Pan Birmingham NHS
Cancer Network

Guideline for the Management of Patients with Squamous Cell Carcinoma of the Skin

Version History

Version	Date	Summary of Change/Process
0.1	13.09.07	National guideline adopted by Skin Network Site Specific Group
1.0	04.09.08	Endorsed by Network Governance Committee following confirmation with Skin Network Site Specific Group Chair that this is the current version from the Association
1.1	30.06.11	Skin Network Site Specific Group agreed to continue adoption of National guidance
2.0	11.07.11	Reviewed and endorsed by Guidelines Sub Group

Date Approved by Network Governance	**July 2011**

Date for Review	**July 2014**

1. Guideline Background

Burton Hospitals NHS Trust, Sandwell and West Birmingham Hospitals NHS Trust, Walsall Healthcare NHS Trust and Worcestershire Acute Hospitals NHS Trust have a local specialist multi disciplinary Team for skin cancer. The specialist multi disciplinary teams are located at Heart of England NHS Foundation Trust and University Hospitals Birmingham NHS Foundation Trust.

2. Guideline Statement

The British Association of Dermatology Multi Professional Guidelines for the Management of the Patient with Primary Cutaneous Squamous Cell Carcinoma have been adopted by the Pan Birmingham Cancer Network to guide the treatment for patients with squamous cell carcinomas (see appendix 1).

Pan Birmingham Cancer Network Governance Committee Chair

Name: Doug Wulff

Signature: Date: July 2011

Pan Birmingham Cancer Network Manager

Name: Karen Metcalf

Signature: Date: July 2011

Network Site Specific Group Clinical Chair

Name: Shireen Velangi

Signature: Date: July 2011

ENDORSED BY GOVERNANCE COMMITTEE

Multi-professional Guidelines

for the Management of the Patient

with Primary Cutaneous Squamous Cell Carcinoma

R J Motley, P W Preston, C M Lawrence

Summary: These guidelines for management of primary cutaneous squamous cell carcinoma present evidence-based guidance for treatment, with identification of the strength of evidence available at the time of preparation of the guidelines, and a brief overview of epidemiological aspects, diagnosis and investigation. These guidelines aim to ensure people with cutaneous squamous cell carcinoma receive the best possible treatment and care.

Disclaimer: These guidelines reflect the best published data available at the time the report was prepared. Caution should be exercised in interpreting the data; the results of future studies may require alteration of the conclusions or recommendations in this report. It may be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. Just as adherence to the guidelines may not constitute defence against a claim of negligence, so deviation from them should not be necessarily deemed negligent.

Footnote: The authors are grateful to Professor PJ Barrett-Lee (Radiotherapy), Dr DAL Morgan (Oncology) Dr DN Slater (Pathology), Mr M Schenker (Plastic Surgery) and Mr A Langford (Skin Care Campaign) for their expert advice and comments on the manuscript.

DEFINITION

Primary cutaneous squamous cell carcinoma (SCC) is a malignant tumour which may arise from the keratinising cells of the epidermis or its appendages. It is locally invasive and has the potential to metastasize to other organs of the body. These guidelines are confined to the treatment of SCC of the skin and the vermilion border of the lip, and exclude SCC of the penis, vulva and anus, SCC in-situ (Bowenôs disease), SCC arising from mucous membranes and keratoacanthoma.

INCIDENCE, AETIOLOGY AND PREVENTION

SCC is the second most common skin cancer and, in many countries, its incidence is rising.[1-7] Its occurrence is usually related to chronic ultra violet light exposure and is therefore especially common in people with sun-damaged skin, fair skin, albinism and xeroderma pigmentosum. It may develop *de-novo*, as a result of previous exposure to ultraviolet or ionising radiation, or arsenic, within chronic wounds, scars, burns, ulcers or sinus tracts and from pre-existing lesions such as Bowenôs disease (intraepidermal SCC).[8-17] Individuals with impaired immune function, for example those receiving immunosuppressive drugs following allogeneic organ transplantation or for inflammatory disease, and those with lymphoma or leukaemia, are at increased risk of this tumour. The risk of SCC with the new wave of ôbiologicô therapies (for inflammatory and haematological disease) has yet to be quantified, although reports identify cases of rapid-onset or reactivation of SCC in patients with risk factors or a past history of the disease.[18-27] Some SCCs are associated with human papilloma virus infection.[28-36] There is good evidence linking SCCs with chronic actinic damage, (including that from the use of tanning devices)[8] and to support sun avoidance, use of protective clothing and effective sunblocks[37] in the prevention of actinic keratoses and SCCs. These measures are particularly important for people receiving long term immunosuppressive medication.[38-41]

