THE ANALYSIS OF DIMENSIONS AND THE RATE OF RECURRENCE OF BASAL CELL CARCINOMA OF PERIORBITAL REGION AFTER EXCISIONAL SURGER

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Basal cell carcinomas (BCC) of periorbital region are often seen in clinical practice and have a potential risk of local recurrence.

This research has been done at the Surgery clinic in Nis - Department of plastic and reconstructive surgery and at the Pathology clinic. 101 patients who had surgery in period from 2000 to 2003, had been analysed. 12 patients had multiple locatcd tumours, so the total numbcr of observed tumours was 121. Tumours have been devided in two groups, depending if they are primary or recurrent: first group - primary tumours (n=l 11), second group - recurrent tumours (n=10).

Patients with recurrent BCC were 56,7 years of age. It is significally less than in patients with primary BCC of periorbital region. They were 66,407 years of age (p=0,037). Ten tumours were recurrent (8,3%). The greatest number of recurrencies vvas on medial canthus (40%), then on uppcr eyelid (30%), on lower eyelid (20%), and on lateral canthus (10%). Tumours larger than 2cm in radius have predispositions to recurrence (p=0,01). There is a positive corrclation between surface and thickncss of tumours ($p<lx!0^6$). There is a positive correlation betvveen the depth of histologic layer to which tumour has penetrated and thickness of tumour (p=0,018).

The average age of patients with recurrence is significally lower than average age of patients with the primar tumour. By defining siže and location of BCCs of periorbital region, it is possible to predict biological behaviour of tumour. *Acta Medica Medianae 2004; 43(2): 13-18.*

Key words: basal cell carcinoma, ***periorbital*** *region, recurrence*

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Intruduction

Basal ćeli carcinomas (BCC) of periorbital region are often seen in clinical practice. There are a lot of pathohistological and clinical types of BCC (ulcerating BCC, superficial BCC, sclerosing BCC, pigmented BCC, basal ćeli nevus syndrome, adnexal BCC, trabecular).

The results of many researches have shovvn that the most aggressive BCCs are in periorbital region. They are most frequently seen on lower eyelids, then at medial canthal region, then at latheral canthal region. They are very rarely seen on upper eyelids (1,2).

On medial canthus (\vhere embrional buds meet), tumours are spread along medial orbit vvall, vvhich enables long subclinic lumour growth, so, this location is malignant (3).

BCCs have a potential risk of local recurrence. Their growth is vvithin parts vvith the least resistance. Becauseof that, infiltration in bones, cartilage and muscles is the late stadium of the disease. When tumour comes to these structures, before infiltration, it spreads along periosteum, perichondrium or tarsus. That is why BCCs on these sites are difficult for surgery and there are many recurrences (4).

So, medial canthus carcinoma has an agressive biological course and bad prognosis.

The basic treatment of BCC is excisional surgery. Skin defects can be closed primarily or vvith skin grafts or local flaps. Defects of evelids, thickness up to 1/4 vvidth, are directly sutured, and up to 1/3 vvidth, they are directly sutured vvith lateral cantotomy (5).

Defects larger than 1/3 of evelid vvidth can be reconstructed by different techniques: Me Gregor, Muštarde, Hughes, Esser, Cutler Beard and so on (2).

Reconstructions in this region are sometimes very complicated, because carcinoma is extremely destructive vvhen it penetrates bones structures.

The treatment of BCC is mainly surgical, radiotherapy has shovvn good results and Mohs surgery is used in treatment of recurrent BCCs. But, this technique is a very complex one and special expertise and training is necessary for skilled support personnel, so il is not suitable for everyday usage.

Nagore et al. claim that incidence of recurrence following surgical excision is 26% in patients with a positive margin, 14% in patients with a close margin. This fact should not be neglected, since the face tumours have positive margins (20-38%), which is more than in tumours at some other sites (8%) (6).

The tumour size is an important factor for recurrence. The bigger basic BCC, the higher rate of recurrence is.

