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Guidelines for the management of basal cell carcinoma

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Summary

This article represents a planned regular updating of the previous British Association of Dermatologists guidelines for the management of basal cell carcinoma. These guidelines 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.

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There are several effective modalities available to treat basal cell carcinoma (BCC).[1,2] Guidelines aim to aid selection of the most appropriate treatment for individual patients. Careful assessment of both the individual patient and certain tumour-specific factors are key to this process.

Definition

BCC is a slow-growing, locally invasive malignant epidermal skin tumour predominantly affecting caucasians. The tumour infiltrates tissues in a three-dimensional fashion[3] through the irregular growth of subclinical finger-like outgrowths which remain contiguous with the main tumour mass.[4,5] Metastasis is extremely rare[6,7] and morbidity results from local tissue invasion and destruction particularly on the face, head and neck. Clinical appearances and morphology are diverse, and include nodular, cystic, superficial, morphoeic (sclerosing), keratotic and pigmented variants. Common histological subtypes include nodular (nBCC), superficial (sBCC) and pigmented forms in addition to morphoeic, micronodular, infiltrative and basosquamous variants which are particularly associated with aggressive tissue invasion and destruction.[8] Perivascular or perineural invasion are features associated with the most aggressive tumours.

Incidence and aetiology

BCC is the most common cancer in Europe, Australia[9] and the U.S.A.,[10] and is showing a worldwide increase in incidence. Inconsistent data collection unfortunately means that accurate figures for the incidence of BCC in the U.K. are difficult to obtain.[11] The age shift in the population has been accompanied by an increase in the total number of skin cancers, and a continued rise in tumour incidence in the U.K. has been predicted up to the year 2040.[12]

The most significant aetiological factors appear to be genetic predisposition and exposure to ultraviolet radiation.[13] The sun-exposed areas of the head and neck are the most commonly involved sites.[14,15] Sun exposure in childhood may be especially important.[16] Increasing age, male sex, fair skin types I and II, immunosuppression and arsenic exposure are other recognized risk factors[17] and a high dietary fat intake may be relevant.[18] Multiple BCCs are a feature of basal cell naevus (Gorlin's) syndrome (BCNS).[19] Following development of a BCC, patients are at significantly increased risk of developing subsequent BCCs at other sites.

Diagnosis and investigation

Dermatologists can make a confident clinical diagnosis of BCC in most cases. Diagnostic accuracy is enhanced by good lighting and magnification and the dermatoscope may be helpful in some cases.[20] Biopsy is indicated when clinical doubt exists or when patients are being referred for a subspecialty opinion, when the histological subtype of BCC may influence treatment selection and prognosis[8] (Table 1). The use of exfoliative cytology has been described.[21] Imaging techniques such as computed tomography or magnetic resonance imaging

Table 1 Factors influencing prognosis of basal cell carcinoma

Tumour size (increasing size confers higher risk of recurrence)
Tumour site (lesions on the central face, especially around the eyes, nose, lips and ears, are at higher risk of recurrence)
Definition of clinical margins (poorly defined lesions are at higher risk of recurrence)
Histological subtype (certain subtypes confer higher risk of recurrence)
Histological features of aggression (perineural and/or perivascular involvement confers higher risk of recurrence)
Failure of previous treatment (recurrent lesions are at higher risk of further recurrence)
Immunosuppression (possibly confers increased risk of recurrence)

scanning are indicated in cases where bony involvement is suspected or where the tumour may have invaded major nerves,[22] the orbit[23,24] or the parotid gland.[25] Other techniques, such as ultrasound, spectroscopy and teraherz scanning, are of academic interest but currently have little or no proven clinical role.

'Low-risk' and 'high-risk' tumours, patient factors and treatment selection

The likelihood of curing an individual BCC strongly correlates with a number of definable prognostic factors (Table 1). These factors[26,27] should strongly influence both treatment selection and the prognostic advice given to patients. The presence or absence of these prognostic factors allows clinicians to assign individual lesions as being at low or high risk of recurrence following treatment.

The recent development of more effective topical and nonsurgical therapies has increased the treatment options for many low-risk lesions, although surgery and radiotherapy (RT) remain the treatments of choice for the majority of high-risk lesions.[28]

Patient-specific factors which may influence the choice of treatment include general fitness, coexisting serious medical conditions, and the use of antiplatelet or anticoagulant medication. A conservative approach to asymptomatic, low-risk lesions will prevent treatment causing more problems than the lesion itself. Even when dealing with high-risk BCC aggressive management may be inappropriate for certain patients, especially the very elderly or those in poor general health, when a palliative rather than a curative treatment regimen may be in the best interests of the patient.

Finally, factors including patient choice, local availability of specialized services, together with the experience and preferences of the specialist involved may influence treatment selection.

Management

A wide range of different treatments has been described for the management of BCC,[29] and both the British Association of Dermatologists (BAD)[30] and the American Academy of Dermatology[31] have published professional guidelines on their appropriate use. Usually the aim of treatment is to eradicate the tumour in a manner likely to result in a cosmetic outcome that will be acceptable to the patient. Some techniques [e.g. cryosurgery, curettage, RT, photodynamic therapy (PDT)] do not allow histological confirmation of tumour clearance. These techniques are generally used to treat low-risk tumours, although RT also has an important role in the management of high-risk BCC. Surgical excision with either intraoperative or postoperative histological assessment of the surgical margins is widely used to treat both low- and high-risk BCC, and is generally considered to have the lowest overall failure rate in BCC treatment.[28] In rare advanced cases, where tumour has invaded facial bones or sinuses, major multidisciplinary craniofacial surgery may be necessary.[32]

There are few randomized controlled studies comparing different skin cancer treatments, and much of the published literature on the treatment of BCC consists of open studies, some with low patient numbers and relatively short follow-up periods.[33]

Broadly, the available treatments for BCC can be divided into surgical and nonsurgical techniques, with surgical techniques subdivided into two categories: excision and destruction.

Surgical techniques

Excision with predetermined margins

The tumour is excised together with a variable margin of clinically normal surrounding tissue. The peripheral and deep surgical margins of the excised tissue can be examined histologically using intraoperative frozen sections[34] or, more commonly, using postoperative vertical sections taken from formalin-fixed, paraffin-embedded tissue.[35] This approach may be used with increasingly wide surgical margins for primary, incompletely excised and recurrent lesions.

Primary basal cell carcinoma

Surgical excision is a highly effective treatment for primary BCC,[35,36] with a recurrence rate of < 2% reported 5 years following histologically complete excision in two different series.[35,37] The overall cosmetic results are generally good,[36] particularly when excision and wound repair are performed by experienced practitioners. The use of curettage prior to excision of primary BCC may increase the cure rate by more accurately defining the true borders of the BCC.[38,39] The size of the peripheral and deep surgical margins should correlate with the likelihood that subclinical tumour extensions exist (Table 1). Although few data exist on the correct deep surgical margin, as this will depend upon the local anatomy, excision through subcutaneous fat is generally advisable. Studies using horizontal [Mohs micrographic surgery (MMS)] sections which can accurately detect BCC at any part of the surgical

margin suggest that excision of small (< 20 mm) well-defined lesions with a 3-mm peripheral surgical margin will clear the tumour in 85% of cases. A 4–5-mm peripheral margin will increase the peripheral clearance rate to approximately 95%, indicating that approximately 5% of small, well-defined BCCs extend over 4 mm beyond their apparent clinical margins.[4,40,41] Morphoeic and large BCCs require wider surgical margins in order to maximize the chance of complete histological resection. For primary morphoeic lesions, the rate of complete excision with increasing peripheral surgical margins is as follows: 3-mm margin, 66%; 5-mm margin, 82%; 13–15-mm margin, > 95%.[4] Standard vertical section processing of excision specimens allows the pathologist only to examine representative areas of the peripheral and deep surgical margins, and it has been estimated that at best 44% of the entire margin can be examined in this fashion, which may partly explain why tumours which appeared to have been fully excised do occasionally recur.[42]

Evidence level: *Surgical excision is a good treatment for primary BCC. (Strength of recommendation A, quality of evidence I – see Appendix 1).*

Incompletely excised basal cell carcinoma

Incomplete excision, where one or more surgical margins are involved with (or extremely close to) tumour, has been reported in 4·7%[43] and 7%[44] of cases reported from British plastic surgical units and 6·3%[45,46] in two retrospective studies from Australia. This usually reflects the unpredictable extent of subclinical tumour spread beyond the apparent clinical margins. However, other relevant factors associated with incomplete excision include operator experience, the anatomical site and histological subtype of the tumour[43] and the excision of multiple tumours during one procedure.[47]

When the surgical margins are examined intraoperatively (excision under frozen section control, MMS), further resection of any involved margins can take place prior to wound repair. Using standard surgery, one approach to minimize the risk of incomplete excision is to excise tumours and delay wound repair until an urgent pathology report is received. In the more common situation, when surgical margins are examined routinely postoperatively, the wound has usually been repaired and the only options are further treatment or prolonged follow up to monitor for tumour recurrence.[48]

Various prospective and retrospective reviews of incompletely excised BCC suggest that not all tumours will recur. Studies using approximately 2–5 years of follow up have reported recurrence rates following histologically incomplete excision of 30%,[46] 38%,[49] 39%[50] and 41%.[51]

In a follow-up study of 140 incompletely excised BCCs 21% of lesions recurred; however, as 31% of the cohort died of other causes during the (minimum 5-year) follow-up period this figure could have been significantly higher.[47] Re-excision of incompletely excised lesions revealed the presence of residual tumour in 45%[47] and 54%[44] of cases when the tissue was examined using standard (vertical) tissue sectioning and in 55% of cases re-excised using MMS.[52]

