Is incisional biopsy helpful in the histopathological classification of basal cell carcinoma?*

*É a biópsia incisional útil na classificação dos carcinomas basocelulares?**

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Abstract: BACKGROUND - Basal cell carcinoma is a tumor with many histologic types, each one with different aggressiveness potential. The known correlation between histologic types found in preoperative biopsy samples and excisional specimens is not absolute. Correspondence rates vary from 42.7 to 80.0% in medical literature.

OBJECTIVE - To evaluate the correlation between histologic types of basal cell carcinoma in preoperative biopsies and their respective excised surgical specimens.

METHODS - A retrospective analysis of 70 primary basal cell carcinoma cases submitted to preoperative biopsies and excisional surgery. The histologic evaluation was performed according to standard practice determining both the predominant and secondary histologic types found in preoperative biopsy materials and surgically excised specimens.

RESULTS - There was a 78.3% correlation rate between the predominant histologic type of the biopsy and the surgical specimen, and an 87% correspondence between the predominant histologic type and/or secondary histologic type of the biopsy and/or predominant histologic type of the surgical specimen.

CONCLUSION - The preoperative biopsy is useful for predicting the predominant basal cell carcinoma histologic type of the surgical excisional specimen in most cases. Nevertheless, when only the predominant histologic type found in biopsy is described, there is a 21.7% failure rate in diagnosis. When both predominant histologic types and secondary histologic types found in the biopsy are described, diagnostic failure drops to 13%.

Keywords: Basal cell carcinoma; Biopsy; Histology; Surgery

Resumo: *FUNDAMENTOS – O carcinoma basocelular é tumor constituído por diferentes tipos histológicos, que demonstram diversificado potencial de agressividade. Sabe-se que a correlação entre os tipos histológicos de carcinoma basocelular encontrados no material de biópsia pré-operatória e no material da peça cirúrgica excisional não é total. Na literatura essa correlação varia de 42,7 a 80%.*

OBJETIVO – Avaliar a correlação entre os tipos histológicos de carcinoma basocelular nas biópsias incisionais e respectivas peças cirúrgicas excisionais.

MÉTODOS – Análise retrospectiva de 70 casos de carcinoma basocelular primário submetidos a biópsia pré-operatória e cirurgia excisional. A avaliação histológica foi feita de modo padronizado, determinando tanto o tipo histológico predominante quanto os tipos histológicos acessórios encontrados no material das biópsias pré-operatórias e nas peças cirúrgicas excisionais.

RESULTADOS – Houve 78,3% de correlação entre tipo histológico predominante da biópsia e peça cirúrgica e 87% de correlação entre tipo histológico predominante e/ou tipo histológico acessório da biópsia e tipo histológico predominante da peça cirúrgica.

CONCLUSÃO – A biópsia pré-operatória é útil para predizer o tipo histológico predominante de carcinoma basocelular da peça cirúrgica excisional na maioria dos casos. No entanto, é importante ressaltar que, quando descrito apenas o tipo histológico predominante encontrado na biópsia, ocorre 21,7% de falha no diagnóstico.

Palavras-chave: Biópsia; Carcinoma basocelular; Cirurgia; Histologia

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INTRODUCTION

Basal cell carcinoma (BCC) is the most frequent malignant cutaneous neoplasm in white individuals, and represents 65% to 75% of all skin tumors.[1]

Over time, histology reports have become more and more detailed. Formerly, the diagnosis furnished by pathologist was merely that of BCC, sometimes accompanied by a description of the different histologic types of the tumor.

This greater degree of detail in tumor analysis and description has enabled an increasingly frequent identification of aggressive histologic types in biopsy materials and calling for more aggressive surgical treatment since the histologic criterion is one of the items considered in the classification of BCC recurrence.[2]

The objective of this study stems from these observations, i.e., to correlate histologic characteristics of BCC preoperative punch biopsies with the histologic characteristics of the surgical specimens to determine consensus between the findings for each specimen.

