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The important role of radiotherapy in patients with non-melanoma skin cancer and other cutaneous entities

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SUMMARY

Non-melanoma skin cancer is the commonest malignancy worldwide and a significant public health issue. Although most non-melanoma skin cancers are small and easily excised or ablated, a recommendation of definitive radiotherapy is often made in patients where the outcome (cosmetic and/or functional) will probably be better with radiotherapy compared to surgery. The aim of adjuvant radiotherapy is to reduce the risk of loco-regional recurrence and the role of palliative radiotherapy is important in improving the quality of life in patients with advanced and/or incurable disease. The aim of this review article is to broadly discuss the various clinical settings in which a recommendation of radiotherapy may be made and also includes a discussion on less frequently encountered cutaneous entities (e.g. *in situ* squamous cell carcinoma, keratocanthoma, lentigo maligna, cutaneous lymphomas and malignant fibrous tumours).

Key words: *basal cell carcinoma; merkel cell carcinoma; squamous cell carcinoma*.

INTRODUCTION

Non-melanoma skin cancer (NMSC) is the commonest malignancy worldwide and a significant public health issue.[1] Although lesions often arise on the sun-exposed head and neck (HN) in older white men, NMSC can also occur in women, younger patients and in non-HN sites (extremities).[2] Basal cell carcinomas (BCC) occur more often than the more serious squamous cell carcinoma (SCC), which can metastasize and may need to be treated more aggressively in certain cases.[3,4]

Most NMSC are small (10–20 mm) and are easily excised or ablated. The recommendation of definitive radiotherapy is often made in patients where the outcome, that is, cosmetic (e.g. nasal BCC) and/or functional (e.g. lower lip SCC) is better with radiotherapy compared with surgery, especially when constrained by the site or size of the lesion.[5,6] Elderly patients (often warfarinized) with advanced lesions where complex surgery (graft or local flap) under general anaesthesia is required are also often better treated with radiotherapy. The aim of adjuvant radiotherapy is to reduce the risk of recurrence (local or regional) and the role of palliative radiotherapy is important in improving the quality of life in patients with advanced and/or incurable disease.

The aim of this review article is to broadly discuss the various clinical settings in which a recommendation of radiotherapy may be made and includes not only NMSC, but also less often seen cutaneous malignancies and conditions (e.g. *in situ* SCC, lentigo maligna (LM), keratocanthoma (KA), cutaneous lymphomas and malignant fibrous tumours). Although there may be site-specific issues, the general principles in recommending radiotherapy will usually still apply in most cases. Wherever possible, relevant articles have been cited to support recommendations and provide for further reading. In other cases where the evidence is lacking, or weak, recommendations are based more on the opinion and experience of the author.

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BASAL CELL CARCINOMA

Definitive setting

Small (<20 mm) BCC can be treated by various methods, including topical patient applied immune–response modifiers.[7] There is a paucity of randomized data comparing different methods with a Cochrane Review[8] reporting surgery or radiotherapy as the most effective treatments with surgery probably showing the lowest recurrence rates. However, local control rates (90–95%)[2,9] and cosmesis (>90% rated as excellent or good)[9] following radiotherapy are excellent and management decisions are often based on multiple factors.

Radiotherapy remains an option when tumour and patient factors favour this and typically these are older patients with a mid-face or nasal (ala nasi or nasal tip) BCC where small skin grafts or flaps may be required. Locations, such as the inner canthus or lower eyelid, may also be better approached with radiotherapy. Larger lesions can still be treated with definitive radiotherapy although with increasing size and deeper invasion local control decreases (80–85%) and excision (+/− adjuvant radiotherapy) may result in better local control.[10] Bone or cartilage invasion (T_4 primary) is not a necessarily a contraindication for recommending definitive radiotherapy with local control rates of 50–75%.[2,10] However, deeply invasive/destructive lesions are best approached (if possible) with combined excision and adjuvant radiotherapy.

