http://www.pjbs.org

PJBS

ISSN 1028-8880

Pakistan Journal of Biological Sciences

ANSInet
Asian Network for Scientific Information
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan

Pakistan Journal of Biological Sciences 12 (21): 1408-1414, 2009
ISSN 1028-8880

Safety Margin in Excision of Basal Cell Carcinoma

[1]S. Babaye-Nazhad, [1]M. Amirnia, [2]H. Alikhah, [1]E. Khodaeyani and [3]N. Atapour
[1]Department of Dermatology, Sina Hospital, Tabriz University of Medical Sciences, Tabriz, Iran
[2]Continuing Medical Education Center, Tabriz University of Medical Sciences, Tabriz, Iran
[3]Tabriz University of Medical Sciences, Tabriz, Iran

Abstract: The aim of this study was to evaluate the intact margin after surgery regarding common method with consideration of 4 mm safe margin. Fifty patients with basal cell carcinoma operated in Tabriz Sina hospital, were chosen randomly and pathological report of these patients after surgery was evaluated with consideration of presence of intact margin. In pathologic report before operation of these patients, Basal cell carcinoma was certified. Also, brief data of these patients history was studied from present cases. Forty eight of 50 (96%) patients had intact margin after surgery and just in two patients (4%), lesion was excised insufficiently and they had involved margin. With brief study of patients' history, most of them had advanced ages and the most common site of tumor presentation was head and neck. The most of these patients had exposure with so much sun light that was accounted an important etiology. With comparison of mentioned statistical results with other reports from other countries, this rate is considered in acceptable range and surgical method is done properly in this hospital and consideration of 4 mm of tumoral margin is enough.

Key words: Basal cell carcinoma, free margin, sun exposure

INTRODUCTION

Basal Cell Carcinoma (BCC) is a common type of slow-growing malignant skin tumor with a rapidly increasing incidence worldwide (Auw-Haedrich *et al*., 2009; Bath-Hextall *et al*., 2004; Delfino *et al*., 2006; Diepgen and Mahler, 2002; Kokoszka and Scheinfeld, 2003; Dieu and Macleod, 2002; Fleischer *et al*., 2001). BCC rarely metastasizes, but it does pursue a locally invasive and sometimes destructive growth pattern. This growth has been described as iceberg-like because the tumor often extends beyond its macroscopically visible borders (Auw-Haedrich *et al*., 2009; Kokoszka and Scheinfeld, 2003; Hsuan *et al*., 2004).

Almost 90% occur on the head and neck with 10% of those involving the eyelid. BCCs are non-metastasising cancers accounting for less than 0.1% of patient deaths, but may cause major complications (Goh *et al*., 2006; Hamada *et al*., 2005; Chadha and Wright, 2009). If left untreated, or inadequately treated, the BCC can cause extensive destruction of tissue, particularly on the face (Bath-Hextall *et al*., 2004). The clinical course of BCC is unpredictable; it may remain small for years, or it may grow rapidly or proceed by successive spurts of extension of tumor and partial regression (Bath-Hextall *et al*., 2004). The tumor may occur at any age, but the incidence of BCC increases markedly after the age of 40 (Bath-Hextall *et al*., 2004; Shinsuke *et al*., 2007). The incidence in younger people is increasing, however, possibly as a result of increased exposure to the sun. Other risk factors are fair skin, tendency to freckle, high degree of sun exposure, excessive use of sun beds, previous radiotherapy, phototherapy, male sex and genetic predisposition (Bath-Hextall *et al*., 2004). The aim of treatment is total tumor eradication with the smallest recurrence risk, employing the most cost effective method that is acceptable to the patient (Goh *et al*., 2006; Hamada *et al*., 2005; Chadha and Wright, 2009). Several treatment modalities are currently available for BCC (Kokoszka and Scheinfeld, 2003; Fleischer *et al*., 2001). These include Mohs surgery, excision surgery, electrodesiccation and curettage, photodynamic therapy, topical imiquimod radiotherapy, laser treatment and cryosurgery (Bath-Hextall *et al*., 2004; Kokoszka and Scheinfeld, 2003). The complete resection is the key to successful outcome with the cure rate of the order of 95%. Incomplete excisions are associated with high rate of recurrence (Hsuan *et al*., 2004; Hussain and Earley, 2003). The most frequently used and most effective therapy is surgical excision, whereby a surrounding margin of macroscopically healthy tissue is removed together with the tumor (Auw-Haedrich *et al*., 2009; Bath-Hextall *et al*., 2004; Goh *et al*., 2006; Kuijpers *et al*., 2002; Szeimies *et al*., 2005).

