Journal of Plastic, Reconstructive & Aesthetic Surgery 88 (2024) 443–451

Revisiting basal cell carcinoma clinical margins: Leveraging natural language processing and multivariate analysis with updated Royal College of Pathologists histological reporting standards

Stephen R. Ali [a,b,*,1], Thomas D. Dobbs [a,b], Matthew Jovic [a], Huw Strafford [c,d], Arron S. Lacey [c,d], Namor Williams [e], William Owen Pickrell [c,f], Hayley A. Hutchings [g], Iain S. Whitaker [a,b]

[a] *Reconstructive Surgery and Regenerative Medicine Research Centre, Institute of Life Sciences, Swansea University Medical School, Swansea, UK*
[b] *Welsh Centre for Burns and Plastic Surgery, Morriston Hospital, Swansea, UK*
[c] *Neurology and Molecular Neuroscience Group, Institute of Life Science, Swansea University Medical School, Swansea University, Swansea, UK*
[d] *Health Data Research UK, Data Science Building, Swansea University Medical School, Swansea University, Swansea, UK*
[e] *Department of Cellular Pathology, Morriston Hospital, Swansea, UK*
[f] *Department of Neurology, Morriston Hospital, Swansea, UK*
[g] *Faculty of Medicine, Swansea University Medical School, Swansea, UK*

Received 6 July 2023; Accepted 18 October 2023

KEYWORDS
Basal cell carcinoma;
Clinical margins;
Natural language processing;
Multivariate analysis;

Summary *Introduction:* Data supporting the current British Association of Dermatologists guidelines for the management of basal cell carcinoma (BCC) are based on historic studies and do not consider the updated Royal College of Pathologists (RCPath) histological reporting standards. The aim of this study was to use natural language processing (NLP)-derived data and undertake a multivariate analysis with updated RCPath standards, providing a contemporary update on the excision margins required to achieve histological clearance in BCC.

* Correspondence to: Reconstructive Surgery & Regenerative Medicine Research Centre, Institute of Life Sciences, Swansea University Medical School, Swansea SA2 8PP, UK.
E-mail address: stephen.ali@swansea.ac.uk (S.R. Ali).
[1] 0000-0002-9917-3432

https://doi.org/10.1016/j.bjps.2023.10.106

Histological reporting guidelines;
Royal College of Pathologists

Methods: A validated NLP information extraction model was used to perform a rapid multicentre, pan-specialty, consecutive retrospective analysis of BCCs, managed with surgical excision using a pre-determined clinical margin, over a 17-year period (2004–2021) at Swansea Bay University Health Board. Logistic regression assessed the relationship between the peripheral and deep margins and histological clearance.
Results: We ran our NLP algorithm on 34,955 BCCs. Out of the 1447 BCCs that met the inclusion criteria, the peripheral margin clearance was not influenced by the BCC risk level ($p = 0.670$). A clinical peripheral margin of 6 mm achieved a 95% histological clearance rate (95% confidence interval [CI], 0.93–0.98). Tumour thickness inversely affected deep-margin histological clearance (OR 0.720, 95% CI, 0.525–0.991, $p < 0.05$). Depth level 2 had a 97% probability of achieving deep-margin histological clearance across all tumour thicknesses.
Conclusion: Updated RCPath reporting standards minimally impact the peripheral margin histological clearance in BCC. Larger clinical peripheral margins than those indicated by current guidelines may be necessary to achieve excision rates of ≥95%. These findings emphasise the need for continuous reassessment of clinical standards to enhance patient care.

Standard surgical excision is an effective treatment for primary basal cell carcinomas (BCCs), with reported 5-year recurrence rates of 3–8%. However, the excision margin plays a crucial role in achieving a balance between cure and minimising morbidity.[1-3] To optimise the treatment outcomes, the British Association of Dermatologists (BAD) guidelines recommend that low-risk BCCs should be excised using a 4 mm peripheral surgical margin, while primary BCCs with high-risk factors should be excised using at least a 5 mm peripheral clinical margin.[4] Additionally, they highlight the importance of adequate excision at the deep-margin, with recommendations to excise to a clear plane, including a fat layer where present, and other deeper structures if needed.

The Royal College of Pathologists (RCPath) has recently updated its guidance on the reporting of BCC histological subtype.[5-7] They now advise that there is no clinical value in distinguishing between the infiltrative, sclerosing, morphoeic, and micronodular subtypes and that these should all be regarded as histological features indicating a high-risk lesion. This allows most BCCs to be categorised as either low-risk or high-risk.

In this study, we expand upon previous research by conducting an analysis using data that is categorised according to the updated RCPath standards. These standards were used to develop the current BAD guidelines and provide recommendations for treatment according to low-risk and high-risk BCC criteria. Notably, the systematic review conducted by the BAD to inform their guideline development included studies that were conducted before the implementation of the RCPath standards. Consequently, there are no studies to date that investigate the impact of the updated RCPath criteria on treatment efficacy for low-risk and high-risk BCC. The aim of this study was to clarify the BCC types that should be treated using wider or deeper clinical margins and inform further guideline updates.

