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A retrospective study of 694 Basal Cell Carcinoma excisions to quantify deep margin documentation and clearance compared to histological type and surgical margin

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Summary *Aims:* Basal cell carcinoma (BCC) is the most common malignancy worldwide. Although rarely a risk to life, they are potentially destructive and disfiguring. Current treatment guidelines are predominantly based on low-risk BCC and make no recommendations regarding the deep excision margin. We aim to clarify the prevalence of high-risk BCC and appropriate surgical management of the deep margin.

Methods: Data of 556 patients presenting for primary excision of 694 basal cell carcinoma to CUH Plastic Surgery between January 2017 and April 2018 were collected by capture of demographics, surgical notes and histology.

We defined the deep surgical margin as numbered anatomical planes, with subcutaneous fat as 0, the first plane under this as 1 and so forth. This allowed comparison of the surgical excision depth, and resulting deep margin histology, across disparate sites.

Histological margin clearance was analysed using ordinal regression of age, site, size, histological type and surgical margin. This allowed identification of factors associated with clear, close or incomplete lesion excision. Subgroup analysis was then performed to make recommendations for surgical margins to achieve adequate lesion clearance.

Results: Six hundred ninety-four BCCs were identified, 66% were male and the average age of patients was 74 years. Of the BCCs, 49% were nodular but 39% were mixed. An infiltrative component was seen in 24% (mixed infiltrative), but only 4% were purely infiltrative. Mean size, site and patient age were similar across histological types.

Deep margin involvement was very rare in nodular or superficial BCCs but occurred in 7% of pure infiltrative and 5% of mixed infiltrative. Peripheral margins were very rarely involved in

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nodular BCCs but occurred in 9% of mixed infiltrative and 10% infiltrative despite similar surgical margins. A deep margin of the first underlying anatomical plane resulted uninvolved margins in 95% of infiltrative or mixed infiltrative BCC, but subcutaneous fat was sufficient for clearance in 95% of nodular, superficial and mixed non-infiltrative BCC.

Conclusions: High-risk BCC was a common finding in our patient population. This was based not only on site and size but also on histological type.

Infiltrative and mixed infiltrative BCCs have a higher risk of close or involved deep margins than other types. We recommend that they are excised to the first underlying anatomical plane. Nodular, superficial and mixed non-infiltrative BCC can usually be safely excised with a cuff of fat alone.

Introduction

Basal cell carcinoma (BCC) is a malignancy of perifollicular keratinocyte stem cells and is the commonest human malignancy.[1] Its incidence is mostly related to a combination of the major risk factors of ageing skin and sun exposure, with a smaller contribution from other risk factors including genetic disorders and immunosuppression.[2] Although rarely life threatening, BCCs are potentially destructive and disfiguring, requiring multidisciplinary surgical, medical and nursing care. An ageing global population with greater UV exposure contributes to a sustained increase in the incidence of BCC, thereby resulting in increasing healthcare expenditure.[3,4] In 2011, the management of non-melanoma skin cancer, of which BCCs form 80%, amounted to nearly $5 billion in the USA alone.[5]

A BCC may be classified as low or high risk related to their risk of incomplete excision, recurrence and the rare incidence of metastatic spread. This classification is based on histological subtype, site and size.[6] Nodular and superficial histological types are regarded as a low-risk lesion, whereas the infiltrative type is regarded as a high-risk lesion. In addition, there is also a population of mixed histology lesions of unpredictable behaviour.[7,8] Head and neck BCCs are all regarded as high risk, particularly those on the central face and ears. Finally, a BCC of more than 20 mm surface diameter is usually regarded as a high-risk lesion.[9]

This classification of BCCs into low or high risk allows triage between the providers predominantly involved in their management, such as dermatologists, plastic surgeons and general practitioners.[10]

There is substantial variation in the international guidelines regarding the surgical management of BCCs.[11] These recommendations are based on studies using either prospective Mohs micrographic surgery (MMS) or retrospective evaluation of peripheral surgical margins.[12,13] For example, the British Association of Dermatology guidelines advise a 4 mm peripheral margin to obtain 95% clearance of low-risk lesions.[9] For high-risk lesions, MMS is often recommended but the availability of this service is variable, the procedure takes longer and it is (at least initially) more expensive.[14] Consequently, the majority of BCCs are excised using standard excision with a pre-determined peripheral margin.

