

Managing Closely Excised Nonmelanoma Skin Cancer

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BACKGROUND: The aim of nonmelanoma skin cancer (NMSC) excision is histologic clearance with margins of ≥ 1 mm, but evidence for close-margin management is scarce. **BACKGROUND:** To compare complete, close, and incomplete excision recurrences. **METHODS:** We performed a retrospective study of a subset of patients who underwent NMSC excision during 2020 to 2021. Lesions were grouped as complete (≥ 1 mm clearance), close (< 1 mm), or incomplete (involved) and recurrence data were collected. Discrete data were analyzed using a χ^2 test. **RESULTS:** There were 421 lesions comprising 194 squamous cell carcinomas (SCCs; 49%) and 227 basal cell carcinomas (BCCs; 51%) included in the analysis. The mean follow-up was 29.3 months (standard deviation: 3.2), and the recurrence rate was 5%. There was a significantly greater risk of recurrence in closely (12%) vs completely (3%) excised SCCs ($\chi^2=4.71$; degrees of freedom [df]=1; $P=0.03$); however, no difference was demonstrated between close (12%) and incompletely (12%) excised SCCs ($\chi^2<0.05$; df=1; $P=0.98$). There was no statistical difference in recurrence rates between completely (1%) and closely (3%) excised BCCs ($\chi^2=1.08$; df=1; $P=0.30$), but a difference was found between closely (3%) and incompletely (16%) excised BCCs ($\chi^2=6.33$; df=1; $P=0.01$). **LIMITATIONS:** Follow-up was < 5 years, after which NMSCs may still recur. **CONCLUSION:** Our results support the clinical practice of treating closely excised SCCs as incomplete and treating closely excised BCCs as complete, perhaps with a follow-up period, in select cases such as when satisfying patient preference or minimising morbidity due to re-excision. **KEYWORDS:** Nonmelanoma skin cancer, close excision, recurrence, squamous cell carcinoma, basal cell carcinoma

Nonmelanoma skin cancers (NMSCs) include both squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) and represent the most common type of skin cancer in the White population.¹ The mainstay of NMSC treatment is surgical excision, including a safety margin surrounding the lesion, with the intent of complete tumor clearance ≥ 1 mm at both the peripheral and deep margins. Updated British Association of Dermatologists (BAD) guidelines on excision margins were published in 2020 and 2021 for SCCs and BCCs, respectively.^{2,3} Involved margins are considered incompletely excised and usually require further treatment, unless contraindicated due to patient comorbidity or patient preference. A clearance < 1 mm is considered a close margin, and the decision to clinically monitor, re-excite, or undergo an alternative form of therapy (such as radiotherapy or immunotherapy) is a patient-tailored decision based on risk factors and patient preference. This decision is often discussed at multidisciplinary team meetings (MDTs), particularly in the case of SCCs. National audit data suggest that NMSC incomplete excision rates are around 2.3% to 3%.^{4,5} However, a more recent meta-analysis by Nolan et al⁶ suggests that incomplete excision rates may be underreported, reporting 11.0% for BCCs and 9.4% for SCCs in a pool of 53,796 patients. Furthermore, ongoing delays and backlogs related to the COVID-19 pandemic are likely to allow for more advanced tumor progression, and with previous studies showing that increasing tumor size is correlated with incomplete excision, it is possible that this incomplete

excision rate may worsen.^{7–9} In either case, close-margin excisions are inconsistently reported and are often included in the complete excision cohort. There is a theoretically higher risk of recurrence with close-margin excisions due to the possibility of malignant cells being missed on microscopic review (ie, a false negative if considered complete).¹⁰ Additionally, close excisions may have occurred in the first place due to more aggressive or insidious disease phenotypes such as infiltrative BCCs, which are less easily marked up pre-operatively.¹¹ However, there are also a fair proportion of incompletely excised lesions that show no residual malignancy on re-excision.¹² Therefore, it remains unclear as to whether close-margin NMSC excisions should be treated as complete or incomplete, though in our center, close margins are often treated as incomplete and re-excised if possible. This is dependent, however, on anatomical location (eg, wider or deeper excision of close-margin excisions on the midface may result in unacceptable morbidity or cosmesis and may be better treated with an alternative modality such as radiotherapy) and patient factors such as ability to travel to our tertiary center for surgery.

