

# Non-melanoma skin cancer in general practice

## *Radiotherapy is an effective treatment option*

**Jeremy Khong**, Peter Gorayski,  
Daniel Roos

### Background

Skin cancer is the most common malignancy that is managed in general practice, and non-melanoma skin cancer (NMSC) comprises the vast majority of presentations. Radiation therapy (RT) plays an important part in the management of NMSC and may be used as definitive treatment for low-risk cancers, as an adjuvant treatment for high-risk disease or alone for inoperable cases.

### Objective

The aims of this article are to discuss: 1) types of RT; 2) role of RT, including its advantages and disadvantages; 3) side effects (toxicity) of RT; 4) outcomes from RT; 5) low- versus high-risk NMSCs and 6) some guidelines for general practitioners on when to refer patients for consideration of RT.

### Discussion

The primary goal of treatment for NMSC is to cure the patient, and a secondary goal is to provide the best cosmetic and functional result with the minimum impact on quality of life. In deciding what modality of treatment to use, clinicians will need to take into account the site of the tumour, clinical stage, histological subtype and any high-risk features, patient comorbidities as well as patient preferences. RT provides a safe and effective alternative to surgery in select cases and is particularly useful for the elderly or where surgery might have a negative impact on function or cosmesis.

**SKIN CANCER** is the most common malignancy in Australia and makes up approximately one-third of diagnosed cancers, resulting in more than 130,000 new cases each year.<sup>1</sup> Non-melanoma skin cancer (NMSC) predominately comprises basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), which account for approximately two-thirds and one-third of NMSCs, respectively.<sup>2</sup> NMSC typically occurs in sun-exposed areas, such as the face, ears, neck, scalp, back and hands. Other cutaneous malignancies are rare, and are discussed later in this article.

Many NMSCs are managed in general practice, where cryotherapy, diathermy, topical treatments and surgery are commonly employed. BCCs and SCCs are not notifiable to cancer registries, while other NMSCs are. The incidence and economic impact of NMSC is profound; it is responsible for the highest expenditure rate of any cancer in Australia. In 2014, 959,243 Medicare Benefits Schedule claims (\$127.6 million) were paid for NMSCs.<sup>2</sup>

Cure rates for NMSC are high, with an estimated 560 deaths from NMSCs in 2016, and a mortality rate of 1.9 deaths per 100,000 people.<sup>2</sup> With such a low death rate, there is a risk that complacency can occur not only from the patient's perspective but also from the treating clinician. Consequently, it is important for the general practitioner (GP) to identify those patients who are at high

risk of relapse and refer them for the appropriate management, which may include radiation therapy (RT), both in the definitive setting and as adjuvant therapy.

NMSC can be classified into low- and high-risk disease on the basis of a number of tumour-, patient- and treatment-related factors. It should be emphasised that risk of locoregional relapse is a continuous rather than categorical variable; nevertheless, this classification is useful for flagging patients who may require referral. The risk classification is summarised in Table 1.

The aims of this article are to discuss:

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- the role of RT, including its advantages and disadvantages
- side effects (toxicity) of RT
- outcomes from RT
- low- versus high-risk NMSCs
- some guidelines for GPs on when to refer patients for consideration of RT.

### Discussion

The primary goal of treatment for NMSC is to cure the patient, and a secondary goal is to provide the best cosmetic and functional result with the minimum impact on quality of life. In deciding what treatment modality to use, clinicians will need to consider the site of the tumour, clinical stage, histological subtype and any high-risk features, patient comorbidities as well as patient preferences.

### Types of radiation treatment

In the modern era, the most common types of RT used to treat skin cancers are superficial radiation treatment (SRT), electrons and megavoltage photons. Brachytherapy surface moulds are rarely used.

SRT uses low-energy X-rays to treat superficial skin cancers up to 8 mm in depth. It is highly effective, with five-year recurrence rates of 4.2% for BCC and 5.8% for SCC, which is comparable to many surgical series.<sup>3</sup>

Electron therapy delivered using a linear accelerator is used to treat larger and more infiltrating skin tumours. Dose levels can also be mapped in three dimensions. Field margins around the tumour are greater than for SRT, and this may create challenges around structures such as the eye.

Megavoltage photons are the preferred treatment for locally advanced skin cancers where large volumes and regional nodes may need to be treated. This is common in the head and neck region.

