Radiotherapy for the treatment of skin cancer

Epithelial skin cancers (basal-cell and squamous-cell cancers) are the most common cancers of the elderly population. These cancers are usually not life-threatening and can be cured easily if recognised early. The treatment options are diverse and should be tailored according to cancer type, site, and patient characteristics. **Dr Navita Somaiah** and **Dr John Paul Glees** review the role of radiotherapy in the management of skin cancer.

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Epithelial skin cancer is a common neoplasm. More than 200 new cases are treated at our hospital (The Royal Marsden, Surrey) each year. The majority of these are basal-cell carcinomas, followed by squamous-cell carcinomas. Both are the result of many years of exposure to ultraviolet light from the sun. With appropriate treatment, preferably at an early stage, excellent local control and cosmesis can be achieved. The treatment options are diverse, including surgical excision, Mohs microsurgery, electrocautery, topical 5-fluorouracil and imiquimod, photodynamic therapy, and superficial radiotherapy.[1,2] Advances in surgical techniques have led to changes in the population of patients treated with radiotherapy. Indeed, radiotherapy for basal-cell carcinoma is used as primary treatment in only 8% of patients in the UK. Radiotherapy, however, has many advantages, including the preservation of anatomy (figure 1) and avoidance of surgery, which is particularly useful in elderly patients who are unsuitable for general anaesthetic or those on anticoagulants.[3–5] Radiotherapy is also used postoperatively for incompletely excised lesions, perineural invasion, and to prevent recurrence. It also provides excellent palliation for painful or bleeding lesions (figure 2).

The spectrum of skin cancers treated by radiotherapy is wide and includes lentigo maligna, Kaposi's sarcoma, cutaneous T-cell and B-cell lymphomas, Merkel cell tumours, and sweat-gland tumours,[6] in addition to basal-cell and squamous-cell carcinomas. Most patients are never given the choice of radiotherapy; they are seen either by a dermatologist or by a surgeon, and treated accordingly. At our institution, there is a bi-monthly skin clinic, with plastic surgeons, dermatologists, and clinical oncologists (radiotherapists), at which all available options are discussed with patients.

Radiotherapy machines

Kilovoltage X-ray equipment producing low-energy photons has been used therapeutically for the treatment of skin cancers for more than 100 years. Superficial, or orthovoltage, radiotherapy using 50–250 kV X-rays is generally used for the treatment of skin tumours. More recently, in some centres, the use of kilovoltage machines has diminished as they have been replaced by megavoltage (the use of high-energy X-rays delivered by linear accelerators) and electron radiotherapy (often preferred because depth of penetration can be accurately prescribed according to energy used) for many clinical applications.

Planning technique

Confirmation of the diagnosis histologically or cytologically is usually recommended so that a rational treatment approach can be made, but

sometimes a clinical diagnosis alone is sufficient. An assessment of the depth of the tumour is then made—it can penetrate deeply at sites of embryonic fusion planes such as the inner canthus, nasolabial fold, ala nasi, tragus, and post-auricular area, and care should be taken to ensure that the radiation energy chosen covers the tumour extent at depth with adequate margins for subclinical excision (at leasat 5 mm).

The gross tumour volume, which is the visible extent of macroscopic disease is marked on the patient with a magnifying glass in a well illuminated room. A margin around the gross tumour volume is then drawn to encompass subclinical extension of disease, to account for any potential change in position of the patient during fractionated radiotherapy (daily divided dose), and also to ensure that the prescribed dose is delivered to the volume. This additional margin is known as the planning target volume. The size is dependent on the tumour size, histology, aggressiveness, and evidence of perineural invasion. Small lesions (less than 0·5 mm) with well defined edges require margins of between 5 and 8 mm, whereas larger lesions—particularly squamous cell carcinomas—require 1 cm margins. The appropriate beam energy can then be chosen for the depth of the lesion.

Most radiology departments have standard lead cut-outs for regular-shaped treatment volumes. Alternatively, in preparation for treatment, patients may attend the 'mould room' for a customised lead cut-out to be fashioned to fit the treatment volume of their tumour. The thickness of lead is dependent on the energy of the beam used. For 90–150 kV, 1·5 mm lead is sufficient. When treating tumours of the eyelid near the inner or outer canthus, an internal lead eye-shield is used to protect the conjunctiva, cornea, and lens. These are either shaped like contact lenses or are spade-shaped. The patient is positioned appropriately on the treatment couch, with the lead cut-out in place over the lesion. With the kilovoltage machine, patients can be treated sitting in a chair (with appropriate immobilisation), if unable to lie down. The machine applicator of suitable diameter is then gently positioned over the area to be treated (figure 3).

The daily dose and fractionation (the number of daily radiotherapy fractions prescribed) of radiotherapy is largely dependent on the site, size, and histology of the lesion, in addition to the age of the patient and their ability to attend for treatment. Many different regimens have been shown to be effective, and the one chosen should have optimum cure rate with least damage to normal tissue. Our institution normally uses 40·5 Gy in nine fractions once-daily for basal-cell carcinomas, and 45 Gy in ten fractions treating daily for squamous-cell carcinomas over 2 weeks. In lesions larger than 6–7 cm in diameter, it may be preferable to use a more fractionated regimen such as 55 Gy in 20 fractions over 4 weeks, in order to reduce the severity of late effects.

An alternative regimen for particularly frail and infirm patients with relatively small lesions involves only two visits, 5 weeks apart, giving 12 Gy at each visit. Other fractionation regimens used include 32·5 Gy in five daily fractions and occasionally single 18 Gy fractions for small basal-cell carcinomas for which cosmesis is relatively unimportant.