The risk of recurrence seems highest in those lesions where both lateral and deep margins were involved with BCC and when the incomplete excision was performed to remove recurrent BCCs, especially those recurrent following radiation therapy.[49] BCCs incompletely excised at the deep margin were considered especially difficult to cure with re-excision.[49] One study calculated the probability of recurrence of incompletely excised BCC and found that it varied according to which margins were involved. When only the lateral margins were involved there was a 17% risk of recurrence, rising to a 33% risk of recurrence if the deep margins were involved.[53]

There is good evidence to support a policy of re-treatment of incompletely excised lesions[44,49,51,52,54–56] especially when they involve critical midfacial sites, where the deep surgical margin is involved, the surgical defect has been repaired using skin flaps or skin grafts[49,57] and where histology shows an aggressive histological subtype. It has been suggested that some incompletely excised lesions may demonstrate a more aggressive histological subtype when the lesion recurs, especially on the central face.[58] If the decision is made to re-treat rather than observe, re-excision (with or without frozen section control) or MMS are the treatments of choice (Table 2). Although there are limited data on the subject, RT appears to have a role in preventing the recurrence of incompletely excised BCC.[53]

Evidence level: *Tumours which have been incompletely excised, especially (i) high-risk lesions; and (ii) lesions incompletely excised at the deep margin, are at high risk of recurrence. (Strength of recommendation A, quality of evidence II-i).*

Recurrent basal cell carcinoma

Recurrent BCC is more difficult to cure than primary disease – the results of all published series on the surgical excision of BCC show cure rates following treatment of recurrent disease that are inferior to those for primary lesions.[59] Recurrent lesions generally require wider peripheral surgical margins than primary lesions with or without standard (non-Mohs) frozen section control.[34] Peripheral excision margins for recurrent BCC of 5–10 mm have been suggested.[60]

Evidence level: *Recurrent tumours, especially on the face, are at high risk of further recurrence following surgical excision even with wide surgical margins. (Strength of recommendation A, quality of evidence II-ii).*

Table 2 Indications for Mohs micrographic surgery

Tumour site (especially central face, around the eyes, nose, lips and ears)
Tumour size (any size, but especially > 2 cm)
Histological subtype (especially morphoeic, infiltrative, micronodular and basosquamous subtypes)
Poor clinical definition of tumour margins
Recurrent lesions
Perineural or perivascular involvement

Mohs micrographic surgery

This specialized surgical procedure was pioneered (as chemosurgery) by Frederic Mohs in the 1940s and later refined into the modern technique of MMS.[61] MMS combines staged resection with comprehensive surgical margin examination and results in extremely high cure rates for even the most high-risk lesions together with maximal preservation of normal tissues.[62,63] The technique, which is generally reserved for high-risk facial lesions, is based upon the principle that all traces of infiltrating BCC must be identified and excised in order to achieve complete cure.[64,65] The indications for using MMS are summarized in Table 2. A review of studies published since the mid-1940s suggested an overall 5-year cure rate of 99% following MMS for primary BCC[66] and 94·4% for recurrent disease.[59] Two prospective studies have been reported from Australia: in one, 5-year cure rates of 100% and 92·2% for primary and recurrent tumours, respectively, were reported in 819 patients with periocular BCC;[67] in the other, 3370 BCCs on the head and neck treated wth MMS resulted in 5-year cure rates of 98·6% for primary BCC and 96% for recurrent disease.[68] A retrospective review of 620 patients with 720 lesions gave estimated 5-year cure rates of 98·8% for primary BCC and 93·3% for recurrent disease.[69] Five-year cure rates of 93·5% for primary BCC and 90% for recurrent disease have been reported.[64]

MMS for BCC performed under local anaesthesia in an outpatient or day-case setting has a good safety record[70,71] and Mohs surgical defects can be repaired by the Mohs surgeon or by facial reconstructive specialists including plastic,[72] otolaryngeal[73] and oculoplastic[74,75] surgeons. The technique is performed using either frozen tissue sections,[76] when resection can take place over a matter of hours, or with formalin-fixed, paraffin-embedded tissues, when the procedure takes place over a number of days.[77,78] Variations of the technique, based upon different techniques of pathological processing of tissue excised in a standard fashion, have been described.[79–82] Both maxillofacial[83] and ophthalmic[84,85] surgeons have reported good results with staged excision of high-risk BCC using standard vertical (non-Mohs) permanent sections and delayed wound repair, as an alternative to MMS which one group felt was too 'labour-intensive'.[84] Several studies have looked at the comparative cost of MMS,[86–89] which (to produce tumour-free margins) has a similar cost to traditional excision[87] but is less expensive than excision using intraoperative frozen section control.[86] A study from the Netherlands found MMS to be more expensive than traditional surgery; however, as MMS is likely to produce extremely high cure rates, it remains cost-effective. The only study to date which tried to compare cure rates following standard excision and MMS[89] appeared to show little difference between the two treatment modalities. However, a failure to adhere to the study design (with 24 of 301 patients randomized to have standard surgical excision being moved into the MMS treatment group) raises concerns about the conclusions of this study.[90]

Evidence levels: *Mohs micrographic surgery is a good treatment for high-risk primary BCC. (Strength of recommendation A, quality of evidence I).*

Mohs micrographic surgery is a good treatment for high-risk recurrent BCC. (Strength of recommendation A, quality of evidence I).

Destructive techniques: surgical

Destructive surgical and nonsurgical techniques are best used for low-risk disease. Unless a confident clinical diagnosis and assessment has been made, a preoperative biopsy is indicated to confirm the diagnosis and to determine the histological subtype. This advice is especially important for facial lesions.

Curettage and cautery

Curettage and cautery (C&C, also known as electrodesiccation and curettage)[91–93] and curettage alone[91,94,95] are traditional methods of BCC removal. Successful outcomes rely heavily on careful selection of appropriate lesions (ideally small nodular or superficial)[94,96] as well as the skill and experience of the operator.[96,97] In a survey of 166 U.K. consultant dermatologists in 1995, 24% of 1597 lesions presenting for the first time were treated by C&C, making it the second most common form of treatment after surgical excision (58%).[98] Variations in technique include the use of different types of curette and the number of cycles of treatment;[93] however, the exact protocol is often unclear in published studies. Curettage and cautery is generally suitable for the treatment of low-risk lesions.[94,96,97,99] Curettage and cautery of high-risk facial lesions is associated with a high risk of tumour recurrence[97,100,101] and is generally contraindicated.

In a study of 69 C&C wounds that were immediately re-excised using MMS, residual tumour was found in 33% of cases overall, with striking differences seen in different body sites (47% of head and neck sites and 8·3% of trunk and limb sites contained residual BCC).[102] This may be one reason why C&C is generally less successful in the treatment of facial lesions. The relatively high incidence of residual BCC but an apparently low incidence of recurrence following C&C has led to suggestions that unidentified wound healing processes following C&C may play a part in tumour destruction, although at least two studies have failed to confirm this theory.[103,104] Tumour debulking by curettage has been combined with various treatment modalities such as imiquimod (IMQ)[105,106] and PDT[107] in attempts to increase efficacy. Curettage has also been combined with cryosurgery – a 5-year follow-up study of 70 noninfiltrative auricular BCCs (not involving the external auditory meatus) treated in this way resulted in one recurrence.[108]

A literature review of all studies published since 1947 suggested an overall 5-year cure rate of 92·3% following C&C for selected primary BCC.[66] Curettage is much less useful for recurrent BCC and a similar review suggested an overall 5-year cure rate of 60%.[59]

Evidence levels: *Curettage and cautery is a good treatment for low-risk BCC. (Strength of recommendation A, quality of evidence II-iii).*

Curettage and cautery is a poor treatment for high-risk BCC. (Strength of recommendation D, quality of evidence II-iii).

Curettage and cautery is a poor treatment for recurrent BCC. (Strength of recommendation D, quality of evidence II-ii).

Cryosurgery

Liquid nitrogen cryosurgery for the destruction of BCC uses the effects of extreme cold (tissue temperatures of −50 to −60 °C) to effect deep destruction of the tumour and surrounding tissues. Individual treatment techniques vary considerably, with both open and closed spray techniques and single or multiple cycles of freezing (freeze/thaw cycles).[109,110] Double freeze/thaw cycles are generally recommended for the treatment of facial BCC, although superficial truncal lesions may require only a single treatment cycle.[111] One report describes the use of 'fractional cryosurgery' where large lesions are treated on multiple separate occasions.[112] The success of cryosurgery relies upon careful selection of appropriate lesions[113] and the experience of the operator.

In one study 12 small nonfacial nBCCs were treated with single freeze-thaw cryosurgery to a monitored temperature of between −50 and −60 °C. When each treatment site was subsequently excised and examined with horizontal step sections, no residual tumour was detected.[114] Cryosurgery is most useful in the treatment of low-risk BCC.[115,116] Five-year cure rates of 99% have been reported by the same author in both 1991[117] and 2004.[118]

In expert hands, cryosurgery also has a role in the management of high-risk lesions, either as the sole treatment[118] or following curettage.[108,119] A follow-up study of 171 high-risk BCCs treated with combined curettage/cryotherapy reported a 8% recurrence rate after a mean follow up of 5·2 years (range 6 months–9·1 years).[119] Although cryosurgery is less useful for the treatment of recurrent BCC,[59] selected lesions may also respond to aggressive expert treatment.[120]

Some authors consider cryosurgery to be an appropriate treatment for selected periocular BCC[121–124] and one series of 158 periocular BCCs treated with double-cycle cryosurgery reported a 8% recurrence rate after a mean 5-year follow-up period. Careful lesion selection was crucial, as factors associated with recurrence included large size, morphoeic histology and involvement of the lid margin.[123] Other than tumour recurrence, adverse results of cryosurgery to eyelid and periocular BCC include conjunctival hypertrophy and ectropion which may require corrective surgery.[123] Cryosurgery (double 25–30-s treatment cycles) has been compared with 5-aminolaevulinic acid (ALA)-PDT in the treatment of low-risk BCC.[125] Histologically verified recurrence rates in the two groups were statistically comparable: 25% (11 of 44) for PDT and 15% (six of 39) for cryosurgery. Additional treatments had to be performed in 30% of the lesions in the PDT group although the healing time was shorter and the cosmetic outcome better with PDT. Pain and discomfort during and after treatment were the same. Additional studies using methylaminolaevulinic acid (MAL)-PDT with longer follow-up periods and including comparison with surgical excision are detailed in the later section on PDT.