Methods

Study design

We undertook a multi-centre, pan-specialty, retrospective analysis of consecutive patients with BCC who were managed with surgical excision using a pre-determined margin at Swansea Bay University Health Board, Swansea, United Kingdom from 2004 to 2021. All lesions were examined by a consultant histopathologist using the bread loafing cross-section technique. Primary, recurrent, and previously excised lesions were grouped together for analysis. Patients with BCC, who were managed by surgical excision, using a pre-determined clinical margin were included. Diagnostic biopsies, including punch biopsy, incision biopsy, shave biopsy, and curettage were excluded, as were patients managed using Mohs micrographic surgery.

Natural language processing (NLP) algorithm

Previous studies have demonstrated that clinical peripheral margins and deep margin planes of excision are commonly missing from the literature and, therefore, not available for analysis. To overcome this and reduce the need to review both operative notes and histopathology reports in a large dataset, we used a novel natural language processing (NLP) technique developed by our group. This used the general architecture for text engineering framework to build an NLP information extraction system using rule-based techniques.[8] This was validated on previously unseen BCC histopathological reports at the same institution as the current study. Mean precision, recall, and F1 score were 86.0% (95% confidence interval [CI], 75.1–96.9), 84.2% (95% CI 72.8–96.1), and 84.5% (95% CI 73.0–95.1), respectively.

Case identification, data extraction and processing

Cases were retrospectively identified from InterSystems TrakCare Laboratory Information Management System (InterSystems TrakCare Lab, Cambridge, Massachusetts, USA), using SNOMED codes for BCC (M-80983, M-80903, M-80943, M-80933, M-80923, M-80943, M-80973, and M-80913). Once the cases were identified, free text pathological reports were retrieved and saved in text file format. Our rule-based NLP pipeline was then applied to this corpus. Comma-separated variable text files were generated from the respective canonical subheadings of the pathology report. Complete case analysis was used as an approach to the treatment of missing data. Owing to the structured nature of the data output by our NLP algorithm, data cleaning was not required, other than to use the first output if there was more than one annotation for the same piece of free text. If a numeric value was extracted the worst prognostic value was selected. For example, in the following statement, 1 mm would be selected as the peripheral margin value: 'peripheral margin 1 mm at 9 o'clock, 3 mm 12 o'clock, 5 mm 3 o'clock and 3 mm 6 o'clock'. Custom Python scripts were used for both these tasks.

Variables

Tumour factors (primary versus recurrent, anatomical site, borders [clinically distinct/indistinct], perineural invasion, lymphovascular invasion, tumour thickness, diameter, level of invasion, subtype, differentiation and stage), patient factors (immunosuppression and previous radiotherapy) and surgical factors (pre-operative peripheral margin [mm] and deep margin) were recorded. The documented deep clinical margin was recorded based on the anatomical plane to which the lesion was excised, with subcutaneous fat recorded as plane 1 (Figure 1). We defined this as the depth level.

The BAD use an adapted National Comprehensive Cancer Network table in their guidelines to define criteria for low-risk and high-risk BCC.[4,9] We used this to categorise BCCs clinicopathologically into low-risk and high-risk groups, equating to the Union for International Cancer Control 8th edition version of tumour-nodes-metastasis (TNM8) and RCPath dataset (Table 1 and Figure 2).[10] The overall clinical risk status of a mixed subtype BCC was judged from the highest risk subtype(s) present, irrespective of percentage or location, in line with current RCPath reporting standards. The primary outcomes were histological margin status and risk status. We defined the margin status as either clear (> 0 mm) or involved (0 mm).

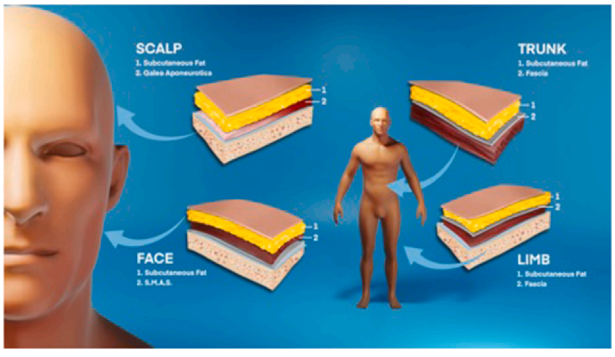

Figure 1 Anatomical planes of deep margin excision demonstrated in different sites across the body. SMAS: superficial musculoaponeurotic system.

