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Archer CMG. Risk stratification key to management of basal cell carcinoma.
Practitioner October 2021;265(1852):21-24

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SPECIAL REPORT

Risk stratification key to management of basal cell carcinoma

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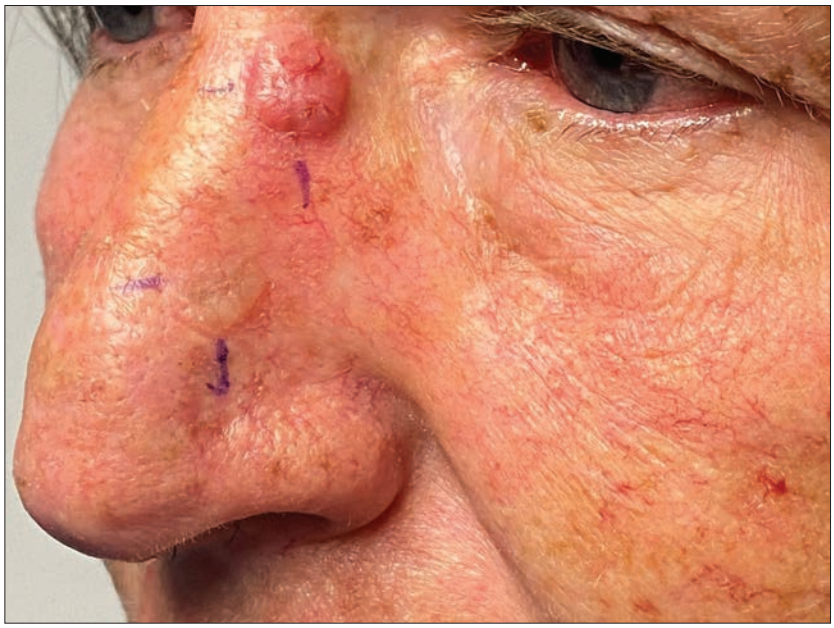


FIGURE 1
Nodular (superior) and mixed nodular and infiltrative (inferior) basal carcinomata on the left nasal sidewall

How should patients be assessed?

How should risk be stratified?

What are the treatment options?

BASAL CELL CARCINOMA (BCC) IS A SLOW GROWING, LOCALLY INVASIVE MALIGNANT EPIDERMAL skin tumour.[1] The tumour infiltrates tissue in a three-dimensional fashion through the irregular growth of finger-like projections which remain continuous with the main tumour mass.[2,3]

Metastasis is extremely rare ranging between 0.0028% and 0.55% of all BCC cases.[4,5] Morbidity results from the localised destruction of tissue particularly on the head and neck.

There are a number of morphological variants including: superficial, cystic, nodular, morphoeic, keratotic and pigmented.

Common histological subtypes include nodular, superficial and pigmented as well as morphoeic, infiltrative, micronodular and basosquamous variants, which show more aggressive tissue infiltration and destruction.[6] Invasion of nerves (perineural) and blood vessels (perivascular) is more common with the more aggressive subtypes.

The incidence of BCC in the UK was 285 per 100,000 person-years between 2013 and 2015.[7] The incidence of BCC continues to rise globally and it is now the most common cancer in Europe, Australasia and the USA.[8] The increasing incidence in the UK is thought to be partly due to an aging population.

RISK FACTORS

The most significant risk factors appear to be genetic predisposition and exposure to ultraviolet radiation (including artificial sources such as sun beds).[9] The sun-exposed sites of the head and neck are most commonly affected.[10,11] Childhood sun exposure may be particularly important.[12] Increasing age, male sex, fair skin (Fitzpatrick types I and II), immunosuppression and arsenic exposure are also risk factors.[13]

Those with basal cell naevus syndrome (Gorlin's syndrome) develop multiple BCCs. The development of one BCC is a strong predictor for the future development of others.