PATIENTS AND METHODS

A retrospective analysis was performed of patients who had been submitted to surgery at the dermatological surgery department of the Dermatology Division at the *Hospital das Clínicas*, Medical School, *Universidade de São Paulo* (HC-FMUSP), in the Ambulatory Surgery Center of the Central HC-FMUSP Institute during the period of February 2001 to January 2004, who met the following inclusion criteria:

1 Histologic diagnosis of BCC by preoperative biopsy,

2 History of primary BCC,

3 Treatment by surgical excision.

In patients who satisfied inclusion criteria, the following information was collected: gender, age, anatomical site of the BCC, histologic examination of preoperative biopsy, lesion measurements according to data recorded in gross examination after fixation in 10% formalin, data from histologic examination of surgically excised lesion, and type of reconstruction utilized.

Preoperative biopsies were performed by the physicians of the Dermatology Division of the HC-FMUSP following standardized procedure, selecting the most typical location of the tumor, generally a pearlescent area or lesion margin. Excisional surgery was performed by the authors at the Ambulatory Surgery Center of the HC-FMUSP.

Previous histologic evaluations of specimens stained by hematoxylin-eosin had been carried out by pathologists of the histology laboratory of the Dermatology Division of the HC-FMUSP. Data on size of the tumors were taken from records of macroscopic examinations of the surgical specimens after fixation in 10% formalin, stored in computer records of the HC-FMUSP central archives.

Slides corresponding to the tumors included in this study were all reviewed independently and randomly by two of the authors, with no pairing of cases; concurrent diagnoses were maintained, and discordant cases were discussed by both raters until consensus.

In order to define histologic types, the standardization shown in chart 1 was used.

Since a large number of cases presented a multiplicity of histologic types and were classified as mixed tumors, these cases were divided by the predominant pattern and secondary patterns. According to a suggestion by the Royal College of Pathologists,[3,4] the predominant histologic type (PHT) is the pattern

CHART 1: Criteria used to determine the histological types of basal cell carcinoma according to growth pattern

Histological type	Histological characteristics			
	Cell clusters	**Palisade**	**Clefts**	**Stroma**
Nodular	Large	Evident	Yes	Myxoid
Superficial	Focal in the epidermis	Evident	Yes or no	Myxoid
Infiltrative / Sclerodermiform	Elongated, irregular	Not Evident	Rare	Collagen
Micronodular	Small ($\leq$ 0.15mm)	Evident	Not very frequent	Slightly collagen
Mixed	Characteristics of two or more types above mentioned			

Sources: Adapted from Sexton M et al[3] e Slater DN et al[4]

CHART 2: Cutoff points for kappa statistics and respective agreement levels

Kappa	Agreement
< 0.2	Weak
0.21 - 0.40	Slight
0.4 - 0.60	Moderate
0.61 - 0.80	Good
0.81 – 1	Excellent

that corresponds to more than 50% of the lesion. Secondary histologic types (SHT) are all patterns found in smaller proportions. These materials were submitted to statistical analysis using the Kappa coefficient (Chart 2) and Fischer's exact test.

RESULTS

As to gender, 54.3% of lesions occurred in male patients, and 45.7% in females. Average age was 67 years (SD = 13 years), ranging from 38 to 93 years; 97% of patients were over 40 years of age. The predominant anatomical site was the cephalic segment (74.3%), especially the malar (20%) and nasal (14.3%) regions. These data intend to show that the specimen is representative of BCCs when compared to medical literature.[5-15]

The average size of the tumors studied was 2 cm along the longest axis, and 55% of lesions required complex reconstruction, such as skin grafts or flaps, demonstrating that the BCCs included in this study had large dimensions.

Statistical analysis of the correlation between histologic type(s) found in the incisional biopsy and the histologic type(s) found in excision surgery materials is displayed on tables 1 to 4.

There was concurrence in 78.3% of 69 cases evaluated, which is considered statistically significant (kappa = 0.42 $p < 0.001$), and the coefficient value shows moderate agreement (Table 1).

In 87% of 69 cases evaluated, the tumor PHT was represented in the biopsy specimen (Table 2).

When the representativeness of the biopsy relative to the tumor size was assessed, there was no statistical difference between the group of tumors 0.5 to 1 cm in size and the group of tumors larger than 1 cm (Table 3).

In evaluating the agreement between the PHT of the biopsy and the surgical sample as to aggressiveness of different histologic types, a 92.7% agreement was noted, which is considered moderate and statistically significant (kappa = 0.51 $p < 0.001$) (Table 4).