People with organ transplants are at high risk of developing cutaneous SCC. Skin surveillance to allow early detection and treatment, and measures to prevent SCC should be part of their routine care. In patients with multiple, frequent or high-risk SCCs consideration should be given to modifying immunosuppressive regimens[42;43] and the prophylactic use of systemic retinoids[44;45] which may also be valuable in other high risk groups.[46] Topical agents, such as imiquimod may have a useful role in preventing the development of skin dysplasia in high-risk renal transplant recipients but substantive evidence is awaited.[47]

CLINICAL PRESENTATION

SCC usually presents as an indurated nodular keratinising or crusted tumour that may ulcerate, or it may present as an ulcer without evidence of keratinisation. All patients where there is a possibility of a cutaneous SCC should be referred urgently to an appropriately trained specialist, usually in the local Dermatology Department, rapid access skin cancer clinic.[48]

DIAGNOSIS

The diagnosis is established histologically. The histology report should include the following: histopathological subtype (for example ácantholyticô, ódesmoplasticô, óspindleô or óverrucous SCCô), degree of differentiation (well, moderately, poorly or un-differentiated; histological grades as described by Broders: Appendix 2), tumour depth (thickness in mm ï excluding layers of surface keratin), the level of dermal invasion (as Clarkôs levels), and the presence or absence of perineural, vascular or lymphatic invasion.[49] The margins of the excised tissue can be stained prior to tissue preparation to allow their identification histologically and comment should be made on the peripheral and deep margins of excision.[50-64]

COMMUNICATION

Having a diagnosis of cancer can evoke many emotions within a person. It is essential that each person with SCC receives very clear and fully informed advice about his or her tumour. A Skin Cancer Clinical Nurse Specialist can provide invaluable information, support and advice. Some people may require additional psychological support and this can often be accessed through the multiprofessional supportive and palliative care team. All clinicians working with people who have cancer should have advanced communication skills training.

PROGNOSIS

The accumulated experience of treating cutaneous SCC by various methods has allowed some predictions to be made about prognosis based on the original lesion.

Factors which influence metastatic potential include anatomical site, size, tumour thickness, level of invasion, rate of growth, aetiology, degree of histological differentiation and host immunosuppression. These details are frequently omitted from reported series of treated SCC and the conclusions of such series must therefore be interpreted with caution. Patient referral patterns may influence local experience of this condition, and series reported from office practices tend to suggest a more favourable prognosis than cases reported from hospital and tertiary centres.[61-72] Changes to the TNM staging system have been proposed to more accurately reflect the prognosis and natural history of cutaneous SCC.[73]

FACTORS AFFECTING METASTATIC POTENTIAL OF CUTANEOUS SCC

A Site

Tumour location influences prognosis: sites are listed in order of increasing metastatic potential[65;74-77]

1 SCC arising at sun-exposed sites excluding lip and ear.
2 SCC of the lip.
3 SCC of the ear.
4 Tumours arising in non sun-exposed sites (e.g. perineum, sacrum, sole of foot).
5 SCC arising in areas of radiation or thermal injury, chronic draining sinuses, chronic ulcers, chronic inflammation or Bowenôs disease.

B Size: Diameter

Tumours greater than 2 cm in diameter are twice as likely to recur locally (15.2% vs. 7.4%), and three times as likely to metastasize (30.3% vs. 9.1%) as smaller tumours.[61;65]

C Size: Depth and level of invasion

Tumours greater than 4 mm in depth (excluding surface layers of keratin) or extending into or beyond the subcutaneous tissue (Clark level V) are more likely to recur and metastasize (metastatic rate 45.7%) compared with thinner tumours. Tumours less than 2 mm in thickness rarely metastasise.[51;55;65] Recurrence and metastases are less likely in tumours confined to the upper half of the dermis and less than 4 mm in depth (metastatic rate 6.7%).[52;55;61;65]

D Histological differentiation and subtype

Poorly differentiated tumours (i.e. those of Broders grades 3 and 4) (Appendix 2) have a poorer prognosis, with more than double the local recurrence rate and triple the metastatic rate of better differentiated SCC.[53;52;65] Acantholytic, spindle and desmoplastic subtypes have a poorer prognosis, whereas the verrucous subtype has a better prognosis. Tumours with perineural involvement, lymphatic or vascular invasion are more likely to recur and to metastasize.[59;62;78]

