

# Characteristics and Recurrence of Primary Eyelid Basal Cell Carcinoma in Central Spain

Alicia Galindo-Ferreiro<sup>1</sup>, Hortensia Sanchez-Tocino<sup>1</sup>, Cecilia Diez-Montero<sup>1</sup>, Minal Belani-Raju<sup>1</sup>, Raquel García-Sanz<sup>1</sup>, Miguel Diego-Alonso<sup>1</sup>, Ines Llorente-Gonzalez<sup>1</sup>, Patricia Callejo Perez<sup>2</sup>, Rajiv Khandekar<sup>3</sup>, Silvana Schellini<sup>4</sup>

<sup>1</sup>Department of Ophthalmology, Rio Hortega University Hospital, Valladolid, Spain, <sup>2</sup>Department of Pathology, Rio Hortega University Hospital, Valladolid, Spain, <sup>3</sup>Research Department, King Khaled Eye Specialist Hospital, Riyadh, Saudi Arabia, <sup>4</sup>Department of Ophthalmology, Botucatu Medical University - UNESP, São Paulo, Brazil

## Abstract

**Purpose:** To define the incidence, characteristics, and management of eyelid basal cell carcinoma (BCC) in Central Spain.

**Methods:** This retrospective study investigates the characteristics and the outcome of eyelid BCC from 2000 to 2016 in a central region of Spain. Data were collected on demographics, skin phenotype, location of the eyelid lesion, clinical and histological diagnosis, surgery, commitment of surgical margins, and recurrence rate.

**Results:** Primary eyelid BCC occurred in a mean of 20.6 lesions a year or 9.4/100,000 inhabitants/year. The mean age of BCC carriers was  $69.4 \pm 16.2$  years, with no gender difference ( $P = 0.479$ ), predominantly affecting Fitzpatrick II–III skin (81.3%) ( $P < 0.001$ ). The most common location was the inner canthus (154/45.7%) ( $P < 0.001$ ) and type nodular (215 cases/63.8%) ( $P < 0.001$ ). The surgical margins were affected in 69 (20.5%) individuals, and the recurrence rate was 5.6 (95% confidence interval, 3.2–8.3) significantly higher in affected margins ( $P < 0.001$ ). The most common location for recurrence was the inner canthus ( $P = 0.003$ ), and the most common histological type for recurrence was sclerosing (16.7%), then multinodular (12.5%), and infiltrating (10.4%) with no significant difference ( $P = 0.27$ ).

**Conclusions:** The frequency of occurrence of eyelid BCC is much less than the estimated crude incidence for skin tumors involving all areas of the body in the Spanish population. Eyelid BCC is more common in the seventh decade of life, with no predilection for gender. Nodular histological type is the most common. The recurrence rate is 5.6%, depending on site and affected margins, even though clear free margins also can present with recurrence.

**Keywords:** Basal cell carcinoma, Eyelid tumors, Periocular, Spain

**Address for correspondence:** Alicia Galindo-Ferreiro, Department of Ophthalmology, Rio Hortega University Hospital, Dulzaina Street, Valladolid, Spain.

E-mail: ali\_galindo@yahoo.es

**Submitted:** 15-Sep-2019; **Revised:** 01-Feb-2020; **Accepted:** 02-Feb-2020; **Published:** 30-Apr-2020

## INTRODUCTION

Basal cell carcinoma (BCC) is the most common skin cancer in the human population,<sup>1,3</sup> and it is also the most common malignant eyelid tumor in Western countries.<sup>4</sup>

In a large series of European cases, BCC was reported in 86% of the malignant eyelid tumors.<sup>5</sup> In many countries, cancer lesions have incomplete or no serious registration, making it extremely difficult to accurately estimate the rates. Besides

this, BCC tumor is, in general, nonfatal with a vast proportion of patients treated only in primary care.<sup>6,7</sup>

In Spain, the incidence of BCC affecting the whole body is 113.05 cases/100,000 population per year (95% confidence interval [CI], 89.03–137.08).<sup>8</sup> Yet, there is a paucity of data involving eyelid BCC. Accurate epidemiological data on eyelid BCC have never been obtained on a national level. Thus,

### Access this article online

#### Quick Response Code:



**Website:**  
www.jcurrophthalmol.org

**DOI:**  
10.4103/JOCO.JOCO\_28\_20

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

**For reprints contact:** WKHLRPMedknow\_advertise@wolterskluwer.com

**How to cite this article:** Galindo-Ferreiro A, Sanchez-Tocino H, Diez-Montero C, Belani-Raju M, Garcia-Sanz R, Diego-Alonso M, *et al.* Characteristics and recurrence of primary eyelid basal cell carcinoma in Central Spain. *J Curr Ophthalmol* 2020;32:183-8.

describing occurrence within our region may reveal important local characteristics.