BCC metastases are rare. They are subcutanous, in the bones, lungs, liver and in the neck lymph nodes (7).

No parameter for biological course and for prognosis of the tumour has been found so far. There are some studies in which prognosis assessment has been done for tumour location, tumour size, immunosupressive therapy and presence of chronic irritations.

The cure rate depends on illness stadium and the type of treatment. It is of great importance to define high risk tumours to be ale to define the proper treatment.

By defining size and location of BCCs of periorbital region, it is possible to predict biological behaviour of tumour. So, it is a challenge to study periorbital region BCCs characteristics and their treatment.

The aim of the research

1. Find out frequency of BCC of periorbital re gion concerning the sex, age and location.
2. Determine rate of recurrence of BCCs of peri orbital region
3. Determine clinical and histological forms of BCC
4. Define tumour size - surface and depth
5. Make histological definitions of tumour inva sion in tissues
6. Determine the way of surgical treatment of pe riorbital region BCCs
7. Compare the obtained results and determine parameters for boiological BCCs characteristics, taking into account previously mentioned parameters, sex, age location, recurrence rate, clinical form, histologic form, surface, depth and tumour invasion rate into tissues.

Material and methods

This research has been done at the Surgery clinic in Nis - Department of plastic and reconstructive surgery and at the Pathology clinic.

101 patients who had surgery in period from 2000 to 2003, had been analysed. 12 patients had multiple located tumours, so the total number of observed tumours was 121.

Tumours have been devided in two groups, depending if they are primary or recurrent.

First group: primary tumours (n=l 11)
Second group:recurrent tumours (n=10).

Ten patients with recurrent tumours were operated in the period between 2000 and 2003. Three of them had both primary and recurrent tumours in that period, seven of them had recurrent tumours. They had had primary tumours before 2000.

The tumour size was determined by clinical examination. Then, according to the tumour radius, tumour surface was calculated in mm^2.

P= D^2/4 x 7i, D-radius, constant rc=3,14 - for the circle

P= Dxd/4 x *n* , D-longer radius, d-shorter radius, constant 7t=3,14 - for ellipse

Measurement of tumour thickness and tumour invasion rate into tissues depth was done. 24 samples with positive margins were not considered, only tumours completely excisioned. (n=97)

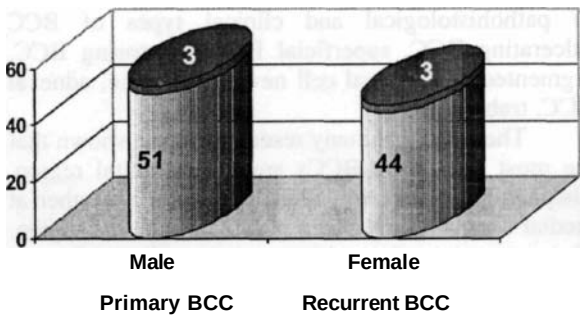
Tumour thickness was measured by occular micrometer, starting from granular layer. The greatest tumour thickness has been measured and expressed in urn. The rate of depth tumour invasion towards the deepest histological layer which tumour reached has been observed.

The results of the research are shown graphycally and in charts (Excel 2000, Word 2000), and SPSS version 10.0 i Statcalc version 5 are used for static analysis. Analytic statistic for scientifis hypothesis testing has also been done. Depending on the types of distribution (normal - unknown), types of statistic caractheristies (numeric - attributive), as well as on number and size of sample, the following statistic tests have been used:

1. Student's t-test for two big independent sam ples, for two small independent samples (for making difference in average values between to samples)
2. X^{2}rtest' Fisher test (to determine connections between examined alributive characteristics)
3. Pearson linear correlation coefficient, Sperman's coefficient of ranking corellation (to determine dependance rate between two variables).