Cryosurgery wounds generally heal with minimal tissue contraction, resulting in good cosmetic results;[113,115,119] however, one study comparing the cosmetic results (but not efficacy) of cryosurgery with excisonal surgery for head and neck found that excision generally gave superior cosmetic results.[126]

Evidence level: *Cryosurgery is a good treatment for low-risk BCC. (Strength of recommendation A, quality of evidence II-ii).*

Carbon dioxide laser

Carbon dioxide (CO_2) laser ablation remains an uncommon form of treatment and there are few published data. When combined with curettage, CO_2 laser surgery may be useful in the treatment of large or multiple low-risk sBCCs. In one small series, the Ultrapulse CO_2 laser appeared effective in treating small BCCs in low-risk areas with minimal post-treatment scarring in three patients with BCNS.[127]

Evidence level: *Carbon dioxide laser ablation may be effective in the treatment of low-risk BCC. (Strength of recommendation C, quality of evidence III).*

Destructive techniques: nonsurgical

Topical immunotherapy with imiquimod

IMQ is an immune-response modifier which acts through toll-like receptors, predominantly expressed on dendritic cells and monocytes, to induce production of cytokines and chemokines which promote both innate and adaptive cell-mediated immune responses.[128] Several studies have reported the efficacy of topical 5% IMQ cream in the treatment of sBCC and dose–response studies indicate that the highest response rates are associated with more frequent or prolonged dosing, together with a significant inflammatory reaction.[129,130]

Pooled results from two randomized vehicle-controlled studies of 5% IMQ cream in the treatment of small sBCC in 724 patients have been reported. Twelve weeks following a 6-week treatment period the histological clearance rates were 82% (application five times weekly, 5x/week), 79% (application seven times weekly, 7x/week) and 3% (vehicle only). An increasing severity of local inflammatory reactions was associated with higher clearance rates. Moderate to severe local site reactions occurred in 87%, including erosion (36%) and ulceration (22%) in subjects in the 5x/week group, with higher figures for the 7x/week group. Rest periods were requested by 10% and 22% of patients in the 5x/week and 7x/week groups, respectively, with resumption of treatment when the reaction had resolved. Eleven patients withdrew from the study due to adverse events.[131]

A multicentre randomized study of the treatment of sBCC with 5% IMQ cream vs. vehicle alone in 84 patients reported similar results. Histological clearance rates following once-daily application for 6 weeks were 80% (IMQ) and 6% (vehicle).[132]

Topical IMQ is approved by the European Medicines Agency for the treatment of small sBCC, using the 5x/week regimen for 6 weeks. This regimen balances therapeutic efficacy with patient tolerability of the common inflammatory reactions.

Long-term data on clinical recurrence rates are limited. An on-going multicentre open-label study of 182 small sBCCs using the 5x/week regimen resulted in 10% of patients failing to respond at 12 weeks. The 90% who did respond then entered a 5-year follow-up phase. Interim results after 2 years of follow up reported an estimated recurrence rate of 20·6% in this group.[133]

Data on the treatment of nBCC using IMQ are limited. Two randomized dose–response studies (reported in the same paper) each evaluated four dosing regimens over a 6- or 12-week application period. Six weeks following treatment the entire treated areas were excised. Histologically confirmed complete response rates were highest in the groups receiving a once-daily dose, with clearance rates of 71% (25 of 35) and 76% (16 of 21) in the 6- and 12-week studies, respectively. Increasing response rates were associated with increasing frequency of dosing over all regimens, and there was a significant correlation between the most intense inflammatory reactions and complete response rate.[134]

A further randomized trial reported complete clinical clearance in 78% of 90 evaluable patients with nBCC following thrice-weekly application of IMQ for 8 or 12 weeks (no difference in outcome between protocols). The treated areas were excised 8 weeks following treatment, and residual BCC was found in 36% of cases, including 12 of 90 (13%) patients considered to have shown complete clinical clearance.[135]

There are currently limited published data on the long-term recurrence rates following IMQ treatment of nBCC. During 5-year follow up of 55 lesions in an open study of different types of BCC treated with IMQ, the long-term clearance rate for the intention-to-treat dataset was 100% (four of four) for sBCC, 75% (six of eight) for nBCC and 60% (26 of 43) for infiltrative BCC.[136]

Two pilot studies investigated the combination of curettage of nBCC prior to the use of topical IMQ.[105,106] In the first, following a single cycle of curettage, IMQ was applied daily for 6–10 weeks and this produced histological clearance of 94% (32 of 34) when the treatment sites were excised 12 weeks after treatment.[105] In the second study, 20 patients received three cycles of C&C followed by IMQ or vehicle once daily for 1 month. Histological examination revealed residual tumour in 10% (one of 10) in the IMQ group and 40% (four of 10) in the vehicle group.[106]

Occlusion of the treatment site does not appear to be beneficial as no difference in efficacy was demonstrated when 5% IMQ cream with and without occlusion was used to treat both sBCC and nBCC.[137] Three separate studies of topical IMQ in a total of seven patients with BCNS have suggested clinical benefit in treating multiple sBCC and nBCC.[138–140]

To date, there are no published randomized trials comparing topical IMQ with an existing standard therapy. One small study compared the efficacy and tolerability of topical IMQ (three times weekly for 3 weeks followed by a 1-week rest period, repeated for a total of 3 months) with MAL-PDT therapy (one cycle of two treatments). Histological clearance in the IMQ group was reported in six of eight (all sBCC) vs. 12 of 13 (sBCC and nBCC) in the PDT group 12 weeks after treatment. Cosmetic results in both groups were similar, although patients tolerated IMQ therapy less well.[141]

On the basis of the currently available data, topical 5% IMQ cream appears to have a role in treating small sBCC, although 5-year follow-up data are awaited. The role of IMQ in the treatment of nBCC remains unclear, as its use has been studied in only small numbers of patients and there are currently limited long-term follow-up data.

Evidence levels: *Topical imiquimod appears effective in the treatment of primary small superficial BCC. (Strength of recommendation A, quality of evidence I).*

Topical imiquimod may possibly have a role in the treatment of primary nodular BCC. (Strength of recommendation C, quality of evidence I).

Photodynamic therapy

Previous BAD guidelines have rated topical PDT using ALA as suitable for the treatment of low-risk sBCC, but a relatively poor option for the treatment of high-risk lesions.[30,142]

ALA-PDT has been compared with cryosurgery in the treatment of both sBCC and nBCC.[125] Clinical recurrence rates at 12 months of 5% (PDT) and 13% (cryotherapy) were underestimates, as histology demonstrated residual BCC in 25% (PDT) and 15% (cryotherapy) of cases, raising concerns both over clinical observation rather than histology as proof of tumour clearance and over the long-term efficacy of PDT. Two further studies of double-cycle ALA-PDT treatment of sBCC reported initial clinical clearance rates of 95% (60 of 62)[143] and 90% (76 of 87),[144] with subsequent recurrence rates of 18%[143] and 4·8%,[144] respectively, after 12 months of follow up.

Since the last BAD guidelines were published,[30] studies have increasingly reported the use of topical MAL, a more lipophilic methyl ester of ALA, which may demonstrate better tumour selectivity. There are currently limited data comparing these two agents, with no difference in tumour response (by histology) in one study of patients with nBCC receiving either ALA-PDT (n = 22) or MAL-PDT (n = 21) using identical regimens including surgical debulking of half of the tumours in each group prior to treatment.[145] MAL-PDT is currently the only licensed form of topical PDT for the treatment of BCC.

The use of MAL-PDT has been compared with both cryotherapy and surgery in the treatment of BCC. Clinical clearance at 3 months of 97% of 102 sBCCs treated by MAL-PDT compared with 95% of 98 lesions treated with cryotherapy in a randomized multicentre study was described in a review article.[146] The cosmetic outcome was superior following PDT, with a good or excellent outcome reported in 89% (PDT) and 50% (cryotherapy). During 48 months of follow up, recurrence rates of 22% (PDT) and 19% (cryotherapy) were reported. In another study previously mentioned in the

curettage section, 91% of 131 sBCCs cleared following MAL-PDT, with 9% of these recurring during 35 months of follow up.[107] The same study also treated nBCCs with MAL-PDT (following curette debulk), with initial clearance of 89% of 168 lesions. Subsequently, 12 thick and six thin tumours (14% and 7%, respectively) recurred during 35 months of follow up.

MAL-PDT (following nonpainful superficial curette or scalpel surface preparation) has been compared with surgical excision (> 5 mm margin) in the treatment of 105 nonfacial nBCCs in a multicentre randomized study. Clearance rates at 3 months were 91% (PDT) and 98% (surgery), and cosmetic outcome rated as good/excellent in 83% (PDT) and 33% (surgery).[147] The same researchers reported long-term (60 months) recurrence rates of 14% (PDT) and 4% (surgery).[148]

A multicentre study of patients considered to be at high risk of complications, poor cosmesis, disfigurement and/or recurrence reported histologically confirmed initial (3 months) clearance rates following MAL-PDT treatment of 85% (40 of 47) for sBCCs and 75% (38 of 51) for nBCCs, with long-term (24 months) recurrence rates of 22% and 18%, respectively.[149] In a similar multicentre study, 148 sBCCs and nBCCs regarded by the authors as 'difficult-to-treat' (defined as large and/or central facial lesions, or patients at increased risk of surgical complications) received MAL-PDT treatment.[150] Histologically confirmed clearance rates at 3 months were 93% (sBCC) and 82% (nBCC). The authors used a time-to-event approach to estimate sustained lesion clearance rates of 82% (sBCC) and 67% (nBCC) at 24 months. These data suggest that MAL-PDT may be an option for high-risk disease when other more effective treatments are either contraindicated or unacceptable to patients.