Adjuvant (postoperative) setting

At least 30% of incompletely excised BCC recur and further treatment is often recommended rather than observation and expectant treatment.[11,12] A positive deep margin resulting in deep recurrence, particularly deep to a local flap, can be difficult to detect. BCC located around the mid-face and periorbital are sites where undetected deep recurrence can result in significant local morbidity. Re-excision is often an option, although in certain circumstances the involved margin precludes simple re-excision and therefore adjuvant radiotherapy is also an option. In a randomized trial of patients with incompletely excised BCC adjuvant radiotherapy improved the 5-year local control from 61 to 91%, although the 10-year local control rates were similar (92 vs 90%) as most recurrences were successfully salvaged with surgery.[13] Although recurrences are rarely ever associated with serious consequences, extensive salvage surgery may be required. Patients with the more aggressive subtypes of sclerosing (morpheaform) and infiltrative BCC are at a higher risk of local recurrence and are best not left untreated in the setting of inadequate excision, especially if located on the mid-face.[14,15]

Dose fractionation schedules

There is no one optimal dose fractionation schedule and an appropriate schedule considers both patient (age, performance status, preference) and tumour factors (site, stage, histology). It should also be noted that dose fractionation schedules often vary considerably with many schedules having evolved over many years as institutional policy rather than based on sound research and evidence. The wide variation in dose fractionation schedules for similar sized lesions can be confusing for clinicians, especially trainees.

As an example, for older (70 years) patients with smaller lesions (20–30 mm) prescribing 40–45 Gy in 10–15 daily fractions will result in acceptable local control and late cosmesis with doses being prescribed at the surface (or D_{max}). Alternatively, clinicians may also prescribe a tumour dose to a depth by estimating the deep extent of a lesion. In at least one large Australian radiation oncology department, a frequently prescribed dose fractionation schedule is 24 Gy in four fractions prescribed at depth (usually 1–4 mm) with a maximum accepted surface dose of 32 Gy.[16]

Elderly or infirm patients can be prescribed single large fractions (10–20 Gy) or even 3–5 fractions of 6–7 Gy. Larger invasive lesions (>3 to 4 cm) and/or younger patients should be approached using a lower fraction size (2–2.5 Gy) and a 'hotter' total dose of 50–60 Gy to achieve the best chance of durable local control and acceptable late effects.

Recent data (n = 806 patients) from a large centre in the UK suggest that small BCC/SCC of the HN, encompassed in a radiotherapy field size of <3 cm, can be treated with a single fraction of 20 Gy.[17] The authors documented a low recurrence rate (<5%), but a necrosis rate of 6%, which is more than expected, or accepted, for small lesions treated with multiple fractions. Of note, late cosmetic outcome was also not reported. In general, single large fractions should not be recommended although in select older patients that decline fractionated treatment, it may be an option.

There is also variation in defining an appropriate field margin; however, a field margin of 5–10 mm beyond macroscopic disease, or a surgical site, is usually adequate for a well-defined nodular BCC, but for SCC and infiltrative BCC a wider margin of 10–15 mm is required to encompass surrounding subclinical spread.[2,16]

SQUAMOUS CELL CARCINOMA

Definitive setting

Patients with SCC are at risk of metastatic spread to regional lymph nodes (especially if recurrent) and it is therefore important to obtain local control.[18] Patients can be considered to have a high-risk SCC if certain unfavourable features (often multiple) are present: thick/invasive lesions (>4 to 5 mm), large lesions (>2 cm), recurrent lesions, high- grade lesions, presence of perineural invasion, lesions in immunocompromised patients and lesions located in the vicinity of the parotid gland.

Patients with high-risk SCC are at increased risk of developing both local recurrence and metastatic nodal disease.[19,20] Radiotherapy is a definitive treatment option although patients with high-risk SCC should ideally have lesions excised with the aim to obtain oncological margins taking into consideration cosmesis and function.[21,22] The British Association of Dermatologists recently published evidenced-based guidelines for managing patients with SCC.[21] The authors ranked the quality of evidence and the strength of recommendations. Patients were considered at greater risk of local recurrence and developing metastases based on six variables: site (lip, ear, non-sun-exposed sites), size (>2 cm), depth (>4 mm or Clark level V), grade (poorly differentiated), host immunosuppression (immunosuppressed) and presentation (recurrent). The authors recommended a multidisciplinary approach to high-risk patients and suggested Mohs micrographic surgery to achieve complete clearance. The National Comprehensive Cancer Network in its guidelines considers patients with tumours ≥4 mm thick, Clark level IV to V, moderate to poor differentiation, perineural invasion present and recurrent as high-risk and recommends wide excision (10-mm margins if achievable), or Mohs micrographic surgery and adjuvant radiotherapy if warranted.[22]