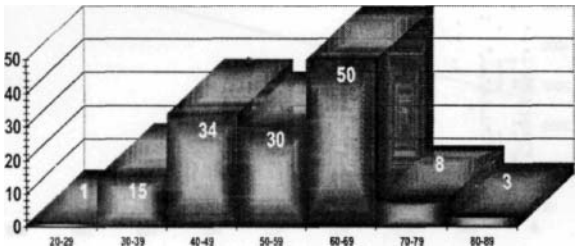
Results

During the observation period, 101 patients were analysed, 54 (53,5%) male and 47 (46,5%) female patients.



*Graph I. Recurrent tumour **distribution** compared to sex*

There is no connection between sex and recurrence (x^2= 0,031, p= 0,861) (Graph 1). Most patients were between 50 and 60 years of age (Graph 2).

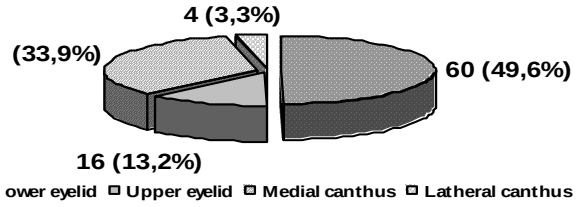


Graph 2. Patients' age

Patients with recurrent BCC were 56,7 years of age. It is significally less than in patients with primary BCC of periorbital region. They were 66,407 years of age (t= 2,376, p= 0,037) (Table 1).

Table I. Difference in average age between patients with primary and recurrent BCC of periorbital region

Age	X-i-SD	t	P
Primary BCC	66,407±1 1,571	2,376	0,037*
Recurrent BCC	56,70112,338		

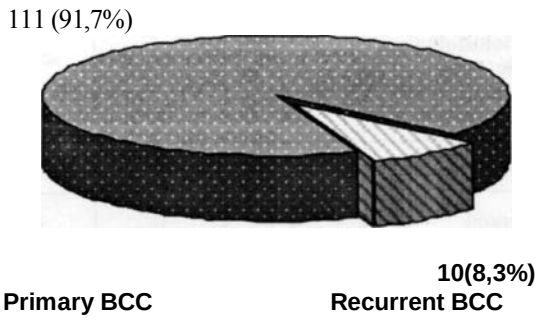


Graph 3. Tumour structure according to location

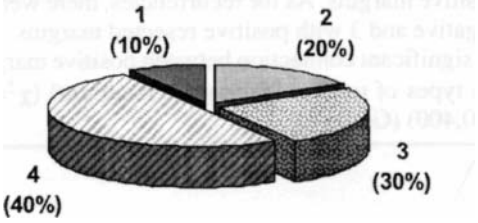
BCC was mostly found on lower eyelid, 60 tumours (49,6%), then on medial canthus, 41 tumours (33,9%), on upper eyelid 16 tumours (13,2%), and on lateral canthus only 4 tumours (3,3%) (Graph 3).

During the period of observation, total of 121 BCCs of periorbital region were operated. Ten of them were recurrent, 8,3% (Graph 4).

The greatest number of recurrencies was on medial canthus, 4 recurrencies (40%), then on upper eyelid, 3 recurrencies (30%), on lower eyelid 2 recurrencies (20%), and on lateral canthus only 1 recurrence (10%) (Graph 5).



Graph 4. Primary and recurrent tumours BCC structure



Graph 5. Recurrent BCC periorbital region structure according to location

In table 2 all clinical forms of BCCs in periorbital region are shown. The most common form was nodular ulcerating: total of 113 tumours (93,4%).

Table 2. BCC structure according to clinical form

Clinical form	n	%
Modulo-ulcerous	113	93,4
Superficial	1	0,8
Sclerosans	2	1,7
Pigmented	1	0,8
Gorlin syndrome	0	0
Syndrome Basex	3	2,5
Trabecular	1	0,8
Score	121	100

As for histological form, most of BCCs were solid, 95 (78,5%), solid-adenoid were significally less, 21 (17,4%) and there were 4 adenoid ones (3,3%) and only one superficial BCC (0,8%).