Statistical analyses

A logistic regression model was used to examine the relationship between the pre-determined clinical peripheral margin value (mm) and complete histological peripheral margin clearance. The model included an interaction term between peripheral margin value (mm) and risk, which was included as a covariate. Predictions of complete histological peripheral margin clearance were made for different levels of clinical peripheral margin value, stratified by risk. Finally, a plot of the probability of complete histological peripheral margin clearance as a function of clinical peripheral margin value was created for high-risk, low-risk, and all BCCs separately. Similarly, we fitted a second logistic regression model to investigate the relationship between complete histological deep margin clearance and the predictor variables such as surgical depth level, risk and tumour thickness. Statistical analysis was undertaken in R version 4.1.1 (R Core Team, R Foundation for Statistical Computing, Vienna, Austria). $p < 0.05$ was deemed statistically significant.

Results

A total of 34,955 BCCs were assessed using our NLP algorithm, identifying 1447 lesions that had complete data and met the inclusion criteria for the study. Each patient received a separate histopathology report describing the lesions excised. Baseline characteristics are shown in Table 2.

Peripheral clearance

Binary logistic regression demonstrated that a lesion, irrespective of its high or low risk, was not influential in determining if the peripheral margin was histologically clear (Table 3, Figures 3 and 4). However, the clinical peripheral margin used was found to be statistically significant in determining if a lesion's histological peripheral margin was clear. As expected, increasing the clinical peripheral margin increased the chance of obtaining histological peripheral margin clearance. To assess the degree to which increasing the clinical peripheral margin influenced the chance of complete histological clearance, the conversion of log odds to probabilities for varying clinical peripheral margins was undertaken and stratified by risk. At a clinical peripheral margin of 6 mm, a 95% histological clearance rate was achieved; this being the same for both high and low-risk BCCs (Figure 5). At a clinical peripheral margin of 11 mm, there was a plateauing of results, and thereafter the probability of obtaining clearance stayed at 99%. Data across all clinical margins and risk statuses are summarised in Table 4.

We also investigated whether the addition of ulceration to upgrade low-risk lesions to high-risk would impact the

Table 1 Criteria for low-risk and high-risk basal cell carcinoma (BCC).

Tumour, patient, and surgical variables collected	Low-risk	High-risk
Location and size	Area A ≤20 mm* Area B ≤10 mm*	Area A >20 mm* Area B >10 mm* Area C
Borders	Well defined	Poorly defined
Primary vs. recurrent	Primary	Recurrent
Immunosuppression	No	Yes
Site of prior radiotherapy	No	Yes
Growth pattern	Nodular, cystic, superficial, and fibroepithelial	Infiltrative (infiltrating, morphoeic, micronodular, and multinodular)
Differentiation: basosquamous	Absent	Present (with or without lymphovascular invasion)
Level of invasion	Dermis, subcutaneous fat	Beyond subcutaneous fat
Depth (thickness)	≤6 mm	>6 mm
Perineural invasion	Absent	Present
Pathological TNM stage	pT1	>pT2

TNM, tumour-nodes-metastasis. One or more criteria satisfies the criteria for high-risk.
* Maximum clinical diameter.

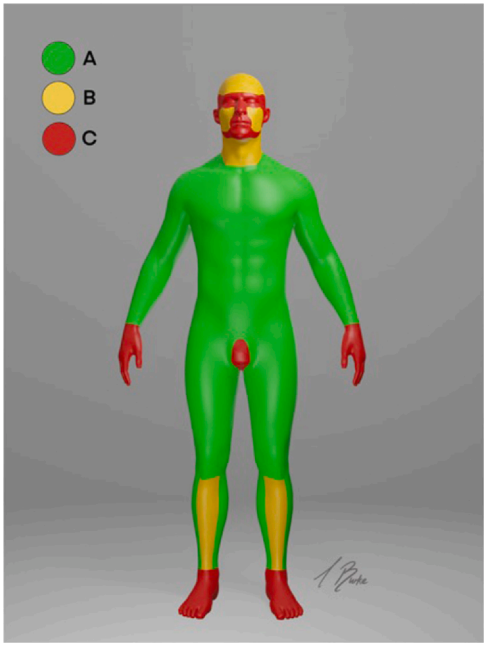

Figure 2 Topographical areas used for classification of low-risk and high-risk basal cell carcinoma (BCC) that corresponds with Table 1. Area A, trunk and extremities excluding hands, nail units, genitalia, pretibial, ankles, and feet; Area B, cheeks, forehead, scalp, neck and pretibial; Area C, 'mask areas' of face (central face, eyebrows, periorbital, eyelids, nose, lips [cutaneous and vermilion], chin, mandible, preauricular, post-auricular, temple, ears); genital areas; hands, nail units, ankles and feet.

likelihood of histological clearance on *post-hoc* analysis. The odds of achieving clearance were found to decrease by a factor of 0.553 when ulceration was present ($p = 0.0257$). This reduced the probability of achieving complete histological peripheral margin clearance for all clinical margins (Supplementary Table 1). Additionally, we investigated

Table 2 Baseline characteristics of the included lesions.

