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Galea vs periosteum: impact of excision depth on outcomes for cutaneous squamous cell carcinoma of the scalp

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ABSTRACT

Cutaneous squamous-cell carcinoma (cSCC) is the second most common skin cancer, with local recurrence rates of up to 10% in the scalp. To date there have been no direct comparisons of recurrence rates or deep margin involvement for surgical excision to different anatomical layers of the scalp. A multi-centre retrospective study of all cSCC excised from the scalp from 2015 to 2020 was conducted. Two hundred and seventy nine patients (17-female, 262-male) met the inclusion criteria (median age 82.2 years), incorporating a total of 302 cSCC's. Primary excision depth was galea in 80 cases and periosteum in 222 (26.5% and 73.5% respectively). A significantly greater proportion of lesions excised to galea had involved or close (<1mm) deep margins ($n=27$, 33.8% galea vs $n=50$, 22.5% periosteum, OR 2.74 [95% CI 1.38–5.45], $p=.004$). Local recurrence rates were also significantly higher for lesions excised to galea vs periosteum ($n=13$, 16.3% vs $n=18$, 8.1% respectively, $p=.039$), although this trend was lost after adjusting for deep margin status. To our knowledge, this study is the first to compare local recurrence rates and margin involvement for cSCC of the scalp excised to different depths. Our findings demonstrate a higher incidence of involved/close deep margins for lesions excised to galea, imposing a higher treatment burden and risk of recurrence for these patients. We therefore advocate including galea in surgical excision.

ARTICLE HISTORY

Received 26 October 2021
Revised 20 December 2021
Accepted 29 March 2022

KEYWORDS

Squamous cell carcinoma; margins; periosteum; galea; recurrence

Introduction

Cutaneous squamous cell carcinoma (cSCC) is the second most common type of skin cancer. Despite a relatively low disease specific mortality rate (2%) [1], recurrence rates following surgical excision are high [2,3]. This can confer significant aesthetic and functional morbidity, especially for lesions situated on the head and neck, which constitute between 26 and 54% of diagnoses [4,5].

Guidelines pertaining to peripheral surgical excision margins for cSCC are relatively consistent, broadly advocating a minimum of 4 mm and 6 mm margins for low and high risk lesions respectively [6]. These have been demonstrated to achieve a histological clearance rate of at least 95% [7,8]. However there is unclear advice regarding excision depth, with different deep margins proposed including hypodermis (assuming deeper layers are macroscopically unaffected) [9], through subcutaneous fat [10] or 'next clear surgical plane' [11].

The scalp consists of five soft tissue layers: skin, connective tissue, galea, loose areolar connective tissue (LAT) and periosteum. Surgical excision of cSCC is typically performed to the galea or periosteum, as these layers can be readily identified and provide an adequate wound bed for skin graft take. Guidelines from the British association of Dermatology (BAD) [11] and the Scottish Intercollegiate Guidelines Network (SIGN) [12] both suggest that excision of cSCC on the scalp should include galea, although the authors of the latter admit that there is currently no evidence to base a recommendation for surgical depth.

Indeed to our knowledge, there have been no studies comparing the histological and clinical outcomes for cSCC excised to different depths of the scalp. This retrospective cohort study was conducted to compare recurrence rates & margin involvement cSCC of the scalp excised to galea vs periosteum.

Materials and methods

A multi-centre retrospective analysis was conducted following institutional approval of all cSCC surgically excised from the scalp during the period 2015 to 2020 inclusive. Data were retrieved from electronic hospital records. No formal power calculation was performed, however all available relevant electronic records in this period were reviewed. Parameters recorded included patient demographics, surgical excision depth and peripheral margins of macroscopically normal tissue, tumour histology and morphology, histological TNM stage, peripheral and deep margin status and local recurrence. The primary and secondary outcomes were deep margin status and local recurrence respectively for lesions excised to galea vs periosteum. The cohorts were not specifically matched, however demographic characteristics were similar (Table 1).

Recurrence was defined as a histologically confirmed cSCC arising within the original excision site of the primary surgery. This was identified through searching through the electronic hospital records and media images for each patient that was identified according to the above criteria up until October 2021. Patients were followed up by Plastic Surgeons in the outpatient

department according to local guidelines and following any re-referral from community teams.

Cases where the cSCC was located in an area of the scalp without underlying galea (e.g. over frontalis and occipitalis muscle), along with those which had no documentation regarding the primary excision depth or were excised down to bone were excluded. In addition, cases which had cSCC recurrence without adequate reporting/imaging detailing the site of the recurrence were also excluded (as this precluded accurate reporting of local recurrence).