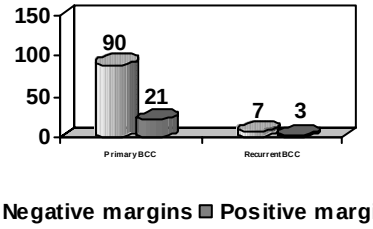
There were 10 recurrencies. They were only in solid and solid - adenoid forms. Despite that, there was not any statistically relevant connection between histological BCC of periorbital region and recurrent tumours (X^2= 0,876, p= 0,645) (Table 3).

Table 3. Distribution of different pathohistological BCC forms of periorbital region at primary and recurrent tumours

Pathohistological form	primary	recurrent	score
Solid	86	9	95
Solid-adenoid	20*	1	21
Adenoid	4	0	4
Superficial	1	0	1
Score	111	10	120

Out of 121 tumours, only 24 (19,8%) were not excisioned in sound tissues. There were 90 primary tumours with negative and 21 pimary tumour with positive margins. As for recurrencies, there were 7 with negative and 3 with positive resected margins. There is no significant connection between positive margins and the types of tumour (primary - recurrent) (x^2= 0,708, p=0,400)(Graph6).

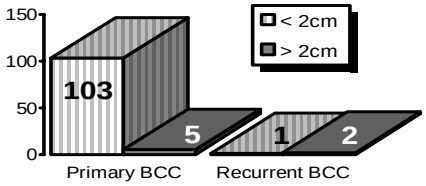
The greatest number of tumours penetrated to the lowest limits of sweat glands (Graph 9) (32).



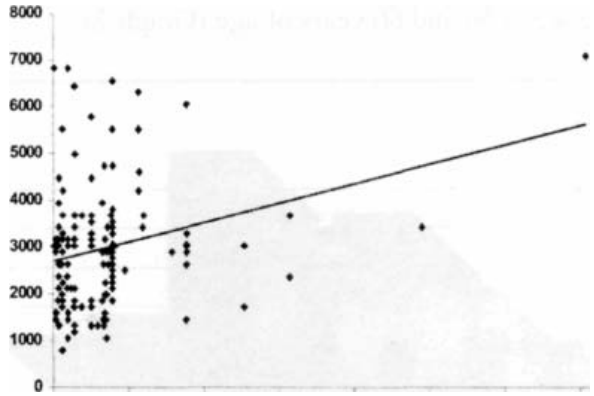
Graph 6. All BCC distribution, with and without recurrency, compared to margins of surgery cut

Tumours larger than 2 cm in radius have predispositions to recurrence (Fisher test p=0,01) (Graph 7).

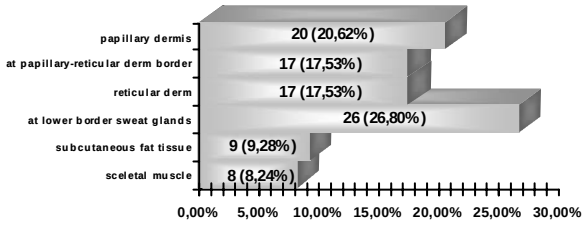
Pearson coefficient of linear correlation for measuring the degree of dependance between surface and thickness of tumours, was r = 0,218 ($p< 1 \times 10^{-6}$), so there was a strong positive correlation, which means that if surface tumour increases, its thickness also increases (Graph 8).