Some patients with BCNS responded to PDT using either red (~630 nm) or blue (~417 nm) light sources, but experience is limited to case reports.[151,152] To date, there is no good evidence to support the use of PDT for infiltrative or recurrent BCC. Topical PDT can be a time-consuming procedure, especially if performed on multiple occasions. Pain during the illumination phase is significant for some patients and ranges from a stinging or burning sensation to occasionally severe discomfort. A number of measures can reduce this pain, including the use of fans, directed cool air, simple analgesia or local anaesthesia. Following PDT the area tends to swell and then form a crust which takes a few weeks to separate.[153]

Evidence levels: *Photodynamic therapy is a good treatment for primary superficial BCC. (Strength of recommendation A, quality of evidence I).*

Photodynamic therapy is a reasonable treatment for primary low-risk nodular BCC. (Strength of recommendation B, quality of evidence I).

Radiotherapy

RT is effective in the treatment of primary BCC,[154–158] surgically recurrent BCC,[159] as adjuvant therapy, and is probably the treatment of choice for high-risk disease in patients who are unwilling or unable to tolerate surgery.[159,160] RT is a complex mix of different techniques including superficial RT (generated at up to 170 kV) which is suitable for lesions up to ~6 mm in depth, electron beam therapy (generated at higher energies) which penetrates deeper tissues, and brachytherapy which is useful for lesions arising on curved surfaces. Due to the expensive nature of the equipment involved, RT is usually available only at major hospital centres. RT can be used in an adjuvant role, for example following incomplete excision of high-risk BCC. Poor long-term cosmetic results which were once a significant problem are much less likely following treatment using modern techniques. Fractionated treatment regimens (which repeatedly exploit the difference in radiosensitivity between malignant and normal tissues) generally produce superior cosmetic outcomes compared with single-fraction treatment, although this obviously requires multiple hospital visits. In the elderly, infirm patient, single-fraction regimens are still used, as the long-term cosmetic result of treatment is less of a concern. All RT treatments are a careful compromise between the likelihood of tumour destruction and an acceptable risk of radionecrosis (a 5% level being generally accepted as a maximum, and most clinical oncologists aiming for a much lower level). Different anatomical areas have different RT tolerances, with the head and neck generally tolerating RT well. However, certain areas such as the upper eyelid can be difficult to treat. The bridge of the nose, where thin skin overlies bone and is often subjected to repeated minor trauma from spectacles, is an area historically associated with a particularly high risk of radionecrosis. However, RT can be used successfully on many facial sites and studies have reported good outcomes following treatment of BCC on the nose,[155,158,159,161] lip,[162] ear[155,163] and periorbital[155,164] skin.

Unfortunately, some studies of RT for facial BCC report treatment of all nonmelanoma cancers (BCC, squamous cell carcinoma and basosquamous cancer), and do not clearly differentiate tumour-specific outcomes. However, in all these studies, BCC was generally the single largest tumour group and consequently some of these studies are referenced in these guidelines.

Review articles have reported overall 5-year cure rates following RT of 91·3%[66] for primary BCC and 90·2%[59] for recurrent disease. Other studies suggest long-term (> 4 years) local control rates of 84%,[165] 86%,[157] 88%,[166] 92·5%[167] and 96%.[158]

Attempts have been made to compare RT with other treatment modalities. A randomized comparison trial of RT against cryotherapy (93 patients) resulted in 2-year cure rates of 96% and 61%, respectively.[168]

Surgical excision (91% with frozen section margin control) of 174 primary facial BCCs < 4 cm in diameter has been compared with RT (mix of interstitial brachytherapy, contact therapy and conventional RT) for 173 lesions.[167] The 4-year recurrence rates were 0·7% (surgery) and 7·5% (RT). Cosmetic outcome at 4 years was significantly superior following surgery (good cosmesis in 79%) compared with RT (good cosmesis in 40%), with altered pigmentation and telangiectasia in over 65% of RT patients, and radiodystrophy in 41%.[169]

RT is contraindicated in the re-treatment of BCC that has recurred following previous RT. RT may promote the growth of new BCC in patients with BCNS, and consequently should either be avoided or used with extreme caution in this patient group.[170]

Evidence levels: *Radiotherapy is a good treatment for primary BCC. (Strength of recommendation A, quality of evidence I).*

Radiotherapy is a good treatment for recurrent (but not radiorecurrent) BCC. (Strength of recommendation A, quality of evidence I).

Follow up

Following treatment of a BCC, all patients are at some degree of risk of both local recurrence (treatment failure) and the development of further primary BCC at other sites (new lesions). These risks form the basis of the arguments both for and against long-term specialist follow up.

The risk of local recurrence is an individual risk, based upon the tumour characteristics and the treatment used. However, for primary BCC treated appropriately by experienced practitioners, the recurrence rate should be low. This is not true for recurrent BCC, where recurrence rates are universally higher than for primary BCC. Patients who have had recurrent (especially multiply recurrent) lesions treated are particularly worthy of follow up in view of their relatively high risk of further recurrence. The timing of follow-up visits should take into account the generally slow growth rate of BCC. Evidence suggests that recurrent disease may take up to 5 years to present clinically, and that up to 18% of recurrent BCC may present even later.[100] In a review of all studies published since 1947 looking at the treatment of primary BCC by various modalities, less than one third of all recurrences presented in the first year of follow up, 50% presented within 2 years, and 66% within 3 years.[66]

The risk of developing further BCC has been studied in a number of ways. Marcil and Stern[171] conducted an English language literature review and meta-analysis and found seven studies assessing the risk of developing a second BCC. Overall, the 3-year cumulative risk ranged from 33% to 70% (mean 44%), representing an approximately 10-fold increase over the rate expected in a comparable general population. The highest rates (60–70%) came from studies including large populations of patients with at least two (sometimes more than two) previous BCCs, suggesting that as the number of BCC lesions increases, so does the risk of developing more. In contrast, patients with only their index BCC who remain disease free for 3 years appear to have a decreased ongoing risk of further BCC. There was no general agreement on particular risk factors which might confer a higher risk of subsequent BCC.

The findings have been supported by the results of a prospective study of two cohorts (total 1183) of private patients in Denmark[172] in whom 299 (25·3%) developed at least 777 new skin cancers during 2 years of follow up, 89·5% of these being BCC. A study based upon data stored by the Swiss Cancer Registry[173] suggested the risk of a second BCC was 8·45 times higher (measured over an unlimited time period) than expected in a comparable general population.

Various authors have tried to identify specific risk factors which might be associated with an increased risk of developing further BCC. Van Iersel *et al.*[174] confirmed an overall increase of subsequent BCC over a 5-year period and identified a possible higher risk in older patients, those with multiple BCC at first presentation, and those with an index tumour > 1 cm in size.

A clinical study of 1200 patients also suggested that the presence of multiple BCC at presentation was associated with increased risk of further BCC[175] and the same group also reported that an index BCC arising on the trunk appeared strongly associated with the development of further (usually also truncal) BCC;[176] this group has suggested that different mechanisms may determine the development of truncal BCC and head and neck BCC.[177]

Two studies have looked at current U.K. practice regarding BCC follow up. Dermatologists in Belfast[178] offered follow up at 12 and 24 months following surgical excision of midfacial primary BCC. They reported attendance rates of 78% at 12 months, falling to 53% at 2 years. A recurrence rate of $< 2\%$ (two of 121) over 2 years was reported, and new BCCs were detected in 11·6% of patients during the first year and 6·3% during the second year of follow up. In 2001 a survey of British dermatologists (68% response) asked about routine follow-up practice following the excision of a primary midfacial BCC. No follow up at all was offered by 27% of responders, 37% would offer one follow-up clinic visit, while 36% would offer more than one hospital-based review.[179]

Clearly, within the British healthcare system it is not possible to offer long-term follow up to all patients who have had their first and only primary BCC treated. Provided treatment has been selected appropriately and performed competently, these patients should, by definition, be at low risk of local recurrence and would benefit from sensible sun protection advice and counselling on the significant (possibly up to 44%) 3-year risk of the development of a second primary lesion. Such patients are probably suitable (with appropriate education and advice) for self-monitoring or follow up in primary care.[50] The case for follow up in either a primary or secondary care setting is stronger for patients who have been treated for recurrent disease (increased risk of further recurrence following all types of treatment) and those with a history of multiple BCCs (significantly increased risk of further BCC), although this would possibly need to be for at least 3 years, to reflect the available evidence base.

Conclusions

Many treatments are known to be effective in the treatment of BCC, ranging from topical therapy (e.g. IMQ) and minimally invasive procedures (e.g. PDT), through destructive modalities (e.g. C&C, cryosurgery) to more specialized treatments such as RT, wide surgical excision and MMS. An assessment of the relative risk of recurrence of an individual lesion will generally

Table 3 Primary basal cell carcinoma (BCC): influence of tumour type, size (large = > 2 cm) and site on the selection of treatment

BCC type: histology, size and site	PDT	Topical imiquimod	Curettage and cautery	Radiation therapy	Cryosurgery	Excision	Mohs surgery
Superficial, small and low-risk site	**	**	**	?	**	?	X
Nodular, small and low-risk site	*	–	**	?	**	***	X
Infiltrative, small and low-risk site	X	X	*	*	*	***	?
Superficial, large and low-risk site	***	**	**	*	**	*	?
Nodular, large and low-risk site	–	–	**	**	**	***	?
Infiltrative, large and low-risk site	X	X	–	*	*	***	**
Superficial, small and high-risk site	*	*	*	**	*	**	*
Nodular, small and high-risk site	–	–	*	**	**	***	**
Infiltrative, small and high-risk site	X	X	–	*	*	**	***
Superficial, large and high-risk site	*	*	–	*	*	**	**
Nodular, large and high-risk site	–	X	X	–	*	**	**
Infiltrative, large and high-risk site	X	X	X	X	X	*	***

PDT, photodynamic therapy; ***, probable treatment of choice; **, generally good choice; *, generally fair choice; ?, reasonable, but not often needed; –, generally poor choice; X, probably should not be used.

