London Cancer
Guidelines for the Treatment and Referral of Squamous Cell Carcinoma (SCC) of the Skin

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1. Definition of SCC

Primary Cutaneous SCC is a malignant tumour that arises from the keratinising cells of the epidermis and its appendages. It is locally invasive but can metastasize to regional lymph node and to other organs of the body.

These guidelines are intended for the treatment of tumours of the skin and the vermillion border and exclude Bowen’s Disease (SCC in situ or intraepidermal SCC), SCCs arising on the penis, vulva, anus, and mucous membranes. For the purposes of these guidelines, keratoacanthomas are regarded as invasive SCC (keratoacanthomatous type), adopting W.H.O terminology (as recommended by the 2012 Royal College of Pathologists dataset for reporting of primary cutaneous SCC).

2. Incidence

SCC is the second most common skin cancer after BCC. Its incidence is rising mainly through chronic exposure to natural or artificial ultraviolet radiation. It is particularly common in those with Fitzpatrick skin type I/II. Other predisposing factors include Bowen’s disease, previous exposure to ionising radiation or arsenic and pre-existing conditions such as chronic wounds, leg ulcers, scars and burns. It is more common in those receiving immunosuppressive drugs such as solid organ transplant recipients (who have up to 150-fold excess risk) and in autoimmune and inflammatory conditions such as rheumatoid arthritis and inflammatory bowel disease. Incidence is also increased in people immunocompromised by conditions such as chronic lymphocytic leukaemia and HIV infection and in certain rare genodermatoses including xeroderma pigmentosum, albinism, Muir-Torre syndrome and Ferguson-Smith syndrome.

3. Clinical Presentation

SCC presents with an indurated, nodular, crusted or keratinising nodule or tumour. It may ulcerate. Occasionally, it presents as a non-keratinising ulcer. It is usually located on chronically sun-exposed anatomic sites, particularly the head and neck, hands and lower legs. It may be both spontaneously painful and/or tender.

4. Referral of suspected SCC

An SCC is clinically suspected when it present with typical features of an indurated nodule or ulcer showing some degree of keratinization. However, a confident diagnosis can only be established histologically. SCCs should not be excised or biopsied in primary care. All patients in whom there is a possibility of a cutaneous SCC should be referred as an urgent
suspected cancer referral through the London Cancer two-week wait referral pathway to an appropriately trained specialist, usually in the local dermatology department.

5. Histological diagnosis

5.1 Primary tumour

The histology report should conform to the minimal data set recommended by the Royal College of Pathologists (RCPPath) in October 2012 and amended in December 2012 (www.rcp.org.uk). In brief, this description should include:

- Macroscopic details: specimen and lesion size
- Microscopic details:
  - Histopathological subtype
  - Grade (well, moderately and poorly)
  - Thickness (≤ 2mm, >2-4mm, >4mm)
  - Level of invasion (Clark level as for melanoma)
  - Lymphovascular invasion
  - Perineural invasion
  - Margins (<1mm, 1-5mm, >5mm)
  - Maximum diameter (≤20mm; >20mm)
  - Pathological risk status (low risk versus high risk)

High-risk pathological and clinical features upstage a lesion from pT1 to pT2. In AJCC7, pT2 is defined as either maximum diameter >20 mm, or pT1 (i.e. ≤20 mm) upstaged two high-risk features:

- grade: poorly differentiated or undifferentiated
- perineural invasion
- thickness > 2 mm
- Clark level ≥ 4
- clinical: ear and hair-bearing (non-glabrous) lip.

Note: There is variation between AJCC7 and the BAD / NICE Skin Cancer MDT Management guidelines with respect to the definition of high-risk SCC (see appendix 1). For the purposes of the London Cancer guidelines, we will the RCPPath recommendation to use BAD / NICE MDT Skin Cancer MDT Management definitions of high risk.

5.2 Locoregional disease

5.2.1 Lymph nodes – number of nodes involved and maximum size of metastatic deposit

The number of involved nodes and the size of largest metastatic deposit are primary pN staging determinants. There are staging breakpoints at 30 and 60 mm. The anatomical site and laterality of the lymph nodes must be recorded.

5.2.2 Lymph nodes – extracapsular invasion (spread/extension)

This is widely regarded as a manifestation of potential biological aggression and
is considered to be associated with a worse prognosis. This finding prompts consideration of the use of adjuvant radiotherapy.