E Host immunosuppression

Tumours arising in patients who are immunosuppressed have a poorer prognosis. Host cellular immune response may be important both in determining the local invasiveness of SCC and the hostôs response to metastases.[35;36;50]

F Previous treatment and treatment modality

The risk of local recurrence depends upon the treatment modality. Locally recurrent disease itself is a risk factor for metastatic disease. Local recurrence rates are considerably less with Mohsô micrographic surgery than with any other treatment modality.[65;75-77;79-82]

TREATMENT

In interpreting and applying guidelines for treatment of SCC, three important points should be noted:

- There is a lack of randomised controlled trials (RCTs) for the treatment of primary cutaneous SCC.
- There is widely varying malignant behaviour of tumours which fall within the histological diagnostic category of óprimary cutaneous SCCô.
- There are varied experiences among the different specialists treating these tumours, which are determined by referral patterns and interests. Plastic and maxillofacial surgeons may encounter predominantly high-risk, aggressive tumours, whereas dermatologists may deal predominantly with smaller and less aggressive lesions.

However, there are three main factors which influence treatment, which are:

- The need for complete removal or treatment of the primary tumour
- The possible presence of local ‘in transit’ metastases
- The tendency of metastases to spread by lymphatics to lymph nodes

The majority of SCC cases are low risk and amenable to various forms of treatment, but it is essential to identify the significant proportion which are high risk. These may be best managed by a multiprofessional team with experience of treating the most malignant tumours.[66;67;69;72;83-86]

The goal of treatment is complete (preferably histologically confirmed) removal or destruction of the primary tumour and of any metastases. In order to achieve this, the margins of the tumour must be identified. The gold standard for identification of tumour margins is histological assessment, but most treatments rely on clinical judgement. It must be recognised that this is not always an accurate predictor of tumour extent, particularly when the margins of the tumour are ill-defined.[60;87-90]

SCC may give rise to local metastases, which are discontinuous with the primary tumour. Such ‘in-transit’ metastases may be removed by wide surgical excision or destroyed by irradiation of a wide field around the primary lesion. Small margins may not remove metastases in the vicinity of the primary tumour. Locally recurrent tumour may arise either due to failure to treat the primary continuous body of tumour, or from local metastases.[50;52;66;67;69;84;91;92]

SCC usually spreads to local lymph nodes and clinically enlarged nodes should be examined histologically (for example by fine needle aspiration or excisional biopsy). Tumour positive lymph nodes are usually managed by regional node dissection, but detailed discussion of the management of metastatic disease is beyond the scope of these guidelines.[74;93-96]

In the absence of clinically enlarged nodes, techniques such as high resolution ultrasound-guided fine needle aspiration cytology may be useful in evaluating regional lymph nodes in patients with high risk tumours.[97-100] The role of sentinel lymph node biopsy has yet to be established.[101-109]

Although there are many large series in which long-term outcome after treatment for cutaneous SCC has been reported (comprehensively summarised in Rowe *et al.*[65]), there are no large prospective randomised studies in which different treatments for this tumour have been compared.[66;90;110-112]

Guidelines for patient treatment

Conclusions from population-based studies do not necessarily indicate the best treatment for an individual patient. In particular, when choosing a treatment modality it is important to be aware of factors which may influence success. Curettage and cautery, cryosurgery, and to a lesser degree radiotherapy are all techniques in which the outcome depends of the experience of the physician. Although the same could be said of surgical excision and Mohsô micrographic surgery, these two modalities provide tissue for histological examination that allows the pathologist to assess the adequacy of treatment and for the physician to undertake further surgery if necessary. For this reason, where feasible, surgical excision (including Mohsô micrographic surgery where appropriate) should be regarded as the treatment of first choice for cutaneous SCC. The other techniques can yield excellent results in experienced hands, but the quality of treatment cannot be assured or audited contemporaneously by a third party.[50;65;70;88;89;94;96;110;113-115]

Surgical Excision

Surgical excision is the treatment of choice for the majority of cutaneous SCC. It allows full characterisation of the tumour and a guide to the adequacy of treatment through histological examination of the margins of the excised tissue.[52;65]

When undertaking surgical excision a margin of normal skin is excised from around the tumour. For clinically well-defined, low risk tumours less than 2 cm in diameter, surgical excision with a minimum 4-mm margin around the tumour border is appropriate and would be expected to completely remove the primary tumour mass in 95% of cases[88] (*Strength of Recommendation A, Quality of Evidence II-iii*). Narrower margins of excision are more likely to leave residual tumour. In order to maintain the same degree of confidence of adequate excision, tumours more than 2 cm in diameter, tumours classified as moderately, poorly or undifferentiated, tumours extending into the subcutaneous tissue and those on the ear, lip, scalp, eyelids or nose should be removed with a wider margin (6 mm or more) and the tissue margins examined histologically, or with Mohsô micrographic surgery.[75-77;88]