Corresponding Author: Mehdi Amirnia, Department of Dermatology, Sina Hospital, Tabriz University of Medical Sciences, Tabriz, Iran Tel: 00989143113577, 00984113378850 Fax: 00984113363485

Because BCC most often occurs in sun-exposed areas such as the head and neck (Kokoszka and Scheinfeld, 2003; Omidian and Emad-Mostofi, 2009; Noorbala and Kafaie, 2007), it is important to save as much healthy tissue as possible while achieving a tumor-free margin for optimum cosmetic and, especially at the eyelids, functional results (Auw-Haedrich *et al*., 2009; Diepgen and Mahler, 2002; Szeimies *et al*., 2005; Bostanci *et al*., 2005; Ducic *et al*., 2009). Some authors prefer a small clinical excision margin of 2 to 4 mm, whereas others recommend a clinical safety margin of =5 to 10 mm in high-risk BCCs such as recurrent BCC or morphea-like BCC (Auw-Haedrich *et al*., 2009; Hamada *et al*., 2005; Hsuan *et al*., 2004).

Treatment of BCC should completely remove the tumor whilst preserving the maximum amount of normal surrounding skin. Therefore, treatment is a compromise between safe excision margins and obtaining a satisfactory cosmetic result (Lalloo and Sood, 2000). The aim of this study was to evaluate the intact margin after surgery regarding common method, which is consideration of 4 mm safe margin.

MATERIALS AND METHODS

This prospective descriptive study was performed on 50 consecutive patients with skin Basal Cell Carcinoma (BCC) which presented to Tabriz Sina Educational and Therapeutic Center and underwent surgical excision in 2004.

The inclusion criteria were patients with newly onset skin BCC confirmed by pathologic examination. Exclusion criteria were concurrent skin lesions or other neoplasia and previous excisional surgery for the same lesion. Also, we excluded the patients with large BCCs which primary closure was impossible for them. The academic ethic commitee confirmed the study. An informed consent was signed by all patients. The information including age, sex, occupation, lesion site and duration of the appearance were collected from patient files or through interview and recorded in questionnaires.

Considering 4 mm of safety margin, the excised tissue was examined by an expert pathologist and the sample margin was reported as normal or affected (Mackie and Calonje, 2004). The patients were visited every week after removing of sutures for one month, every month for one year and then every 6 month for 48 month.

The collected data was analyzed by SPSS-13 statistical software and the results were expressed as percentage and diagrams (Hassanpour *et al*., 2006).

RESULTS

Of all 50 BCC patients 29 (57%) were male and 21 (42%) were female. The age distribution of patients is showed in Fig. 1.

As showed in Fig. 1, the men aged less than 50 are free of the disease. The most susceptible age range in males was 69-70 years with 34.5%. However, the disease onset in women is seen in earlier ages and 4.7% of female patients are seen in age range of 20-29 years.

Regardless of patients' sex, the most susceptible age ranges in all cases were 50-59 and 69-70 years with 34 and 30%, respectively.

For evaluation of sun exposure as a risk factor of BCC, the patients were classified in two groups as Usual-exposure and High-exposure according to their occupation. The housekeeper women were excluded from this analysis because of their vague status about sun exposure. Of 29 men, 22 (76%) were in high exposure group and 7 were in normal exposure group ($p<0.05$).

Table 1 shows the anatomic distribution of BCC tumors in studied patients. Of all cases, 49 (98%) had the lesion on head and neck and only in one man (2%) the lesion was on the chest (over the sternum). The most common sites of tumor in men were nose (27.6%), Scalp

Table 1: The distribution of basal cell carcinoma in body areas of studied patients

Location of tumor	Male	Female	Total	p-value
	---------- (%) ----------			
Head and neck				
Brow (frontal)	6.9	14.3	10	0.05
Nose	27.6	47.5	36	0.05
Eye	6.9	4.8	6	0.05
Cheek	24.1	14.3	20	0.05
Scalp	24.1	14.3	20	0.05
Neck	3.4	0.0	2	0.05
Ear	3.4	4.8	4	0.05
Body	3.4	0.0	2	0.05
Limbs	0.0	0.0	0	0.05