Due to a paucity of literature available regarding the outcomes following close-margin NMSC excision, recurrence rates of such cases remain unclear. The aim of this study is to investigate recurrence rates from a cohort of NMSC incomplete excisions and in particular to compare these rates between incomplete, closely, and completely excised lesions.

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ORIGINAL RESEARCH

METHODS

Clinical governance approval was granted prior to commencing the study (CA21-089).

This cohort study was based on a subset of data used in a previous study conducted at our institution.¹³ In the previous study, we identified patients who underwent standard surgical excision for NMSC (both SCCs and BCCs) at our tertiary plastic surgery center hub site (our center operates at multiple sites in a hub-and-spoke model, serving a population of approximately 3.2 million)¹⁴ over 1 year from April 1, 2020, to March 31, 2021. Cases were therefore included in the study after being identified at our National Health Service trust via a computerized operative theater database. Our center practice generally treats close-excision margins as incomplete, especially in the case of SCC. For closely excised SCCs, re-excision or alternative therapy (eg, immunotherapy) are offered, though sometimes patients will be monitored only due to patient preference or other factors such as multiple comorbidities. Closely excised patients with BCCs are offered re-excision, radiotherapy, or clinical monitoring. Mohs surgery is sometimes offered to these patients, but due to difficulty of access at our centre, this is often declined by patients. Our aim was to examine recurrence rates in these lesion excisions. Therefore, for comparison, we obtained data for similarly sized cohorts of completely, closely, and incompletely excised SCCs and BCCs from the previous study.¹³

Data collected included age, gender, comorbidities, operation date, anatomical site, histologic type, margins, recurrence, follow-up time, and further re-excisions. For individuals with multiple lesions, each lesion was treated as a discrete data point. Regarding margins, a tumor excised by ≥ 1 mm was considered complete, < 1 mm as close, and involved margins incomplete. Patients without follow-up data due to being followed up at other sites in the trust or with other specialties were excluded from the study.

In order to analyze if closely excised lesions should be treated as completely or incompletely excised, statistical analysis was performed using Microsoft Excel for Office 365 (Microsoft Corporation) for a χ^2 test to examine if the proportion of recurrences was statistically similar between close and complete excisions, between close and incomplete excisions, and finally between complete and incomplete