The diagnosis of BCC is clinical in the majority of cases. Examining the patient in a well lit room with the option for dermoscopy improves clinical accuracy.[14] Biopsy is useful to confirm diagnosis and delineate the histological subtype of BCC where this may affect the choice of treatment.

Imaging in the form of CT or MRI is indicated when the tumour has infiltrated bone, large nerves, the orbit or the parotid gland.[15,16,17]

CLINICAL PRESENTATION

BCCs most commonly present on the head and neck and sun-exposed sites but may occur at any site on the body. Patients will often report a non-healing wound that recurrently bleeds, crusts and scabs but does not heal. BCCs can present as slow growing papules, nodules, plaques or ulcers with a rolled edge. They can be pearly, red, pink or pigmented and some have a degree of translucency. Surface blood vessels are often visible. Generally, BCCs grow slowly over months to years.

ASSESSMENT

The history should involve a thorough review of the patient's risk factors and consider the following details, which are always useful to include in the referral letter:

- The site and size of the lesion
- How long the lesion has been present
- Rate of growth
- Bleeding, crusting, scabbing
- Keratotic vs non-keratotic
- Whether the lesion is painful
- History of previous skin cancers
- Skin type (I-VI)
- Occupational sun exposure (e.g. farming, military, construction)
- Medication particularly anticoagulants and any clotting abnormalities that may influence surgery

»

Table 1

Factors influencing prognosis of basal cell carcinoma

- Tumour size (larger size confers greater risk of recurrence)
- Tumour site (lesions on central face particularly around the eyes, nose, lips and ears have a high risk of recurrence)
- Definition of clinical margins (poorly defined margins have greater risk of recurrence)
- Histological subtype
- Aggressive histological features including perineural or perivascular involvement
- Failure of previous treatment i.e. recurrent tumours
- Immunosuppression

A full skin check should be performed which helps to give a context to the background sun exposure as well as identifying other potential lesions of concern. The lesion itself should be palpated and it may be necessary to remove some of the surface crust with gloved fingers to allow for a more accurate diagnosis.

Although BCCs rarely metastasise it is good practice to examine regional lymph nodes given the common differential of squamous cell carcinoma (SCC).

If the clinician is confident in the diagnosis then patients can generally be referred for routine assessment in the skin cancer clinic.

Suspected high-risk BCCs on the central face (around the eyes, nose, lips and ears) should be referred for an urgent opinion. It is the anatomical site which makes rapid assessment more pressing as the main concern is local tissue destruction which may have poor functional and cosmetic outcomes if left.

DERMOSCOPY

Dermoscopy is a useful adjunct in the diagnosis and classification of BCC but should be used carefully in conjunction with the clinical history and examination of the skin with the naked eye.

Table 2

Indications for Mohs micrographic surgery

- Tumour site (central face, around the eyes, nose, lips and ears)
- Tumour size (particularly > 20 mm)
- Histological subtype (particularly morphoeic, infiltrative, micronodular and basosquamous subtypes)
- Poorly distinct tumour margins
- Recurrent lesions
- Perineural or perivascular involvement

Dermoscopic features can be varied and are dependent on the morphology (superficial, nodular, pigmented etc). Features which may be seen include:

- Arborising or linear fine vessels
- Maple leaf-like structures at the periphery
- Ovoid blue/grey pigment clumps or nests
- Speckled brown pigment
- Surface ulceration
- Surface scaling
- Perpendicular white lines
- Milky pink structureless areas
- Shiny white, red areas

DIFFERENTIAL DIAGNOSIS

This includes malignant and benign growths including but not limited to: SCC, melanoma, actinic keratosis, Bowen's disease, trichoepithelioma, chondrodermatitis, sebaceous hyperplasia, fibrous papule of the face and molluscum contagiosum.