Table 4 Recurrent basal cell carcinoma (BCC): influence of tumour type, size (large = > 2 cm) and site on the selection treatment

BCC type: histology, size and site	PDT	Topical imiquimod	Curettage and cautery	Radiation therapy	Cryosurgery	Excision	Mohs surgery
Superficial, small and low-risk site	**	*	*	*	**	**	–
Nodular, small and low-risk site	–	X	**	**	**	***	–
Infiltrative, small and low-risk site	X	X	–	**	**	***	*
Superficial, large and low-risk site	**	*	*	**	**	*	*
Nodular, large and low-risk site	X	X	–	*	*	***	*
Infiltrative, large and low-risk site	X	X	–	*	*	**	**
Superficial, small and high-risk site	?	X	*	*	*	**	**
Nodular, small and high-risk site	X	X	*	*	*	***	**
Infiltrative, small and high-risk site	X	X	X	*	*	**	***
Superficial, large and high-risk site	?	X	X	*	–	**	**
Nodular, large and high-risk site	X	X	X	–	–	**	***
Infiltrative, large and high-risk site	X	X	X	–	–	*	***

PDT, photodynamic therapy; ***, probable treatment of choice; **, generally good choice; *, generally fair choice; ?, reasonable, but not often needed; –, generally poor choice; X, probably should not be used.

be a useful way of identifying the most appropriate treatment modalities. For example, low-risk disease is generally suitable for topical therapy, C&C, cryotherapy, simple excision and PDT, while high-risk BCC is generally better managed with wide surgical excision, RT and MMS.

An indication of the relative value of the various treatment modalities covered in these guidelines is summarized in Table 3 (primary BCCs) and Table 4 (recurrent BCCs). While heavily based upon the overall likelihood of cure, these recommendations also take into account practicality of use, side-effects, cosmetic outcomes, and patient acceptability.

Disclaimer

These guidelines have been prepared for dermatologists on behalf of the British Association of Dermatologists and are based on the best data available at the time the report was prepared. Caution should be exercised when interpreting the data where there is a limited evidence base. The results of future studies may require alteration of the conclusions or recommendations in this report. It may be necessary to depart from the guidelines in the interests of specific patients and special circumstances. Just as adherence to guidelines may not constitute defence against a claim of negligence, so deviation from them should not necessarily be deemed negligent.

References

1 Kuijpers DI, Thissen MR, Neumann MH. Basal cell carcinoma: treatment options and prognosis, a scientific approach to a common malignancy. *Am J Clin Dermatol* 2002; **3**:247–59.

2 Thissen MR, Neumann MH, Schouten LJ. A systematic review of treatment modalities for primary basal cell carcinomas. *Arch Dermatol* 1999; **135**:1177–83.

3 Braun RP, Klumb F, Girard C *et al.* Three-dimensional reconstruction of basal cell carcinomas. *Dermatol Surg* 2005; **31**:562–6.
4 Breuninger H, Dietz K. Prediction of subclinical tumor infiltration in basal cell carcinoma. *J Dermatol Surg Oncol* 1991; **17**:574–8.
5 Hendrix JD Jr, Parlette HL. Duplicitous growth of infiltrative basal cell carcinoma: analysis of clinically undetected tumor extent in a paired case–control study. *Dermatol Surg* 1996; **22**:535–9.
6 Lo JS, Snow SN, Reizner GT *et al.* Metastatic basal cell carcinoma: report of twelve cases with a review of the literature. *J Am Acad Dermatol* 1991; **24**:715–19.
7 Ting PT, Kasper R, Arlette JP. Metastatic basal cell carcinoma: report of two cases and literature review. *J Cutan Med Surg* 2005; **9**:10–15.
8 Costantino D, Lowe L, Brown DL. Basosquamous carcinoma – an under-recognized, high-risk cutaneous neoplasm: case study and review of the literature. *J Plast Reconstr Aesthet Surg* 2006; **59**:424–8.
9 Gilbody JS, Aitken J, Green A. What causes basal cell carcinoma to be the commonest cancer? *Aust J Public Health* 1994; **18**:218–21.
10 Miller DL, Weinstock MA. Nonmelanoma skin cancer in the United States: incidence. *J Am Acad Dermatol* 1994; **30**:774–8.
11 Goodwin RG, Holme SA, Roberts DL. Variations in registration of skin cancer in the United Kingdom. *Clin Exp Dermatol* 2004; **29**:328–30.
12 Diffey BL, Langtry JA. Skin cancer incidence and the ageing population. *Br J Dermatol* 2005; **153**:679–80.
13 Gailani MR, Leffell DJ, Ziegler A *et al.* Relationship between sunlight exposure and a key genetic alteration in basal cell carcinoma. *J Natl Cancer Inst* 1996; **88**:349–54.
14 Roenigk RK, Ratz JL, Bailin PL, Wheeland RG. Trends in the presentation and treatment of basal cell carcinomas. *J Dermatol Surg Oncol* 1986; **12**:860–5.
15 Lindgren G, Diffey BL. Basal cell carcinoma of the eyelids and solar ultraviolet radiation exposure. *Br J Ophthalmol* 1998; **82**:1412–15.
16 Corona R, Dogliotti E, D'Errico M *et al.* Risk factors for basal cell carcinoma in a Mediterranean population: role of recreational sun exposure early in life. *Arch Dermatol* 2001; **137**:1162–8.
17 Zak-Prelich M, Narbutt J, Sysa-Jedrzejowska A. Environmental risk factors predisposing to the development of basal cell carcinoma. *Dermatol Surg* 2004; **30**:248–52.
18 McNaughton SA, Marks GC, Green AC. Role of dietary factors in the development of basal cell cancer of the skin. *Cancer Epidemiol Biomarkers Prev* 2005; **14**:1596–607.
19 Gorlin RJ. Nevoid basal cell carcinoma (Gorlin) syndrome. *Genet Med* 2004; **6**:530–9.
20 Felder S, Rabinovitz H, Oliviero M, Kopf A. Dermoscopic differentiation of a superficial basal cell carcinoma and squamous cell carcinoma *in situ*. *Dermatol Surg* 2006; **32**:423–5.
21 Bakis S, Irwig L, Wood G, Wong D. Exfoliative cytology as a diagnostic test for basal cell carcinoma: a meta-analysis. *Br J Dermatol* 2004; **150**:829–36.
22 Williams LS, Mancuso AA, Mendenhall WM. Perineural spread of cutaneous squamous and basal cell carcinoma: CT and MR detection and its impact on patient management and prognosis. *Int J Radiat Oncol Biol Phys* 2001; **49**:1061–9.
23 Leibovitch I, McNab A, Sullivan T *et al.* Orbital invasion by periocular basal cell carcinoma. *Ophthalmology* 2005; **112**:717–23.
24 Meads SB, Greenway HT. Basal cell carcinoma associated with orbital invasion: clinical features and treatment options. *Dermatol Surg* 2006; **32**:442–6.
25 Farley RL, Manolidis S, Ratner D. Aggressive basal cell carcinoma with invasion of the parotid gland, facial nerve, and temporal bone. *Dermatol Surg* 2006; **32**:307–15.
26 Randle HW. Basal cell carcinoma: identification and treatment of the high-risk patient. *Dermatol Surg* 1996; **22**:255–61.
27 Batra RS, Kelley LC. A risk scale for predicting extensive subclinical spread of nonmelanoma skin cancer. *Dermatol Surg* 2002; **28**:107–12.
28 Bath-Hextall F, Perkins W, Bong J, Williams H. Interventions for basal cell carcinoma of the skin. *Cochrane Database Syst Rev* 2007; **1**:CD003412.
29 Ceilley RI, Del Rosso JQ. Current modalities and new advances in the treatment of basal cell carcinoma. *Int J Dermatol* 2006; **45**:489–98.
30 Telfer NR, Colver GB, Bowers PW. Guidelines for the management of basal cell carcinoma. *Br J Dermatol* 1999; **141**:415–23.
31 Drake LA, Ceilley RI, Cornelison RL *et al.* Guidelines of care for basal cell carcinoma. The American Academy of Dermatology Committee on Guidelines of Care. *J Am Acad Dermatol* 1992; **26**:117–20.
32 Backous DD, DeMonte F, El-Naggar A *et al.* Craniofacial resection for nonmelanoma skin cancer of the head and neck. *Laryngoscope* 2005; **115**:931–7.
33 Smeets N. Little evidence available on treatments for basal cell carcinoma of the skin. *Cancer Treat Rev* 2005; **31**:143–6.
34 Cataldo PA, Stoddard PB, Reed WP. Use of frozen section analysis in the treatment of basal cell carcinoma. *Am J Surg* 1990; **159**:561–3.
35 Walker P, Hill D. Surgical treatment of basal cell carcinomas using standard postoperative histological assessment. *Australas J Dermatol* 2006; **47**:1–12.
36 Marchac D, Papadopoulos O, Duport G. Curative and aesthetic results of surgical treatment of 138 basal-cell carcinomas. *J Dermatol Surg Oncol* 1982; **8**:379–87.
37 Griffiths RW, Suvarna SK, Stone J. Do basal cell carcinomas recur after complete conventional surgical excision? *Br J Plast Surg* 2005; **58**:795–805.
38 Johnson TM, Tromovitch TA, Swanson NA. Combined curettage and excision: a treatment method for primary basal cell carcinoma. *J Am Acad Dermatol* 1991; **24**:613–17.
39 Chiller K, Passaro D, McCalmont T, Vin-Christian K. Efficacy of curettage before excision in clearing surgical margins of nonmelanoma skin cancer. *Arch Dermatol* 2000; **136**:1327–32.
40 Wolf DJ, Zitelli JA. Surgical margins for basal cell carcinoma. *Arch Dermatol* 1987; **123**:340–4.
41 Kimyai-Asadi A, Goldberg LH, Peterson SR *et al.* Efficacy of narrow-margin excision of well-demarcated primary facial basal cell carcinomas. *J Am Acad Dermatol* 2005; **53**:464–8.
42 Kimyai-Asadi A, Goldberg LH, Jih MH. Accuracy of serial transverse cross-sections in detecting residual basal cell carcinoma at the surgical margins of an elliptical excision specimen. *J Am Acad Dermatol* 2005; **53**:469–74.
43 Kumar P, Orton CI, McWilliam LJ, Watson S. Incidence of incomplete excision in surgically treated basal cell carcinoma: a retrospective clinical audit. *Br J Plast Surg* 2000; **35**:563–6.
44 Griffiths RW. Audit of histologically incompletely excised basal cell carcinomas: recommendations for management by re-excision. *Br J Plast Surg* 1999; **52**:24–8.
45 Dieu T, Macleod AM. Incomplete excision of basal cell carcinomas: a retrospective audit. *Aust NZ J Surg* 2002; **72**:219–21.
46 Sussman LA, Liggins DF. Incompletely excised basal cell carcinoma: a management dilemma? *Aust NZ J Surg* 1996; **66**:276–8.
47 Wilson AW, Howsam G, Santhanam V *et al.* Surgical management of incompletely excised basal cell carcinomas of the head and neck. *Br J Oral Maxillofac Surg* 2004; **42**:311–14.
48 Grabski WJ, Salasche SJ. Positive surgical excision margins of a basal cell carcinoma. *Dermatol Surg* 1998; **24**:921–4.