Margin	Risk	Margin (mm)	Number of lesions
Peripheral	Low	=0	28
Peripheral	Low	>0	319
Peripheral	High	=0	55
Peripheral	High	>0	745
Total peripheral	-	-	1147
Deep	Low	=0	4
Deep	Low	>0	48
Deep	High	=0	19
Deep	High	>0	229
Total deep	-	-	300
Total peripheral and deep	-	-	1447

Table 3 Odds ratios for obtaining histological peripheral clearance based on low-risk versus high-risk and peripheral clinical margin.

Coefficients	OR	95% CI	p-value
Peripheral margin	1.270	(1.066-1.551)	0.0128
Low-risk	0.901	(0.563-1.471)	0.670

OR: odds ratio.

whether low-risk BCCs and differing anatomical sites and diameters could be managed with smaller clinical margins on *post-hoc* analysis. Univariate analysis of low-risk BCCs (satisfying low-risk criteria *except* high-risk anatomical site) at area C showed that the clinical margin was a significant predictor of clearance (estimate = 0.8033, standard error = 0.3876, z-value = 2.072, $p = 0.0382$) but not in other anatomical areas with smaller margins (<10 mm or 10-20 mm). In this group, the probability of achieving a complete peripheral margin was higher for most clinical

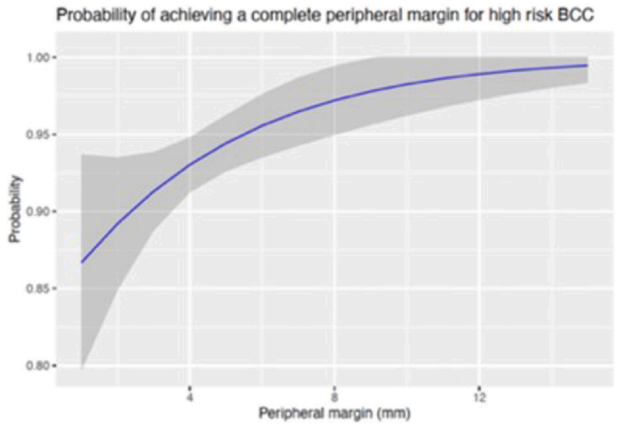

Figure 3 Probability of achieving a complete peripheral margin for *high-risk* basal cell carcinoma (BCC).

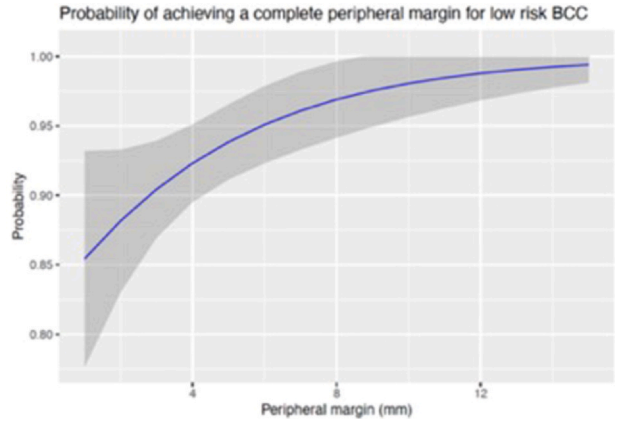

Figure 4 Probability of achieving a complete histological peripheral margin for *low-risk* basal cell carcinoma (BCC).

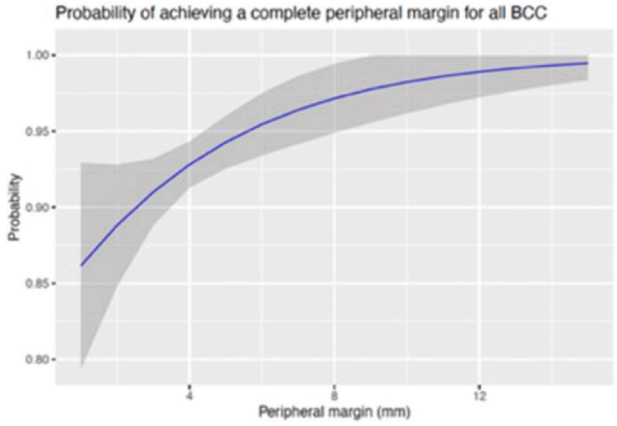

Figure 5 Probability of achieving a complete peripheral margin for *all* basal cell carcinoma (BCC).

margins (Supplementary Table 2), with a 4 mm margin giving a 95% clearance rate.

Deep clearance

Assessment of tumour thickness with depth level stratified by risk was not possible owing to the low frequency of lesions which were low-risk and had incomplete deep margins. To avoid bias, we did not add risk as a variable in the model. After removing outliers, we analysed tumour thickness up to a maximum of 6 mm.

Regression analysis indicated that increasing tumour thickness decreased the chance of obtaining deep histological clearance (odds ratio [OR] 0.720, 95% CI, 0.525-0.991, $p < 0.05$ [Table 5]). This is reflected in the results from the analysis of the depth levels (Table 6). The ORs of the depth

Table 4 Probability (95% CI) of achieving a complete peripheral histological margin.