It is only meaningful to consider such margins when the peripheral boundary of the tumour appears clinically well-defined. The concept of a ósurgical marginô (i.e. normal-appearing tissue around the tumour) is based upon an assumption that the clinically visible margin of the tumour bears a predictable relationship to the true extent of the tumour, and that excision of a margin of clinically normal-appearing tissue around the tumour will encompass any microscopic tumour extension. The wider the surgical margin the greater the likelihood that all tumour will be removed. Large tumours have greater microscopic tumour extension and should be removed with a wider margin. This concept is equally valid for non-surgical treatments such as radiotherapy and cryotherapy in which a margin of clinically normal-appearing tissue is treated around the tumour. Mohsô micrographic surgery, does not make this assumption but displays the margins of the tissue for histological examination, and allows a primary tumour mass, growing in-continuity to be excised completely with

minimal loss of normal tissue. There are important lessons to be learnt from the experiences of micrographic surgery in treating cutaneous SCC (see below).[60;65;75-77;79;89]

Local Metastases

Microscopic metastases may be found around high-risk primary cutaneous SCC.[67;92;95] Under these circumstances a ówideô surgical margin extending well beyond the primary tumour may include such metastases and thus have a higher cure rate than a narrower margin. Mohsô micrographic surgery removes tumour growing in-continuity but does not identify in-transit micro-metastases. For this reason some practitioners of Mohsô micrographic surgery will excise a further surgical margin when treating high risk tumours after the Mohsô surgical wound has been histologically confirmed to be clear of the primary tumour mass.[67;95]

Histological Assessment of Surgical Margins

Conventional histological examination of one or more transverse sections of excised tissue displays a cross-section of the tumour and tissue margins. This is the best way of assessing and categorising the nature of the tumour, and it is usual to comment on whether tumour extends to the tissue margin, or if not, to record the margin of uninvolved skin around the tumour.[49;60] The value of such comments depends on how closely the section examined reflects the excised tissue in general. If SCC appears to extend to the margin of the examined tissue, then it should be assumed, particularly if the true margin of the tissue has been stained prior to sectioning, that excision is incomplete. Orientating markers or sutures should be placed in the surgical specimen by the surgeon to allow the pathologist to report accurately on the location of any residual tumour. A pathologist, using the conventional óbreadloafô technique for examining tissue, typically views only a small sample of the specimen microscopically,[60] and this may allow incompletely excised high-risk tumour to go undetected. There are several alternative tissue preparations that allow the peripheral margins of the excised tissue to be more comprehensively examined.[87] The clinician and pathologist must work closely together in order

to ensure appropriate sampling and microscopic examination of excised tissue, particularly with high-risk tumours.[60;87]

Mohsô micrographic surgery differs because the tissue is not displayed in cross-section and, if the first level of excision is adequate, tumour may not be seen at all in the microscopic sections. There are technical factors that may occasionally hamper identification of SCC in frozen sections and under these circumstances final histological examination should be undertaken on formalin-fixed tissue.[116;117]

Mohs' Micrographic Surgery

Mohsô micrographic surgery allows precise definition and excision of primary tumour growing in-continuity, and as such would be expected to reduce errors in primary treatment which may arise due to clinically invisible tumour extension. There is good evidence that the incidence of local recurrent and metastatic disease are low after Mohsô 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 impairment.[52;65] (*Strength of Recommendation B, Quality of Evidence II-iii*). The best cure rates for high risk SCCs are reported in series treated by Mohsô micrographic surgery.[65;81;82;116-118] Where Mohsô micrographic surgery is indicated but not available then one of the other histological techniques to examine the peripheral margin of the excised tissue should be employed.[87]

However, there are no prospective randomised studies comparing therapeutic outcome between conventional or wide surgical excision versus Mohsô micrographic surgery for cutaneous SCC.

It is firmly established that incomplete surgical excision is associated with a worse prognosis and, when doubt exists as to the adequacy of excision at the time of surgery, it is desirable, where

practical, to delay or modify wound repair until complete tumour removal has been confirmed histologically.[50;65-69;78]

Curettage and Cautery

Excellent cure rates have been reported in several series and experience suggests that small (<1 cm) well-differentiated, primary, slow growing tumours arising on sun-exposed sites can be removed by experienced physicians with curettage.[65;90;110;114;119] There are few published data relating outcome after curettage of larger tumours and different clinical tumour types.