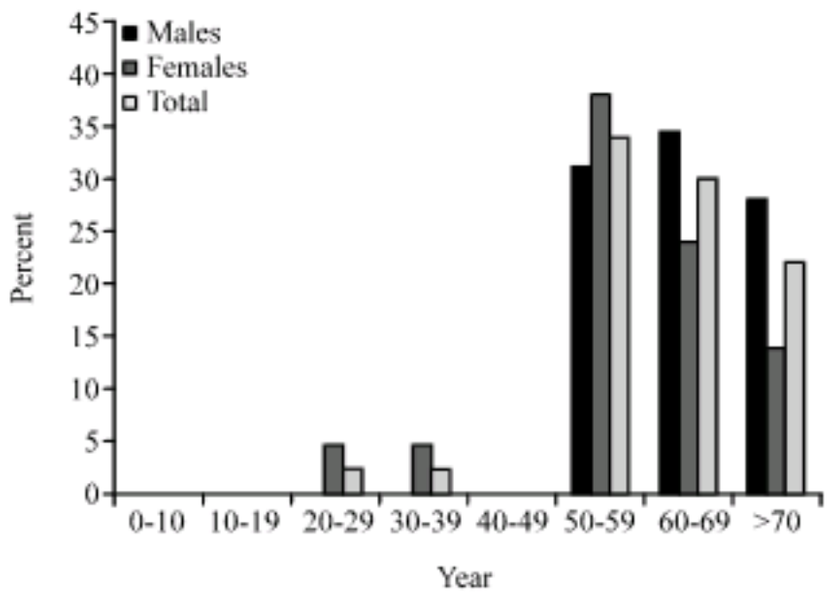

Fig. 1: Age distribution of patients with basal cell carcinoma

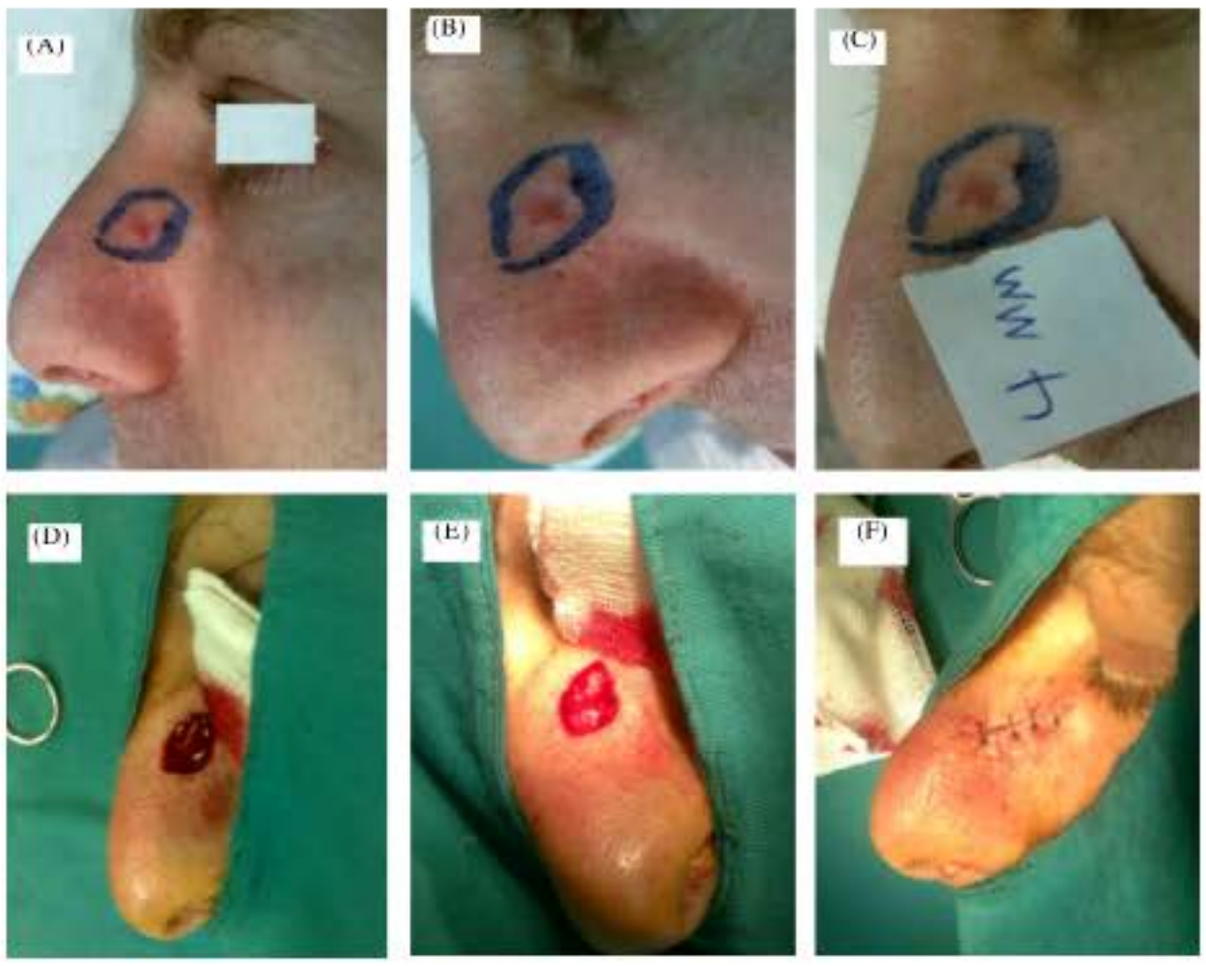

Fig. 2: One of operated patients with BCC, before (A-C), during (D, E) and after (F) excisional biopsy