Peripheral margin (mm)	Risk	Probability	Lower limit	Upper limit
1	High	0.87	0.80	0.94
2	High	0.89	0.85	0.94
3	High	0.91	0.89	0.94
4	High	0.93	0.91	0.95
5	High	0.94	0.93	0.96
6	High	0.96	0.93	0.98
7	High	0.96	0.94	0.99
8	High	0.97	0.95	0.99
9	High	0.98	0.96	1.00
10	High	0.98	0.96	1.00
11	High	0.99	0.97	1.00
12	High	0.99	0.97	1.00
13	High	0.99	0.98	1.00
14	High	0.99	0.98	1.00
15	High	0.99	0.98	1.00
1	Low	0.85	0.78	0.93
2	Low	0.88	0.83	0.93
3	Low	0.90	0.87	0.94
4	Low	0.92	0.90	0.95
5	Low	0.94	0.91	0.97
6	Low	0.95	0.92	0.98
7	Low	0.96	0.93	0.99
8	Low	0.97	0.94	1.00
9	Low	0.98	0.95	1.00
10	Low	0.98	0.96	1.00
11	Low	0.98	0.96	1.00
12	Low	0.99	0.97	1.00
13	Low	0.99	0.97	1.00
14	Low	0.99	0.98	1.00
15	Low	0.99	0.98	1.00
1	Overall	0.86	0.79	0.93
2	Overall	0.89	0.85	0.93
3	Overall	0.91	0.89	0.93
4	Overall	0.93	0.91	0.94
5	Overall	0.94	0.93	0.96
6	Overall	0.95	0.93	0.98
7	Overall	0.96	0.94	0.99
8	Overall	0.97	0.95	0.99
9	Overall	0.98	0.96	1.00
10	Overall	0.98	0.96	1.00
11	Overall	0.99	0.97	1.00
12	Overall	0.99	0.97	1.00
13	Overall	0.99	0.98	1.00
14	Overall	0.99	0.98	1.00
15	Overall	0.99	0.98	1.00

Table 5 Summary of logistic regression analysis results assessing deep clearance subject to depth level and tumour thickness.

Coefficients	OR	95% CI	p-value
Depth level 2	2.726	(0.659–18.428)	0.213
Tumour thickness	0.720	(0.525–0.991)	0.041

OR: odds ratio.

Table 6 Probability (95% CI) of achieving a complete deep margin using a logistic regression model of depth level and tumour thickness for high-risk and low-risk lesions combined.

Depth level	Tumour thickness (mm)	Probability	Lower limit	Upper limit
1	1	0.97	0.93	1.00
1	2	0.95	0.92	0.99
1	3	0.94	0.90	0.98
1	4	0.91	0.86	0.98
1	5	0.89	0.79	0.98
1	6	0.85	0.70	1.00
2	1	0.99	0.97	1.00
2	2	0.98	0.96	1.00
2	3	0.98	0.94	1.00
2	4	0.97	0.92	1.00
2	5	0.95	0.89	1.00
2	6	0.94	0.84	1.00

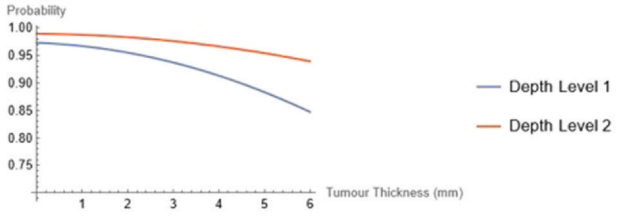

Figure 6 Probability of achieving a complete deep margin when considering tumour thickness for *all* basal cell carcinomas (BCCs) stratified by depth level.

levels fluctuated with large CIs in most cases. As in the peripheral margin example, probabilities of deep clearance were computed for varying tumour thickness stratified by depth level. The results can be seen in Figure 6. All depth levels showed a decreasing chance of deep clearance with increasing tumour thickness. Depth level 2 had the greatest probability of achieving deep clearance (97%) at all tumour thicknesses, followed by depth level 1 (92%).

The ratio of depth level to tumour thickness was used as a variable in the model with risk; probabilities were computed based on the relationship of these variables to demonstrate the distribution of this ratio relative to the likelihood of achieving a complete deep clearance. While both coefficients indicated no statistical significance (Table 7), the probability plot showed an increasing trend of ratio and probability in an almost linear trend (Figure 7). No real change was evident between the high and low-risk probabilities (Table 8). For lower values of ratio (i.e. low values of depth level and high values of tumour thicknesses)

Table 7 Summary of logistic regression analysis results assessing deep clearance subject to ratio and risk status.

Coefficients	OR	95% CI	p-value
Ratio	1.366	(0.778–2.850)	0.355
Low-risk	0.901	(0.294–3.101)	0.847

OR: odds ratio.