The high cure rates reported following curettage and cautery of cutaneous SCC (*Quality of Evidence II-iii*), may reflect case selection, with a greater proportion of small tumours treated by curettage than by other techniques, but also raise the question as to whether curettage per se has a therapeutic advantage. The experienced clinician undertaking curettage can detect tumour tissue by its soft consistency and this may be of benefit in identifying invisible tumour extension and ensuring adequate treatment. Conventionally, cautery or electrodesiccation is applied to the curetted wound and the curettage-cautery cycle then repeated once or twice. Curettage is routinely undertaken to ódebulkô the tumour prior to Mohsô micrographic surgery, but is of no proven benefit prior to standard surgical resection.[120] Curettage provides poorly orientated material for histological examination and no histological assessment of the adequacy of treatment is possible. Curettage and cautery is not appropriate treatment for locally recurrent disease or high risk tumours.

Cryosurgery

Good short term cure rates have been reported for small histologically confirmed SCC treated by cryosurgery in experienced hands. Prior biopsy is necessary to establish the diagnosis histologically. There is great variability in the use of liquid nitrogen for cryotherapy and significant transatlantic variations in practice. For this reason caution should be exercised in the use of cryotherapy for SCC

although it may be an appropriate technique for selected cases in specialised centres.[65;113;121] Cryosurgery is not appropriate for locally recurrent disease or high risk tumours.

Radiotherapy

Radiotherapy is generally contraindicated in the younger patient because the scar from surgery is usually less noticeable than the pallor and telangiectases which develop as a late effect in irradiated skin. In some circumstances radiotherapy will give a better cosmetic effect, particularly where loss of tissue is likely to cause cosmetic or functional impairment. For example, the lower eyelid, the inner canthus of the eye, the lip, the tip of the nose and in some cases the ear. SCC can be cured by radiotherapy in more than 90% of cases.[52;65;110;122-125] Choice of radiotherapy modality (electrons or photons) dose and technique require experience and the involvement of a qualified clinical oncologist.

Some skin sites tolerate radiotherapy poorly, e.g. the back of the hand, the abdominal wall and the lower limb, and surgical excision is preferable at these sites. Any tumour invading cartilage or bone, e.g. over the ear or nose is best treated surgically to avoid radio-necrosis.

In all cases where there is debate about whether radiotherapy or surgery is the best option, close liaison should take place between the dermatologist, clinical oncologist and plastic surgeon ideally in a multi-disciplinary clinic.

Other Treatments

Other reported treatments include: topical Imiquimod, intralesional Interferon Alpha, intralesional 5-Fluorouracil, and photodynamic therapy.[126-135] Evidence for the role of these treatments is lacking and limited to isolated case reports (*Strength of Recommendation C, Quality of Evidence IV*).

Elective prophylactic lymph node dissection / sentinel lymph node biopsy

Elective prophylactic lymph node dissection has been proposed for SCC on the lip greater than 6 mm in depth and cutaneous SCC greater than 8 mm in depth, but evidence for this is weak[70;74] (*Strength of Recommendation C, Quality of Evidence II-iii*). Elective lymph node dissection is not routinely practised and there is no compelling evidence of benefit over morbidity.[51;56]

There has been recent interest in the application of sentinel lymph node biopsy in the management of high risk SCC. The procedure is technically feasible and may help avoid unnecessary lymph node dissection. However, the overall benefit of the technique in patients with SCC has yet to be determined.[101-109]

The multiprofessional oncology team

Patients with high risk SCC and those presenting with clinically involved lymph nodes should ideally be reviewed by a multiprofessional skin oncology team which includes a dermatologist, pathologist, appropriately trained surgeon (usually a plastic, ENT or maxillo-facial surgeon), clinical oncologist, radiologist and a clinical nurse specialist in skin cancer.[48] Some advanced tumours are not surgically resectable and these should be managed in a multiprofessional setting in order that other therapeutic options are considered. Patients should be provided with suitable written information concerning diagnosis, prognosis, self-examination and follow up support, local and national support organisations and, where appropriate, access to a multiprofessional palliative care team.