Table 2: Duration of the disease before excisional surgery

Duration of disease (year)	Male	Female	Total	p-value
	---------- (%) ----------			
<1	24.1	14.3	20	0.05
1-2	27.6	33.3	30	0.05
2-3	27.6	19.0	24	0.05
3-4	0.0	14.3	6	0.05
4-5	3.4	4.8	4	0.05
>5	17.2	14.3	16	0.05

(24.1%) and cheek (24.1%). These sites in women were nose (47.5%), Scalp (14.3%) and cheek (14.3%). Totally, the most common sites of tumor in all patients were nose (36%), Scalp (20%) and cheek (20%). Figure 2 shows one of BCC tumors on nose skin, which excised with 4 mm safe margin.

Table 2 shows the duration of the disease before excisional surgery. Totally, most of patients (54%) underwent excisional surgery within 1-3 years after disease appearance.

All patients underwent surgical excision by one dermatologist with 4 mm safe margin. Pathologic examination of excised lesion confirmed the presence of safe margin (complete excision) in 48 patients (96%).

However, there were two cases (4%) of incomplete excision. Both of these tumors were pertaining to head region (one was in brow of a 50 year old man and another in cheek of a 45 year old woman). Pathologic examination revealed the remaining tumoral cells in depth and borders of tissue excised from brow but only in borders of tissue excised from cheek. Both incompletely excised tumors were re-excised with a delay of less than 2 months successfully. Then, no clinical evidence of recurrence of BCCs was recorded after a mean follow-up time of 48 month. Discussion

Ultraviolet radiation is generally accepted to be a major risk factor for BCC (Goh *et al*., 2006; Omidian and Emad-Mostofi, 2009; Noorbala and Kafaie, 2007). Noorbala and Kafaie (2007) reported a total of 3,930 patients with cancer between 1987 and 2001 in Yazd (a hot, dry, desert area in the center of Iran). Skin cancer with a mean frequency of 28.6 percent was the most commonly reported cancer, of which 76.9% were BCC (Noorbala and Kafaie, 2007). In our study, 76% of men were in high sun-exposure group.

The principal aim of any proposed method of management should be complete eradication of the tumor, which will be reflected in a very low recurrence rate. It also should preserve as much normal tissue as possible and thereby allow the best chance of a good reconstructive result with minimal intervention (Hsuan *et al*., 2004). In addition it is important to be as simple and cost effective as possible (Hsuan *et al*., 2004). Surgical excision has the advantages of simplicity, economy and the availability of a histological report. The reported rates of incomplete excision of BCC vary widely (5-25%) among centers around the world (Dieu and Macleod, 2002). Incomplete excision of skin malignancy is one of the 57 clinical indicators developed by the Royal Australasian College of Surgeons and the Australian Council on Healthcare Standards to act as a measure of the standard of surgical care (Dieu and Macleod, 2002).

Surgical excision is a rapid and ambulatory treatment, usually performed under local anesthesia (Bonvallot *et al*., 1993). Traditionally, wide excision margins were adopted in an attempt to ensure total clearance, but this has been shown to be an unreliable method of guaranteeing complete excision (Hsuan *et al*., 2004). Dieu and Macleod (2002) conducted a study to determine the rate of incomplete excision of BCC. Of 3558 BCC excised, 223 (6.3%) were reported to have histologically positive margin. Lateral margins were involved in 182 lesions (82%), deep margins were present in 30 lesions and 11 lesions had both deep and lateral margins that were positive. Of the 223 excised BCC with positive margin, 62 (28%) were recurrent BCC. Of the 62 recurrent BCC, 30 had been excised surgically, 24 had received radiotherapy, seven had cryotherapy and one was curetted (Dieu and Macleod, 2002). Collin reported a recurrence rate of 2.3% when combining 3-5 mm margins (Hsuan *et al*., 2004). While in some patients wide margins may leave residual tumor, in others excessive normal tissue is lost, necessitating complicated reconstructive techniques which might have been avoided (Hsuan *et al*., 2004).