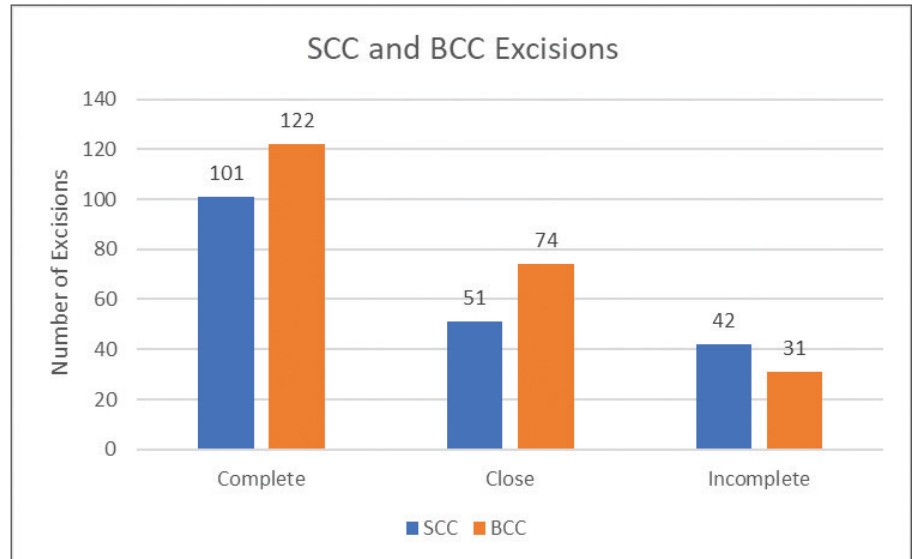


FIGURE 1. Number of patients included in each nonmelanoma skin cancer cohort by completeness of excision. There were 101 patients with squamous cell carcinoma (SCC) with complete excisions, 51 with close, and 42 with incomplete. There were 122 patients with basal cell carcinoma (BCC) with complete excisions, 74 close, and 31 incomplete.

excisions (with the null hypothesis of no difference in recurrence between the groups). The χ^2 statistic, degrees of freedom (df), and *P* values for the χ^2 test are reported. Significance was set to $P < 0.05$.

RESULTS

We identified a pool of 468 NMSC lesions that had been excised; 47 lesions that were followed up externally at other sites or lacked follow-up data were excluded, leaving 421 lesions for analysis in 380 patients (247 male, 133 female) with median age of 81 years (interquartile range [IQR]: 75–87). The lesions comprised 194 SCCs (49%, 194/421) and 227 BCCs (51%, 227/421), and 85% (357/421) were located on the head and neck. Mean follow-up time for high-risk monitored lesions was 29.3 months (SD: 3.2; range: 18.1–38.2 months), while mean follow-up times for low-risk lesions discharged at first follow-up was 2.3 months (SD: 3.3; range: 0.3–25.3 months).

The selected SCC group ($n=194$) comprised 52% (101/194) complete excisions, 26% (51/194) close excisions, and 22% (42/194) incomplete excisions. In the selected BCC group ($n=227$), there were 54% (122/227) complete excisions, 32% (74/227) close, and 14% (31/227) incomplete (**Figure 1**).

In the closely excised SCC group, 14% (7/51) were planned for re-excision at first follow-up. Regarding anatomical site, 92% (47/51) of close

excisions were in the head and neck region vs 8% (4/51) in the lower-risk anatomical sites of the limbs.

In the closely excised BCC group ($n=74$), only 1 was planned for re-excision at first follow-up; 93% (69/74) of close excisions were in the head and neck region vs 7% (5/74) in the lower-risk areas of the trunk or limbs.

The overall NMSC recurrence rate was 5% (22/421), with 64% (14/22) of recurrences being SCCs (3 from completely excised lesions, 6 from closely excised, and 5 from incomplete excisions) and 36% (8/22) being BCCs (1 from a completely excised lesion, 2 from closely excised, and 5 from incomplete excisions). Therefore, the SCC close-excision recurrence rate was 12% (6/51) and the BCC close-excision recurrence rate was 3% (2/74). Overall, 91% (20/22) of recurrences were in lesions from the head and neck, with the remaining 9% (2/22) from the forearm and chest. Of the recurrent lesions that were closely or incompletely excised at initial histology ($n=18$), only 1 patient (6%, 1/18) was referred for radiotherapy with an incompletely excised SCC; the other 94% (17/18) either listed for re-excision or monitored if not suitable for re-excision. One patient (25%, 1/4) of the completely excised lesions that recurred had additionally developed multiple new SCCs at follow-up and was referred for immunotherapy. Median time to recurrence was 5.7 months (range: 1.8–23.2; IQR: 4.4–8.1). Further recurrence data are presented in **Table 1**.