STRATIFYING RISK

The cure rates for individual BCCs depend on a number of prognostic factors (see table 1, above left). The presence, or absence, of these factors helps guide treatment selection and prognostic advice given to patients. Low-risk subtypes may be amenable to treatment with topical preparations or nonsurgical treatments, while those with higher-risk features would generally be treated by surgery or radiotherapy.[18]

Individual patient factors will influence treatment choice including performance status (i.e. their ability to perform activities of daily living without the help of others), concurrent medical conditions and the use of anticoagulant medications.

A conservative watch and wait approach may be reasonable for low-risk tumours and it is important that the risks of treatment are weighed against the benefits.

In certain clinical circumstances clinicians and patients may mutually choose to manage high-risk tumours conservatively where palliation is kinder than curative treatment which may cause significant morbidity.

TREATMENT

There are a broad range of potential treatments for BCC and guidance on the appropriate use of these treatments is set out in detail in the British Association of Dermatologists guidelines.[1] Striking a balance between tumour eradication and acceptable cosmetic and functional outcomes is key.

Some modalities of treatment (such as curettage, cryosurgery, radiotherapy) do not allow for histological confirmation of clearance of the tumour.

Excision of BCC with intraoperative or postoperative examination of tissue margins remains the gold standard for treatment of low- and high-risk BCCs and has the highest overall cure rate.[18]

Surgical excision

The tumour is removed with predetermined margins of normal tissue (4-10 mm). The peripheral and deep margins of the specimen are then examined histologically with frozen sections intraoperatively[19] or more commonly postoperative vertical sections using formalin-fixed, paraffin-embedded tissue.[20]

Surgical excision of primary BCC is very effective and has a recurrence rate < 2% at 5 years for histologically completely excised tumours.[20]

Studies of well defined small BCCs (< 20 mm) have shown that a 3 mm peripheral surgical margin will clear the tumour in 85% of cases and this figure rises to 95% with a 4-5 mm margin. This means that 5% of well defined tumours will stretch more than 4 mm beyond the apparent clinical margin.[21,22]

For morphoeic BCCs, a 3 mm peripheral margin predicts a 66% completion of excision; 5 mm margin 82% and 13-15 mm margin > 95%. Vertical sectioning by the pathologist allows sampling of the peripheral and deep margins and is estimated to examine up to 44% of total margin. This explains why some seemingly completely excised BCCs show recurrence.[23]

Mohs micrographic surgery (MMS)

This procedure is the staged resection of tumour with comprehensive examination of surgical margins. It has the highest rates of cure even for lesions with high-risk features (see table 1, above left) and aims to conserve normal tissue.

This technique is generally used for high-risk lesions on the head and neck. The indications for MMS are summarised in table 2, left.

Cure rates at 5 years are reported as > 99% following MMS for primary BCC[24] and 93-96% for recurrent BCC.[25] MMS is performed under a local anaesthetic as a day case.

Once tumour clearance is achieved, reconstruction is either undertaken by dermatological, plastic or oculoplastic surgeons. The reconstruction may happen the same day or shortly after the procedure.

Curettage and cautery
Curettage and cautery (or electro-dessication and curettage) is best reserved for low-risk tumours on the trunk and limbs (small well defined nodular or superficial BCCs). Its success rate depends on appropriate case selection and is heavily operator dependent.

Cryosurgery
Cryosurgery employs liquid nitrogen to destroy the BCC and surrounding tissue using the effects of extreme cold (-50 to - 60°C). It is best reserved for low-risk BCCs not on the head and neck.

Carbon dioxide laser
This technique uses an ablative laser to destroy the tumour. It is not commonly used in UK practice but has potential for the quick and effective treatment of multiple superficial BCCs (low-risk tumours) and has reasonable cosmetic results.

Imiquimod
Imiquimod is an immune response modifier which acts through toll-like receptors and elicits both innate and adaptive cell-mediated immune responses. It is effective for the treatment of superficial BCCs. Treatment regimens may vary but typically patients are treated daily 5 days a week for 6 weeks. Patients sometimes complain of flu-like symptoms and temperatures with treatment.