Clinically, BCC has a typical appearance, and histologic analysis represents the definitive diagnosis. Surgical excision is considered effective, yet the management of incompletely excised BCC remains controversial.<sup>9-11</sup>

The purpose of this study is to estimate the eyelid BCC occurrence, describing the characteristics, outcome of treatment, and recurrence rate in a Spanish population. To our knowledge, this is a unique study on eyelid BCC in the Spanish population.

## METHODS

This retrospective study included consecutive patients who underwent excision of eyelid BCC over a 17-year period (from 2000 to 2016) at Rio Hortega University Hospital, Valladolid, Spain. The institutional research board approved this study, and consent was waived due to the retrospective nature of the research.

Three oculoplastic surgeons, one maxillofacial surgeon, and one plastic surgeon were responsible for surgery and care of the patients.

A chart review was used to collect data on patient demographics (gender and age at the time of surgery) and color of skin (Fitzpatrick skin type). Skin was categorized into five types according to the behavior in the sun applying the Fitzpatrick scheme – Type I: very white skin with red or blond hair, light eyes, and freckles. It always burns, unable to tan, more sensitive to sun exposure (Northern Europe or the ethnicity of Ireland); Type II: usually clear skin. It suffers burns easily and tans minimally, even when it comes to tanning; Type III: light skin. It burns moderately and tans gradually and evenly to light brown. Most Caucasians are Type II or Type III; Type IV: olive skin. It burns minimally, and the medium brown is always well tanned; and Type V: brown skin. It rarely burns, profusely tan to dark brown. Most Hispanics, Asians, and those in the Middle East are Type IV or V and people with Indian and some African ethnic heritage are Type V.<sup>12</sup> Clinical details of the lesions, including size, presence of other lesions on the face or body, location, and extension of the tumor according to the affected lid ( $\leq 1/3$ ,  $1/3-1/2$  or  $>1/2$  of palpebral length), and clinical diagnosis before the surgical procedure were noted. After excision, the lesion was macroscopically measured (height  $\times$  length in mm), and histological details were noted.

Recurrence was defined clinically as the presence of another tumor within 5 mm of the site of the excised lesion. Otherwise, the lesion was classified as new.

Exclusion criteria were a patient who had had surgery elsewhere, follow-up  $<1$  year, or unavailable histologic analysis.

### Characteristics of the studied population

Rio Hortega University Hospital is a public tertiary hospital. It serves a population of 261,033 people and is located in

Valladolid city. Valladolid is the biggest city of the autonomous community of Castile and León, located in the central region of Northwest Spain, at an altitude of 735 m, with Mediterranean climate characterized by a hot summer with influences of a cold semi-arid climate. The population is estimated to be 526,223 people, distributed across a total of 225 municipalities in an area of 8110 km<sup>2</sup> and with a population density of 64.88 people per km<sup>2</sup>.<sup>13</sup> It is the region with one of the highest life expectancies in Spain and Europe at 65.4% between 16 and 64 years. Seventeen and seven tenth percent are aged 65 years or more, and 16.9% are children or adolescents.<sup>13</sup>

### Tumor removal procedure

Excisional margins were marked previously to the procedure with marking pen leaving clear margins of 2–3 mm around a tumor with well-defined borders or 5 mm margins if the borders were ambiguous. Under local anesthesia using 0.5% lidocaine/1:200,000 with adrenaline, complete excision was performed. A marker suture was placed at the 12 o'clock position on the specimen for orientation during histopathological assessment.<sup>14</sup> If there was concern about completeness of excision, peripheral and/or deep biopsies were performed beyond the main resection. These specimens were embedded in paraffin for sectional analysis. If there was histological positive margin in an inner canthus lesion, we re-excised the affected margin. If the lesion was in another location, the patient was just closely followed even with positive margin detected.

