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GROWTH RATE OF DIFFERENT BASAL CELL CARCINOMA SUBTYPES

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5 **Short title: Basal cell carcinomas growth rate**

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3 Basal Cell Carcinoma (BCC) subtypes seem to have different biological behaviour [1,2]. The speed of growth
4 of tumours is one of the factors that can account for their tissue invasiveness. Interviewing patients
5 currently is the only method of measuring the growth of a tumour over time[3,4]. Studies on BCCs' speed of
6 growth have been carried out on rare occasions [5] and they never concerned the speed of the different
7 BCC subtypes.

8 **Patients and Methods**

9 Patients affected by BCCs were studied by Our Clinic between January 01, 2015 and December, 2015. BCC
10 subtypes were classified according to the simplified classification under superficial, infiltrative-
11 morpheaform/micronodular and nodular subtypes. We measured the maximum lateral and depth
12 extension of the surgically removed tumours in millimetres of the histological sample. We
13 quantified the kinetics of the visible according to a simplified method [3]: each patient was only asked to
14 recall the date (T1) they had first noticed a lesion where the BCC developed later and the time of
15 surgical excision (T2). The rate of growth (ROG) is defined as the ratio between the maximum lateral
16 extension and/or depth in millimetres (mm) of the tumour and the time of tumour growth in months (mo)
17 (T2-T1). Inclusion criteria: complete surgical excision. Exclusion criteria: mixed histology BCCs and inability
18 to provide precise information about ROG. Statistical analyses were performed using SPSS for Windows
19 (version 15.0; SPSS Inc. Chicago, IL, USA), BCC subtype groups were compared using the student t-test for
20 differences in ROG and the value of $P < 0.05$ was considered significant.

21

22 **Results**

23 A total of 127 patients with BCCs were summoned; of these, 83 refused to participate or their answers
24 were judged as poorly reliable. The remaining 44 patients (23 male, 21 female) were hence enrolled in the

1 study. Age of the patients in years: superficial subtype 66.13 ± 10.88 ; nodular subtype 69.94 ± 9.34 ;
2 infiltrative subtype 74.42 ± 8.58 ($p < 0.04$ vs. superficial subtype.) The table shows respectively the values of
3 depth and lateral extension in millimetres in the observed subtypes (Table 1, upper part) and the ROG of
4 the same subtypes (Table 1, lower part).

5 **Discussion**

6 Although BCCs are said to take years to double in size [1], direct evidence of BCC growth rate is lacking.
7 More recently, Kricker et al. have investigated the growth rate of BCCs [5] and stated that superficial and
8 infiltrative/micronodular subtypes were more at risk of spreading extensively. The rate of growth (ROG) is
9 currently the only method of measuring the growth of a tumour over time [6]; this method was then
10 externally validated, thus confirming its usefulness [7]. Our results indicate a significant difference among
11 infiltrative/micronodular and nodular subtypes versus superficial ones as regards the depth extension and a
12 difference in lateral extension of the nodular subtype vs. the superficial one. This observation is consistent
13 with the usual clinical view and histological confirmation. On the contrary the lateral extension has the
14 highest value in the superficial subtype and the lowest in the nodular one. These observations seem to be
15 the effect of the different ROGs measured. There is indirect evidence supporting the hypothesis that local
16 conditions may favour a certain subtype [8,9]. These conditions may restrain the depth development of
17 superficial subtypes as well as speed up the nodular or infiltrative ones. Sun-damaged skin may represent a
18 tissue permissive stoma environment for nodular and more aggressive subtypes, which have a well-known
19 preference for sun-exposed sites [12]. With ageing and cumulative environmental assault, senescent cells
20 build up in the stoma and secrete factors that can disrupt tissue architecture and/or stimulate cells to
21 proliferate. Local conditions (sun-exposed skin, increasing age) may effect the higher ROG of these more
22 aggressive subtypes vs. the superficial one. The main limitation of this study concerns the medical history
23 criteria used for the evaluation of the ROG, which nevertheless remains the only method currently possible
24 to assess the growth speed of a tumour. ROG also assumes that tumour growth is constant and linear.
25 Another limitation regards the number of patients and the high percentage of data that was lost, although

1 we did not admit the great number of patients, who were unable to provide precise information, to the
2 study.

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6 References

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3 Table 1: Mean **depth and lateral extension** in millimetres of the BCC subtypes studied. In the lower part of
 4 the table are indicated the mean **Rates of Growth** in millimetres/month of the same subtypes considered.

BCC Subtypes		Depth Extension (mm)	P	Lateral extension (mm)	p
Infiltrative	n=12	3.02+2.3	0.3°	5.29+2.62	0.11°
Nodular	n=17	2.32+1.18	0.0001**	3.98+1.70	0.025**
Superficial	n=15	0.895+0.49	0.0018*	5.83+2.69	0.6*
BCC Subtypes		ROG for depth extension mm/month		ROG for lateral extension mm/month	
Infiltrative	n=12	0.195+0.13	0.4 °	0.377+0.40	0.6°
Nodular	n=17	0.278+0.32	0.02**	0.464+0.5	0.7**
Superficial	n=15	0.075+0.08	0.008*	0.402+0.4	0.8*

5 ° p value of Infiltrative-Micronodular subtype versus Nodular subtype

6 * p value of Infiltrative-Micronodular subtype versus Superficial subtype

7 ** p value of Nodular subtype versus Superficial subtype

8 n = number of patients

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