5-fluorouracil cream
5-fluorouracil interferes with DNA synthesis and promotes cell death. It has a role in the treatment of superficial BCCs. Treatment regimens will vary based on response and should be tailored to the individual patient. Treatment may be once or twice daily and last for 4-6 weeks. Patients will experience sore inflamed skin while on treatment and regular use of a moisturiser should be helpful.

Photodynamic therapy
Photosensitising agents, oxygen and light are used to create a photochemical reaction, which destroys skin cancer cells. Methyl aminolevulinic acid or an alternative preparation is applied to the »

FIGURE 2
A poorly defined infiltrative and superficial BCC on the left temple

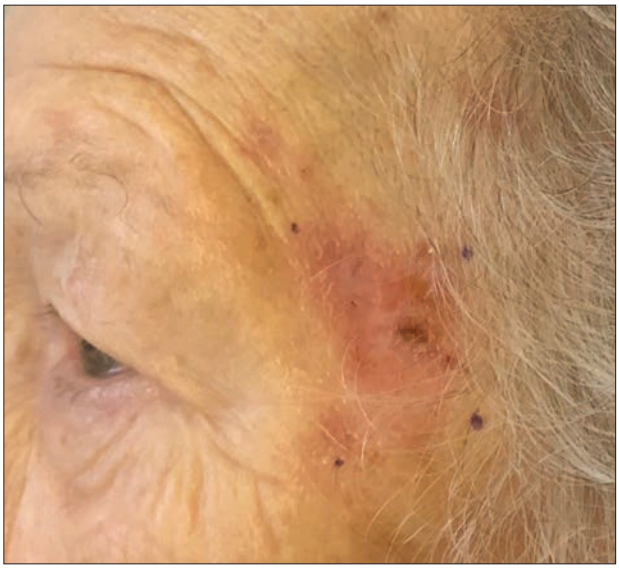


FIGURE 3
An ulcerated nodular and infiltrative BCC on the left inner canthus

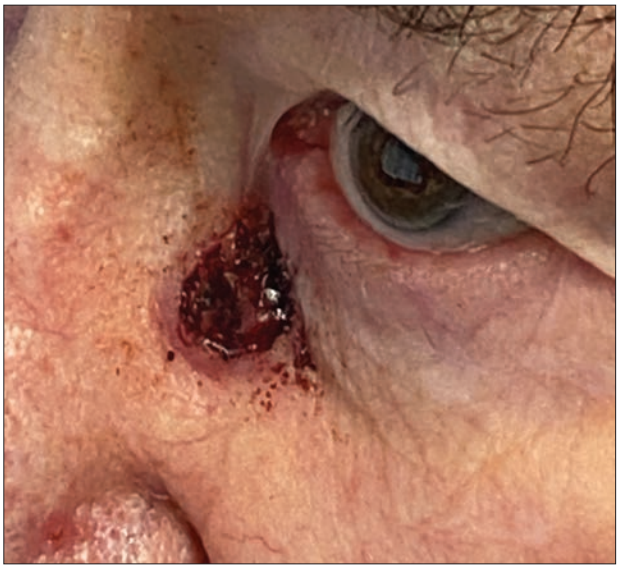


FIGURE 4
A pigmented, basosquamous carcinoma on the right superior nasolabial cheek