TABLE 1. Recurrent lesion data

| SEX | AGE | ANATOMICAL SITE | SCC/ BCC | HISTOLOGICAL SUBTYPE | T STAGE | DEPTH OF INVASION | DIFFERENTIATION | PERINEURAL/ LYMPHOVASCULAR INVASION | EXCISION | HISTOLOGICAL MARGINS, NEAR × DEEP (mm) | FOLLOW-UP PLAN | RE-EXCISIONS | TIME TO RECURRENCE (MONTHS) | COMORBIDITIES |
|-----|-----|-----------------|-------------|--------------------------|---------|-----------------------|------------------|--|------------|--|---|---|-----------------------------|--|
| M | 82 | Pre-auricular | SCC | Keratoacanthoma-like | pT1 | Reticular dermis | Moderate | No | Complete | 5 × 6 | Immunotherapy (multiple lesions at follow-up) | N/A | 12.6 | Type 2 diabetes, hypercalcemia, pancreatic cancer |
| M | 81 | Scalp | SCC | Classical | pT2 | Reticular dermis | Moderate-to-poor | No | Complete | 13 × 8 | Monitor | N/A | 1.9 | Diabetes, angina |
| M | 80 | Scalp | SCC | Classical | pT2 | Deep dermis | Moderate | No | Complete | 5 × 1 | Monitor | N/A | 4.9 | None |
| M | 84 | Forearm | SCC | Keratoacanthoma-like | pT2 | Subcutis | Moderate | Lymphatic | Close | 7 × <0.1 | Monitor | N/A | 5.3 | High cholesterol, asthma |
| M | 92 | Scalp | SCC | Classical | pT2 | Subcutis | Poor | No | Close | 6 × <0.5 | Monitor | N/A | 5.0 | None |
| M | 71 | Scalp | SCC | Infiltrative | pT2 | Subcutis | Moderate | Perineural | Close | 8.5 × <1 | Re-excision, bone burring and integra | 1 re-excision; margins 5.5 × 0.8 (bone burrings not sent) | 6.6 | Osteoarthritis, memory impairment |
| M | 71 | Scalp | SCC | Keratoacanthoma-like | pT2 | Deep reticular dermis | Well | No | Close | 6.5 × 0.8 | MDT: Re-excision to scalp | 3 re-excisions; most recent scar only with no residual malignancy | 7.9 | Colon cancer, thrombocytopenia, atrial fibrillation |
| F | 92 | Nasal bridge | SCC | Classical | pT1 | Subcutis and muscle | Moderate | No | Close | 4.5 × <1 | Monitor | N/A | 7.8 | None |
| M | 82 | Postauricular | SCC | Acantholytic | pT2 | Subcutis | Moderate | No | Close | 6 × 0.6 | Immunotherapy (multiple lesions at follow-up) | N/A | 4.2 | Type 2 diabetes, hypercalcemia, pancreatic cancer |
| M | 58 | Scalp | SCC | Infiltrative keratinized | pT2 | Subcutis | Poor | Perineural, possible lymphovascular | Incomplete | 7.5 × 0 | Re-excision: deeper excision and local flap | 2 re-excisions, most recent positive peripheral and deep margins; referred for radiotherapy | 3.0 | Gastroesophageal reflux disease |
| M | 84 | Scalp | SCC | Classical | pT2 | Subcutis | Moderate | No | Incomplete | 11 × 0 | Monitor (outer table burred) | N/A | 9.6 | Atrial fibrillation, tubular adenoma, vasculitis, rheumatoid arthritis, colon cancer |
| M | 97 | Chest | SCC | Classical | pT2 | Skeletal muscle | Moderate | No | Incomplete | 5 × 0 | Radiotherapy | N/A | 1.8 | Hypertension, ischemic heart disease |

BCC: basal cell carcinoma; F: female; M: male; MDT: multidisciplinary team meeting; SCC: squamous cell carcinoma

