2 courses (QUAD shot, also used in reirradiation), 20 Gy in 2 fractions 1 week apart, 30 Gy in 10 fractions over 14 days, 30.6 Gy in 3 fractions over 14 days, 40.2 Gy in 6 fractions over 35 days, 35 Gy in 5 fractions 3 times a week, and 8 Gy per fraction delivered on days 0, 7 and 21.[1–5]

Longer treatment schedules should be considered in patients with favourable prognosis and expected longer-term disease control.[2]

Palliative radiotherapy schedules should be distinguished from radical treatment used in older or frail patients, such as adaptive split-course radiotherapy or mono- or biweekly hypofractionation.[6,7]

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Cutaneous and subcutaneous metastasis from non-skin primaries

Background

Local radiotherapy is an underused modality for the palliative treatment of symptomatic cutaneous and subcutaneous metastases from non-skin primary cancers.[8] Radiotherapy schedules used in cutaneous and subcutaneous metastases are consistent with those used in palliative radiotherapy for a skin cancer primary. Field size and dose per fraction will need to be kept in consideration to avoid skin necrosis.

Recommendations

Palliative radiotherapy:

- Single exposure of 12–20 Gy field size <3 cm (Grade C)
- 14.8 Gy in 4 fractions twice daily over 2 consecutive days and repeated at 4-weekly intervals for a further 2 courses (QUAT shot, also used in reirradiation) (Grade C)
- 20 Gy in 2 fractions 1 week apart (Grade C)
- 20 Gy in 5 fractions over 5 days (Grade C)
- 30 Gy in 10 fractions over 14 days (Grade C)
- 30.6 Gy in 3 fractions over 14 days (Grade C)
- 40.2 Gy in 6 fractions over 35 days (Grade C)
- 35 Gy in 5 fractions 3 times a week (Grade C)
- 8 Gy per fraction delivered on days 0, 7 and 21 (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.[9]

References

1. Vuong W, Lin J, Wei RL. Palliative radiotherapy for skin malignancies. *Ann Palliat Med* 2017 Apr; **6**(2): 165–172. doi:10.21037/apm.2016.11.10.
2. Staackmann C, Schild SE, Rades D. Palliative radiotherapy for cutaneous squamous cell carcinoma of the head-and-neck region. *In Vivo* 2021 Jul-Aug; **35**(4): 2283–2288. doi:10.21873/invivo.12501.
3. Veness M, Richards S. Role of modern radiotherapy in treating skin cancer. *Australas J Dermatol* 2003 Aug; **44**(3): 159–66; quiz 167–8.
4. Barnes EA, Breen D, Culleton S *et al*. Palliative radiotherapy for non-melanoma skin cancer. *Clin Oncol (R Coll Radiol)* 2010 Dec; **22**(10): 844-9. doi:10.1016/j.clon.2010.07.014.
5. Grewal AS, Jones J, Lin A. Palliative radiation therapy for head and neck cancers. *Int J Radiat Oncol Biol Phys* 2019; **105**(2): 254–266. doi:10.1016/j.ijrobp.2019.05.024.
6. Fogarty GB, McLaren KR, Moutrie Z, Poon TSC, Izard MA. Locally advanced skin cancers of the frail and elderly: consider adaptive split-course radiotherapy. *Br J Dermatol* 2018 Dec; **179**(6): 1416–1417.
7. Valeriani M, Nicosia L, Agolli L *et al*. Mono- and bi-weekly hypofractionated radiation therapy for the treatment of epithelial skin cancer in very elderly patients. *Anticancer Res* 2017 Feb; **37**(2): 825–830.

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8. Spratt DE, Gordon Spratt EA, Wu S *et al*. Efficacy of skin-directed therapy for cutaneous metastases from advanced cancer: a meta-analysis. *J Clin Oncol* 2014 Oct 1; **32**(28): 3144–55. doi:10.1200/JCO.2014.55.4634.
9. www.cebm.ox.ac.uk/resources/levels-of-evidence/oxford-centre-for-evidence-based-medicine-levels-of-evidence-march-2009 (last accessed 28/11/2023).

Acknowledgements

With thanks to lead authors Dr Agata Rembielak (The Christie NHS Foundation Trust), Dr Brendan McCann (Beatson West of Scotland Cancer Centre) and Dr Romaana Mir (Mount Vernon Cancer Centre) for reviewing and updating this chapter of the guidance.