

SUCCESS OF SURGICAL TREATMENT OF BASAL CELL CARCINOMA: ROLE OF INTRAOPERATIVE FROZEN SECTION

Amna Babar, Shahid Jamal, Syed Salman Ali, Saba Anjum, Dilawar Abbas Rizvi*

Armed Forces Institute of Pathology/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, *Pak Emirates Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan

ABSTRACT

Objective: To determine the success rate of surgical excision assisted with intra operative frozen section technique; in patients with high clinical suspicion of basal cell carcinoma at aesthetically important areas.

Study Design: Descriptive cross-sectional.

Place and Duration of Study: Department of Histopathology, Army Medical College and Armed Forces Institute of Pathology, Rawalpindi in collaboration with department of Dermatology, Pak Emirates Military Hospital, Rawalpindi from Dec 2016 to Jun 2017.

Material and Methods: A total of fifty one (n=51) patients between age 35-75 years with high clinical suspicion of basal cell carcinoma of any size or histology on aesthetically important areas who were planned for surgical excision were enrolled in the study. Success rate was assessed in terms of tumor free margin on histopathology report.

Results: Mean age of study subjects was 54.7 years \pm 13.4 SD with M:F of 1.43:1. Success rate was found to be 84.3% (n=43/51). No significant difference was observed in success rate after stratification with respect to gender, age, types of BCC ($p>0.05$ in all cases), but success of excision according to aesthetic areas was significant ($p=0.029$).

Conclusion: Conventional surgical excision for BCC at aesthetically important areas assisted with intra operative frozen section technique resulted in high success rates in terms of tumor free margins.

Keywords: Basal cell carcinoma, Frozen section, Tumour free margin.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Basal cell carcinoma (BCC) is the most common skin malignancy (75% to 80%) arising from the basal layer of epidermis and its appendages¹⁻³. The majority of these cancers occur on areas of skin that are regularly exposed to sunlight or other ultraviolet radiation including scalp^{4,5}. The goal of treatment of BCC is to completely remove the tumor with maximally preservation of function and cosmesis at the site of treatment⁶. Surgical removal remains the standard mode of treatment for basal cell carcinoma and classically it was used as method of choice for treating BCC but is associated with recurrence and unacceptable cosmetic results due to wide margins excision⁷. The frozen section procedure also called cryosection is a

pathological laboratory procedure to perform rapid microscopic analysis of a specimen. It is used most often in oncological surgery^{6,8}. One of the uses of frozen section is to inform the surgeon if the surgical margin is clear of residual cancer, or if residual cancer is present at the surgical margin. This technique is also being used in the surgeries for BCC for better cure rates and cosmetic outcomes in one step surgery with encouraging results^{9,10}. It allows surgeons to excise the tumors with minimum margins and to take intraoperative consultation from pathologist while patient remains on surgery table. With this improvised surgical technique and intraoperative pathologist consultation cure rates of 99% has been achieved for primary BCC with maximally preserved tissue¹¹. In a recent study, authors reported the success rate (complete surgical excision) in the intra-operative frozen section biopsy cohort as 84.51%, with a completely excised tumor in 60 of 71 cases¹². In view of

Correspondence: Dr Shahid Jamal, House No 71-C, Lane No. 8 Askari Road Adyala, Rawalpindi Pakistan

Email: sjarawj@gmail.com

Received: 22 Nov 2017; revised received: 18 Jul 2018; accepted: 21 Jul 2018

above, present study was planned to establish the role of intra operative frozen section technique for assisting surgical excision of BCC. It may offer several advantages including better cure rate, maximal tissue preservation in cosmetically and anatomically sensitive areas with immediate reconstruction in most cases.