Radiotherapy reactions and late effects

During a course of radiotherapy, patients can expect to see erythema of the skin as part of an acute radiotherapy reaction characterised by desquamation, oozing, crusting of the lesion, and increased skin pigmentation. This reaction usually appears 2 weeks after radiotherapy commences and lasts for about 2–4 weeks. Patients should be informed and reassured that it is temporary and reversible. We have before and after treatment photographs available in our clinic to show patients what to expect. To the untrained eye, the acute skin reaction over the treatment site may look like an infection, but infection is very unusual. Within a few weeks, the appearance improves, leaving healed skin underneath. Commonly observed late adverse effects, seen over subsequent months or years, include skin hypo-pigmentation or hyper-pigmentation, skin atrophy, telangiectasia, and epilation. These effects are variable and acceptable to most patients if informed appropriately (figure 4).

Spectrum of treatable disease

The treatment of basal-cell carcinoma and squamous-cell carcinoma using radiotherapy is well documented and provides excellent local control and cure, equivalent to that of surgery.

Radiotherapy also plays an important role in the treatment of other less common skin tumours as described below.

Bowen's disease[7]
This condition is also known as squamous-cell carcinoma in situ and is generally treated by dermatologists. Cases may be referred for radiotherapy when non-responsive areas become troublesome to the patient or thicken, bleed, or are painful. Bowen's disease is treated as a squamous-cell carcinoma to a dose of 45 Gy in 10 fractions over 2 weeks. Guidelines from the British Dermatology Association suggest that Bowen's disease of the lower limb in elderly people does not necessarily need treatment and can be monitored.

Lentigo maligna[8]
This neoplasm is the in-situ phase of lentigo maligna melanoma. Typically located on the face in older Caucasian women, these tumours are often present for 5–15 years. They are generally large, flat lesions that may be tan or brown coloured. Lentigo maligna has low metastatic potential; however, if left untreated, less than 5% of cases progress to lentigo maligna melanoma, which is thought to be as aggressive as any other melanoma. Conventional surgery, cryosurgery, and radiotherapy all have recurrence rates of 5–10% and can be offered to patients. Radiotherapy has the advantage of preserving normal anatomy and function, and provides good cosmesis for facial lesions. The dose used is 45 Gy in 10 fractions over 2 weeks (figure 5).

Merkel cell tumours[9,10]
These rare neuroendocrine tumours arise from the mechanoreceptors of the basal epidermis. They are particularly aggressive and have a propensity for head and neck and extremity sites. The tumour has many similarities to small-cell carcinoma of the lung, both histologically, with its intrinsic sensitivity to chemo-radiation, and in metastatic potential. Surgery is the treatment of choice. Post-operative radiotherapy to doses of 45–60 Gy is advocated to reduce local recurrence rates. Generous planning margins of 3–5 cm around the scar are included.

Cutaneous T-cell lymphoma[11, 12]
Also known as mycosis fungoides, this rare condition is a malignancy of T-helper cells. These skin lesions are very radiosensitive, and superficial radiotherapy can be used for the localised plaque stage or small tumour stage, with complete response rates cited as 60–90%.[11,12] More diffuse plaque disease is an indication for total skin electron beam therapy. Margins of 0·5–1 cm are used and lesions treated to a dose of 8 Gy in two fractions or 12 Gy in three fractions daily.

Primary cutaneous B-cell lymphoma[13]
This indolent form of lymphoma has a good prognosis. Although local cutaneous recurrences are observed in 25–68% of patients, dissemination to internal organs is rare. 5-year survival rates typically range from 89% to 96%. Overly aggressive treatment of this lymphoma

has not been shown to improve survival or prevent relapse.[13] Polychemotherapy should be reserved for involvement of non-contiguous anatomic sites or those with extracutaneous spread. Once the diagnosis of primary cutaneous B-cell lymphoma is established, history, physical examination, and staging investigations should be performed to rule out systemic involvement. Radiotherapy is the treatment of choice for localised disease at presentation or for relapse. Photons or electrons are used as appropriate with a 2–3 cm margin to a dose of 15 Gy in five fractions over 1 week or 20 Gy in five fractions over a week.

Cutaneous angiosarcoma[14]

Cutaneous angiosarcoma is a rare and aggressive endothelial-derived sarcoma that usually affects elderly people. A combined modality approach is often required including surgery, radiotherapy, and chemotherapy. Photons or electrons are used as appropriate. A margin of at least 1 cm is required as sub-microscopic disease can extend beyond the clinical tumour margin. The common dosage schedule is 55 Gy in 20 fractions over 4 weeks or 60 Gy in 30 fractions over 6 weeks.

Kaposi's Sarcoma[1]

Classical Kaposi's sarcoma is an unusual vascular sarcoma occurring in the skin of the lower extremities of elderly patients of Jewish or Mediterranean descent. It usually follows an indolent course, but can metastasise to the lungs or gastrointestinal tract. Other types of Kaposi's sarcoma include endemic (seen in Africa), epidemic (AIDS-related), and in association with immunosuppressant therapy (iatrogenic). Highly-active antiretroviral therapy[15] is the treatment of choice for epidemic Kaposi's sarcoma, and can be given alone or in combination with systemic or local therapy. For localised lesions, superficial radiotherapy is usually the preferred treatment option as an 8 Gy single fraction or 12 Gy in three fractions.[16] Excision, cryotherapy, and intralesional chemotherapy have also been described.

Conclusion

Radiotherapy has a very important role in the treatment of skin cancers with cure rates equivalent to surgery. It should be offered to patients as an alternative to surgery especially in elderly patients and in areas of the body—ears, near the eyes, nose, lips—where preservation of anatomy and cosmesis is important. Radiotherapy also offers good palliation for locally advanced and symptomatic lesions.

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