Follow-up

Early detection and treatment improves survival of patients with recurrent disease. All patients should be instructed in self-examination of the surgical scar site, local skin and lymph nodes and should receive written information sheets giving clear instructions and actions to take should they

suspect recurrent disease. Elderly patients may have difficulty in undertaking adequate self-examination. A specialist or appropriately trained clinical nurse specialist or primary care physician may undertake regular follow-up examination for recurrent disease. Seventy five percent of local recurrences and metastases are detected within 2 years and 95% within 5 years.[52;65] It would therefore seem reasonable for the patient who has had a high-risk SCC to be kept under close medical observation for recurrent disease for at least 2 and up to 5 years (*Strength of Recommendation A, Quality of Evidence II-ii*; Table 1). The decision as to who follows the patient will depend upon the disease risk, local facilities and interests.[52;65]

Summary of treatment options for primary cutaneous squamous cell carcinoma

Please see Table 2 for recommendations.

Table 1: Risk Factors: Primary Cutaneous Squamous Cell Carcinoma

	Site	**Diameter**	**Tumour Depth and level of invasion**	**Histological Features and subtype**	**Host Immune status**
Low risk	SCC arising at sun-exposed sites excluding lip and ear	Tumours up to 20 mm in diameter	Tumours up to 4 mm in depth and confined to dermis	Well-differentiated tumour or Verrucuous subtype	No evidence of immune dysfunction
High risk	SCC of lip or ear	Tumours more than 20 mm in diameter	Tumours more than 4 mm in depth or invading beyond dermis	Moderately-differentiated tumour	Immunosupressive therapy ï such as Organ Transplant Recipients
	Recurrent SCC			Poorly-differentiated tumour	Chronic immunosuppressive disease ï e.g. CLL
	SCC arising in non exposed sites such as perineum, sacrum, sole of foot			Perineural invasion Acantholytic, Spindle, or Desmoplastic subtypes	
	SCC arising in radiation or thermal scars, chronic ulcers or inflammation or Bowenôs disease			Incomplete excision	

Tumours with features confined to the first row are considered ólow riskô all others are óhigh riskô

Table 2: Summary of Treatment Options for Primary Cutaneous Squamous Cell Carcinoma

Treatment	Indications	Contraindications	Notes
Surgical Excision	All resectable tumours	Where surgical morbidity is likely to be unreasonably high	General treatment of choice for SCC
Mohs Micrographic Surgery / Excision with histological control	High risk tumours	Where surgical morbidity is likely to be unreasonably high	High risk tumours need wide margins or histological margin control
Radiotherapy	Non-resectable tumours	Where tumour margins are ill-defined	
Curettage and Cautery	Small, well-defined, low-risk tumours	High risk tumours	Only suitable for experienced practitioners
Cryotherapy	Small, well-defined, low-risk tumours	High risk tumours, recurrent tumours	Only suitable for experienced practitioners

AUDIT POINTS

1 Surgical excision margins: Are the margins of excision (recommended: 4 mm for well-defined, low risk tumours and 6 mm for high risk tumours) appropriate and clearly documented in the medical notes?

2 Are those involved in the care of patients with SCC able to show evidence of advanced communications skills training?

3 Has the prognosis of the tumour ï low-risk or high-risk been documented in the notes?

4 Is there evidence of the patient being instructed in self-examination and being provided with written information sheets?

5 Is there evidence of appropriate follow up examination by suitably trained persons?

Appendix 1

STRENGTH OF RECOMMENDATIONS

A There is good evidence to support the use of the procedure.

B There is fair evidence to support the use of the procedure.

C There is poor evidence to support the use of the procedure.

D There is fair evidence to support the rejection of the use of the procedure.

E There is good evidence to support the rejection of the use of the procedure.

QUALITY OF EVIDENCE

I Evidence obtained from at least one properly designed, randomised control trial.

II-i Evidence obtained from well designed controlled trials without randomisation.

II-ii Evidence obtained from well designed cohort or case control analytic studies, preferably from more than one centre or research group.

II-iii Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the introduction of penicillin treatment in the 1940ôs) could also be regarded as this type of evidence.

III Opinions of respected authorities based on clinical experience, descriptive studies or reports of expert committees.

IV Evidence inadequate owing to problems of methodology (e.g. sample size, or length or comprehensiveness of follow-up or conflicts in evidence).

Appendix 2

BRODERS HISTOLOGICAL CLASSIFICATION OF DIFFERENTIATION IN SCC

Broders devised a classification system in which grades 1, 2 and 3 denoted ratios of differentiated to undifferentiated cells of 3:1, 1:1 and 1:3 respectively. Grade 4 denoted tumour cells having no tendency towards differentiation.

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