MATERIAL AND METHODS

This cross-sectional study was carried out at Pathology department of Army Medical College in collaboration with Armed Forces Institute of Pathology and department of Dermatology, Pak Emirates Military Hospital, Rawalpindi, from 16 December 2016 to 15 June 2017, after taking

treatment that seriously impairs wound healing, diabetics and pregnant women were excluded from the study. Patient data including age, gender, BCC type and site of tumour were noted. The tissue specimen, labelled with the patients name and Lab ID No. accompanied by a surgical pathology request form, were delivered by the dermatology department Pak Emirates Military Hospital by the patient attendant. The cryostat LEICA CM 1900 (Germany) was used for the procedure. All the designated margins were taken and labelled slides of each designated margin were prepared using the standard protocol of frozen section, followed by H&E

Table: Stratification of success rate according to age groups, gender, BCC type and aesthetic areas involved.

Clinicopathological variable	Cases (n)	Percentage (%)	Success		p-value
			Present	Absent	
Age Groups (years) (n=51)					
35-50	21	41%	16	5	0.249 (FE test)
>50	30	59%	27	3	
Gender (n=51)					
Male	30	59%	26	4	0.702 (FE test)
Female	21	41%	17	4	
BCC Type (n=51)					
Nodular	25	49%	19	6	0.529 (FE test)
Ulcerative	20	39%	18	2	
Pigmented	4	8%	4	0	
Infiltrative	2	4%	2	0	
Aesthetic Areas (n=51)					
Peri-Orbital	25	49%	24	1	0.029 (FE test)
Central Face	15	29%	10	5	
Peri-Nasal	11	22%	9	2	

approval from the Ethical Review Committee. Fifty one patients were selected by consecutive, non-probability sampling (Sample size was calculated by using WHO calculator 1.1 taking confidence interval 95%, anticipated population proportion 84.5%¹² and absolute precision required as 10%). Patients of both genders between 35-75 years of age, with high clinical suspicion of basal cell carcinoma of any size or histology on aesthetically important areas, planned for surgical excision were included in the study. Patients with recurrent tumour, residual tumour, who were receiving any sort of

staining. The stained slides were examined by the resident pathologist. Presence or absence of any invasive BCC was determined. Identification of the type of BCC was ascertained from the sections of main lesion. The margin assessment and final diagnosis was rendered by the consultant histopathologist. All the information, whether the margin was positive or negative was communicated to the operating dermatologist/surgeon over telephone. All the patients who had positive margins, underwent re-excision. Thus a one-step surgery, ultimately leading to negative margins was obtained. When all the necessary

information was provided to the operating dermatologist, the frozen section sample in the cryostat was transferred from the specimen block holder into the labelled embedding cassette, followed by routine processing and H&E staining. The data was entered and analyzed using SPSS version 19. Mean and standard deviation were calculated for the quantitative variable like age. Qualitative variables like gender, type of BCC, area involved and success were represented as frequency and percentage.

basal cell carcinoma of any size or histology on aesthetically important areas, planned for surgical excision were recruited in this study. Mean age in present study was 54.7 ± 13.4 SD. There were 30 (59%) male and 21 (41%) females with a M:F of 1.43:1. Most of the patients were over 50 years of age (59%, n=30). Clinically out of 51 cases of BCC, 25 cases (49%) were nodular, 20 cases (39%) were ulcerative, 4 cases (8%) were pigmented and 2 cases (4%) were of infiltrative type. A total of 25 cases (49%) were on peri-