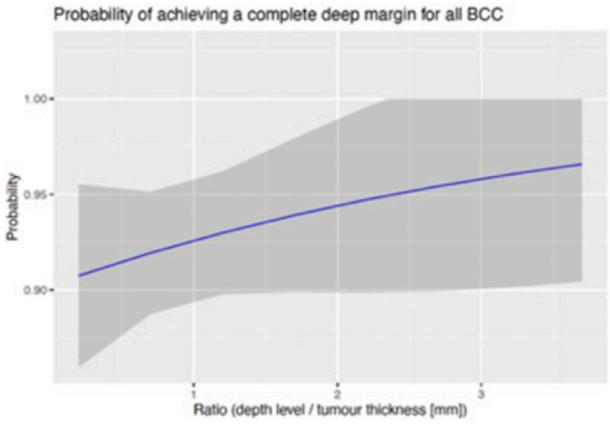

Figure 7 Probability of achieving a complete deep margin for *all* basal cell carcinomas (BCCs) when considering the ratio of depth level: tumour thickness (mm).

Table 8 Probability (95% CI) of achieving a complete deep margin using a logistic regression model of ratio = depth level/tumour thickness for high-risk and low-risk lesions combined.

Ratio	Prediction	Lower limit	Upper limit
0	0.90	0.84	0.96
0.5	0.91	0.88	0.95
1	0.93	0.90	0.96
1.5	0.94	0.90	0.97
2	0.94	0.90	0.99
2.5	0.95	0.90	1.00
3	0.96	0.90	1.00
3.5	0.96	0.90	1.00
4	0.97	0.91	1.00

we found a lower probability of achieving complete deep clearance. For higher values of the ratio (i.e. high values of depth level and low values of tumour thickness), we found an increase in the likelihood of a deep clearance. Therefore, we can conclude that increasing depth level relative to decreasing tumour thickness increases the probability of complete deep clearance; however, this result was not statistically significant.

Sensibility analysis based on variability in F1 score

Given the pivotal role of the F1 score in appraising the equilibrium between precision and recall, we undertook a sensibility analysis to envisage the potential implications of its variability on our outcomes. For this analysis, we adopted two primary modelling assumptions. Firstly, we postulated that the influence of the F1 score on clearance is

linear. Secondly, we surmised that fluctuations in the F1 score would yield proportional modifications in the reported outcomes. This assumption can be represented as:

$$\text{Best-case scenario: Adjustment factor} = \frac{\text{Upper CI of F1}}{\text{Reported F1}}.$$

$$\text{Worse-case scenario: Adjustment factor} = \frac{\text{Lower CI of F1}}{\text{Reported F1}}.$$

Our reported F1 score in validation was 84.5%, with a 95% CI spanning from 73.0% to 95.1%. Drawing upon this data, we devised two hypothetical scenarios. In the best-case scenario, with the F1 score at its upper bound of 95.1%, the adjustment factor was determined to be 1.125. Under this assumption, the peripheral clearance for a 6 mm margin, previously cited at a 95% clearance rate, would essentially top out at 100% after adjustment. Similarly, the 11 mm clinical margin, initially reported at 99%, would also peak at 100% following adjustment. Pertaining to deep clearance, the original clearance of 97% of depth level 2 would be adjusted to 100%, and depth level 1, which had an earlier clearance rate of 92%, would also escalate to 100% post-adjustment. Conversely, the worst-case scenario emanates from the lower threshold of CI of the F1 score: 73.0%. The corresponding adjustment factor for this scenario is 0.8637. For peripheral clearance at a 6 mm clinical margin, the original 95% clearance rate would be adjusted downwards to 82.05%. The 11 mm clinical margin would have its clearance rate diminish from the original 99–85.49%. In terms of deep clearance, clearance of depth level 2 would recede from 97% to 83.9%, while that of depth level 1 would drop from the initial 92–79.5%. These observations highlight the susceptibility of our results to alterations in the F1 score.

Discussion

This is the first study to date to use NLP for large volume assessment of the completeness of excision margins for BCC. Despite the availability of destructive and topical treatments, surgical excision with a pre-determined clinical margin has been the mainstay of BCC management for decades. As microscopic tumour extension is not identifiable at the time of surgical excision, the aim of a pre-determined clinical excision margin is to gain complete histological clearance in as many cases as possible, while balancing against the functional and aesthetic considerations of larger excisions. These clinical margins serve only as a guide aimed at achieving a 1 mm histological margin for oncological clearance. This means that while they provide a helpful benchmark, they do not guarantee complete excision in all cases.

In their systematic review, the BAD aimed to evaluate appropriate clinical margins for standard surgical excisions of BCC.[4] They compared non-standard clinical margins (< 4 mm, > 5 mm) to specified clinical margins (4–5 mm) and assessed incomplete excision rates. Overall, the findings of the included studies suggest that standard excision margins of 4–5 mm are appropriate for surgical excision of BCC. However, our results indicate that 4 mm and 5 mm peripheral margins result in incomplete excision rates of 8% and 6%, respectively. To achieve the BAD recommended target rate of ≥95% for complete excision, our study suggests that a peripheral margin of 6 mm for both high and low-risk BCCs would be more appropriate.