To date, the majority of studies have concentrated on the excision of low-risk BCCs in low-risk sites. Most have only involved low patient numbers.[15] It might therefore be argued that these guidelines are not entirely applicable to plastic surgeons, who are more likely to manage high-risk lesions. Patients in the UK are also poorly represented in studies of BCC management, and it is possible that this cohort may differ from those seen in Australia, Europe, Asia or the USA.

High-risk BCCs are comparatively poorly studied.[16] Current guidelines generally advise either substantially wider initial excision of such lesions, up to 13–15 mm, or MMS.[6] However, this is not always possible because of both direct referral for excision and the high rate of discordance between incisional and excisional biopsy results.[17] Furthermore, it appears that the proportions of the different types vary geographically and by body site, impacting applicability of guidelines.[18]

Once obtained, the specimens are processed by the local histopathology department, and the margins are examined for completeness of excision. As only a portion of the margin is studied, there is a known risk of incorrectly diagnosed margin status and later recurrence.[19] Furthermore, an incompletely excised tumour may recur with a more aggressive subtype.[20]

To date, the optimal deep margin for complete excision of a BCC has not been defined, and indeed, it is not even referenced in many national guidelines.[11] Given the sheer number of patients presenting with this condition, this is a surprising omission.

Some studies suggest assessing deep margin status intraoperatively, which may be appropriate for florid involvement.[3] However, given that the recommended peripheral surgical margins are based on subclinical tumour extension, clinical assessment alone of deep margin status is also likely to be inaccurate. Re-excision of close or involved deep margins is known to be challenging, in addition to increasing the burden on the patient and local healthcare resources.[21,22] It is therefore important to maximise the chances of complete excision in a single procedure while avoiding unnecessarily aggressive surgery.

We therefore aimed to establish what the deep margin for BCC excision should be.

Materials and methods

A retrospective study of all patients presenting with a primary excision of a BCC to the Plastic Surgery Department at

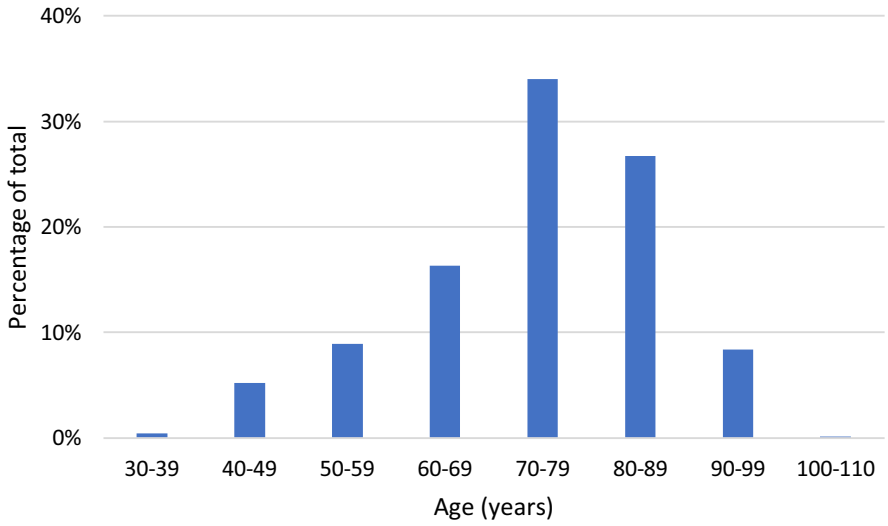

Figure 1 BCC incidence versus Age.