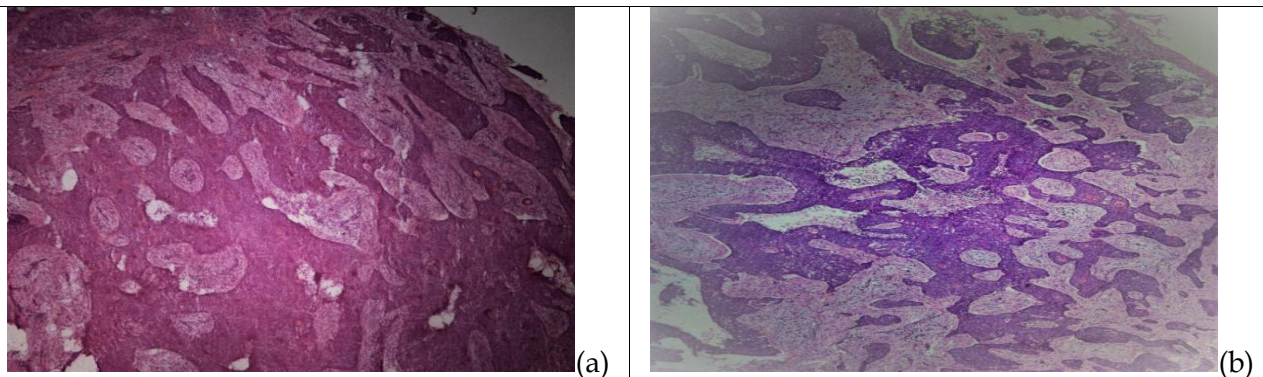


Figure-1: Photomicrographs showing a positive margin (a): Frozen section (H&E x200), (b): Permanent sections (H&E x200).

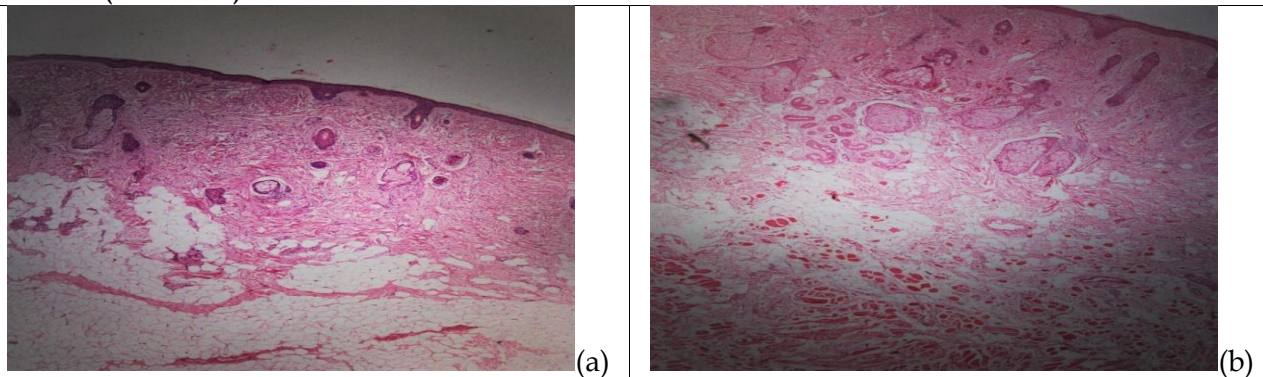


Figure-2: Photomicrographs showing a negative margin (a): Frozen section (H&E x100); (b): Permanent section of the same (H&E x100).

Effect modifiers like age, gender, type of BCC and area involved were controlled by stratification. Post stratification Chi-square/ Fischer’s exact tests (where individual cell count was <5) were applied. The p -value ≤ 0.05 was considered significant.

RESULTS

A total of fifty one (n=51) patients between age 35-75 years with high clinical suspicion of

orbital area, 15 cases (29%) were on central face while 11 cases (22%) were peri-nasal in location. Success rate was assessed in terms of tumor free margin on histopathology of the surgical excision specimen and was found to be 84.3% (n=43/51) in this study (figure-1 & 2). Data was stratified for gender, age groups, types of BCC and aesthetic areas involved to deal with effect modifiers. No significant difference was observed in success rate after stratification with respect to gender,

age, types of BCC ($p>0.05$ in all cases), but success of excision according to aesthetic areas was significant ($p=0.029$). Results are summarized in table.