It is not appropriate that incompletely excised SCC be observed as recurrent SCC are associated with a higher incidence of regional metastases spread of up to 25–45% depending on the site of the recurrence.[18] In a study of patients with cutaneous SCC <2 cm in diameter, the authors report that with a 4-mm excision margin 95% achieved negative excision margins and SCC >2 cm required a 6-mm margin to achieve a 95% rate of negative excision margins.[23]

There is no consensus as to which high-risk patients should be offered elective treatment (surgery or radiotherapy) to regional nodes and a need for research to better identify patients at risk of having subclinical nodal metastases.[24] However, patients with recurrent thick SCC (>4 to 5 mm) in the vicinity (temple, forehead, preauricular area) of the parotid gland should be considered candidates for elective treatment.[3] The role of sentinel node biopsy (SNB) in patients with HN cutaneous SCC is unclear and lacking data from high-quality prospective trials to guide clinicians.[25,26]

The control rate for recurrent BCC/SCC is lower by at least 10% when compared with untreated lesions of equivalent size, emphasizing the importance of reducing the risk of local relapse.[2] The local control rate for SCC is also lower by 10–15% than an equivalent sized BCC.[2,27] However, definitive radiotherapy still remains an excellent option. The need for extensive surgery may preclude patients with multiple medical comorbidities. In some sites, such as the lip in a moderately advanced lower lip SCC, radiotherapy achieves excellent maintenance of oral function and cure rates similar to surgery.[28]

Radiotherapy to lower-limb lesions, although not contraindicated, should be considered cautiously. Patients often have poorly vascularized and oedematous tissues that may limit the effectiveness of radiotherapy and/or result in delayed healing. Surgery should be considered as a better option particularly considering that cosmesis and function are usually not important factors.

Adjuvant (postoperative) setting

A patient with an incompletely excised (positive or close margin) SCC is at risk of both local recurrence and also developing regional metastases. However, there is no consensus in regard to the definition of an acceptable surgical margin. Recommendations in published reports in the setting of lip and other cutaneous SCC range from 3 to 10 mm.[29,30] Choo *et al.* documented a mean distance of 5.2 mm of microscopic extension in 71 NMSC (57 BCC, 14 SCC) and a requirement for 10-mm margins to achieve a 95% chance of negative excision margins.[31] This finding, and of others also, supports the need for radiation oncologists to use adequate field margins of 10–15 mm, in most cases. The significance of local recurrence is well documented and adjuvant radiotherapy is an effective option when excision is incomplete and re-excision is not possible. Babington *et al.* documented a 37% local recurrence rate in excised patients not receiving adjuvant radiotherapy compared with a 6% local recurrence rate in patients treated with surgery and adjuvant radiotherapy in the setting of lip SCC.[32]

In situ *SCC (Bowen's disease)*

Definitive radiotherapy is an option in patients with non-invasive *in situ* disease. *In situ* SCC (or Bowen's disease) is limited to the epidermis and its appendages and usually presents as a slowly growing scaly erythematous facial plaque. A minority (<5%) become invasive although this figure may be higher (10–30%) in genital lesions such as Erythroplasia of Queyrat (*in situ* SCC of the penis). A dose fractionation schedule of 40–50 Gy in 10–20 fractions using superficial (110–150 kVp) energy photons will achieve a local control rate of 95–100%.[33] Recent review articles on managing patients with Bowen's disease emphasize the multitude of treatments (including radiotherapy) for patients with this disease.[34,35] Despite this, in select cases radiotherapy is an efficacious and well-tolerated option to be considered.