ORIGINAL RESEARCH

TABLE 1 CONTINUED. Recurrent lesion data

| SEX | AGE | ANATOMICAL SITE | SCC/ BCC | HISTOLOGICAL SUBTYPE | T STAGE | DEPTH OF INVASION | DIFFERENTIATION | PERINEURAL/ LYMPHOVASCULAR INVASION | EXCISION | HISTOLOGICAL MARGINS, NEAR × DEEP (mm) | FOLLOW-UP PLAN | RE-EXCISIONS | TIME TO RECURRENCE (MONTHS) | COMORBIDITIES |
|-----|-----|-----------------|----------|----------------------------------|---------|-------------------|-----------------|-------------------------------------|------------|--|---|--|-----------------------------|---|
| M | 82 | Tragus | SCC | Acantholytic | pT2 | Dermis | Poor | No | Incomplete | 3 × 0 | Immunotherapy (multiple lesions at follow-up) | N/A | 4.2 | Type 2 diabetes, hypercalcemia, pancreatic cancer |
| M | 91 | Cheek | SCC | Classical | pT2 | Subcutis | Moderate | No | Incomplete | 0 × 1 | MDT and imaging: re-excision | 1 re-excision; 8 × clear deep specimen | 2.5 | Gastritis |
| M | 82 | Lower eyelid | BCC | Nodular and infiltrative | | Reticular dermis | | No | Complete | 1 × 4.5 | Monitor | N/A | 5.3 | Hypertension |
| F | 79 | Canthus | BCC | Nodular | | Reticular dermis | | No | Close | 2 × 0.4 | Monitor | N/A | 23.2 | Anemia, atrial fibrillation |
| F | 77 | Lower lip | BCC | Nodular and superficial | | Reticular dermis | | No | Close | 0.8 × 1.5 | Monitor | N/A | 11.2 | Prediabetes |
| F | 86 | Forehead | BCC | Nodular and infiltrative | | Subcutis | | No | Incomplete | 0 × 3 | Monitor | N/A | 4.8 | Hypertension, osteoporosis |
| M | 79 | Nose | BCC | Nodular | | Reticular dermis | | No | Incomplete | 2.7 × 0 | Re-excision | 1 re-excision; no residual malignancy | 5.3 | Hypertension, ischemic heart disease |
| M | 78 | Cheek | BCC | Nodular | | | | No | Incomplete | 0 × 0.4 | Monitor | N/A | 13.6 | Chronic kidney disease, hypothyroidism |
| M | 90 | Ear | BCC | Infiltrative | | Deep dermis | | No | Incomplete | 0 × 2.5 | Offered re-excision; declined | N/A | 6.1 | None |
| M | 93 | Temple | BCC | Nodular infiltrative superficial | | Deep dermis | | No | Incomplete | 0 × 2 | Monitor | N/A | 6.4 | None |

BCC: basal cell carcinoma; F: female; M: male; MDT: multidisciplinary team meeting; SCC: squamous cell carcinoma

On χ^2 testing, when comparing the recurrence rates between the completely excised (3%, 3/101) and closely excised (12%, 6/51) SCCs, the chance of recurrence was statistically different ($\chi^2=4.71$; $df=1$; $P=0.03$). However, when comparing recurrence rates in the close (12%, 6/52) and incomplete (12%, 5/42) SCC groups, there was no difference ($\chi^2<0.05$; $df=1$; $P=0.98$). As expected, there was a statistically significant difference between the complete (3%, 3/101) and incomplete (12%, 5/42) excision groups ($\chi^2=4.48$; $df=1$; $P=0.03$).

For BCCs, in the completely (1%, 1/122) vs closely (3%, 2/74) excised groups, there was no statistical difference in recurrence rates ($\chi^2=1.08$; $df=1$; $P=0.30$). Looking at the closely (3%, 2/74) and incompletely (16%, 5/31) excised groups, there was a statistical difference in recurrence ($\chi^2=6.33$; $df=1$; $P=0.01$). Once again, recurrence rates in completely (1%, 1/122) vs incompletely (16%, 5/31) excised BCCs were statistically different ($\chi^2=15.48$; $df=1$; $P<0.01$).