DISCUSSION

The BCC is a common skin cancer that arises from the cells of the basal layer of the epithelium or from the external root sheath of the hair follicle. Surgical excision is the standard mode of treatment for BCC1. Frozen section analysis has been used to increase the likelihood of complete excision of skin cancers and to minimize the risk for recurrence, however, its use remains controversial and commonly considered an optional tool, the reliability and effectiveness of which remain questionable². Findings of the present study have demonstrated ineffectiveness of intra-operative frozen section biopsy in about 15% ($n=8/51$) of cases who required subsequent re-excision. This might be attributed to the intrinsic limitations of such a procedure and subjective indications. Identifying a definite clinical margin may be difficult in various circumstances like sclerosing basal cell carcinoma that usually features ill-defined borders resembling small patches of scleroderma with peripheral growth and central sclerosis. Our results are comparable with report of Manstein *et al* (2003)¹³ on 60 consecutive cases in which frozen section diagnoses was compared with permanent sections. It was found that in 85% of the cases the frozen sections were accurate compared with the permanent sections, but in 13% of the total cases the margins were less than 1mm. In another report by Goto *et al* (2012)¹⁴, 256 cases treated surgically assisted with intraoperative frozen section biopsy over the period of 10 years, a success rate of 91.8% was achieved while incomplete excisions occurred in 21 (8.2%) cases. In their retrospective study, Ghauri *et al* (1999)¹⁷ used frozen section analysis on 76% of the 277 lesions evaluated, and found that frozen section examination were 91% accurate in detecting the presence or absence of tumor involvement at the surgical margins. However, some studies show contradictory

result. Nicoletti *et al* (2013)¹² conducted a large retrospective study to examine 670 surgical excisions of non-melanoma skin cancers of the head and neck in 481 patients over a period of nine years. Their results demonstrated the paradoxical ineffectiveness of an intra-operative frozen section biopsy in pursuing higher rates of radical excision in non-melanoma skin cancers. In a review by Cataldo *et al* (1990)¹⁵, 450 cases of BCC showed frozen section to be most helpful in treating recurrent tumors where microscopic tumor foci extend beyond clinical margins in 45% of cases. They suggested that frozen section analysis may be of value in selected patients with primary tumors, but its routine use is not indicated for the majority of these lesions, since complete excision is possible without relying on frozen section in 90% of cases. In analysis of cutaneous basal and squamous cell carcinomas by Bogdanov-Berezovsky *et al* (2008)¹⁶ false negative margins were found in 19 cases (11.2%) and false positive margins in 11 (6.6%) and they supported the use of frozen section margin control in selected patients suffering from non-melanoma skin cancer of the head and neck⁷. In another study of 6 patient using frozen section for margin analysis approximately 71% of the excision margins were clear after primary excision, 27% at second excision and 1% at third excision. In present study, an intra-operative frozen section was required to check a complete excision of the BCC in one or more specimen marginal spots. In particular, it is mostly required in the critical anatomical sites of the head, such as the nose, cheeks, eyelids, chin, lips and forehead. Thus, a potentially persistent disease from an incomplete primitive excision would demand a far more aggressive and disabling secondary surgery. Nonetheless, the effectiveness of an intra-operative frozen section biopsy is always correlated with the surgeon's subjective clinical assessment. Other authors consider the frozen section as an optional tool utilized to intra-operatively assess one or more margins of a surgically excised specimen. Its advisability, reliability and effectiveness are as debated as

Mohs micrographic surgery with a corresponding equal distribution of supporters and critics^{6,8,11,18,19}. Furthermore, the forthcoming use of the promising confocal laser scanning microscopy is likely to provide a non-invasive view to pre-operatively identify adequate resection margins^{9,10}.