DISCUSSION

At the Dermatology Division of the HC-FMUSP, the number of patients with BCC is very expressive and has been progressively increasing, a fact that correlates with the current tendency worldwide. In face of the clinical diagnosis of BCC, several factors are considered when choosing a treatment option: size, anatomical location, primary condition or recurrence, and histologic type. Small tumors in areas of low recurrence risk are treated by simpler methods, such as curettage and electrocoagulation or cryosurgery with liquid nitrogen. Extensive and poorly delimited tumors in areas of high recurrence risk, or recurrent tumors, with aggressive histologic type, are preferably treated with Mohs micrographic surgery (MMS). For large primary tumors that are well delimited and show non-aggressive histologic types, depending on the patient's clinical picture, treatment of choice is usually excisional surgery.

Authors who consider preoperative biopsies important[2,16] base their opinions on the fact that one of the criteria for classifying BCCs as having a high or low recurrence risk is the histologic type. Nodular and superficial types are considered low risk for recurrence and are called non-aggressive. Micronodular, sclerodermiform, and infiltrative types are considered high risk for recurrence and are called aggressive. Since surgical aggressiveness is determined by the histologic type found in the preopera-

TABLE 1: Agreement between predominant histological types in biopsies and surgical specimens of 69 basal cell carcinomas

PHT in biopsy	PHT in surgical specimen				Total
	NOD	MIC	SUP	SCL	
NOD	68.1%	1.4%	7.2%		76.8%
MIC	4.3%	1.4%		2.9%	8.7%
SUP	4.3%		8.7%		13%
SCL	1.4%				1.4%
Total	78.1 %	2.9%	15.9%	2.9%	100%

PHT – Predominant histological type; NOD – nodular; MIC – micronodular; SUP – superficial; SCL – sclerodermiform

Table 2: Presence or absence, in biopsy, of the predominant histological types found in surgical specimens in 69 basal cell carcinomas

PHT in surgical specimen	PHT or SHT in the biopsy		Total
	Present	Absent	
Nodular	50 (92.6%)	4 (7.4%)	54
Superficial	8 (72.7%)	3 (27.3%)	11
Micronodular	2 (100%)	-	2
Sclerodermiform	-	2 (100%)	2
Total	60 (87%)	9 (13%)	69

PHT – Predominant histological type;
SHT – Secondary histological type;

tive biopsy, it was important to verify if the histologic types found in biopsies are represented in the surgical specimens.

Orengo et al. (1997) evaluated 342 primary BCCs operated by MMS in order to correlate the number of MMS phases with the histologic type of the BCC. In this study, 81.6% of the tumors removed in the first or second phase of MMS were of the nodular type. Of those tumors that required three or more phases for complete removal, most were micronodular, sclerodermiform, infiltrative, or mixed types. One interesting fact was identified in this study - a mere 42.7% correlation between the type present in the preoperative biopsy and the type present at the final phase of MMS. The authors attribute this to the occurrence of more than one histologic type in the same tumor and the impossibility of adequately representing the tumor totality with one small biopsy fragment.[17]

With the objective of determining if the best biopsy method is punch or saucerization, Russell et al. assessed the histologic correlation between the preoperative biopsy by punch or saucerization and the surgical specimen in 86 cases of BCC. Their aim was to determine which of the two would be the better method of obtaining a biopsy specimen. Results were 80% for the first option, and 75.9% for the second, with a statistically insignificant difference, showing an equivalence of the two methods.[18]

In the study by Russell et al. for the histologic classification of tumors, only the predominant histologic type in samples was considered, and BCCs were divided in a simplified manner into nodular, superficial, and infiltrative.[18]

In this study, the descriptive classification proposed by Sexton et al.[3] was used because of its detail (Chart 1), as well as the standardized classification of the Royal College of Pathologists since it defines predominant and secondary patterns (Chart 3). The BCC cases were subdivided into nodular, micronodular, superficial, sclerodermiform (including the type some authors define as infiltrative), and mixed (with two or more histologic types in the same material). In mixed tumors, the predominant histologic type (PHT) corresponds to more than 50% of specimen, and the secondary histologic types (SHT) represent smaller proportions. In this way, it was possible to identify a greater degree of correlation among the histologic types of BCC.