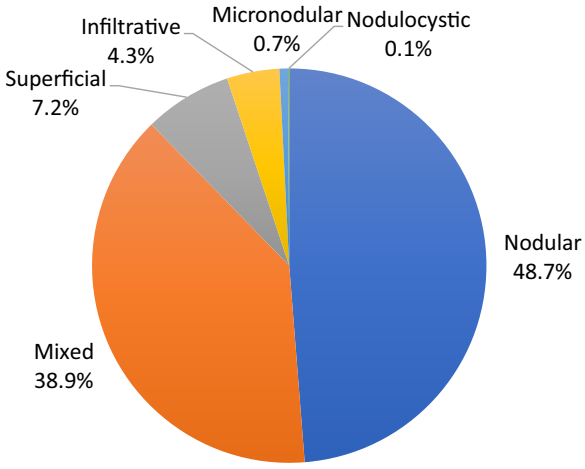

Figure 2 Basal Cell Carcinoma histological type.

Cambridge University NHS Foundation Trust (CUH) was performed. Patients who were seen in a 15-month period from January 2017 to April 2018 were included. Excisions were performed by 30 surgeons across our department, consisting of 14 consultants, 1 associate specialist and 15 specialist registrars, with a small number of supervised procedures by more junior trainees. Approval for this study was obtained from the Clinical Audit department, and the study was conducted in accordance with the STROBE statement.

Patient records were examined for standard demographics, tumour site and documented surgical peripheral and deep margins. Histological results were reviewed for tumour size, subtype and peripheral and deep margin status. Microsoft Excel and IBM SPSS 25 were then used to analyse the results.

Limited data exist regarding the appropriate deep surgical margin for BCC excision, and it is difficult to study this across body sites. We assessed the surgical notes for the documented deep margin, defining a 'cuff of fat' as 0, the first underlying anatomical plane as 1 and so on. For example, in the scalp after fat, the first anatomical plane is the galea (defined as plane 1), and the second is periosteum (defined as plane 2) and the third is bone (defined as plane 3). In the ear, plane 1 is the perichondrium and plane 2 is excision with cartilage. This was then used as an ordinal variable to compare deep surgical margins across the body.

Although CUH is a transplant centre, as a group, transplant patients comprised only a very small proportion of the BCC population and were not studied separately. Similarly, patients with other uncommon risk factors such as genetic disorders were rare or absent in our population. The study group therefore comprised patients with the most common risk factors such as age and UV exposure.

We did not capture BCC recurrence during this period, as this has previously been characterised by other authors. Recurrence is problematic to study owing to a combination of high dropout rates, length of time to recurrence and development of coincidental lesions.

Results

Six hundred ninety-four BCCs were identified affecting 556 patients. Sixty-six per cent of them were male, and patients were most commonly in their eighth decade of life, with a mean age of 69 years (Figure 1). Nodular BCC was the most common form (49%), but mixed histology was also frequent (39%). Micronodular and nodulocystic BCCs were uncommon - both $<1\%$; therefore, they were not available for further analysis (Figure 2). Eighty-eight per cent of lesions were <20 mm in peripheral diameter and 10% were ≥ 20 mm (1.7% unrecorded).

Mixed BCCs contained a variety of subtypes. Nodular BCC was seen in nearly all lesions (93%), but infiltrative and superficial components were seen in 57% and 41%, respectively (Figure 3).

As infiltrative BCC is known to be more difficult to treat,[23] we grouped mixed histology as 'mixed infiltrative' (where an infiltrative component was seen) and 'mixed non-infiltrative' for further study (Table 1).