KERATOCANTHOMA

Keratocanthoma presents typically as a rapidly enlarging lesion with a central keratin plug and may be difficult to distinguish on biopsy from a well-differentiated SCC. Radiotherapy is an effective option if excision is not contemplated. Relatively low doses of 25 Gy in five fractions have been reported as resulting in durable regression. However, particularly, if a diagnosis of KA is uncertain, a dose fractionation schedule similar to a SCC should be prescribed. In one study of 55 patients with KA and treated with radiotherapy most were prescribed 40 Gy in 10

fractions twice weekly with the authors reporting complete regression of all lesions and a satisfactory cosmetic outcome.[36] Spontaneous regression is documented to occur in up to 20% of patients with KA. In a case series of 14 patients with spontaneously regressing KA (five on the hand) the mean time to complete regression was 27 weeks with none subsequently recurring. The author reported minimal scarring and no need for revision surgery.[37] If a confident diagnosis of KA is established select patients may elect close observation (e.g. extremity KA) although patients with enlarging facial lesions may choose treatment.

Lip SCC

Lip SCC (usually the sun-exposed lower lip) is a skin cancer in Australia and not a subsite of mucosal oral cancer. Similar to other early to moderate-sized SCC the outcome with surgery or radiotherapy is similar. The laxity of the lip means that wedge excision with primary closure is usually achieved. However, when >30 to 50% of the lip is involved surgery to achieve oncological margins is not possible without risking function (oral competency). Radiotherapy is therefore an excellent option. In a large series of Dutch patients with a T1 lip SCC (n = 89) and treated with definitive radiotherapy (51 Gy in 17 fractions or 48 Gy in 12 fractions) only one patient experienced local relapse.[38] The lower lip can be treated with orthovoltage photons following insertion of an intraoral lead shield to protect the mandible and teeth. Prescribed doses should be similar to any other equivalent-sized SCC in the vicinity of 50 to 55 Gy in 20–25 fractions.[28,32]

Metastatic nodal SCC

Metastatic SCC to regional lymph nodes of the HN (usually parotid +/− upper cervical nodes) necessitates referral to a multidisciplinary cancer service. An obvious index lesion is not identified in 20–30% of patients, but common sites include the anterior scalp, forehead/temple or ear. Operable patients should proceed to surgery. In most patients adjuvant radiotherapy (60 Gy in 30 fractions) is also recommended to improve loco-regional control, as the risk of nodal relapse remains high despite surgery.[39] Patients usually have multiple unfavourable features (multiple nodes, extranodal spread, close margins, perineural invasion), but with surgery and adjuvant radiotherapy can still expect a 5-year disease-free survival of 70–75%.[40] The role of concurrent adjuvant chemotherapy is unclear and currently being investigated in a Trans Tasman Radiation Oncology Group randomized trial.

Patients can also develop metastatic cutaneous SCC to non-HN nodal regions, such as the groin or axilla. These patients should similarly be recommended surgery (if operable) and adjuvant radiotherapy (50 Gy in 2-Gy fractions) with the aim to decrease the risk of regional recurrence.[41] Patients treated with radiotherapy alone to sites of nodal metastases are less likely to be cured, although most will experience nodal regression with good palliation. Definitive doses should be at least 60–66 Gy using a shrinking field technique and palliative doses approximately 40 Gy in 15 fractions (or similar) to achieve a worthwhile response.

Perineural invasion

Perineural invasion (PNI) occurs uncommonly in patients with cutaneous SCC and rarely in patients with aggressive (usually morpheaform) BCC and is usually an incidental (microscopic) finding.[42] The incidence of metastatic nodal spread is higher in patients with PNI. In a study of patients with PNI treated with radiotherapy +/− surgery, half of all relapses in patients with microscopic PNI were in regional nodes, prompting the authors to recommend elective nodal treatment.[43] PNI can lead to significant morbidity (neuropathic pain and cranial nerve palsies) and mortality from the involvement of cranial nerves (usually facial or trigeminal) leading to orbita/skull base/intracranial spread. The optimal treatment remains unclear although wide-field radiotherapy is an important treatment used in many patients. Patients with focal PNI, especially if located in the periorbital region, should be recommended appropriate treatment. This may involve wider re-excision or alternatively adjuvant radiotherapy.[44] The finding of PNI away from the actual tumour mass, and often extending to excision margins, indicates progressive PNI and a need for further treatment. Data from the University of Florida suggest that patients with asymptomatic microscopic (incidental) PNI have a better outcome compared with patients presenting with clinically or radiologically positive PNI (local control at 5 years 87 vs 55%).[45] Patients with advanced (symptomatic or image positive) PNI may still be curable with high-dose radiotherapy. Various techniques and fractionation schedules have been proposed, including using hyperfractionation[43] (74.4 Gy in 1.2-Gy twice-daily fractions), intensity-modulated radiation therapy[46] or an electron/photon beam arrangement.[47] All approaches aim to deliver high dose (>60 Gy) radiotherapy to areas of risk (including neural pathways) yet minimize late toxicity.