Clinically, poorly demarcated tumors were simply padded firmly with a nonstick dressing while awaiting histological confirmation of clear margins in 2–3 days (Slow Mohs with formalin-fixed sections).<sup>15</sup>

The technique utilized for reconstruction of the lid was dependent on the size of tissue removal and was performed by direct closure or required flaps, grafts, or a complex technique.

### Histopathology analysis

On removal, the specimen was fixed in formalin. The main tissue specimen was measured and sectioned, including the margins of the lesion, then embedded in paraffin, sectioned using microtome into 4  $\mu$ m slices, mounted on glass slides, and stained with hematoxylin/eosin for microscopic evaluation. All of the pathology specimens were examined by the Pathology Department at our center.

BCC diagnosis and classification was based on the World Health Organization<sup>16</sup> classification criteria as nodular (solid), micronodular, superficial (multifocal), sclerosing, infiltrating, and others (fibroepithelial, pigmented, cystic, basosquamous, plexiform [adenoid pattern], keratotic, and metatypical). We added mixed subtypes when various subtypes of BCC lesions were impinging onto one another.

On histopathologic examination, clear margins or commitment of surgical margins (incomplete resection) by tumor cells were noted, considering the presence of residual tumor at or within 1 mm of the lateral or deep margins of the excised specimen.

The follow-up of patients was every 3–6 months initially and annually thereafter.

### Statistical analysis

Data were collected using a pretested data collection form and transferred to an Excel Spreadsheet (Microsoft Corp®, Redmond, WA, USA). The Statistical Package for the Social Sciences (SPSS 23; IBM Corp., Armonk, NY, USA) was used to perform the statistical analysis. For quantitative variables, the mean and standard deviation were reported. For qualitative variables, the frequencies and percentage proportions were calculated. To associate the outcomes for unilateral or bilateral involvement, the odds ratio, 95% CI, and two-sided *P* values were calculated. *P* < 0.05 was considered statistically significant. A multivariate analysis was also performed to evaluate the interaction of all risk factors on the rates of BCC.

## RESULTS

Over the 17-year period assessed in this study, 337 patients were detected with BCC of the periocular skin at our hospital. The estimated mean frequency of occurrence of primary eyelid BCC was 20.6 lesions a year or 9.4/100,000 inhabitants/year.

The analysis according to age groups revealed no gender preponderance (*P* = 0.515) [Figure 1]. Table 1 summarizes the descriptive characteristics of patients with periocular BCC. The left side of the periocular area was affected in 179 (53.1%) (*P* = 0.25). Type II or III Fitzpatrick skin was presented in 274 (81.3%) (*P* < 0.001). The majority of the BCC patients (190/56.4%) had lesions <1/3 of the length eyelid, mainly located in the inner canthus (154/45.7%) (*P* < 0.001).

BCC had a significant agreement in clinical and histological diagnosis (Cohen's kappa coefficient = 0.975) (*P* < 0.001), with correct clinical diagnostic in 95% of cases.

Table 2 shows the characteristics and histopathological diagnosis of BCC in Central Spain. Histopathological examination indicated that the majority (215/63.8%) of the BCC cases were nodular (*P* < 0.001). BCC excision had clear margins in 267 (79.2%, 95% CI: 74.8–83.6) cases. Surgical repair was performed by direct closing for 229 (68%: 95% CI: 63–73.2). Recurrence occurred in 19/337 (5.6%, 95%

CI: 3.2–8.3) cases. Orbital involvement with necessity to go for exenteration occurred in 2 cases (0.6%).

The relationship between affected margins, location, histopathological subtype, and recurrence is presented in Table 3. Eight (3%) cases of free margins had recurrence, and 11 patients (15.9%) of affected margins had recurrence (*P* < 0.001). The recurrence rate was higher in tumors located in the inner canthus (12/63.2%) (*P* = 0.003).

There was no significance regarding the recurrence depending on histological subtype (*P* = 0.27) although the most common recurrence according to histology type was sclerosing (16.7%), then multinodular (12.5%), and infiltrating (10.4%).