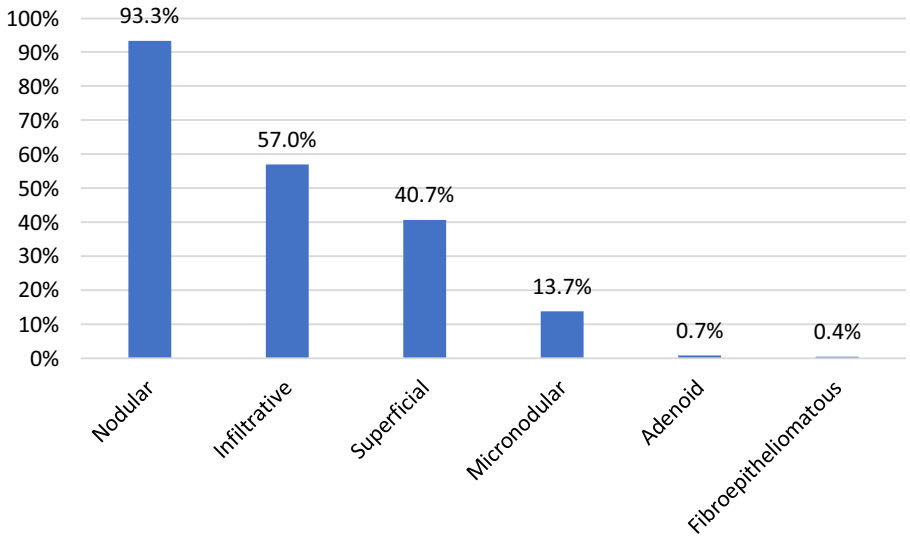

Figure 3 Mixed Basal Cell Carcinoma subcomponent histological types.

Table 1 BCC types and lesion characteristics.

Histology	Number of BCCs in study (% total)	Sex (% Male)	Age in years (95% CI)	Diameter in mm (95% CI)
Nodular	338 (48.7)	68.0	73.6 (72.3-75)	9.6 (9-10.3)
Mixed Infiltrative	154 (22.2)	63.6	76.3 (74.6-78)	12.3 (11.1-13.6)
Mixed Non-Infiltrative	116 (16.7)	68.1	72.1 (69.7-74.4)	10.5 (9.5-11.6)
Superficial	50 (7.2)	60.0	73.3 (69.4-77.2)	11.3 (8.7-13.8)
Infiltrative	30 (4.3)	66.0	70.2 (65.2- 75.1)	11.1 (9.2- 13.1)

While pure nodular BCC was the most common type, it did not contribute to the majority of tumours in this study. Twenty-two per cent were mixed infiltrative, a subtype that has been shown to behave in a similar way as that of infiltrative BCC.[23]

We then assessed whether histological type in our population could be predicted based on age, sex or size. Mixed infiltrative and infiltrative BCC tended to be larger and seen in older patients; however, this between-type difference was not statistically significant (Table 1). Overall, we found that a similar type distribution was regardless of sex, age and size, and hence, these factors cannot be used to guide management.

Although there was some variation in the distribution of BCC subtype across the body, high-risk types were seen across the body, and hence, site alone cannot be used to guide treatment (Figure 4). Superficial BCC was uncommon in the head and neck, which concurs with previous work.[18]

Assessment of peripheral margins for all BCC excisions showed that 88% of lesions had peripheral margins more than 1 mm clear, 8% were close (<1 mm) and 5% were involved. Assessment of deep margins showed that 86% had deep margins more than 1 mm clear, 13% were close (<1 mm) and 1.4% were involved.

The surgical notes were reviewed for documentation of the deep excision margin (Table 2). Although the first underlying anatomical plane was used in 39%, this margin was not documented in 27%. Operation notes for samples from the independent sector were only partially available to the investigators. These patients and those with full-thickness excisions were excluded from regression analysis of excision margins.

Table 2 Documented deep surgical margin.

Documented deep surgical margin	Proportion of total excisions (%)
Subcutaneous fat	23.7
First anatomical plane (e.g. Perichondrium of ear)	39.4
Second anatomical plane (e.g. with Cartilage)	7.3
Full thickness (e.g. Wedge excision)	2.5
Not documented	27.1
Independent sector sample	23.5

By comparing histological findings and surgical notes, we were able to compare the peripheral and deep margin clearance across BCC histological subtypes (Figures 5 and 6).