Merkel cell carcinoma

Merkel cell carcinoma (MCC) is a primary cutaneous neuroendocrine (small cell) carcinoma with a high propensity for loco-regional and distant relapse.[48] Radiotherapy has an essential role in decreasing the risk of loco-regional relapse and improving the survival of patients with MCC.[49,50] Although recommendations are for wide local excision with appropriate oncological margins (10–20 mm) there is evidence that extensive local surgery does not necessarily lead to a better outcome when adjuvant loco-regional radiotherapy is used.[51] However, adjuvant loco-regional radiotherapy should be recommended in most patients and be considered best practice. In the largest study of its type the addition of adjuvant radiotherapy significantly

improved overall median survival in patients with lesions >2 cm from 21 to 50 months ($P = 0.0003$).[52] Treatment should ideally include the excision site, in-transit tissue and regional lymph nodes. In select conditions, such as in distal limb lesions, regional nodes cannot always be treated in continuity with in-transit tissues.

The aim of adjuvant radiotherapy is to reduce the risk of loco-regional relapse that occurs in 40–50% of cases treated with surgery alone. A typical dose fractionation schedule is 50 Gy in 20–25 daily fractions using megavoltage photons or moderate energy (9–12 MeV) electrons plus bolus. The role of adjuvant chemotherapy is currently unresolved although the results of recent trials may ultimately lead to the incorporation of carboplatin/etoposide-based chemotherapy in this systemic disease.[53]

Cutaneous angiosarcoma

Despite a vascular (endothelial) origin cutaneous angiosarcomas often present as a skin lesion that is difficult to diagnose clinically. Most lesions arise on the face and scalp of older men and usually extend widely well beyond any clinical disease. Excision alone usually results in local recurrence because of the multicentric and insidious nature of this disease. Relapse often occurs quickly and usually outside treated areas, including regional and distant metastases. Angiosarcomas are radioresponsive and treatable with radiotherapy. In situations of scalp involvement, patients can be treated by a technique encompassing the entire scalp using a combination of matching photon and electron fields.[54] Alternatives to matching photon and electron fields include multiple static electron fields or electron arcs. Patients with limited and operable disease should undergo excision to achieve negative margins followed by wide-field adjuvant radiotherapy (55–60 Gy). Patients treated with definitive radiotherapy and having widespread loco-regional disease are unlikely to be cured. The outcome of patients diagnosed with cutaneous angiosarcomas is poor despite curative intent adjuvant radiotherapy although a minority may be cured if disease is truly localized (5-year survival 10–30%).[55]

Kaposi's sarcoma

Kaposi's sarcoma (KS) is a spindle cell malignancy arising from the vascular endothelium and occurring anywhere in the body, although KS often involves the skin and oral cavity. Lesions may be multiple and coalesce to form large plaques. Previously seen in elderly men of Mediterranean or Jewish origin (the so-called classic KS) it is now more common as a consequence of the AIDS epidemic. The role of radiotherapy in treating patients with AIDS-related KS has markedly diminished with the advent of highly active antiviral therapies. Despite this KS are radioresponsive and various dose fractionation schedules have been used to treat cutaneous lesions with good effect, ranging from a single 8 Gy to 30–40 Gy in 10–20 daily fractions.[56] A dose of 20 Gy in 10 daily fractions would be acceptable in most clinical scenarios.