Graph 7. Recurrence occurence distribution compared to primary tumour size

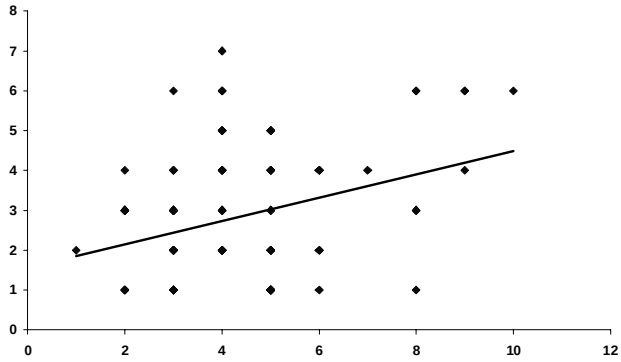


Graph 8. Correlation between surface and thickness of tumours



Graph 9. Tumour distribution according to different depths of histologic layers to which they penetrated

There is a positive correlation between the depth of histologic layer to which tumour has penetrated and thickness of tumour. (Sperman's coefficient of rang correlation p= 0,240, p= 0,018), which means that greater the depth of tumour penetrating, the greater its thickness is (Graph 10).



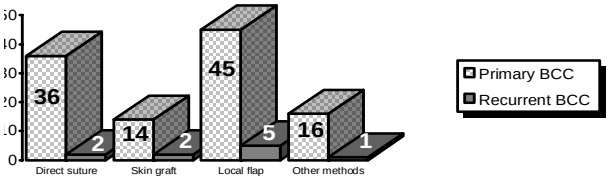
Graph 10. Correlation between the depth of histologic layer to which tumour has penetrated and thickness of tumour

In primary tumours there is also positive correlation between depth and thickness of tumour, (p= 0,025), while in recurrent tumours there was no correlation, (p= 0,157) (Table 4).

Table 4. Correlation between the depth of histologic layer to which BCC penetrated and thickness of all BCCs, primary BCCs and recurrent BCCs

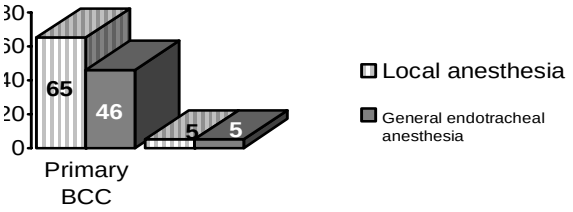
	All tumours thickness	Primary BCCs thickness	Recurrent BCCs thickness
ρ	0,240	0,235	0,636
p	0,018*	0,025*	0,157

There is no significant connection between primary and recurrent tumours and the way of defect reconstruction (x^2=l,156, p= 0,764) (Graph 11).



Graph 11. Primary and recurrent rumour distribution compared to defect reconstruction

There is no significant connection between the types of anesthesia (local, general endotrahial) and the types of tumour (primary, recurrent), (x^2= 0,276, p= 0,600) (Graph 12).



Graph 12. Primary and recurrent tumours compared to types of anesthesia

Discussion

BCC is the most frequent epithel tumour of eyelids. It is estimated to be 80-90% ot all tumour in thr West countries (8).

Early BCC treatment enables its cure. To choose the best therapy it is necessary to know biological, histological and clinical behaviour of this tumour (5).

Average age of patients with recurrency was 56,7 years of age, significally less compared to average age of patients with primary tumour (66,407 years of age), (p= 0,037). Because of UV exposure, chemical agenses, smoking..., and because elderly persons have skin BCC more often than younger ones, it could be thought that recurrences more often appear in elderly persons also. But, researches have shown a contradictory fact that recurrences more often occur in younger patients. So, there are probably some risk factors that cause these recurrences, but they are not defined yet. Recently, at chromosome 9 there has been found a specific tumour - surpressor gene which could have a part in development of individual BCC, as well as in BCC which occurs in syndrome nevoid BCCs (9). Presence of cancer genes shows that recurrencies of BCC do not depend on surgery intervention only, but on malignant potential in genetic code as well.

The tumour occured at lower eyelid most frequently (56,4%), then on medial canthus (28,2%), then on upper eyelid (12,2%) and on lateral canthus (3,2%). The same data were found in world's literature also (1).