DISCUSSION

This study builds upon previous work by our team, which highlighted the need for clarity on whether close excisions should be considered complete or incomplete.¹³ Our main findings are that regarding recurrence, closely excised SCCs recur in a manner similar to incompletely excised tumors whereas for BCCs, closely excised lesions appear to behave more similarly to completely excised tumors. The logical conclusion is that closely excised SCCs should be managed with further treatment (re-excision, Mohs surgery, or radiotherapy) or at least discussion in an MDT as for incompletely excised SCCs. This lends some evidence to the most recent iteration of the British Association of Dermatologists guidelines for SCCs, which suggest managing closely excised lesions similarly to incompletely excised tumors, though they report there is little strong evidence to support this practice.² Conversely, as closely excised BCCs have recurrence rates statistically similar to completely excised BCCs, we may be able to treat these more conservatively, as wider or deeper re-excisions, particularly in cosmetically sensitive areas such as the nose and eyelids, may be associated with higher morbidity and impairments to social functioning for some patients.¹⁵ To our knowledge, there is a paucity of literature regarding the best treatment options for closely excised lesions, which has also contributed to the inconsistently reported nature of close

margins, with some authors considering these completely excised,^{16–27} while others consider them incomplete.^{28–32} Therefore, the results of our study offer some evidence toward the ongoing debate of best practice for closely excised lesions.

In our selected cohort of patients, there were 42 incompletely excised SCCs from the total 194 SCCs (22%) in the dataset and 31 incompletely excised BCCs from the total of 227 (13%). Due to the study design (looking for recurrences in cohorts matched to the incomplete and close excisions), this is not a proportion of total NMSCs excised over the study period. The total incomplete excision rate in our previous study was 6.6% for SCC rate and 3.2% for BCC, from a total pool of 2,554 NMSC excisions, which is in line with other studies in the literature.^{6,13} Head and neck lesions are known to confer a high risk of incomplete excision, partly due to a difficult balance between oncologic control and functional or cosmetic concerns.^{33,34}

Interestingly, in the time since our study cohort of patients received surgery, the British Association of Dermatologists guidance for standardized excision margins has been updated, with suggested peripheral-excision margins for low-risk BCCs increasing from 3 mm to 4 mm, the same as for low-risk SCCs.^{2,3} Therefore, it is possible that newer populations of patients with BCC with excisions based on the updated guidelines may have an even lower rate of close or incomplete margins; this should be investigated in the future to clarify the merits of a wider excision, particularly in cosmetically sensitive areas.

As a final point, with regards to re-operation, one might argue that closely excised lesions are an ideal case use for Mohs surgery given ability for immediate margin control. However, there is large variability in availability of Mohs surgeons worldwide, with countries such as the United States having far greater access than some European countries. Therefore, this study offers most benefit to areas in which there are fewer Mohs services and treatment of closely excised lesions is more of a dilemma.

Limitations of this study include the lack of data on lesion size or intra-operative margins (peripheral or deep plane) and, for close-margin excisions, our histologic data were limited in some cases as reports only mentioned a margin <1 mm but not the specific measurement. Follow-up is also <5 years, a period in which NMSCs may still recur. While continuous data on closeness of excision were not required for our current study, future work using regression analysis

could investigate closeness of excision with recurrence as well as the differences in recurrence rates between close-peripheral and close-deep margins. Finally, given that we had a high caseload of head and neck cases, these results may not be entirely generalizable to a general lower-risk population.

CONCLUSION

Our study demonstrated that closely excised SCCs recur as frequently as incompletely excised lesions, while closely excised BCCs have a similar recurrence pattern to completely excised lesions. In this area where there is a paucity of literature and ongoing debate, our results provide some support to the clinical practice of treating closely excised SCCs as incomplete and to consider treating closely excised BCCs as complete, perhaps with a period of follow-up, which may help to decrease the excess morbidity caused by wider re-excision.

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ORIGINAL RESEARCH

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