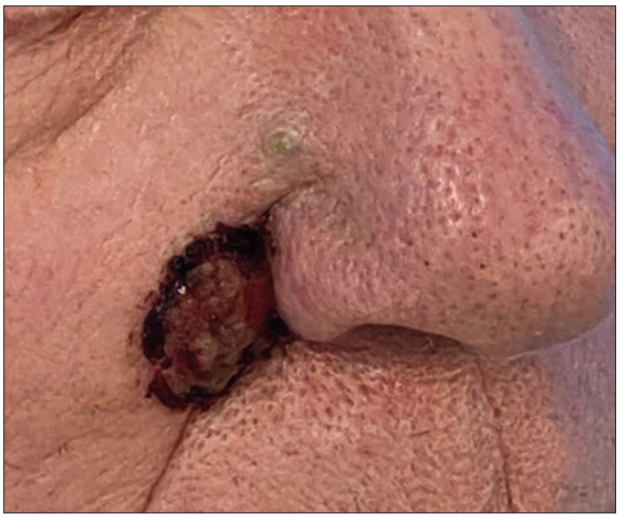
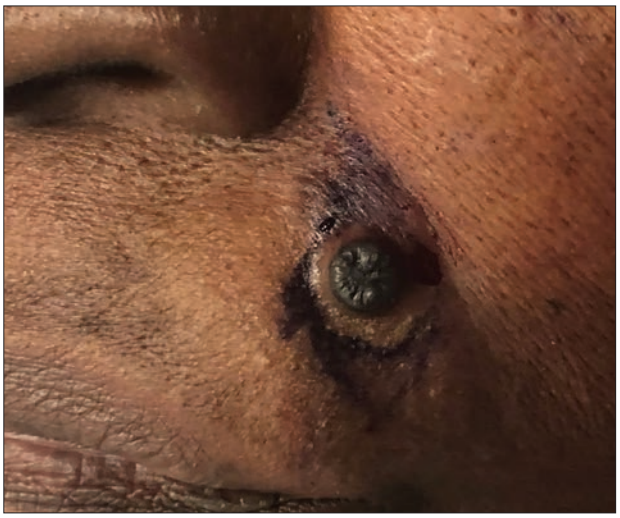


FIGURE 5
A pigmented, nodular BCC on the left upper cutaneous lip in a patient with Fitzpatrick skin type 6



key points

SELECTED BY

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Basal cell carcinoma (BCC) is a slow growing, locally invasive malignant epidermal skin tumour. The tumour infiltrates tissue in a three dimensional fashion through the irregular growth of finger-like projections which remain continuous with the main tumour mass. Metastases are very rare and morbidity results from the localised destruction of tissue particularly on the head and neck. Suspected high-risk BCCs on the central face (around the eyes, nose, lips and ears) should be referred for an urgent opinion.

BCCs most commonly present on the head and neck and sun-exposed sites but may occur at any body site. Patients will often report a non-healing wound that recurrently bleeds, crusts and scabs but does not heal. BCCs can present as slow growing papules, nodules, plaques or ulcers with a rolled edge. They can be pearly, red, pink or pigmented and some have a degree of translucency. Surface blood vessels are often visible. Generally, BCCs grow slowly over months to years.

The history should involve a thorough review of the patient's risk factors and consider: the site and size of the lesion; how long the lesion has been present; rate of growth; bleeding, crusting, scabbing; keratotic vs non-keratotic; whether the lesion is painful; history of previous skin cancers; skin type (I-VI); occupational sun exposure (e.g. farming, military, construction); patient's medication particularly anticoagulants and any clotting abnormalities that may influence surgery.

A full skin check should be performed which helps to give a context to the background sun exposure as well as identifying other potential lesions of concern. The lesion itself should be palpated and it may be necessary to remove some of the surface crust with gloved fingers to allow for a more accurate diagnosis. Differential diagnosis includes malignant and benign growths including but not limited to: SCC, melanoma, actinic keratosis, Bowen's disease, trichoepithelioma, sebaceous hyperplasia, chondrodermatitis, fibrous papule of the face and molluscum contagiosum.

Individual patient factors will influence treatment choice including performance status, concurrent medical conditions and the use of anticoagulant medications. A conservative watch and wait approach may be reasonable for low-risk tumours and it is important that the risks of treatment are weighed against the benefits. In certain clinical circumstances clinicians and patients may mutually choose to manage high-risk tumours conservatively where palliation is kinder than curative treatment which may cause significant morbidity. Striking a balance between tumour eradication and acceptable cosmetic and functional outcomes is key. Excision of BCC with intraoperartive or postoperative examination of tissue margins remains the gold standard for treatment of low- and high-risk BCCs and has the highest overall cure rate.

surface of superficial BCCs and is absorbed. This is then activated by a particular wavelength of light either from a laser or non-laser light.