Statistical analysis was performed using Jamovi 1.2 software [13]. Means \pm standard deviation (SD) and medians \pm interquartile range (IQR) were used to compare continuous data with and without skew respectively. The Mann–Whitney U test and Chi-squared test were used to compare tumour characteristics between both groups. The relationships between recurrence rates and margin involvement with surgical excision depth were investigated using Chi-squared tests and multivariable logistic regression. A probability (p) value less than .05 was considered significant.

Results

A total of 279 patients (17 female and 262 male) met the inclusion criteria, incorporating 302 cSCC's (Figure 1). Median age was 82.2 years (IQR = 10.7, Q1 = 75.8, Q3 = 86.5).

Tumour characteristics

Two hundred and ninety six lesions had a pathological TNM (pT) stage recorded according to the Union for International Cancer

Table 1. Comparison of demographics and tumour characteristics.

	Galea	Periosteum	Total	p value
Age				
Median (Years)	82.2	82.2	82.2	.38
Q1	75.6	76.0	75.8	
Q3	86.0	86.9	86.5	
Gender	n (%)	n (%)	n	
F	1 (1.3)	16 (7.2)	17 (5.6)	
M	79 (98.8)	206 (92.3)	285 (94.3)	
Histological pT stage				
pT1	36 (45.0)	99 (44.6)	135	
pT2	38 (47.5)	97 (43.7)	135	
pT3	5 (6.3)	21 (9.5)	26	.60
Not staged	1	5	6	
Differentiation				
Well	12 (15.0)	42 (18.9)	54	
Moderate	56 (70.0)	138 (62.2)	194	
Poor	10 (12.5)	30 (13.5)	40	.59
Not recorded	2	12	14	
Maximum tumour depth				
Median (mm)	3.5	4.0		.20
Q1	2.5	2.5		
Q3	5.0	6.1		

Control (UICC) TNM classification version 8 for lesions post 2017 and version 7 for all others (Table 1) [14]. Fifty four lesions were reported as well differentiated (17.9%), 194 moderately differentiated (64.2%) and 40 poorly differentiated (13.2%), whilst 14 cases were unreported. Median depth of invasion was 3.9 mm (IQR = 3.5 mm, Q1 = 2.5 mm, Q3 = 6.0 mm).

There was no significant difference in histological tumour characteristics between the two groups (Table 1).

Peripheral margins

The majority of lesions (70.5%) were excised with 4–6mm macroscopic peripheral margins. Only seven lesions (2.3%) had involved or close peripheral histopathological margins, all of which had been excised with 4–6mm margins.

Deep margins

Primary excision depth was galea in 80 cases and periosteum in the other 222 (26.4% and 73.5% respectively). A significantly greater proportion of lesions excised to galea had involved or close (<1mm) deep margins ($n = 27$, 33.8% galea vs $n = 50$, 22.5% periosteum, $p = .048$) (Table 2). This trend remained after adjusting for potential confounders (tumour stage, depth of invasion, differentiation status) using multivariable logistic regression (Odds ratio 2.74 [95% CI 1.38–5.45], $p = .004$).

All of these patients had their pathology reviewed in a specialist MDT to review and confirm diagnosis.

All patients with involved margins were offered radiotherapy or re-excision, although four declined any further treatment. Thirty-one (47.6%) cases with close deep margins went on to have further intervention for the primary lesion (radiotherapy $n = 25$, re-excision $n = 6$) as they were deemed high risk. The remainder has close observation as per national guidelines [12].

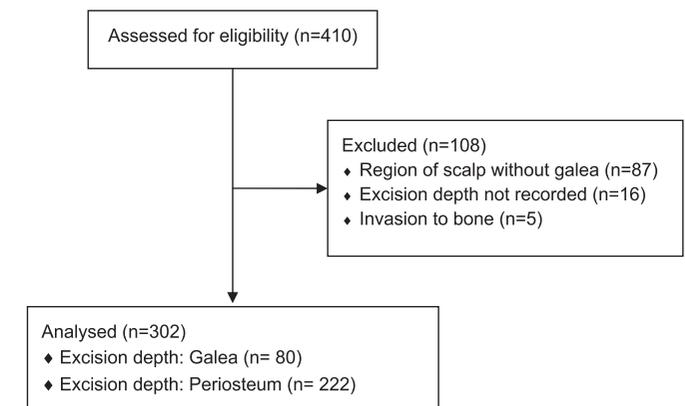


Figure 1. CONSORT diagram.

Table 2. Deep margin involvement and recurrence rates.