In 2018, the World Health Organisation classified infiltrative, micronodular, and sclerosing/morphoeic subtypes of BCC as 'high-risk', citing a heightened potential for local recurrence, invasion, and metastasis.[11] The refined 2019 RCPath dataset supplied precise and exhaustive guidelines for reporting these subtypes and suggested categorisation of certain subtypes as high-risk, advancing the accuracy and uniformity in BCC reporting.[7] Interestingly, our study discerned that the designated risk status had little influence on the clarity of the peripheral margin. Notably, our study found that the presence of ulceration, not acknowledged as a negative prognostic factor in current guidelines, negatively impacted the probability of clearance. Additionally, applying narrower margins for managing low-risk BCCs < 10 mm in size at body area C could secure equivalent clearance rates, potentially resolving the absence of observed disparity in clearance rates between various risk statuses. These findings have important implications for clinical management and underscore the need for further refinement of risk stratification in the management of BCCs.

While clinical peripheral margin size has been relatively well studied, the depth to which a BCC should be excised to gain complete histological clearance is poorly evidenced. BAD guidelines recommend excision to a clear plane at the deep margin, including any deeper structures if necessary. Kiely et al. showed that excising to the first underlying anatomical plane resulted in uninvolved margins in 95% of infiltrative or mixed infiltrative BCC, while subcutaneous fat was adequate for clearance in 95% of nodular, superficial, and mixed non-infiltrative BCC.[12] Our data would support this finding; however, we were not able to add risk in the regression model owing to the low frequency of lesions that were both low-risk and had incomplete deep margins. Therefore, we cannot comment on the impact of the RCPath standards on the recommended excision plane differentially for high-risk and low-risk lesions. However, we can demonstrate that depth level 2 has the greatest probability of achieving deep clearance at all tumour thicknesses included in the analysis. In our investigation of the relationship between the probability of complete deep-margin clearance of skin cancer and the anatomical plane it is excised at, we found that tumour thickness potentially confounds this relationship.

In the pursuit of increased oncological safety with lower incomplete excision rates, the BAD recommends that individual operators and units should regularly audit their outcomes, with a target of ≥95% clearance.[13,14] While these recommendations provide clarity and a unified direction, they also bring forth questions about the broader implications of achieving such high rates. Would pushing for a higher complete excision rate necessitate wider and deeper clinical margins? If so, at what cost? Every excision inherently brings forth risks. Therefore, decisions about excision margins must be made using a holistic perspective.

The onus falls on both the plastic surgery and dermatology communities to question whether the reduction of an incomplete excision rate by a few percentages justifies a potentially increased risk of complications or a compromise in aesthetic or functional outcomes. Secondary procedures, bring with them added emotional stress, potential financial implications, and risks associated with surgery. Nevertheless, for certain patients, particularly those who are concerned about scarring or functional impairment, a smaller initial clinical margin with an elevated risk of a secondary excision or even radiotherapy might be more desirable than a larger primary excision or reconstruction. The debate on margins for BCCs should be seen not just as a matter of millimetres but as a multifaceted issue interlacing oncological safety, aesthetic or functional considerations, patient preferences, and quality of life. The challenge lies in crafting an approach that seamlessly integrates all these facets and epitomises the essence of holistic patient care.

Strengths and limitations

Using NLP, our study provides novel insights into the importance of assessing peripheral margins in the context of the RCPath 2019 standards for the completeness of BCC excisions which no other study has performed to date. By using new statistical modelling techniques, we could add to the literature on the optimal deep margin for the complete excision of BCCs. Even with a considerable amount of missing data, our research includes a complete dataset for 1447 lesions. This sizeable dataset compares favourably with many studies cited in the BAD systematic review, which spanned 29 studies with an average lesion count of 744.[4]

However, despite using an NLP algorithm on over 34,000 BCCs over a 17-year period, only 5% had complete data. The credibility of our results hinges on consistent and unbiased data documentation. Furthermore, the potential variability in surgeons' measurement and definition of clinical margins and depth levels introduces inconsistencies in the data. To address this limitation, we advocate the use of the UK National Histopathology Request Form for skin biopsies, which has been approved by the BAD.[7] Although the measured clinical peripheral margin is a non-core clinical item in this form, incorporating this information would significantly improve the completeness of data for similar future studies. Notwithstanding our sensibility analysis, it is paramount to emphasise that our study's foundation rests heavily on the accuracy of the NLP algorithm that fuels the multivariate analysis. Accordingly, any inaccuracies or biases within the algorithm can cascade into the multivariate model, potentially impacting the validity of our conclusions. Thus, our results should be interpreted with an added degree of caution.

Conclusion

This study has shed light on the impact of updated RCPath histological reporting standards on clearance rates in the surgical management of BCC. Our findings suggest that peripheral margin clearance is not influenced by RCPath risk criteria and that larger peripheral margins may be necessary to achieve complete excision rates ≥95%. We also suggest that risk stratification should include ulceration in the future, and guideline updates should consider the requirement for smaller clinical margins depending on anatomical sites and tumour diameter.