BCC excision rates were strongly influenced by histological subtype. Mixed tumours with an infiltrative component were similar in this aspect to purely infiltrative tumours. These lesions were at risk of involved peripheral and deep excision margins. By contrast, nodular lesions rarely had involved deep or peripheral margins. Superficial lesions were more likely to have involved peripheral margins than nodular but had no involved deep margins in this study.

Ordinal regression was performed between peripheral margin clearance and BCC type while using site, lesion

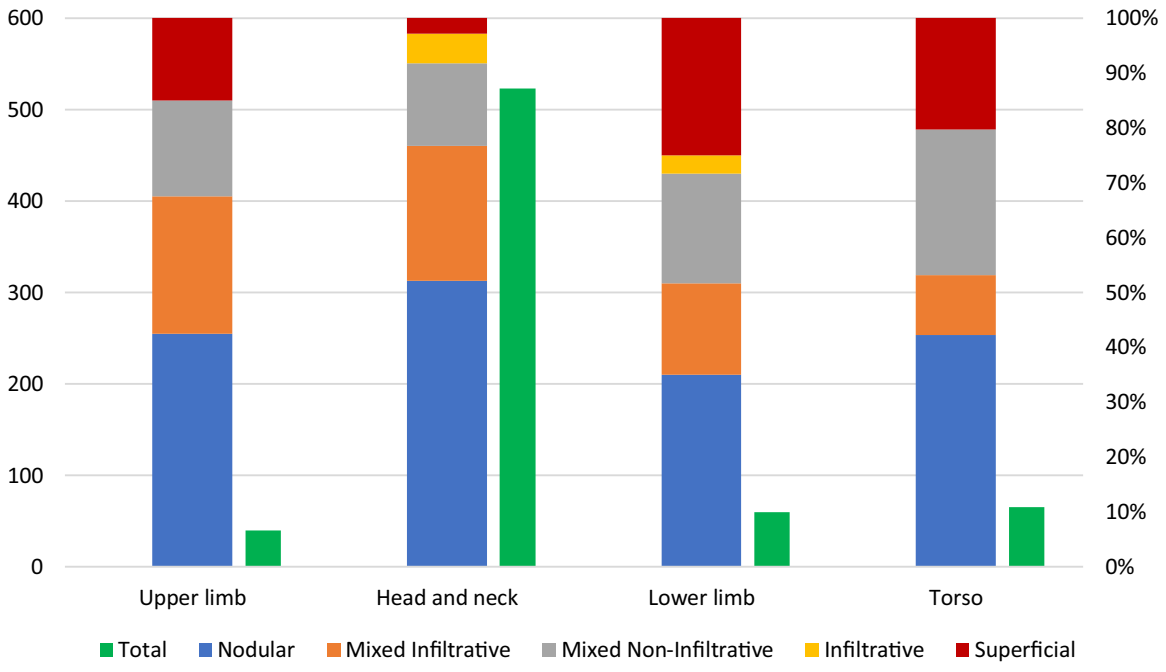

Figure 4 BCC subtype by site.