Radiotherapy

Radiotherapy is an effective treatment for primary BCC. It can be used in cases of recurrence after surgery as well as adjuvant therapy. It should be avoided in younger patients where possible as it can encourage the growth of non-melanoma skin cancers years after treatment. It should not be used in patients with Gorlin's syndrome for this reason.

FOLLOW-UP

Follow-up varies widely across different centres in the UK. While all patients with a previous BCC have a potential risk of local recurrence and the development of new primary BCCs, many would not be followed up routinely in secondary care. Individual patient risk stratification is important and more regular follow-up would generally be reserved for those with multiple recurrent tumours. Shortly after the diagnosis and treatment of a primary BCC is the ideal opportunity to educate patients on the benefits of self-examination and sun protection.

CONCLUSION

There are many different types of treatment for BCC. Selecting the appropriate treatment for the individual patient is based on calculating the risk of recurrence in that individual. Individual patient factors will influence treatment choice including performance status, concurrent medical conditions as well as the anatomical site affected and the specific morphology of the tumour.

Early identification of BCCs in the community and appropriate referral is associated with better treatment outcomes. High-risk BCCs warrant urgent referral whereas low-risk tumours can be seen routinely.

Competing interests: None

REFERENCES

1 Telfer NR, Colver GB, Morton CA. Guidelines for the management of basal cell carcinoma. *Br J Dermatol* 2008;159:35-48
2 Breuninger H, Dietz K. Prediction of subclinical tumor infiltration in basal cell carcinoma. *J Dermatol Surg Oncol* 1991;17:574-78
3 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;22:535-39
4 Seo SH, Shim WH, Shin DH et al. Pulmonary metastasis of basal cell carcinoma. *Ann Dermatol* 2011;23(2):213-16
5 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
6 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;59:424-28
7 Venables ZC, Nijsten T, Wong KF et al. Epidemiology of basal and cutaneous squamous cell carcinoma in the UK 2013-15: a cohort study. *Br J Dermatol* 2019;181(3):474-82
8 Miller DL, Weinstock MA. Nonmelanoma skin cancer in the United States: incidence. *J Am Acad Dermatol* 1994;30:774-78
9 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
10 Roenigk RK, Ratz JL, Bailin PL, Wheeland RG. Trends in the presentation and treatment of basal cell carcinomas. *J Dermatol Surg Oncol* 1986;12:860-65
11 Lindgren G, Diffey BL. Basal cell carcinoma of the eyelids and solar ultraviolet radiation exposure. *Br J Ophthalmol* 1998;82:1412-15
12 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;137:1162-68
13 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
14 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;32:423-25
15 Leibovitch I, McNab A, Sullivan T et al. Orbital invasion by periocular basal cell carcinoma. *Ophthalmology* 2005;112(7):17-23
16 Meads SB, Greenway HT. Basal cell carcinoma associated with orbital invasion: clinical features and treatment options. *Dermatol Surg* 2006;32:442-46
17 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
18 Bath-Hextall F, Perkins W, Bong J, Williams H. Interventions for basal cell carcinoma of the skin. *Cochrane Database Syst Rev* 2007;1:CD003412
19 Cataldo PA, Stoddard PB, Reed WP. Use of frozen section analysis in the treatment of basal cell carcinoma. *Am J Surg* 1990;159:561-63
20 Walker P, Hill D. Surgical treatment of basal cell carcinomas using standard postoperative histological assessment. *Australas J Dermatol* 2006;7:1-12
21 Wolf DJ, Zitelli JA. Surgical margins for basal cell carcinoma. *Arch Dermatol* 1987;123:340-44
22 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;53:464-68
23 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
24 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
25 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;53:452-57

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