49 Richmond JD, Davie RM. The significance of incomplete excision in patients with basal cell carcinoma. *Br J Plast Surg* 1987; **40**:63–7.

50 Park AJ, Strick M, Watson JD. Basal cell carcinomas: do they need to be followed up? *J R Coll Surg Edinb* 1994; **39**:109–11.

51 De Silva SP, Dellon AL. Recurrence rate of positive margin basal cell carcinoma: results of a five-year prospective study. *J Surg Oncol* 1985; **28**:72–4.

52 Bieley HC, Kirsner RS, Reyes BA, Garland LD. The use of Mohs micrographic surgery for determination of residual tumor in incompletely excised basal cell carcinoma. *J Am Acad Dermatol* 1992; **26**:754–6.

53 Liu FF, Maki E, Warde P *et al.* A management approach to incompletely excised basal cell carcinomas of skin. *Int J Radiat Oncol Biol Phys* 1991; **20**:423–8.

54 Hauben DJ, Zirkin H, Mahler D, Sacks M. The biologic behavior of basal cell carcinoma: part I. *Plast Reconstr Surg* 1982; **69**:103–9.

55 Robinson JK, Fisher SG. Recurrent basal cell carcinoma after incomplete resection. *Arch Dermatol* 2000; **136**:1318–24.

56 Berlin J, Katz KH, Helm KF, Maloney ME. The significance of tumor persistence after incomplete excision of basal cell carcinoma. *J Am Acad Dermatol* 2002; **46**:549–53.

57 Koplin L, Zarem HA. Recurrent basal cell carcinoma: a review concerning the incidence, behavior, and management of recurrent basal cell carcinoma, with emphasis on the incompletely excised lesion. *Plast Reconstr Surg* 1980; **65**:656–64.

58 Boulinguez S, Grison-Tabone C, Lamant L *et al.* Histological evolution of recurrent basal cell carcinoma and therapeutic implications for incompletely excised lesions. *Br J Dermatol* 2004; **151**:623–6.

59 Rowe DE, Carroll RJ, Day CL. Mohs surgery is the treatment of choice for recurrent (previously treated) basal cell carcinoma. *J Dermatol Surg Oncol* 1989; **15**:424–31.

60 Burg G, Hirsch RD, Konz B, Braun-Falco O. Histographic surgery: accuracy of visual assessment of the margins of basal-cell epithelioma. *J Dermatol Surg Oncol* 1975; **1**:21–4.

61 Mohs FE. Chemosurgery for skin cancer: fixed tissue and fresh tissue techniques. *Arch Dermatol* 1976; **112**:211–15.

62 Lawrence CM. Mohs' micrographic surgery for basal cell carcinoma. *Clin Exp Dermatol* 1999; **24**:130–3.

63 Nelson BR, Railan D, Cohen S. Mohs' micrographic surgery for nonmelanoma skin cancers. *Clin Plast Surg* 1997; **24**:705–18.

64 Wennberg AM, Larko O, Stenquist B. Five-year results of Mohs' micrographic surgery for aggressive facial basal cell carcinoma in Sweden. *Acta Derm Venereol (Stockh)* 1999; **79**:370–2.

65 Williford PM, Feldman SR. Surgery for basal-cell carcinoma of the face. *Lancet* 2004; **364**:1732–3.

66 Rowe DE, Carroll RJ, Day CL Jr *et al.* Long-term recurrence rates in previously untreated (primary) basal cell carcinoma: implications for patient follow-up. *J Dermatol Surg Oncol* 1989; **15**:315–28.

67 Malhotra R, Huilgol SC, Huynh NT, Selva D. The Australian Mohs database, part II: periocular basal cell carcinoma outcome at 5-year follow-up. *Ophthalmology* 2004; **111**:631–6.

68 Leibovitch I, Huilgol SC, Selva D *et al.* Basal cell carcinoma treated with Mohs surgery in Australia II. Outcome at 5-year follow-up. *J Am Acad Dermatol* 2005; **53**:452–7.

69 Smeets NW, Kuijpers DI, Nelemans P *et al.* Mohs' micrographic surgery for treatment of basal cell carcinoma of the face – results of a retrospective study and review of the literature. *Br J Dermatol* 2004; **151**:141–7.

70 Kimyai-Asadi A, Goldberg LH, Peterson SR *et al.* The incidence of major complications from Mohs micrographic surgery performed in office-based and hospital-based settings. *J Am Acad Dermatol* 2005; **53**:628–34.

71 Cook JL, Perone JB. A prospective evaluation of the incidence of complications associated with Mohs micrographic surgery. *Arch Dermatol* 2003; **139**:143–52.

72 Dobke MK, Miller SH. Tissue repair after Mohs surgery. A plastic surgeon's view. *Dermatol Surg* 1997; **23**:1061–6.

73 Stein JM, Hrabovsky S, Schuller DE, Siegle RJ. Mohs micrographic surgery and the otolaryngologist. *Am J Otolaryngol* 2004; **25**:385–93.

74 Inkster C, Ashworth J, Murdoch JR *et al.* Oculoplastic reconstruction following Mohs surgery. *Eye* 1998; **12**:214–18.

75 Sciscio A, Stewart K, Grewal J *et al.* Periocular Mohs micrographic surgery: results of a dual-site day-surgery service. *Orbit* 2001; **20**:209–15.

76 Breuninger H. Micrographic surgery of malignant skin tumors: a comparison of the frozen technique with paraffin sectioning. *Facial Plast Surg* 1997; **13**:79–82.

77 der Plessis PJ, Dahl MG, Malcolm AJ *et al.* Mohs' surgery of periocular basal cell carcinoma using formalin-fixed sections and delayed closure. *Br J Dermatol* 1998; **138**:1003–8.

78 Skaria AM, Salomon D. Mohs' surgery of periocular basal cell carcinoma using formalin-fixed sections and delayed closure. *Br J Dermatol* 1999; **140**:775.

79 Wong VA, Marshall JA, Whitehead KJ *et al.* Management of periocular basal cell carcinoma with modified *en face* frozen section controlled excision. *Ophthal Plast Reconstr Surg* 2002; **18**:430–5.

80 Strong JW, Worsham GF, Hagerty RC. Peripheral in-continuity tissue examination: a modification of Mohs' micrographic surgery. *Clin Plast Surg* 2004; **31**:1–4.

81 Boztepe G, Hohenleutner S, Landthaler M, Hohenleutner U. Munich method of micrographic surgery for basal cell carcinomas: 5-year recurrence rates with life-table analysis. *Acta Derm Venereol (Stockh)* 2004; **84**:218–22.

82 Bentkover SH, Grande DM, Soto H *et al.* Excision of head and neck basal cell carcinoma with a rapid, cross-sectional, frozen-section technique. *Arch Facial Plast Surg* 2002; **4**:114–19.

83 Niederhagen B, von Lindern JJ, Berge S *et al.* Staged operations for basal cell carcinoma of the face. *Br J Oral Maxillofac Surg* 2000; **38**:477–9.

84 Hsuan JD, Harrad RA, Potts MJ, Collins C. Small margin excision of periocular basal cell carcinoma: 5 year results. *Br J Ophthalmol* 2004; **88**:358–60.

85 David DB, Gimblett ML, Potts MJ, Harrad RA. Small margin (2 mm) excision of peri-ocular basal cell carcinoma with delayed repair. *Orbit* 1999; **18**:11–15.

86 Cook J, Zitelli JA. Mohs micrographic surgery: a cost analysis. *J Am Acad Dermatol* 1998; **39**:698–703.

87 Bialy TL, Whalen J, Veledar E *et al.* Mohs micrographic surgery vs traditional surgical excision: a cost comparison analysis. *Arch Dermatol* 2004; **140**:736–42.

88 Essers BA, Dirksen CD, Nieman FH *et al.* Cost-effectiveness of Mohs micrographic surgery vs surgical excision for basal cell carcinoma of the face. *Arch Dermatol* 2006; **142**:187–94.

89 Smeets NW, Krekels GA, Ostertag JU *et al.* Surgical excision vs Mohs' micrographic surgery for basal-cell carcinoma of the face: randomised controlled trial. *Lancet* 2004; **364**:1766–72.