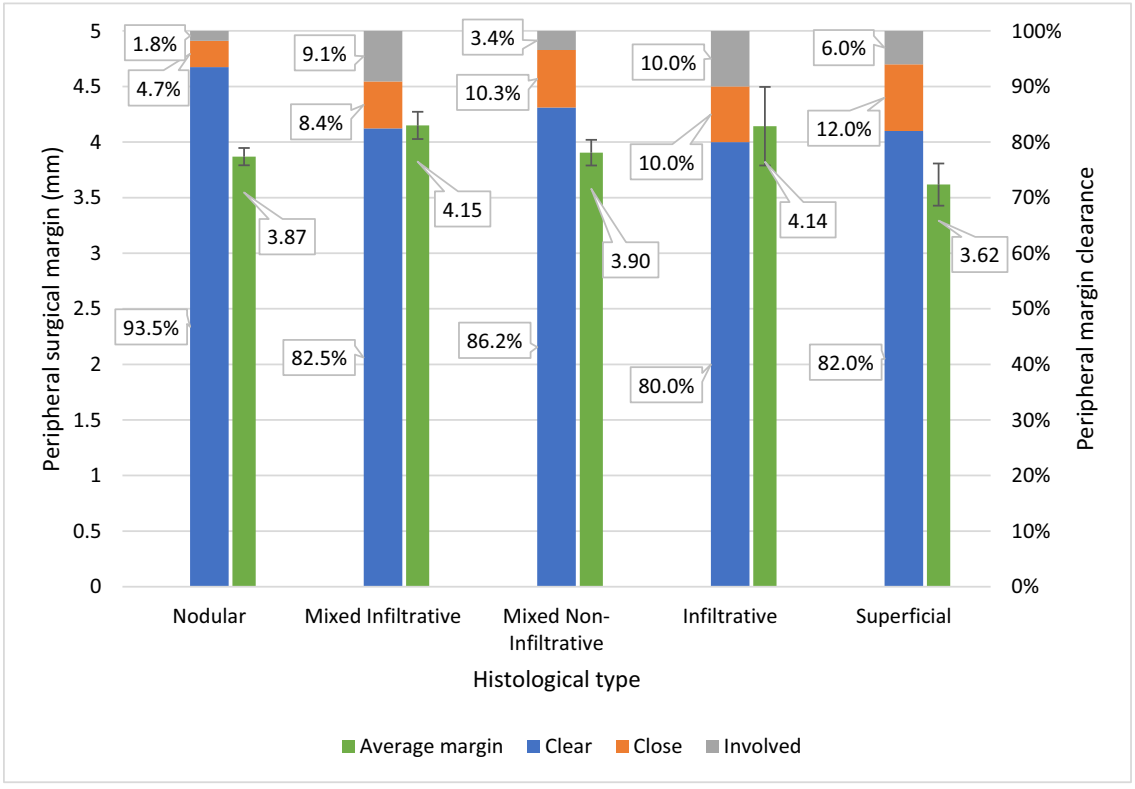

Figure 5 Peripheral margin clearance compared to peripheral surgical margin with standard errors.

diameter and preoperative margin as covariates. Compared to nodular BCC, all other types were more likely to have involved peripheral margins (Table 3).

Ordinal regression was also performed between deep margin clearance and BCC type while using site, lesion diameter and surgical deep margin as covariates. Compared to nodular BCC, infiltrative and mixed infiltrative BCCs were more likely to have an involved deep margin (Table 4). None of the mixed non-infiltrative or superficial samples had an involved deep margin.

BCC type, documented deep surgical margin and deep margin status were analysed as subgroups. Nodular, superficial and mixed non-infiltrative BCC samples excised with a deep margin of subcutaneous fat had clear deep