Thissen *et al*. (2000) compared cosmetic results after cryosurgery and excision for primary BCC. Forty eight tumors were treated by excisional surgery and 48 tumors underwent cryosurgery. In one year follow-up, recurrence occurred in 3 of cryosurgery and none of the excision patients. All clinical professionals evaluated excision surgery as much better than cryosurgery (Thissen *et al*., 2000). Surgical excision for primary BCC remains the gold standard (Dieu and Macleod, 2002; Avril *et al*., 1997), with cure rates in the order of 95-99%. To achieve this cure rate, it is imperative that surgical excision is complete. The rate of incomplete excision varies widely in the literature (Bath-Hextall *et al*., 2004; Dieu and Macleod, 2002; Fleischer *et al*., 2001; Avril *et al*., 1997). The excellent result of 0.7% (10/1411), as recorded by Emmett and Broadbent was achieved in a sample of private patients treated by excision margins (3-10 mm) wider than those currently practiced (Dieu and Macleod, 2002). Kumar *et al*. (2000) have reported a rate of 4.7% (41/879), which is the best in recent times. The highest rate, 49.5%, came from 95 BCC on eyelids excised by ophthalmologists. All other published series in the past two decades have rates ranging from 7 to 25% (Dieu and Macleod, 2002; Collopy *et al*., 2000).

In Fleischer *et al*. (2001) study, tumor was present at the surgical margins in 243 (16.6%) of 1459 specimens. Tumors of the head and neck were more likely to be incompletely excised than truncal tumors in all the analyses. In Fleischer *et al*. (2001) study, incomplete excisions were more common in women, although this difference was not significant. It has been hypothesized that tumor excision in cosmetically sensitive areas on women may lead physicians, in an attempt to minimize cosmetic morbidity, to treat them differently than men (Fleischer *et al*., 2001). We found no evidence to support this hypothesis.

The most common site for incomplete excisions is the head and neck (86%), particularly the midface (nose, ears and periorbital), which account for 70% of cases (Dieu and Macleod, 2002; Kumar *et al*., 2000). In Dieu and Macleod (2002) study, the head and neck accounted for 86% (192/223) of all incomplete BCC; 70% (131/223) were on the nose, ears and periorbital regions. The most common sites of incomplete excision were the nose (20.2%); ear, including periauricular (18.4%); forehead and temple (17.5%); cheek and malar (10.7%) and periorbital (9.4%). The remaining 14% occurred on the limbs (8%) and trunk (6%) (Dieu and Macleod, 2002). The mean follow-up time was 18 months. There were seven recurrences within the follow-up period. Of those incompletely excised lesions managed by observation alone, four (4.5%) recurred. In the re-excised group, three (2.4%) recurred (Dieu and Macleod, 2002).

In present study, 98% of BCCs were located on head and neck region. Both of two cases (4%) of incomplete excision were pertaining to head region (one was in brow of a 50 year old man and another in cheek of a 45 year old woman). Pathologic examination revealed the remaining tumoral cells in depth and borders of tissue excised from brow but only in borders of tissue excised from cheek. Both incompletely excised tumors were re-excised with a delay of less than 2 months successfully. Then, no clinical evidence of recurrence of BCCs was recorded after a mean follow-up time of 48 month. The present series is important from a single point; that is, from a tertiary referral hospital, with an overall rate of incomplete excision (4%) being better than all published rates to date except for Hamada *et al*. study (Hamada *et al*., 2005). This was achieved with conventional 4 mm margins. Hamada *et al*. (2005) studied 223 consecutive cases with histologically confirmed eyelid BCC. Excision with 4 mm margins gave a zero recurrence rate. The overall 5 year and over recurrence rate including previously recurrent BCCs was 4.35%, only one of which was in the primary BCC group (1.6%) (10). The mean follow up was 48.6 months (range 2-120 months), the female to male ratio 1.1:1 (85:77), the mean age 71.2 (33-97) years (Hamada *et al*., 2005). Goh *et al*. (2006) studied 166 BCCs patients. There were 81 males and 85 females (male to female ratio, 0.95). The highest proportion (27.1%) was in the 81-90-year age group. The average patient age was 70.9 years (range, 32-101 years).

Seventy five percent were over the age of 60 years, with the highest proportion (27.1%) in the 81-90-year age group (Goh *et al*., 2006). In our study, the mean follow up was 48 months, the female to male ratio 1:1.4 (21:29), the mean age 68.8 (22-76) years. In Goh *et al*. (2006) study, BCCs were present for an average duration of 41.6 months (range, 0.25-360 months) before medical diagnosis. Of the 185 lesions, 156 (84.3%) were in the head and neck region, 18 (9.7%) were on the trunk and 11 (5.9%) were on the limbs. The most common site for BCCs was the nose (24.3%). The average diameter of the lesions was 12.0 mm (range, 1-70 mm) (Goh *et al*., 2006). Totally, the most common sites of tumor in all patients were nose (36%), Scalp (20%) and cheek (20%). Most of our patients (54%) underwent excisional surgery within 1-3 years after disease appearance (range, 6-60 months).