90 Otley CC. Mohs' micrographic surgery for basal-cell carcinoma of the face. *Lancet* 2005; **365**:1226–7.

91 Reymann F. 15 years' experience with treatment of basal cell carcinomas of the skin with curettage. *Acta Derm Venereol (Stockh)* 1985; **120** (Suppl.):56–9.

92 Sheridan AT, Dawber RP. Curettage, electrosurgery and skin cancer. *Australas J Dermatol* 2000; **41**:19–30.

93 Edens BL, Bartlow GA, Haghighi P *et al.* Effectiveness of curettage and electrodesiccation in the removal of basal cell carcinoma. *J Am Acad Dermatol* 1983; **9**:383–8.
94 Barlow JO, Zalla MJ, Kyle A *et al.* Treatment of basal cell carcinoma with curettage alone. *J Am Acad Dermatol* 2006; **54**:1039–45.
95 McDaniel WE. Therapy for basal cell epitheliomas by curettage only. Further study. *Arch Dermatol* 1983; **119**:901–3.
96 Spiller WF, Spiller RF. Treatment of basal cell epithelioma by curettage and electrodesiccation. *J Am Acad Dermatol* 1984; **11**:808–14.
97 Kopf AW, Bart RS, Schrager D *et al.* Curettage-electrodesiccation treatment of basal cell carcinomas. *Arch Dermatol* 1977; **113**:439–43.
98 Motley RJ, Gould DJ, Douglas WS, Simpson NB. Treatment of basal cell carcinoma by dermatologists in the United Kingdom. British Association of Dermatologists Audit Subcommittee and the British Society for Dermatological Surgery. *Br J Dermatol* 1995; **132**:437–40.
99 Carlson KC, Connolly SM, Winkelmann RK. Basal cell carcinoma on the lower extremity. *J Dermatol Surg Oncol* 1994; **20**:258–9.
100 Silverman MK, Kopf AW, Grin CM *et al.* Recurrence rates of treated basal cell carcinomas. Part 2: curettage-electrodesiccation. *J Dermatol Surg Oncol* 1991; **17**:720–6.
101 Salasche SJ. Curettage and electrodesiccation in the treatment of midfacial basal cell epithelioma. *J Am Acad Dermatol* 1983; **8**:496–503.
102 Suhge d'Aubermont PC, Bennett RG. Failure of curettage and electrodesiccation for removal of basal cell carcinoma. *Arch Dermatol* 1984; **120**:1456–60.
103 Spencer JM, Tannenbaum A, Sloan L, Amonette RA. Does inflammation contribute to the eradication of basal cell carcinoma following curettage and electrodesiccation? *Dermatol Surg* 1997; **23**:625–30.
104 Nouri K, Spencer JM, Taylor JR *et al.* Does wound healing contribute to the eradication of basal cell carcinoma following curettage and electrodesiccation? *Dermatol Surg* 1999; **25**:183–7.
105 Wu JK, Oh C, Strutton G, Siller G. An open-label, pilot study examining the efficacy of curettage followed by imiquimod 5% cream for the treatment of primary nodular basal cell carcinoma. *Australas J Dermatol* 2006; **47**:46–8.
106 Spencer JM. Pilot study of imiquimod 5% cream as adjunctive therapy to curettage and electrodesiccation for nodular basal cell carcinoma. *Dermatol Surg* 2006; **32**:63–9.
107 Soler AM, Warloe T, Berner A, Gierckskey KE. A follow-up study of recurrence and cosmesis in completely responding superficial and nodular basal cell carcinomas treated with methyl 5-aminolaevulinate-based photodynamic therapy alone and with prior curettage. *Br J Dermatol* 2001; **145**:467–71.
108 Nordin P, Stenquist B. Five-year results of curettage-cryosurgery for 100 consecutive auricular non-melanoma skin cancers. *J Laryngol Otol* 2002; **116**:893–8.
109 Graham G. Statistical data on malignant tumors in cryosurgery: 1982. *J Dermatol Surg Oncol* 1983; **9**:238–9.
110 Zacarian SA. Cryosurgery of cutaneous carcinomas. An 18 year study of 3,022 patients with 4,228 carcinomas. *J Am Acad Dermatol* 1983; **9**:947–56.
111 Mallon E, Dawber R. Cryosurgery in the treatment of basal cell carcinoma. Assessment of one and two freeze-thaw cycle schedules. *Dermatol Surg* 1996; **22**:854–8.
112 Goncalves JC. Fractional cryosurgery. A new technique for basal cell carcinoma of the eyelids and periorbital area. *Dermatol Surg* 1997; **23**:475–81.
113 Holt PJ. Cryotherapy for skin cancer: results over a 5-year period using liquid nitrogen spray cryosurgery. *Br J Dermatol* 1988; **119**:231–40.
114 Giuffrida TJ, Jimenez G, Nouri K. Histologic cure of basal cell carcinoma treated with cryosurgery. *J Am Acad Dermatol* 2003; **49**:483–6.
115 Kokoszka A, Scheinfeld N. Evidence-based review of the use of cryosurgery in treatment of basal cell carcinoma. *Dermatol Surg* 2003; **29**:566–71.
116 Bernardeau K, Derancourt C, Cambie M *et al.* [Cryosurgery of basal cell carcinoma: a study of 358 patients]. *Ann Dermatol Venereol* 2000; **127**:175–9.
117 Kuflik EG, Gage AA. The five-year cure rate achieved by cryosurgery for skin cancer. *J Am Acad Dermatol* 1991; **24**:1002–4.
118 Kuflik EG. Cryosurgery for skin cancer: 30-year experience and cure rates. *Dermatol Surg* 2004; **30**:297–300.
119 Jaramillo-Ayerbe F. Cryosurgery in difficult to treat basal cell carcinoma. *Int J Dermatol* 2000; **39**:223–9.
120 Kuflik EG, Gage AA. Recurrent basal cell carcinoma treated with cryosurgery. *J Am Acad Dermatol* 1997; **37**:82–4.
121 Buschmann W. A reappraisal of cryosurgery for eyelid basal cell carcinomas. *Br J Ophthalmol* 2002; **86**:453–7.
122 Anders M, Sporl E, Krantz H *et al.* [Cryotherapy of malignant eyelid tumors]. *Ophthalmologe* 1995; **92**:787–92.
123 Tuppurainen K. Cryotherapy for eyelid and periocular basal cell carcinomas: outcome in 166 cases over an 8-year period. *Graefes Arch Clin Exp Ophthalmol* 1995; **233**:205–8.
124 Gunnarson G, Larko O, Hersle K. Cryosurgery of eyelid basal cell carcinomas. *Acta Ophthalmol (Copenh)* 1990; **68**:241–5.
125 Wang I, Bendsoe N, Klinteberg CA *et al.* Photodynamic therapy vs. cryosurgery of basal cell carcinomas: results of a phase III clinical trial. *Br J Dermatol* 2001; **144**:832–40.
126 Thissen MR, Nieman FH, Ideler AH *et al.* Cosmetic results of cryosurgery vs. surgical excision for primary uncomplicated basal cell carcinomas of the head and neck. *Dermatol Surg* 2000; **26**:759–64.
127 Nouri K, Chang A, Trent JT, Jimenez GP. Ultrapulse CO_2 used for the successful treatment of basal cell carcinomas found in patients with basal cell nevus syndrome. *Dermatol Surg* 2002; **28**:287–90.
128 Stockfleth E, Trefzer U, Garcia-Bartels C *et al.* The use of toll-like receptor-7 agonist in the treatment of basal cell carcinoma: an overview. *Br J Dermatol* 2003; **149** (Suppl. 66):53–6.
129 Marks R, Gebauer K, Shumack S *et al.* Imiquimod 5% cream in the treatment of superficial basal cell carcinoma: results of a multicenter 6-week dose–response trial. *J Am Acad Dermatol* 2001; **44**:807–13.
130 Geisse JK, Rich P, Pandya A *et al.* Imiquimod 5% cream for the treatment of superficial basal cell carcinoma: a double-blind, randomized, vehicle-controlled study. *J Am Acad Dermatol* 2002; **47**:390–8.
131 Geisse J, Caro I, Lindholm J *et al.* Imiquimod 5% cream for the treatment of superficial basal cell carcinoma: results from two phase III, randomized, vehicle-controlled studies. *J Am Acad Dermatol* 2004; **50**:722–33.
132 Schulze HJ, Cribier B, Requena L *et al.* Imiquimod 5% cream for the treatment of superficial basal cell carcinoma: results from a randomized vehicle-controlled phase III study in Europe. *Br J Dermatol* 2005; **152**:939–47.
133 Gollnick H, Barona CG, Frank RG *et al.* Recurrence rate of superficial basal cell carcinoma following successful treatment with imiquimod 5% cream: interim 2-year results from an ongoing 5-year follow-up study in Europe. *Eur J Dermatol* 2005; **15**:374–81.
134 Shumack S, Robinson J, Kossard S *et al.* Efficacy of topical 5% imiquimod cream for the treatment of nodular basal cell carcinoma: comparison of dosing regimens. *Arch Dermatol* 2002; **138**:1165–71.
135 Eigentler TK, Kamin A, Weide BM *et al.* A phase III, randomized, open label study to evaluate the safety and efficacy of imiquimod