Classic KS in immunocompetent patients usually has a long and indolent course. Death rarely occurs as a direct result of KS. Patients with localized resectable lesions may undergo excision. Radiotherapy is also effective in palliating areas of symptomatic disease that are often multifocal. Single, small doses of 8–12 Gy are reported to result in symptom relief and tumour reduction in most patients.[57] Higher total doses (more fractionated) may be delivered to sites of limited disease in select circumstances.

CUTANEOUS LYMPHOMAS

Cutaneous lymphomas are exquisitely radiosensitive and respond to relatively low doses of radiotherapy. With the exception of primary cutaneous B-cell lymphoma (CBCL) and selected patients with cutaneous T-cell lymphoma, of which Mycosis fungoides is the most common type, the role of radiotherapy in lymphomas is essentially palliative. Patients with sites of symptomatic local disease (lymph nodes/dermal lesions/ulcers) can be palliated with doses of 20–30 Gy often requiring orthovoltage or low-energy electrons. In CBCL, a form of indolent extranodal non-Hodgkin's lymphoma, local radiotherapy to doses of 36–40 Gy may be curative.[58] Select patients with Mycosis fungoides and Sezary syndrome may be treated with total skin electron beam therapy to a dose of 36 Gy over 9 weeks.[59] This treatment is complex and is usually delivered by centres of excellence that treat haematological malignancies.

Adnexal carcinomas

Adnexal (appendage) carcinomas, such as sebaceous carcinomas, eccrine/apocrine carcinomas and microcystic adnexal carcinomas, are rare and treatment should be individualized.[60] There are limited data to suggest these carcinomas are not as radiosensitive as NMSC. However, these are often aggressive in nature with a propensity to regional and distant metastases. Patients with operable lesions should have these excised with appropriate margins. Inoperable lesions may respond to radiotherapy and this should be considered an option. Adjuvant radiotherapy may also be recommended in cases of incomplete excision. Radiotherapy doses similar to NMSC should be prescribed.

MALIGNANT FIBROUS TUMOURS

Dermatofibrosarcoma protuberans (DFSP) is an uncommon cutaneous soft tissue sarcoma (STS) that may be locally aggressive and invade surrounding tissues and structures.[61] Most lesions are indolent in nature with 10% containing fibrosarcoma. Lesions arise often on the trunk and extremities in men more frequently than women. Treatment should be wide excision to obtain clear (2–3 mm) margins. Patients with

positive or close margins at a risk of local recurrence (20–30%) and may be recommended further treatment.[61] Adjuvant radiotherapy is reported to significantly reduce the risk of local recurrence and is therefore an option especially if re-excision is not feasible.[61,62] Doses of 55–70 Gy in 2–2.5 Gy fractions have been used and most lesions can be treated with low-energy photons.

Atypical fibroxanthoma (AFX) often arise in older men with actinically damaged skin, especially on the scalp, forehead or ear.[63] Although presenting as a fleshy nodule, it is usually a superficially invasive tumour that can be easily excised. Local recurrence with complete excision is low and the role of radiotherapy is unclear although patients with positive margins should be recommended further treatment. Dose fractionation schedules similar to DFSP should be considered. Rare cases of AFX metastasizing are reported.

Malignant fibrous histiocytoma (MFH) is a more aggressive STS that should be excised with wide oncological 3- to 5-cm margins. Often categorized as deep (muscle) in most cases, or superficial (subcutis, dermis) in the minority, lesions may arise as large (>5 cm) relatively superficial lesions. The pleomorphic subtype is the most often found variant (65% of cases). The role of radiotherapy is usually in the adjuvant setting and as MFH invades deeper prognosis worsens secondary to the development of distant metastases (usually lung).[64,65]

In situ *melanoma (LM)*

Lentigo maligna and LM melanoma (early invasive LM) often present as large superficial (1–2 mm thick) pigmented facial lesions in elderly patients. The size and location often precludes simple excision and radiotherapy remains a well-established option with excellent control rates (90–95%).[66,67] Reported radiotherapy doses range from 35–100 Gy in 5–10 fractions although dose fractionation schedules of 40–50 Gy in 10–20 fractions would also be considered effective with similar control rates and excellent cosmesis.[68,69] Treatment only requires a superficially penetrating beam with a field margin of 10–15 mm beyond any observed disease.