The rate of re-excision for incomplete BCC (4%) was less than many series which average at 30% (Dieu and Macleod, 2002; Kumar *et al*., 2000). In our study, pathology report of 'incomplete margins' was indicative of the presence of residual tumor. We did not use frozen section. This method is rarely used because of its unreliability and its inefficiency. Ghauri *et al*. (1999) have demonstrated that the accuracy of frozen sections in detecting the presence of tumor at the margins is 91.1%. Coupled with the fact that standard frozen section may take longer than the operation itself, it is reserved for selected difficult re-excisions (Dieu and Macleod, 2002).

The rate of recurrence in those having a wait and see approach (3.1%) is much lower than many published reports. This reflects the short follow up (mean 18 months) and is not statistically significant when compared with the rate of recurrence after re-excision (2.4%). However, Gooding *et al*. have found that the mean interval of recurrence was 15-16 months and Pascal *et al*. found it to be 24 months (Dieu and Macleod, 2002). However, we did not use'wait and see approach.

Incomplete excision of skin tumors is seen more commonly in instances where the tumor margins are rendered difficult to discern clinically by scarring from previous treatment, or when the tumor is large and infiltrating and occurs at difficult anatomical sites (Dieu and Macleod, 2002). Controversy remains as to how to manage incompletely excised BCC. A case can be made for observing those lesions in which the surgeon is confident that there is no macroscopic residual disease, the patient is elderly and the recurrence. If this approach is adopted, the patient should be followed for at least 5 years. Generally it is more efficient to re-excise incomplete BCC (Dieu and Macleod, 2002).

Lalloo and Sood reported the results of a prospective study of 63 patients who underwent excision of well-demarcated BCCs in the head and neck region. The surgical excision margin used was 2 mm. Histological assessment confirmed complete excision in 95% and there was no evidence of recurrence of the BCC over a 24 month follow-up period in all patients. They propose that a clinical excision margin of 2 mm is adequate for treatment of simple, well demarcated BCCs arising in the head and neck (Lalloo and Sood, 2000). However, in the periocular region, especially when the lid margin is involved, such wide excision results in large defects requiring complex reconstruction. Hsuan *et al*. have reported excellent results following the use of 2 mm margins in periocular BCCs excised in a staged manner (Hsuan *et al*., 2004). However, the traditional surgical management of nodular adnexal BCC involves excision with 3-4 mm margins and primary repair. This may remove a significant area of healthy tissue, often necessitating a complicated reconstruction, without the confirmation that tumor excision is complete (Hsuan *et al*., 2004). Conventionally, BCCs are excised with 3-4 mm margins, combined with primary repair (Hsuan *et al*., 2004; Chadha and Wright, 2009). To achieve the best functional and cosmetic results it is important to minimize the amount of normal tissue loss. Surprisingly, even 3-4 mm margins are insufficient to guarantee complete excision and in up to 54% histological clearance is not achieved (Hsuan *et al*., 2004).

Goh *et al*. (2006) studied 185 BCCs in 166 patients. All BCCs were excised with at least a 4 mm margin according to hospital guidelines. Postoperatively, all specimens were examined histologically for margin clearance. Of the 185 lesions, 28 (15.1%) were incompletely excised. Conventional surgical excision with margin control achieves a satisfactory tumor clearance rate of 84.9% (Goh *et al*., 2006).

A number of factors may influence the tumor clearance rate for surgical excision of BCCs. BCCs of larger size are more likely to be incompletely excised. Location of the tumor seems to be significant because most incompletely excised or recurrent BCCs reported in previous studies have been located on the head and neck. Female sex has occasionally been found to be associated with a higher incidence of BCC recurrences; however, other studies have not been confirmatory (Fleischer *et al*., 2001) and we found no evidence to support this hypothesis.

Incompletely excised BCCs are those most likely to recur. Because most recurrent tumors are situated on the head and neck and have an infiltrative growth pattern, pathologists should report on the microscopic growth pattern of BCCs as well as completeness of excision (Rippey and Rippey, 1997). Clinicians must attempt to excise head and neck BCCs with wide margins initially. Tumors extending to the margin of excision which are infiltrative in pattern and located on the head and neck may be particularly likely to recur and immediate

re-excision should be considered in these patients (Rippey and Rippey, 1997). Rippey and Rippey (1997) studied 268 patients with 353 BCCs, of which 16% (58/353) extended to the margin of surgical excision. Most of these were situated on the head or neck (43/58; 74%). Seven of the 28 (25%) (28/353; 8%) recurrent BCCs were incompletely excised.