Treatment doses are delivered typically over a 6–7-week period, although under some circumstances, shorter courses may be appropriate.

Brachytherapy involves the delivery of radiation from a radioactive source. An individualised surface mould that is highly conformal to the patient contour and tumour is especially useful in situations where the tumour is located on anatomical curves or near critical organs. Iridium-192 is typically used in the treatment of NMSC. This allows delivery of a high dose of radiation to the tumour, with rapid dose fall-off and subsequent sparing of nearby healthy tissues, resulting in excellent cosmesis with high tumour control. Treatment is more convenient for the patient because it is usually delivered two or three times per week, rather than daily, which is especially useful for elderly or frail patients.<sup>4</sup> Several studies report five-year local control rates of >95%.<sup>5</sup>

**Table 1. Risk profile for non-melanoma skin cancer (adapted from National Comprehensive Cancer Network Guidelines<sup>12,13</sup> and American Joint Committee on Cancer Guidelines<sup>14</sup>)**

| Risk factor                   | Low risk  | High risk   |
|-------------------------------|---|---|
| <b>Tumour factors</b>         |   |   |
| Tumour size                   | ≤2 cm   | >2 cm   |
| T stage                       | T1–2  | T3–4  |
| Thickness                     | ≤6 mm   | >6 mm   |
| Depth of invasion             | No invasion beyond papillary dermis                                 | Invasion of deep reticular dermis or subcutaneous fat   |
| Site                          | Not involving lip or mask area of face                              | Lip or mask area of face  |
| Differentiation               | Well or moderate  | Poor or undifferentiated  |
| Subtype                       | SCC: verrucous and keratoacanthomatous<br>BCC: nodular, superficial | SCC: acantholytic, adenosquamous, desmoplastic, carcinosarcomatous<br>BCC: micronodular, infiltrative, sclerosing, desmoplastic |
| Perineural invasion           | Absent or single small nerves                                       | Multifocal small nerve or named nerves >0.1 mm diameter   |
| Rapid growth                  | Absent  | Present   |
| Borders                       | Well defined  | Poorly defined or in transit metastases   |
| Lymphovascular invasion       | Absent  | Present   |
| Margin status                 | Negative  | Positive or close (<2 mm)   |
| <b>Patient factors</b>        |   |   |
| Immune status                 | Immunocompetent   | Immunosuppressed  |
| Chronic inflammation or scars | Absent  | Present   |
| Previous radiation therapy    | No  | Yes   |

BCC, basal cell carcinoma; SCC, squamous cell carcinoma

### Surgery versus radiation treatment

Surgery is often employed as the primary treatment modality because it offers an effective and efficient method for accomplishing cure. However, because of patient and/or tumour factors, RT may achieve superior functional and cosmetic outcomes. Although there is a paucity of randomised data comparing surgery to RT, local control rates (90–95%) and cosmesis (>90% excellent or good) following RT are typically reported.<sup>6</sup> Most retrospective studies suggest that both surgery and RT can achieve five-year local control rates of 85–95%.

Surgery has the advantage of being a single-day procedure that provides histology on the resection specimen so that margins can be assessed and high-risk features identified. The disadvantages of surgery are that it is invasive, may require the patient to suspend anticoagulation and may negatively affect cosmesis or function.

The advantages of RT are that it is non-invasive and may be better able to preserve cosmesis and function. This is particularly useful around the nose, ear and lips. The disadvantages of RT are that treatments are typically given daily for 1–7 weeks, and confirmation of margin

coverage is not available. Associated radiation dermatitis may take 3–4 weeks to settle post-treatment. Tumours, especially BCCs, may take weeks to months to resolve. While cosmesis with RT may be excellent at six months, this tends to worsen with time, whereas surgical results continue to improve.<sup>7</sup> For this reason, RT is often better suited to the older patient.

The acute and late effects of RT are confined to the treatment area. Skin erythema and desquamation are commonplace. Late effects of treatment include atrophy, hypopigmentation, alopecia and telangiectasia. Cartilage, soft tissue or bone necrosis are rare complications. There is a very small risk of radiation-induced secondary cancers, but the latent period is approximately 10 years. Dose to sensitive organs such as the thyroid and eye can be reduced by shielding the organ during treatment.