The greatest number of recurrencies was at medial canthus (n=4), then on upper eyelid (n=3), lower eyelid (n=2) and on latheral canthus only one. Pieh et al. claim that the greatest risk of recurrencies in periorbital region is on medial canthus, then on lower and upr_er eyelids, and the least on latheral canthus. This can be connected with complex anatomy of medial canthal ligament, duct system and orbital septal attachments (10).

Incomplete excision was applied in 19,8% cases. Researches about connections of positive resected margins and recurrent tumours showed no significant data. Literature data concerning this problem are different (3,6).

Comparing size of primary tumours without recurrence with the size of primary tumour with occurence of recurrence, we got statistically significant difference (p= 0,01), which means that tumour greater than 2 cm in radius are high risk recurrent tumours. The size of tumour is an important factor for recurrence rate (11).

Comparing tumour surface and thickness, it was found that there is a strong positive correlation, the larger surface, the greter thickness (p= 0,024).

On the other hand, there is significant positive correlation between tumour depths and its thickness. Greater tumour thickness, deeper tumour depth penetration (p = 0,24*, p = 0,018).

Conclusion

BCC periorbital region is more often seen in older patients, mostly in the period between the age of 60 or 70**.** The average age of patients with recurrence is

significally lower than average age of patients with the primar tumour. It is most often lacated on lower eyelids, then on medial canthus, on upper eyelids and most rarely on lateral canthus. Recurrence is on medial canthus in most cases, then on upper eyelids, lower eyelids and it is rarely seen on lateral canthus.

There is significant connection between primary tumour size and its recurrence. Tumours larger than 2 cm in radius have recurrence predispositions. There is also positive correlation between BCC tumour surface and its thickness, and also between BCC thickness and depth of histologic layer to which tumour penetrated.

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ANALIZA DIMENZIJA I STOPE RECIDIVA BAZOCELULARNOG KARCINOMA PERIORBITALNE REGIJE NAKON HIRURSKE EKSCIZIJE

Irena Janković, Milan Višnjić, Dragon Mihailović i Dimitrije Janković

Bazocelularni karcinomi (BCK) periorbitalne regije česti su u kliničkoj praksi i imaju potencijalni rizik za nastanak lokalnog recidiva.

Ispitivanje je sprovedeno u Odeljenju za plastičnu i rekonstruktivnu hirurgiju Hirurške klinike Kliničkog centra u Nišu i Klinici za patologiju. Analiziran je 101 bolesnik operisan u periodu od 2000. do 2003. godine. Kako je 12 bolesnika imalo tumor na više lokalizacija, broj ukupno posmatranih tumora bio je 121. Tumori su podeljeni prema tome po koji se put javljaju u dve grupe: I grupa - primarni tumori (n=l 11) i II grupa - recidivantni tumori (n=10).

Starost bolesnika sa recidivom BCK koja je iznosila 56,7 godina, bila je signifikantno manja od starosti bolesnika sa primamim BCK periorbitalne regije koja je iznosila 66,407 godine (p= 0,037). Bilo je 10 recidiva (8,3%). Najveći broj recidiva bio je na medijalnom kantusu (40%), zatim na gornjem kapku (30%), donjem kapku (20%), a najmanji na lateralnom kantusu (10%). Tumori veći od 2 cm u prečniku signifikantno su predisponirani za kasniju pojavu recidiva (p= 0,01). Između površine i debljine tumora postojala je jaka pozitivna korclacija ($p<lxl0^{-6}$). Između dubine histološkog sloja do koga je tumor prodro i debljine tumora postojala je pozitivna korelacija (p= 0,018).

Prosečna starost bolesnika sa recidivom je signifikantno manja od prosečne starosti bolesnika sa primarnim tumorom. Utvrdivanjem dimenzija i lokalizacije BCK periorbitalne regije moguće je predvideti biološko ponašanje tumora. *Acta Medica Medianae 2004; 43(2): 13-18.*

Ključne reči: hazocelularni karcinom, periorhitcilna regija, recidiv