The 5 year recurrence rate for excised BCCs was 0.7% for neck, trunk and extremities vs. 20.2% for head. Surgical excision is a highly effective method for removal of BCCs with a good to excellent cosmetic outcome in about 85% of the recurrence-free treatment sites (Hussain and Earley, 2003). When BCCs are completely excised, only 1% will recur, compared with 33-39% if they are incompletely excised (Goh *et al*., 2006). Bonvallot *et al*. (1993) studied 81 patients with BCC of the nose to present the oncological and cosmetic results of surgical treatment. Surgery had a recurrence rate of 3.7 to 12.6%. Recurrences were due to insufficient excision. The cosmetic result was good (85 to 90%). They concluded that surgical treatment of nasal BCC is safe, effective and rapid, with good oncological and cosmetic results and it has many advantages over the other treatments (Bonvallot *et al*., 1993). In Goh *et al*. study, the head and neck accounted for 82.1% (23/28) of all incompletely excised BCCs; 53.6% (15/28) were on the mid-face (nose, nasolabial folds, inner canthi of the eyes and medial aspect of the cheeks). The most common site of incomplete excision was the nose (32.1%). The remaining 17.9% occurred on the trunk. When compared with completely excised tumors, incompletely excised BCCs were more likely to be located on the mid-face and trunk (71.4% vs. 43.3%) (Goh *et al*., 2006).

Bath-Hextall *et al*. searched for all published randomized controlled trials. The only study of surgical excision versus radiotherapy showed significantly more persistent tumors and recurrences in the radiotherapy group compared with surgery. One study compared cryotherapy with surgery, with inconclusive results at one year (Bath-Hextall *et al*., 2004). Preliminary studies suggest a short term success rate of 87-88% for imiquimod cream in the treatment of superficial basal cell carcinoma, although this cream has not been compared with surgery. Surgery and radiotherapy seem to be the most effective treatments; however, surgery showed the lowest failure rates (Bath-Hextall *et al*., 2004). Other treatments might have some use but need to be compared with surgery.

Despite the fact that there are many publications reporting on recurrence rates for other treatment options such as Mohs surgery, cryosurgery, or radiotherapy (Kokoszka and Scheinfeld, 2003; Caccialanza *et al*., 2001), these studies are not uniform and the results cannot be directly compared. Consequently, there is a need for randomized clinical trials providing data on the efficacy of excisional surgery as contrasted with other techniques. Future investigators should consider the use of histologic clearance as an outcome measure (Kokoszka and Scheinfeld, 2003).

CONCLUSION

BCC predominantly affects the elderly. In present experience, conventional surgical excision for BCCs with postoperative margin assessment achieves an acceptable success rate of 96%. With comparison of statistical results with other reports from other countries, this rate is considered acceptable and surgical method is done properly in our center and consideration of 4 mm of tumoral margin is enough.

REFERENCES

Auw-Haedrich C., S. Frick, D. Boehringer and H. Mittelviefhaus, 2009. Histologic safety margin in basal cell carcinoma of the eyelid: correlation with recurrence rate. Ophthalmology, 116: 802-806.

Avril, M.F., A. Auperin, A. Margulis, A. Gerbaulet and P. Duvillard, 1997. Basal cell carcinoma of the face: Surgery or radiotherapy? Results of a randomized study. Br. J. Cancer, 76: 100-106.

Bath-Hextall, F., J. Bong, W. Perkins and H. Williams, 2004. Interventions for basal cell carcinoma of the skin: Systematic review. BMJ., 25: 705-705.

Bonvallot, T., Y. Raulo, J. Zeller, J.M. Faivre, G. Horn and J. Baruch, 1993. Basal cell carcinoma of the nose. Ann. Dermatol. Venereol., 120: 209-214.

Bostanci, S., P. Kocyigit, A. Alp, C. Erdem and E. Gürgey, 2005. Treatment of basal cell carcinoma located in the head and neck region with intralesional interferon alpha-2a: Evaluation of long-term follow-up results. Clin. Drug Investig., 25: 661-667.

Caccialanza, M., R. Piccinno and A. Grammatica, 2001. Radiotherapy of recurrent basal and squamous cell carcinomas in 229 patients. Eur. J. Dermatol., 11: 25-28.

Chadha, V. and M. Wright, 2009. Small margin excision of periocular basal cell carcinomas. Br. J. Ophthalmol., 93: 803-806.

Collopy, B.T., L. Rodgers, P. Woodruff and J. Williams, 2000. Early experience with clinical indicators in surgery. Aust. N. Z. J. Surg., 70: 448-451.

Delfino, S., D. Innocenzi, G. Di Lorenzo, M. Scalvenzi, V. Montesarchio, F. Feroce, A. Baldi and P. Persichetti, 2006. An increase in basal cell carcinoma among the young: An epidemiological study in a Middle-South Italian population. Anticancer Res., 26: 4979-4983.