CONCLUSION

Conventional surgical excision for BCC at aesthetically important areas assisted with intraoperative frozen section technique resulted in high success rates in terms of tumor free margins, particularly so at the aesthetic sites.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

REFERENCES

1. Kasper M, Jaks V, Hohl D, Toftgård R. Basal cell carcinoma molecular biology and potential new therapies. *J Clin Invest* 2012; 122: 455-63.
2. Marzuka AG, Book SE. Basal Cell Carcinoma: Pathogenesis, Epidemiology, Clinical Features, Diagnosis, Histopathology, and Management. *Yale J Biol Med* 2015; 88: 167-79.
3. Hallaji Z, Rahimi H, Shahshahani MM. Comparison of risk factors of single basal cell carcinoma with multiple basal cell carcinomas. *Indian J Dermatol* 2011; 56: 398-402.
4. Kwasniak LA, Garcia-Zuazaga J. Basal cell carcinoma: evidence-based medicine and review of treatment modalities. *Int J Dermatol* 2011; 50: 645-58.
5. Chung S. Basal Cell Carcinoma. *Arch Plast Surg* 2012; 39: 166-70.
6. Tan J, Joblin L, Davenport E. Accuracy of frozen sections for breast cancer sentinel lymph node biopsies within a peripheral New Zealand hospital. *N Z Med J* 2016; 129: 46-50.
7. Luz FB, Ferron C, Cardoso GP. Surgical treatment of basal cell carcinoma: an algorithm based on the literature. *An Bras Dermatol* 2015; 90: 377-83.
8. Abudukadeer A, Azam S, Zunong B, Mutailipu AZ, Huijun B, Qun L. Accuracy of intra-operative frozen section and its role in the diagnostic evaluation of ovarian tumors. *Eur J Gynaecol Oncol* 2016; 37: 216-20.
9. Gill HS, Moscato EE, Seiff SR. Eyelid margin basal cell carcinoma managed with full-thickness en-face frozen section histopathology. *Ophthalm Plast Reconstr Surg* 2014; 30: 15-9.
10. Gurunluoglu R, Kubek E, Arton J, Olsen A, Bronsert M. Nonpersistence of Basal Cell Carcinoma After Diagnostic Shave Biopsy: Reconstruction When Specimen Is Negative During Surgery. *Ann Plast Surg* 2015; 74: 695-8.
11. Morrissey M, Beachkofsky T, Ritter S. When to consider Mohs surgery: A long-standing malignant lesion or a tumor in a cosmetically sensitive area are 2 instances in which Mohs micrographic surgery yields superior results. *The Journal of Family Practice* 2013; 62: 558-64.
12. Nicoletti G, Brenta F, Malovini A, Musumarra G, Scevola S, Faga A. Study to determine whether intraoperative frozen section biopsy improves surgical treatment of non-melanoma skin cancer. *Mol clin oncol* 2013; 1: 390-94.
13. Manstein ME, Manstein CH, Smith R. How accurate is frozen section for skin cancers? *Ann Plast Surg* 2003; 50(6): 607-9.
14. Goto M, Kai Y, Arakawa S, Oishi M, Ishikawa K, Anzai S, et al. Analysis of 256 cases of basal cell carcinoma after either one-step or two-step surgery in a Japanese institution. *J Dermatol* 2012; 39(1): 68-7.
15. Cataldo PA, Stoddard PB, Reed WP. Use of frozen section analysis in the treatment of basal cell carcinoma. *Am J Surg* 1990; 159(6): 561-3.
16. Bogdanov-Berezovsky A, Rosenberg L, Cagniano E, Silberstein E. The role of frozen section histological analysis in the treatment of head and neck skin basal and squamous cell carcinomas. *Isr Med Assoc J* 2008; 10(5): 344-5.
17. Ghauri RR, Gunter AA, Weber RA. Frozen section analysis in the management of skin cancers. *Ann Plast Surg* 1999; 43(2): 156-60.
18. Vohra LM, Gulzar R, Saleem O. Intra operative frozen examination of sentinel lymph node in breast cancer. *J Ayub Med Coll Abbottabad* 2015; 27: 40-4.
19. Nigam J, Misra V, Dhingra V, Jain S, Varma K, Singh A. Comparative study of intra-operative cytology, frozen sections, and histology of tumor and tumor-like lesions of nose and paranasal sinuses. *J Cytol* 2013; 30: 13-7.