5% cream applied thrice weekly for 8 and 12 weeks in the treatment of low risk nodular basal cell carcinoma. *J Am Acad Dermatol* 2007; **57**:616–21.
136 Vidal D, Matias-Guiu X, Alomar A. Fifty-five basal cell carcinomas treated with topical imiquimod: outcome at 5-year follow-up. *Arch Dermatol* 2007; **143**:266–8.
137 Sterry W, Ruzicka T, Herrera E *et al.* Imiquimod 5% cream for the treatment of superficial and nodular basal cell carcinoma: randomized studies comparing low-frequency dosing with and without occlusion. *Br J Dermatol* 2002; **147**:1227–36.
138 Kagy MK, Amonette R. The use of imiquimod 5% cream for the treatment of superficial basal cell carcinomas in a basal cell nevus syndrome patient. *Dermatol Surg* 2000; **26**:577–8.
139 Stockfleth E, Ulrich C, Hauschild A *et al.* Successful treatment of basal cell carcinomas in a nevoid basal cell carcinoma syndrome with topical 5% imiquimod. *Eur J Dermatol* 2002; **12**:569–72.
140 Micali G, De Pasquale R, Caltabiano R *et al.* Topical imiquimod treatment of superficial and nodular basal cell carcinomas in patients affected by basal cell nevus syndrome: a preliminary report. *J Dermatolog Treat* 2002; **13**:123–7.
141 Nikkels AF, Pierard-Franchimont C, Nikkels-Tassoudji N *et al.* Photodynamic therapy and imiquimod immunotherapy for basal cell carcinomas. *Acta Clin Belg* 2005; **60**:227–34.
142 Morton CA, Brown SB, Collins S *et al.* Guidelines for topical photodynamic therapy: report of a workshop of the British Photodermatology Group. *Br J Dermatol* 2002; **146**:552–67.
143 Varma S, Wilson H, Kurwa HA *et al.* Bowen's disease, solar keratoses and superficial basal cell carcinomas treated by photodynamic therapy using a large-field incoherent light source. *Br J Dermatol* 2001; **144**:567–74.
144 Clark C, Bryden A, Dawe R *et al.* Topical 5-aminolaevulinic acid photodynamic therapy for cutaneous lesions: outcome and comparison of light sources. *Photodermatol Photoimmunol Photomed* 2003; **19**:134–41.
145 Kuijpers D, Thissen MR, Thissen CA, Neumann MH. Similar effectiveness of methyl aminolevulinate and 5-aminolevulinate in topical photodynamic therapy for nodular basal cell carcinoma. *J Drugs Dermatol* 2006; **5**:642–5.
146 Braathen LR, Szeimies R-M, Basset-Seguin N *et al.* Guidelines on the use of photodynamic therapy for nonmelanoma skin cancer. An international consensus. *J Am Acad Dermatol* 2007; **56**:125–43.
147 Rhodes LE, de Rie M, Enström Y *et al.* Photodynamic therapy using topical methyl aminolevulinate vs surgery for nodular basal cell carcinoma. Results of a multicenter randomized prospective trial. *Arch Dermatol* 2004; **140**:17–23.
148 Rhodes LE, de Rie MA, Leifsdottir R *et al.* Five year follow-up of a randomized, prospective trial of methyl aminolevulinate photodynamic therapy vs surgery for nodular basal cell carcinoma. *Arch Dermatol* 2007; **143**:1131–6.
149 Horn M, Wolf P, Wulf HC *et al.* Topical methyl aminolevulinate photodynamic therapy in patients with basal cell carcinoma prone to complications and poor cosmetic outcome with conventional treatment. *Br J Dermatol* 2003; **149**:1242–9.
150 Vinciullo C, Elliott T, Francis D *et al.* Photodynamic therapy with topical methyl aminolaevulinate for 'difficult-to-treat' basal cell carcinoma. *Br J Dermatol* 2005; **152**:765–72.
151 Oseroff AR, Shieh S, Frawley NP *et al.* Treatment of diffuse basal cell carcinomas and basaloid follicular hamartomas in nevoid basal cell carcinoma syndrome by wide-area 5-aminolevulinic acid photodynamic therapy. *Arch Dermatol* 2005; **141**:60–7.
152 Itkin A, Gilchrest BA. delta-Aminolevulinic acid and blue light photodynamic therapy for the treatment of multiple basal cell carcinomas in two patients with nevoid basal cell carcinoma syndrome. *Dermatol Surg* 2004; **30**:1054–61.
153 Morton CA. Methyl aminolevulinate (Metfix) photodynamic therapy – practical pearls. *J Dermatolog Treat* 2003; **14** (Suppl. 3):23–6.
154 Al-Othman MO, Mendenhall WM, Amdur RJ. Radiotherapy alone for clinical T4 skin carcinoma of the head and neck with surgery reserved for salvage. *Am J Otolaryngol* 2001; **22**:387–90.
155 Rio E, Bardet E, Ferron C *et al.* Interstitial brachytherapy of periorificial skin carcinomas of the face: a retrospective study of 97 cases. *Int J Radiat Oncol Biol Phys* 2005; **63**:753–7.
156 Guix B, Finestres F, Tello J *et al.* Treatment of skin carcinomas of the face by high-dose-rate brachytherapy and custom-made surface molds. *Int J Radiat Oncol Biol Phys* 2000; **47**:95–102.
157 Kwan W, Wilson D, Moravan V. Radiotherapy for locally advanced basal cell and squamous cell carcinomas of the skin. *Int J Radiat Oncol Biol Phys* 2004; **60**:406–11.
158 Childers BJ, Goldwyn RM, Ramos D *et al.* Long-term results of irradiation for basal cell carcinoma of the skin of the nose. *Plast Reconstr Surg* 1994; **93**:1169–73.
159 Caccialanza M, Piccinno R, Grammatica A. Radiotherapy of recurrent basal and squamous cell skin carcinomas: a study of 249 re-treated carcinomas in 229 patients. *Eur J Dermatol* 2001; **11**:25–8.
160 Finizio L, Vidali C, Calacione R *et al.* What is the current role of radiation therapy in the treatment of skin carcinomas? *Tumori* 2002; **88**:48–52.
161 Caccialanza M, Piccinno R, Moretti D, Rozza M. Radiotherapy of carcinomas of the skin overlying the cartilage of the nose: results in 405 lesions. *Eur J Dermatol* 2003; **13**:462–5.
162 Huynh NT, Veness MJ. Basal cell carcinoma of the lip treated with radiotherapy. *Australas J Dermatol* 2002; **43**:15–19.
163 Silva JJ, Tsang RW, Panzarella T *et al.* Results of radiotherapy for epithelial skin cancer of the pinna: the Princess Margaret Hospital experience, 1982–1993. *Int J Radiat Oncol Biol Phys* 2000; **47**:451–9.
164 Morrison WH, Garden AS, Ang KK. Radiation therapy for nonmelanoma skin carcinomas. *Clin Plast Surg* 1997; **24**:719–29.
165 Zagrodnik B, Kempf W, Seifert B *et al.* Superficial radiotherapy for patients with basal cell carcinoma; recurrence rates, histologic subtypes, and expression of p53 and Bcl-2. *Cancer* 2003; **98**:2708–14.
166 Caccialanza M, Piccinno R, Kolesnikova L, Gnecchi L. Radiotherapy of skin carcinomas of the pinna: a study of 115 lesions in 108 patients. *Int J Dermatol* 2005; **44**:513–17.
167 Avril MF, Auperin A, Margulis A *et al.* Basal cell carcinoma of the face: surgery or radiotherapy? Results of a randomized study. *Br J Cancer* 1997; **76**:100–6.
168 Hall VL, Leppard BJ, McGill J *et al.* Treatment of basal-cell carcinoma: comparison of radiotherapy and cryotherapy. *Clin Radiol* 1986; **37**:33–4.
169 Petit JY, Avril MF, Margulis A *et al.* Evaluation of cosmetic results of a randomized trial comparing surgery and radiotherapy in the treatment of basal cell carcinoma of the face. *Plast Reconstr Surg* 2000; **105**:2544–51.
170 Caccialanza M, Percivalle S, Piccinno R. Possibility of treating basal cell carcinomas of nevoid basal cell carcinoma syndrome with superficial X-ray therapy. *Dermatology* 2004; **208**:60–3.
171 Marcil I, Stern RS. Risk of developing a subsequent nonmelanoma skin cancer in patients with a history of nonmelanoma skin cancer: a critical review of the literature and meta-analysis. *Arch Dermatol* 2000; **136**:1524–30.
172 Veien K, Veien NK. Risk of developing subsequent nonmelanoma skin cancers. *Arch Dermatol* 2001; **137**:1251.
173 Levi F, Randimbison L, Maspoli M *et al.* High incidence of second basal cell skin cancers. *Int J Cancer* 2006; **119**:1505–7.

174 van Iersel CA, van de Velden HV, Kusters CD *et al.* Prognostic factors for a subsequent basal cell carcinoma: implications for follow up. *Br J Dermatol* 2005; **153**:1078–80.
175 Ramachandran S, Fryer AA, Smith AG *et al.* Basal cell carcinoma. *Cancer* 2000; **89**:1012–18.
176 Lear JT, Smith AG, Bowers B *et al.* Truncal tumor site is associated with high risk of multiple basal cell carcinoma and is influenced by glutathione S-transferase, *GSTT1*, and cytochrome P450, *CYP1A1* genotypes, and their interaction. *J Invest Dermatol* 1997; **108**:519–22.
177 Ramachandran S, Fryer AA, Smith A *et al.* Cutaneous basal cell carcinomas: distinct host factors are associated with the development of tumors on the trunk and head and neck. *Cancer* 2001; **92**:354–8.
178 Mc Loone NM, Tolland J, Walsh M, Dolan OM. Follow up of basal cell carcinomas: an audit of current practice. *J Eur Acad Dermatol Venereol* 2006; **20**:698–701.
179 Bower CP, Lear JT, de Berker DA. Basal cell carcinoma follow-up practices by dermatologists: a national survey. *Br J Dermatol* 2001; **145**:949–56.
180 Griffiths CEM. The British Association of Dermatologists guidelines for the management of skin disease. *Br J Dermatol* 1999; **141**:396–7.
181 Cox NH, Williams HC. The British Association of Dermatologists therapeutic guidelines: can we AGREE? *Br J Dermatol* 2003; **148**:621–5.

Appendix 1

The consultation process and background details for the British Association of Dermatologists guidelines have been published elsewhere.[180,181]

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, randomized controlled trial.
II-i Evidence obtained from well-designed controlled trials without randomization.
II-ii Evidence obtained from well-designed cohort or case–control analytical 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 1940s) 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 of evidence).