Diepgen, T.L. and V. Mahler, 2002. The epidemiology of skin cancer. Br. J. Dermatol., 146: 1-6.

Dieu, T. and A.M. Macleod, 2002. Incomplete excision of basal cell carcinomas: A retrospective audit. Aust. N. Z. J. Surg., 72: 219-221.

Ducic, Y., D.E. Marra and C. Kennard, 2009. Initial Mohs surgery followed by planned surgical resection of massive cutaneous carcinomas of the head and neck. Laryngoscope, 119: 774-777.

Fleischer, A.B. Jr., S.R. Feldman, J.O. Barlow, B. Zheng and H.B. Hahn *et al*., 2001. The specialty of the treating physician affects the likelihood of tumor-free resection margins for basal cell carcinoma: Results from a multi-institutional retrospective study. J. Am. Acad. Dermatol., 44: 224-230.

Ghauri, R.R., A.A. Gunter and R.A. Weber, 1999. Frozen section analysis in the management of skin cancers. Ann. Plastic Surg., 43: 156-160.

Goh, B.K., P. Ang, Y.J. Wu and C.L. Goh, 2006. Characteristics of basal cell carcinoma amongst Asians in Singapore and a comparison between completely and incompletely excised tumors. Int. J. Dermatol., 45: 561-564.

Hamada, S., T. Kersey and V.T. Thaller, 2005. Eyelid basal cell carcinoma: Non-mohs excision, repair and outcome. Br. J. Ophthalmol., 89: 992-994.

Hassanpour, S.E., A. Kalantar-Hormozi, S. Motamed, S.M. Moosavizadeh and R. Shahverdiani, 2006. Basal cell carcinoma of scalp in patients with history of childhood therapeutic radiation: A retrospective study and comparison to nonirradiated patients. Ann. Plastic Surg., 57: 509-512.

Hsuan, J.D., R.A. Harrad, M.J. Potts and C. Collins, 2004. Small margin excision of periocular basal cell carcinoma: 5 year results. Br. J. Ophthalmol., 88: 358-360.

Hussain, M. and M.J. Earley, 2003. The incidence of incomplete excision in surgically treated basal cell carcinoma: A retrospective clinical audit. Irish Med. J., 96: 18-20.

Kokoszka, A. and N. Scheinfeld, 2003. Evidence-based review of the use of cryosurgery in treatment of basal cell carcinoma. Dermatol. Surg., 29: 566-571.

Kuijpers, D.I., M.R. Thissen and M.H. Neumann, 2002. Basal cell carcinoma: Treatment options and prognosis, a scientific approach to a common malignancy. Am. J. Clin. Dermatol., 3: 247-259.

Kumar, P., C.I. Orton, L.J. McWilliam and S. Watson, 2000. Incidence of incomplete excision in surgically treated basal cell carcinoma: A retrospective clinical audit. Br. J. Plastic Surg., 53: 563-566.

Lalloo, M.T. and S. Sood, 2000. Head and neck basal cell carcinoma: Treatment using a 2-mm clinical excision margin. Clin. Otolaryngol. Allied Sci., 25: 370-373.

Mackie, R.M. and E. Calonje, 2004. Non-Melanoma Skin Cancers and Other Epidermal Skin Tumors. 7th Edn., Wiley-Blackwell, USA., ISBN: 0632064293.

Noorbala, M.T. and P. Kafaie, 2007. Analysis of 15 years of skin cancer in central Iran (Yazd). Dermatol. Online J., 13: 1-1.

Omidian, M. and N. Emad-Mostofi, 2009. Basal cell carcinoma arising from traditional tattoo. Arch. Iran Med., 12: 198-198.

Rippey, J.J. and E. Rippey, 1997. Characteristics of incompletely excised basal cell carcinomas of the skin. Med. J. Aust., 166: 581-583.

Shinsuke, K., K. Hirohiko, T. Yasuhiro, H. Kazuo and I. Masayoshi, 2007. Linear basal cell carcinoma in an Asian patient. Open. Ophthalmol. J., 1: 20-22.

Szeimies, R.M., S. Karrer and H. Backer, 2005. Therapeutic options for epithelial skin tumors: Actinic keratoses, Bowen disease, squamous cell carcinoma and basal cell carcinoma. Hautarzt, 56: 430-440.

Thissen, M.R., F.H. Nieman, A.H. Ideler, P.J. Berretty and H.A. Neumann, 2000. Cosmetic results of cryosurgery versus surgical excision for primary uncomplicated basal cell carcinomas of the head and neck. Dermatol. Surg., 26: 759-764.