6. Treatment of primary cutaneous SCC

6.1 Background

In planning the treatment of a primary SCC several factors should be considered:
1. Most SCCs are low risk and may be managed through the LSMDT. However, it is essential to identify high-risk lesions (see above) and manage in an SSMDT.
2. There is a lack of randomised controlled trials for the treatment of primary cutaneous SCCs.
3. Tumours have a widely varying behaviour within the histological category of SCC.
4. Varied experiences between and within the specialties of dermatology and plastic and reconstructive surgery.
5. The primary aim of treatment is the complete removal of the tumour.
6. The possible presence of ‘in-transit metastases’ that have not as yet involved lymph node or blood vessels should be considered and dealt with through wide excision and/or wide field post-excision radiotherapy.
7. Regional draining lymph nodes if enlarged or palpable should be examined histologically and, if tumour positive, should be managed by regional dissection and clearance. The role of sentinel lymph node biopsy has not yet been established in the management of SCCs.

6.2 Surgical Excision

Surgical excision is the treatment of choice for most SCCs. It allows for histological examination of the tumour and the assessment of clearance margins, both lateral and deep. The following recommendations for adequate excision are based on BAD guidelines. For clinically well-defined, low risk, pT1 tumours, a minimum 4 mm margin around the tumour provides 95% completeness of excision. In order to maintain the same degree of confidence for high-risk tumours, a minimum 6 mm margin is recommended where possible.

6.3 Mohs’ Micrographic Surgery

There are no prospective randomized trials comparing conventional wide margin surgical excision with Mohs’ micrographic surgery for primary cutaneous SCC. However, there is some evidence that the incidence of local recurrent and metastatic disease are low after Mohs’ micrographic surgery and it should therefore be considered in the surgical treatment of high-risk SCC, particularly at difficult sites where wide surgical margins may be technically difficult to achieve without functional compromise.

6.4 Histological Assessment of Surgical Margins

Histological examination of multiples levels of the excised tissue displays a cross section of the tumour and the excised margins. This allows histological characterisation of the tumour and to record the margin of uninvolved skin around the tumour. Orientation markers or
skin sutures allow the pathologist to report accurately on the location of any residual tumour if present. Whilst Mohs’ micrographic surgery allows for a more accurate assessment of tumour clearance, technical factors with frozen sections occasionally hamper the identification of SCC tissue. Formalin fixed specimens should then be used for the final histological examination.

6.5 Curettage and Cautery

Excellent cure rates have been reported in several studies suggesting that small tumours less than 1 cm that are well differentiated, primary, slow growing and on sun exposed sites can be adequately removed by experienced physicians. This result may simply be a reflection of case selection by highly experienced operators. By convention, one or two curettage/cautery cycles are carried in order to achieve an adequate clearance. It provides poorly orientated material for histological examination and therefore assessment of the adequacy of excision is not possible.

Curettage and cautery should only be undertaken when surgical excision is deemed inappropriate. It may be used to debulk the tumour prior to using other treatment modalities like radiotherapy, cryotherapy, excision or Mohs’ surgery. It is not appropriate for recurrent tumour.

6.6 Cryosurgery

Cryosurgery should be used with caution in the treatment of SCC. Prior histological confirmation is required. It should only be used to treat small SCCs or to effect short-term cure in those where other methods of treatment are contra-indicated, e.g. in patients with poor general health or in those with shortened life expectancy. It is not appropriate in recurrent disease.

6.7 Radiotherapy

Radiation therapy for SCCs offers reported long and short-term cure rates comparable to other treatments especially in elderly or those with multiple co-morbidities, although there are no well-designed RCTs directly comparing surgery and radiotherapy. Radiotherapy should be used for non-resectable SCCs or in large tumours where margins are poorly defined. In other circumstances, radiotherapy will offer the best cosmetic and/or functional result. This will often be the case for lesions of the lips, nose and ears amongst many others particularly tumours occurring in special sites. Certain very advanced tumours, where surgical morbidity would be unacceptably high may also be best treated by radiotherapy.