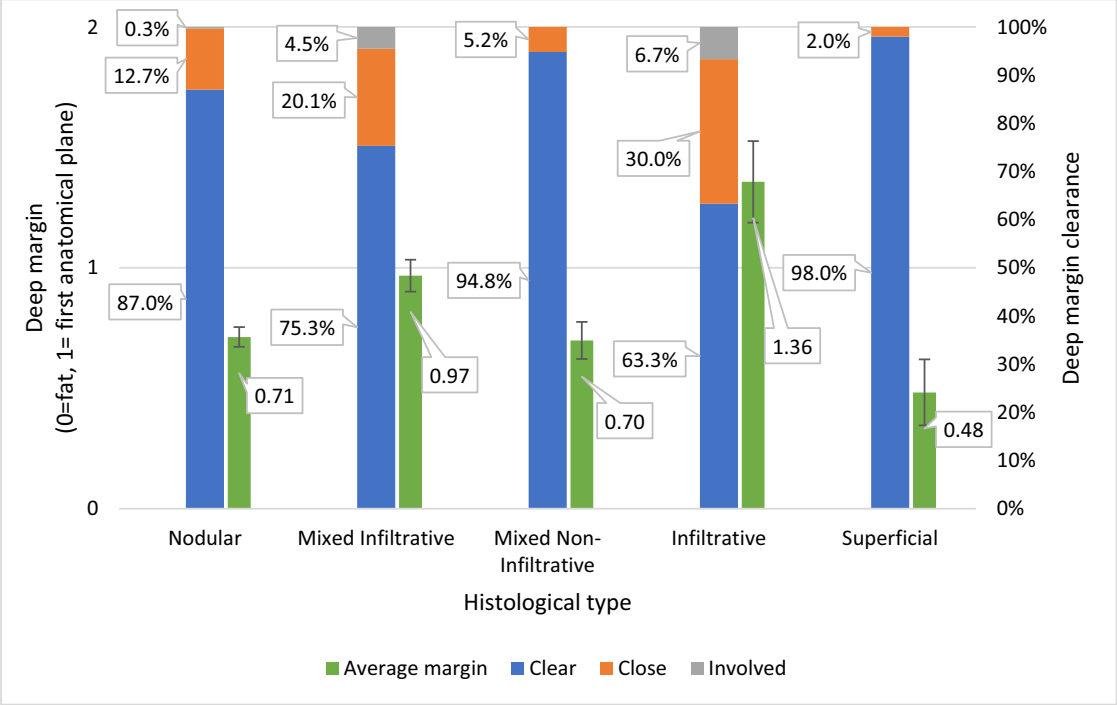

Figure 6 Deep margin clearance compared to anatomical excision plane with standard errors.

Table 3 Odds ratios for close/involved peripheral margins compared to those for nodular BCC (site, lesion diameter and peripheral margin as covariates).

Histology	Odds Ratio for close or involved margins	95% CI	p value
Infiltrative	4.4	1.0-19.7	0.055
Superficial	3.6	0.7-17.6	0.112
Mixed Infiltrative	2.6	1.2-6.0	0.022
Mixed Non-Infiltrative	2.0	0.7-5.5	0.189
Nodular	1	-	-

Table 4 Table 2- Odds ratios for close/involved deep margins compared to those for Nodular BCC (site, lesion diameter, deep surgical margin as covariates).

Histology	Odds Ratio for close or involved margins	95% CI	p value
Infiltrative	9.9	2.3-43.3	0.002
Mixed Infiltrative	1.8	0.8-3.9	0.14
Nodular	1	-	-
Mixed Non-Infiltrative	0.5	0.2-1.6	0.25
Superficial	0	0	0.99

margins in 94.6%. However, infiltrative and mixed infiltrative BCC samples required a deeper excision, with only 80% of margins clear at this excision depth. For these lesions, a deep margin of the first underlying anatomical plane resulted in 95.3% uninvolved margins (99.4% for nodular, superficial and mixed non-infiltrative).

Discussion

In this study, we have demonstrated that the deep margin of BCC excision is often poorly documented and likely seen as less important than the peripheral margins. To some extent, this may be justifiable, as involved deep margins are uncommon. However, where margins are involved or close and further treatment is advised, undocumented margins make planning this more difficult. We therefore recommend that peripheral and deep surgical excision margins should be formally documented for all BCC excisions.

Mixed infiltrative and pure infiltrative lesions have a greater tendency for subclinical spread both deep and peripherally, resulting in a higher incidence of involved margins. This is unlike nodular, superficial and mixed non-infiltrative BCCs; while these lesions are at risk of

involved peripheral margins, an involved deep margin was very unusual for these subtypes. This was despite a non-significant trend to excise these lesions with shallower sample depth. This may explain the finding that some BCCs recur with a more aggressive subtype; if a mixed lesion is excised, the infiltrative component could be more likely to be incompletely removed.[20,24]

For nodular, superficial and mixed non-infiltrative BCC, excision with a cuff of fat was usually adequate for confident excision. However, infiltrative and mixed infiltrative lesions can require a deeper excision. Where clinical suspicion or incisional biopsy suggests an infiltrative component, we recommend that these lesions should be excised to the first underlying anatomical plane. This level resulted in 95% uninvolved deep margins – a rate that is likely to be acceptable to patients and providers. Careful intraoperative assessment should be made regarding the need for further excision of the deep margin, although we recognise the inaccuracy of clinical assessment alone. Where possible, patients should be advised that these lesions are at a higher risk of needing further treatment.