### Low-risk BCC and SCC

Low-risk tumours are usually early-stage tumours (T1–2N0M0) with no adverse prognostic features. These make up more than 90% of NMSCs, and the vast majority will be managed by surgical excision with excellent cure rates. For lesions in difficult sites such as the nose, lower eyelid or pinna, RT may provide a viable alternative. Areas that are not suitable for RT are poorly vascularised areas such as the lower leg, the upper eyelid or areas that are prone to physical trauma over bony prominences. For cosmetic reasons, surgery may be preferable in hair-bearing regions such as the upper lip in males, as RT will produce permanent alopecia.

Most low-risk NMSCs may be treated with SRT or electrons, the choice depending on tumour size and depth of infiltration. Treatments are usually given in 5–15 fractions with daily treatments given Monday to Friday. Fractionated treatment allows a better therapeutic ratio between tumour kill and normal tissue damage. Shorter schedules of 3–4 fractions 1–2 weeks apart may be given for elderly, frail patients for whom any increased risk of late RT effects is less of a concern. Margins around the gross disease are usually 5–20 mm depending on the size of

the lesion and its perceived invasiveness peripherally. Sensitive normal structures such as the conjunctiva can be shielded.

### High-risk BCC and SCC

High-risk tumours are those with advanced T stage (T3–4) and/or associated adverse features such as perineural or lymph node involvement and/or in a setting of immunosuppression. The best results are usually achieved with combined modality treatment using surgery and adjuvant RT. However, RT may be used alone for inoperable cases, where surgery would have an adverse impact on cosmesis or function, or when patients refuse operation. These patients and those with advanced complex skin cancers should be discussed in multidisciplinary team meetings (MDTMs) where surgeons, radiation oncologists, medical oncologists, radiologists, pathologists and allied health teams can formulate a coordinated treatment plan.

RT is usually given 4–6 weeks post-surgery when healing is well established. Excessive delays in commencing RT may adversely affect tumour control, especially for SCCs, which proliferate more rapidly than BCCs. For inoperable cases, RT may be used alone; this will achieve long-term control in approximately 70% of cases. Control is poorer for recurrent tumours, SCC, bone erosion and nodal disease.<sup>8–11</sup>

For high-risk lesions, treatment volumes are often complex and may require the primary site and regional nodes to be treated in continuity. For lesions with extensive perineural spread, the treatment may need to include the course of affected cranial nerves (usually branches of the trigeminal or facial nerves). Newer techniques such as intensity-modulated radiation therapy (IMRT) or volumetric modulated arc therapy (VMAT) allow complex dose distributions to be given to the tumour with greater sparing of normal tissues. Doses are delivered over a 6–7-week period.

Megavoltage photons are the preferred modality of treatment for high-risk NMSCs in the vast majority of cases. The primary site and nodes are usually

included for SCC; however, for BCCs, the primary site alone is treated, as lymph node involvement is rare.

### Rare histologies

Rare histologies (eg Merkel cell carcinoma, lymphomas, microcystic adnexal carcinoma, sebaceous carcinoma) will be an infrequent occurrence in general practice. All of these cases should be referred for assessment at an MDTM.

### Referral guidelines

The GP will be able to manage the vast majority of NMSCs and achieve excellent control rates.

Referral to a radiation oncologist should be considered in the following circumstances:

- low-risk NMSCs where a non-surgical approach is favoured; this may relate to patient preference or it may be a clinical decision based on the impact of surgery on cosmesis or function
- high-risk NMSCs where there are two or more high-risk features
- rare malignancies (as described previously).

### Authors

Jeremy Khong MBBS, Radiation Oncology Registrar, Department of Radiation Oncology, Royal Adelaide Hospital, SA. jeremy.khong@sa.gov.au

Peter Gorayski BSc (Hons), BMBS, FRACGP, FRANZCR, Radiation Oncologist, Department of Radiation Oncology, Royal Adelaide Hospital, SA; Associate Professor, University of South Australia, SA  
Daniel Roos BSc (Hons), Dip Ed, MBBS, MD, FRANZCR Senior Radiation Oncologist, Department of Radiation Oncology, Royal Adelaide Hospital, SA; Professor, School of Medicine, University of Adelaide, SA

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correspondence [ajgp@racgp.org.au](mailto:ajgp@racgp.org.au)