PALLIATION

Locally advanced lesions

Elderly or debilitated patients may present with advanced skin cancers, which, although not curable, can be palliated. Lesions are often painful, bleeding and infected, causing problems for both the patient and the carer. Single large fractions of 12–20 Gy can be given quickly using megavoltage photons, if warranted, with the addition of bolus. Uncooperative patients may require oral sedation before treatment. These large, single fractions are well tolerated with minimal toxicity. Alternative regimen include multiple medium-sized fractions given once or twice a week (eg 3×8 Gy). In elderly patients, who are otherwise well, higher total dose fractionation schedules, such as 35 Gy in 5–7 fractions, or 40 Gy in 10 fractions, may be more appropriate and can be considered more radical in intent and can be delivered as two or three fractions per week.

Metastatic lesions

Dermal-based metastases may arise in patients with lung and breast cancer and can present as rapidly enlarging subcutaneous masses with intact overlying skin. Fungation and bleeding may occur and palliative radiotherapy using orthovoltage photons or megavoltage photons with bolus using a single 8-Gy fraction or 20 Gy in five fractions are effective.

Cutaneous SCC, MCC and malignant melanoma can also manifest dermal-based (or in-transit) lesions in proximity to an excised primary. The face and scalp are sites where in-transit metastases arise, especially from SCC. Patients are potentially curable, although any treatment approach (including radiotherapy) should include generous field margins to encompass any subclinical dermal metastases.[70] Relapse often occurs just outside treated fields.

MISCELLANEOUS

Late reactions

The late (years) cosmetic effects (telangiectasia, epidermal atrophy, altered pigmentation) of radiotherapy may be suboptimal: with continued unprotected sun exposure, when prescribing a large dose per fraction (>3 to 4 Gy), if the total dose is >55 Gy, or following treatment to larger fields and/or deeply invasive lesions. Patients are strongly advised to use sun protection to decrease both, the incidence of further NMSC and maintain the best infield cosmetic result. A randomized French study (surgery vs radiotherapy) of patients with facial BCC suggested that at 4 years follow up the cosmetic outcome was rated significantly better by both the patient (good result; 87 vs 69%) and the clinician (good result; 79 vs 40%) in favour of surgery.[71] This further reinforces the need for ongoing sun protection in Australian patients if late cosmesis is important. Smaller treatment fields (2–3 cm) tolerate hypofractionation better than larger areas, but even so, if cosmesis is important larger fractions should still be avoided. Patients should also be warned of the small risk (<5%) of late soft tissue and cartilage necrosis, which is related to increasing tumour size and larger doses per fraction.

Younger patients

When irradiating younger patients, especially women, a better long-term cosmetic outcome is likely to be achieved by prescribing a low dose per fraction (2 Gy/fraction). A typical dose for a small BCC would be 50–60 Gy in 25–30 daily fractions.[72] However, even with this dose fractionation schedule patients can still expect some degree of infield hypopigmentation and telangiectasia. Other options, if possible, therefore should be considered before recommending radiotherapy to younger

patients. In addition, these patients are at risk of developing new NMSC close to, or within a radiotherapy field and this will preclude further radiotherapy as an option. Radiation induced malignancies following small field superficial radiotherapy for skin cancers are rare, but remains a consideration when discussing radiotherapy in younger patients.

Immunosuppression

Patients that are immunosuppressed (organ transplant recipients, non-Hodgkin's lymphoma, chronic lymphocytic leukaemia) and diagnosed with SCC, MCC or unfavourable BCC are at much greater risk of developing loco-regional recurrence and ultimately even death.[73] Treatment must be aimed at eradicating all disease, including potential sites of subclinical spread. In select cases, adjuvant radiotherapy is an especially important (potentially life saving) addition to other treatment (usually surgery).[74]

CONCLUSION

Radiation oncologists and clinicians that treat patients with cutaneous malignancies (including less often found entities) should have an understanding of the important role of radiotherapy in the various clinical settings that may present to them. Despite recent advances in treating patients by non-radiotherapy approaches (e.g. Mohs microsurgery, laser treatment, topical immune modifiers etc.) radiotherapy offers specific advantages unavailable to other methods.

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