7. Treatment of locoregional disease

1. The role of sentinel lymph node biopsy has not yet been established in the management of SCCs but may be considered on case-by-case basis in high-risk individuals.
2. Regional draining lymph nodes if enlarged or palpable should be examined histologically. If tumour positive, they should be managed by regional dissection and clearance. Post-operative radiotherapy may be considered for cases of incomplete lymph node dissection or extracapsular spread. Primary radiotherapy may be considered where surgery is deemed inappropriate.
8. Imaging

<table>
<thead>
<tr>
<th>Imaging modality</th>
<th>Indications and notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td>None</td>
</tr>
<tr>
<td>Staging</td>
<td>CT, MRI</td>
</tr>
<tr>
<td></td>
<td>Ultrasonography +/-FNA</td>
</tr>
<tr>
<td></td>
<td>Bone scans</td>
</tr>
<tr>
<td>Surveillance</td>
<td>None routine.</td>
</tr>
</tbody>
</table>

9. Involvement of the Multidisciplinary team

All SCCs should be reviewed at the MDM (low risk SCC at the LSMDT and high risk SCC at the SSMDT). All management decisions should be discussed with the patient and/or their relatives. Information leaflet where available should be given to the patient with ample opportunity to discuss their treatment and their concerns with the clinical nurse specialist and their respective medical/surgical member of the team.

10. Follow-up of patients with primary SCC

Early detection and treatment of recurrences improves survival. Ninety-five percent of recurrences and metastases are detected within the first 5 years. It is therefore reasonable to follow up all patients with high risk SCCs for that period. For low risk SCC, the decision as to who follows the patient will depend upon the disease risk, local facilities and interests. If followed in primary care, the patient should be instructed on how to carry out self examination and report any possible recurrence to the primary care physician who can in turn decide on whether referral back to the specialist is necessary.

11. Referral Guidelines For SCC

11.1 Primary care referral guidelines
GP referral pathway is described on the London Cancer suspected cancer 2-week wait referral proforma. It provides guidance on the type of skin cancer and where they can be referred.

11.2 Referral guidelines between skin teams

1. LSMDT may diagnose and treat all low risk primary SCC. All SCC should be discussed in the MDM.
2. All complex / high risk SCC should be referred on to the SSMDT for discussion and further management.
3. Once definitive treatment has been completed patients should be referred back to the local unit for follow up.
4. The exceptions to this practice are if the patient has been entered into a clinical trial or if the patient has expressed a wish to have part or all of their follow up through the SSMDT.
5. SCCs in specific anatomical sites may be managed by more than one specialist MDT. This is detailed in the site-specific skin cancer document.
### Appendix E  Comparison table for high-risk factors for NICE MDT management and AJCC7 TNM pT1 upstaging

<table>
<thead>
<tr>
<th></th>
<th>MDT</th>
<th>AJCC/TNM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pathology</strong></td>
<td>Pathology high risk</td>
<td>≤ 20mm max diameter</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Upstage pT1 to pT2</td>
</tr>
<tr>
<td><strong>Minimum number</strong></td>
<td>One required</td>
<td>Two required</td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
<td>Not included in pathology risk assessment</td>
<td>Ear or hair-bearing lip</td>
</tr>
<tr>
<td></td>
<td>There are complementary clinical criteria to be used by the clinician or MDT</td>
<td></td>
</tr>
<tr>
<td></td>
<td>A low pathology risk may, however, still be associated with a high clinical MDT risk</td>
<td></td>
</tr>
<tr>
<td><strong>Pathology</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Grade</strong></td>
<td>Poorly differentiated</td>
<td>Poorly differentiated</td>
</tr>
<tr>
<td><strong>Thickness (Breslow)</strong></td>
<td>&gt; 4 mm</td>
<td>&gt; 2 mm</td>
</tr>
<tr>
<td><strong>Clark level</strong></td>
<td>≥ 5 (subcutaneous fat)</td>
<td>≥ 4 (reticular dermis)</td>
</tr>
<tr>
<td><strong>Perineural invasion</strong></td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td><strong>Lymphovascular invasion</strong></td>
<td>Present</td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>TNM</strong></td>
<td>pT 2, 3, 4</td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>High-grade histological subtype</strong></td>
<td>Present</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

* Acantholytic, desmoplastic, spindle/metaplastic/sarcomatoid/adenosquamous, squamous cell carcinoma with Bowens