Institutional ethical approval

Ethical committee approval has been obtained from Swansea University Medical School Research Ethics Subcommittee (reference no: 2020-0025). The study was performed in accordance with the Declaration of Helsinki.

Financial support

SRA and TDD are funded by the Welsh Clinical Academic Training Fellowship. ISW is the surgical specialty lead for Health and Care Research Wales and reports active grants from the American Association of Plastic Surgeons and the European Association of Plastic Surgeons. SRA received a grant from the British Association of Plastic, Reconstructive, and Aesthetic Surgeons specifically for this work. The Reconstructive Surgery & Regenerative Medicine Research Centre is funded by The Scar Free Foundation and Health and Care Research Wales. The Scar Free Foundation is the only medical research charity focused on scarring with the mission to achieve scar-free healing within a generation.

CRediT authorship contribution statement

All listed authors contributed to 1) the conception and design, acquisition of data, analysis, and interpretation of data; 2) drafting the article or revising it critically for important intellectual content; 3) final approval of the version to be published; 4) agreement to be accountable for all aspects of the work.

Declaration of Competing Interest

None.

Acknowledgements

We thank Mr Octavian Parkes, Research Programme Manager at the Reconstructive Surgery & Regenerative Medicine Research Centre, for his critical review of the manuscript.

Data availability

All data were anonymised prior to collection. We do not have a data sharing agreement for the data; however, we

are exploring ways of obtaining patient consent and endeavour to produce a minimum dataset for cross-platform testing.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.bjps.2023.10.106.

References

1. Thissen MR, Neumann MH, Schouten LJ. A systematic review of treatment modalities for primary basal cell carcinomas. *Arch Dermatol* 1999;**135**(10):1177–83.
2. 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**(9447):1766–72.
3. Mosterd K, Krekels GA, Nieman FH, et al. Surgical excision versus Mohs' micrographic surgery for primary and recurrent basal-cell carcinoma of the face: A prospective randomised controlled trial with 5-years' follow-up. *Lancet Oncol* 2008;**9**(12):1149–56.
4. Nasr I, McGrath EJ, Harwood CA, et al. British Association of Dermatologists guidelines for the management of adults with basal cell carcinoma 2021. *Br J Dermatol* 2021;**185**(5):899–920.
5. Ali SR, Abdulla M, Ibrahim N, Dobbs TD, Haj-Basheer M, Whitaker IS. The incidence and risk of involved margins in surgically resected basal cell carcinoma: A multi-centre consecutive case series. *J Plast Reconstr Aesth Surg* 2021;**74**(11):3196–211.
6. Warren H, Ali SR, Abdulla M, et al. What depth of surgical excision results in adequate histological deep margin clearance in basal cell carcinoma? A retrospective cohort study of 1126 basal cell carcinomas. *J Plast Reconstr Aesthetic Surg* 2022;**75**(7):2387–2440.
7. Slater D, Barrett P. Standards and datasets for reporting cancers: Dataset for histopathological reporting of primary basal cell carcinoma. London: Royal College of Pathologists. Available at URL: https://www.rcpath.org/uploads/assets/53688094-791e-4aaa-82cec42c3cb65e35/Dataset-for-histopathological-reporting-of-primary-cutaneous-basal-cell-carcinoma.pdf [Accessed February 24, 2023].
8. Ali SR, Strafford H, Dobbs TD, et al. Development and validation of an automated basal cell carcinoma histopathology information extraction system using natural language processing. *Front Surg* 2022;**9**:870494https://www.frontiersin.org/articles/10.3389/fsurg.2022.870494/full.
9. National Comprehensive Cancer Network (NCCN). NCCN Guidelines. Basal cell skin cancer. Available at URL: https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1416 [Accessed February 24, 2023].
10. Gospodarowicz MK, Brierley JD, Wittekind C. *TNM Classification of Malignant Tumours*. Chichester: John Wiley & Sons; 2017.
11. Elder DE, Massi D, Willemze R, editors. 4th ed.*WHO Classification of Skin Tumours*, Vol. 11. Lyon: International Agency for Research on Cancer; 2018.
12. Kiely JR, Patel AJK. A retrospective study of 694 basal cell carcinoma excisions to quantify deep margin documentation and clearance compared to histological type and surgical margin. *J Plast Reconstr Aesthetic Surg* 2019;**72**(11):1805–12.
13. Keith DJ, de Berker DA, Bray AP, et al. British Association of Dermatologists' national audit on nonmelanoma skin cancer excision. *Clin Exp Dermatol 2014* 2017;**42**(1):46–53.
14. Keith DJ, Bray AP, Brain A, et al. British Association of Dermatologists (BAD) national audit on non-melanoma skin cancer excision 2016 in collaboration with the Royal College of Pathologists. *Clin Exp Dermatol* 2020;**45**(1):48–55.