In order to evaluate the histologic agreement between the preoperative biopsy and the surgical specimen as to the PHT (Table 1), a statistical test was used that demonstrated a 78.3% concurrence rate, i.e., in 78.3% of cases, the PHT identified in the biopsy material was also the PHT found in the surgical specimen. This is considered a moderate agreement (kappa = 0.42 $p < 0.001$), on a scale comprised by weak, slight, moderate, good, and excellent agreements. This information is obtained by pairing diagnoses of the biopsy and the surgical sample, and demonstrates the precision of histologic type detection for the entire surgical sample.

Later, the agreement between any of the types found by biopsy (PHT and/or SHT) and the PHT of the surgical material was analyzed (Table 2). An 87% correlation was shown, demonstrating that it is important to describe all types of BCC found on the preoperative biopsy since this raises the possibility of the surgical specimen PHT being represented in the biopsy by 8.7%. Theoretically, the most precise diagnosis by preoperative biopsy would lead to the best treatment choice.

Considering that the size of the tumor might preclude consensus since larger tumors could have a greater multiplicity of histologic types, the agreement rates of tumors up to 1 cm and those with more than 1 cm along the longest axis was compared. There was no statistically significant difference between the two

Table 3: Presence or absence, in biopsy, of the predominant histological type found in surgical specimens in 61 basal cell carcinomas, according to tumor size

PHT in surgical specimen	Tumor size		Total
	0.5 to 1cm	> 1cm	
Present in biopsy	23 (88.5%)	31 (88.6%)	54 (88.5%)
Absent in biopsy	3 (11.5%)	4 (11.4%)	7 (11.5%)
Total	26 (87%)	35 (3%)	61 (100%)

PHT – Predominant histological type
Fisher´s exact test: $p = 1.000$

TABLE 4: Agreement between predominant histological types in biopsies and surgical specimens of 69 basal cell carcinomas, according to histological classification for recurrence risk

Predominant histological type in biopsy	Predominant histological type in surgical specimens				Total	
	AG*		NAG**			
	N	%	N	%	N	%
AG	3	4.3	4	5.8	7	10.1
NAG	1	1.4	61	88.4	62	89.9
Total	4	5.8	65	94.2	69	100

*AG – aggressive **NAG – not aggressive

groups (Table 3), i.e., a larger tumor did not necessarily imply a smaller representativeness of the biopsy. Bearing in mind that one of the objectives of preoperative biopsies is to determine if the histologic type of the BCC has a low or high risk for recurrence, BCCs were subdivided into aggressive (micronodular, sclerodermiform/infiltrative) and non-aggressive (nodular and superficial) forms.

In assessing the agreement between the PHT in biopsies and the PHT in surgical specimens as to aggressiveness of the BCCs (Table 4), a 92.7% agreement rate was found, which is considered moderate (kappa = 0.52 p?0.001), but larger than that observed for individual tumor types. This fact is extremely important, since tumor aggressiveness determines a more aggressive intervention, that is, the use of wider safety margins for tumor removal. We emphasize, however, that the ideal situation would be an excellent correlation (kappa = 0.81 to 1), which would lead to the best treatment choice.

CHART 3: Histological classification of basal cell carcinomas

Type of growth pattern	Nodular* Superficial Infiltrative / sclerodermiform Micronodular Others
Type of differentiation	Presence of very atypical or malignant squamous component
Perineural invasion	Parainfiltrative, sclerodermi form, micronodular and basal-squamous
Excision margins Distance to the closest periphery	Not involved (...mm) or involved
Distance to depth	Not involved (...mm) involved

Source: Slater DN et al.[4]
*The nodular types comprises solid, cystic, adenoid BCCs, and those with follicular differentiation or with formation of keratin cysts

CONCLUSIONS

Agreement between the predominant histologic type by biopsy and the predominant histologic type of the surgical specimen was 78.3%, which is considered statistically moderate.

The description of both predominant and secondary histologic types by biopsy leads to an 8.7% increase in correlation with the predominant histologic types of the surgical material, which reaches, therefore, an 87% agreement rate.

When BCCs are classified as aggressive and non-aggressive, histologic correlation reaches 92.7%, which is still considered moderate, rendering the anatomo-clinical correlation indispensable. ❑

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