	Galea n (%)	Periosteum n (%)	Total n	p value
Deep margin involvement				
Close margins	22 (27.5)	43 (19.4)	65	.13
Involved margins	5 (6.3)	7 (3.2)	12	.22
Total	27 (33.8)	50 (22.5)	77	.048*
Tumour recurrence				
Local recurrence (excluding close/involved margins)	6 (7.5)	16 (7.2)	22	.93
Total local recurrence	13 (16.3)	18 (8.1)	31	.039*

*Indicates statistical significance ($p < .05$).

Local tumour recurrence

Thirty one lesions developed local recurrence (10.2%). The overall recurrence rate for cSCC was significantly higher for lesions excised to galea vs periosteum ($n=13$, 16.3% and $n=18$, 8.1% respectively, $p=.039$), however this trend lost in after excluding lesions which had close/involved margins at initial excision (Table 2).

Mean time to recurrence was 17.7 months (± 11.9 months). Of the lesions that recurred, nine had close or involved deep or peripheral margins at primary excision respectively, six of which had either radiotherapy or further surgery following the primary excision.

Discussion

To the best of our knowledge, this study is the first to directly compare local recurrence rates and margin involvement for cSCC of the scalp excised to different anatomical depths. Our findings demonstrate a significantly higher incidence of close/involved deep margins and local recurrence rates for cSCC excised to galea vs periosteum ($p=.048$ and $p=.039$ respectively). Given the increasing incidence of scalp cSCC worldwide, these findings are important for surgical decision making.

The overall incidence of local recurrence of cSCC in our study was 10.2%, which is broadly consistent with the literature for wide local excision in the scalp [15,16]. A 5-year multi-centre follow up study by Khan et al., found an overall (local + regional lymph node) recurrence rate of 10% for cSCC of the scalp, the second highest of all anatomical categories [16]. Similarly, a retrospective study of 101 cSCC excised from the scalp reported by Jenkins et al., demonstrated a local recurrence rate of 8%. The authors of the latter study noted that local recurrence was exclusively limited to cases where the deep clearance was ≤ 2 mm. In our study, only 29% of cases with local recurrence had deep margins of ≤ 1 mm, although limited histological reporting of margins > 1 mm precluded analysis of the entire 0–2mm category.

Nevertheless, surgeons operate at the macroscopic level, which was the rationale for our direct comparison of local recurrence following excision to different anatomical layers. Moreover, fascial/aponeurotic layers theoretically provide physical barriers to tumour invasion and metastases. Indeed in this study, we found a significantly higher incidence of close/involved deep margins for lesions excised to galea vs periosteum. This may suggest that the galea might help impede the vertical invasion element of cSCC, and hence should be included with the excision. Moreover, given that almost half of cases with involved/deep margins went on to have further therapy, this strategy may help reduce the treatment burden for affected patients.

Local recurrence rates for cSCC were also significantly higher for lesions excised to galea vs periosteum, although this trend was lost after excluding cases with involved/close deep margins. This may suggest that deep margin status is the predominant driver for increased recurrence risk in lesions excised to galea.

The majority of local recurrence within our cohort occurred within the first two years following primary excision (80.9%). This is similar to the study by Jenkins et al., who found that all local recurrence occurred within the first 18 months [15]. Nevertheless, there were four cases of recurrence in the 24–36 month category in our study, all of which were categorised as low-high risk lesions. According to national guidelines, these patients did not have scheduled follow up beyond two years from primary excision [11], potentially delaying diagnosis. This provides further evidence to support higher risk stratification of cSCC of the scalp,

similar to cSCC of the lip and ear, in order to warrant longer follow up [17].

Peripheral excision margins observed in our data-set broadly followed the international guidelines which aim to achieve $> 95\%$ clearance [6]. Indeed, only seven lesions (2.4%) had close or involved peripheral margins on histology, indicating relatively low anatomical constraints for adequate surgical excision of lesions on the scalp.

Based on our findings, we advocate surgical excision of cSCC of the scalp to periosteum where possible, to minimise the risk of margin involvement, further treatment burden and local tumour recurrence. In addition, we suggest that the scalp should be placed in a higher category when risk stratifying cSCC by anatomical location, given the higher incidence of local recurrence compared to other sites (10.2% in our study vs 6.7% all sites published by Khan et al., [16] and potentially longer interval to recurrence.