We found that high-risk BCCs may often be excised successfully with substantially narrower peripheral margins than those currently recommended, albeit less reliably than those of low-risk BCCs. Although not the primary purpose of this study, this is reassuring given the frequency with which these lesions are encountered. Previous studies have shown that when excised completely, even high-risk lesions are not at greater risk for recurrence than their low-risk counterparts.[25]

As incisional biopsy is uncommon and its results inaccurate, and clinical histological diagnosis is likely to be similarly imprecise, it may be difficult to decide the deep excision margin preoperatively.[17] While excising all BCCs to the first underlying plane is an option, it will represent over-excision for many patients. Although there may be surgical advantages to this approach, such as easier haemostasis or reconstruction, the risk of accidental injury, particularly to nerves, is increased. Dermoscopy has been shown to be useful for assessing BCC histological type and may therefore be of benefit in planning excision margins.[26]

There are some sites, such as the medial canthus, where a deep excision plane is unclear. In the UK, these BCCs would often be considered for MMS due to the similar difficulty in determining peripheral excision margins and reconstructive options. As this is common practice at our institution, we did not capture many of these lesions and are not able to make recommendations regarding this difficult site.

As our data are solely from a single tertiary UK Plastic Surgery centre, it is possible that the lesions studied here were at higher risk in terms of site or larger size. We have not been able to identify another study assessing the deep surgical margin for BCC excision across the body, and hence, it is difficult to demonstrate external validity in this aspect. However, this is also a large study on peripheral excision margins for BCCs, with the rate of incomplete excision in line with previous published data.[22]

During recent years, excision of low-risk BCC in the UK has shifted from secondary care towards primary care. This potentially reduces expenditure and increases patient convenience but probably increases incomplete excision rates.[10,27] Our recommendations could have the effect of reducing this shift. We do not, however, anticipate that this should result in a substantial change in health expenditure or departmental staffing; truly low-risk BCC by site, size and type is relatively rare.[10]

It is difficult to know whether our results can be applied to patients in other countries. In other settings, patients may present at different disease stages, be referred to different specialities and be treated using different methods – particularly regarding MMS. It has been shown that the proportions of BCC type vary internationally, likely driven by variation in genetics, culture and UV exposure.[18]

We appreciate the limitations to this study. First, we rely on reporting using serial transverse sections ('bread-loafing') rather than the en-face technique used for MMS. This has known limitations regarding the proportion of margin visualised – estimated at 1–2%.[28] As a result, a margin reported as clear or close might instead be involved where complete histological assessment is performed.

A further limitation results from the poor documentation of excision margins. Our patients were treated by 30 surgeons of varying seniority, and although a pragmatic approach, this introduces variation in the terminology used in surgical notes. More junior surgical grade has previously been suggested as a risk factor for incomplete BCC excision.[29] However, we expect that measured peripheral margins and documented deep planes should be consistent across consultants and surgical registrars.

Conclusions

High-risk BCC was common in our population by both site and size and also by tumour type. Infiltrative histology is seen both as a primary type and as a common component of mixed tumours. In both, it is associated with incomplete peripheral and deep excision margins.

Infiltrative or mixed infiltrative BCCs should be excised to a deep margin of the first underlying anatomical plane. BCCs of nodular, mixed non-infiltrative and superficial types can usually be safely excised with subcutaneous fat alone.

Conflicts of interest

The authors confirm that they have no conflicts of interest to declare.

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