The main limitation of this study is the relatively small number of local recurrences and potential uncontrolled confounding risk factors (e.g. tumour size, history of previous SCC, comorbidities). Nevertheless, this is one of the largest studies of scalp cSCC's to date, and other tumour characteristics were broadly similar between both groups (Table 1). An additional limitation is the potential for reporting bias due to some surgeons not documenting the depth of primary excision (excluding these cases from analysis). The numbers of these cases were low however, constituting less than 5% of the total patients identified from the primary search.

Conclusion

This study is the first to compare local recurrence rates and margin between for cSCC of the scalp excised to different anatomical depths. Our findings demonstrate a higher incidence of close/involved deep margins and local recurrence for cSCC excised to galea vs periosteum. We therefore advocate including galea in surgical excision of cSCCs of the scalp.

Disclosure statement

No potential conflict of interest was reported by the author(s).

References

- [1] Karia P, Han J, Schmults C. Cutaneous squamous cell carcinoma: estimated incidence of disease, nodal metastasis, and deaths from disease in the United States, 2012. *J Am Acad Dermatol.* 2013;68(6):957–966.
- [2] Lee CB, Roorda BM, Wakkee M, et al. Recurrence rates of cutaneous squamous cell carcinoma of the head and neck after Mohs micrographic surgery vs. standard excision: a retrospective cohort study. *Br J Dermatol.* 2019;181(2): 338–343.
- [3] Rowe D, Carroll R, Day C. Prognostic factors for local recurrence, metastasis, and survival rates in squamous cell carcinoma of the skin, ear, and lip. Implications for treatment modality selection. *J Am Acad Dermatol.* 1992;26(6): 976–990.
- [4] Jung G, Metelitsa A, Dover D, et al. Trends in incidence of nonmelanoma skin cancers in Alberta, Canada, 1988–2007. *Br J Dermatol.* 2010;163(1):146–154.
- [5] Youl P, Janda M, Aitken J, et al. Body-site distribution of skin cancer, pre-malignant and common benign pigmented

- lesions excised in general practice. *Br J Dermatol.* 2011; 165(1):35–43.
- [6] Nahhas A, Scarbrough C, Trotter S. A review of the global guidelines on surgical margins for nonmelanoma skin cancers. *J Clin Aesthet Dermatol.* 2017;10(4):37–46.
- [7] Brodland D, Zitelli J. Surgical margins for excision of primary cutaneous squamous cell carcinoma. *J Am Acad Dermatol.* 1992;27(2):241–248.
- [8] Motley R, Kersey P, Lawrence C. Multiprofessional guidelines for the management of the patient with primary cutaneous squamous cell carcinoma. *Br J Dermatol.* 2002; 146(1):18–25.
- [9] Stratigos A, Garbe C, Lebbe C, et al. Diagnosis and treatment of invasive squamous cell carcinoma of the skin: European consensus-based interdisciplinary guideline. *Eur J Cancer.* 2015;51(14):1989–2007.
- [10] Cancer Council Australia, Clinical practice guidelines for keratinocyte cancer, <https://www.wiki.cancer.org.au/australia>. 2021; [cited 2021 Mar 20]. Available from: https://wiki.cancer.org.au/australia/Guidelines:Keratinocyte_carcinoma.
- [11] Keohane S, Botting J, Budny P, et al. British association of dermatologists guidelines for the management of people with cutaneous squamous cell carcinoma 2020. *Br J Dermatol.* 2021;184(3):401–414.
- [12] SIGN. Scottish Intercollegiate Guidelines Network, Management of primary cutaneous squamous cell carcinoma, 2014; [cited 2021 Mar 13]. Available from: <https://www.sign.ac.uk/media/1094/sign140.pdf>.
- [13] The jamovi project 2021. jamovi (Version 1.6) [Computer Software]. Retrieved from <https://www.jamovi.org>. [computer program]. 2020.
- [14] Brierley J, Gospodarowicz M, Wittekind C. TNM classification of malignant tumours. 8th ed. New York: Union for International Cancer Control; 2016.
- [15] Jenkins G, Smith A, Kanatas A, et al. Anatomical restrictions in the surgical excision of scalp squamous cell carcinomas: does this affect local recurrence and regional nodal metastases? *Int J Oral Maxillofac Surg.* 2014;43(2):142–146.
- [16] Khan K, Mykula R, Kerstein R, et al. A 5-year follow-up study of 633 cutaneous SCC excisions: rates of local recurrence and lymph node metastasis. *J Plast Reconstr Aesthet Surg.* 2018;71(8):1153–1158.
- [17] Mo J, Miller C, Karakousis G, et al. The scalp is a high-risk site for cutaneous squamous cell carcinoma metastasis. *J Am Acad Dermatol.* 2021;84(6):1742–1744.