## DISCUSSION

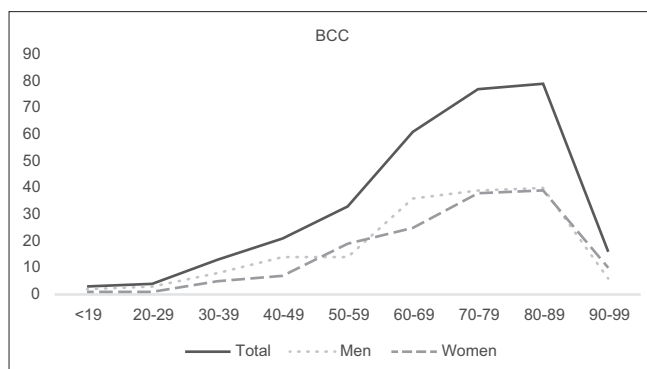
This study was conducted in Central Spain in order to determine the estimated occurrence, demographic characteristics, and the outcomes after treatment of BCC. To our knowledge, this is the first study involving those aspects of eyelid BCC in Spain.

The estimated mean annual frequency of occurrence of eyelid BCC in the studied population was 20.6 lesions a year, occurring in 9.4/100,000 inhabitants/year, much less than the estimated crude incidence for skin tumors involving all areas of the body in the Spanish population (113.05 BCC cases/100,000 inhabitants/year; 95% CI: 89.03–137.08) or for other European

**Table 1: Demographic and clinical characteristics of patients with basal cell carcinoma in Central Spain; *n* (%) of occurrence of cases from 2000-2016 (*n* = 337)**

BCC	<i>n</i> (%)	<i>P</i>
Age (years)		
Mean±SD	69.4±16	
Gender		
Male	175 (51.9)	0.47
Female	162 (48.1)	
Side involved		
Left	179 (53.1)	0.25
Right	158 (46.9)	
Skin color		
Fitzpatrick II-III	274 (81.3)	<0.001
Others	63 (18.7)	
Size of the lesion		
<1/3	190 (56.4)	<0.001
1/3-1/2	86 (25.5)	
>1/2	19 (5.6)	
Missing	42 (12.5)	
Location of lesion		
Inner canthus	154 (45.7)	<0.001
Lower lid	126 (37.4)	
Upper lid	32 (9.5)	
Lateral canthus	17 (5)	
Overlapping two locations	6 (1.8)	
Missing data	2 (0.6)	

*P* < 0.05 is statistically significant. BCC: Basal cell carcinoma, *n*: Sample size, SD: Standard deviation



**Figure 1: Analysis of basal cell carcinoma according to age groups**

**Table 2: Characteristics and histopathological diagnosis of basal cell carcinoma and in Central Spain**

Histopathological diagnosis	BCC (n=337), n (%)	P
Clinical diagnosis		
BCC	320 (95)	<0.001
SCC	6 (1.8)	
Other malignant	0 (0)	
Benign	8 (2.4)	
Missed data	6 (1.8)	
Subtype histological		
BCC nodular	215 (63.8)	<0.001
BCC infiltrative	48 (14.2)	
BCC mixed	39 (11.6)	
BCC others*	12 (3.6)	
BCC micronodular	9 (2.7)	
BCC superficial multifocal	8 (2.4)	
BCC sclerosing	6 (1.8)	
Margin		
Free	267 (79.2)	<0.001
Committed	69 (20.5)	
Missed data	1 (0.3)	
Surgical technique		
Direct closure	229 (68)	<0.001
Flap	70 (20.9)	
Graft	25 (7.4)	
Complex technique	13 (3.9)	
Recurrence		
No	318 (94)	<0.001
Yes	19 (45.6)	
Orbit involved		
Yes	4 (1.2)	<0.001
Exenteration	2 (0.6)	
No	327 (97)	
Missed data	6 (1.8)	

P<0.05 is statistically significant. \*Others: Adenoid, pigmented, keratotic, infundibulocystic, fibroepithelioma, cystic, basosquamous. BCC: Basal cell carcinoma, n: Sample size, SCC: Squamous cell carcinoma

countries such as Germany, Slovakia, Sweden, Wales, and Ireland.<sup>7,8</sup> Despite the incidence in any body location of BCC, in Europe, it is lower compared to the USA or Australia.<sup>17</sup>

Our study provides novel demographic information and histological features of eyelid tumors in this region and documented differences in the behavior of BCC confirming some aspects of this lesion reported in other regions as a preponderance in aging (69.4 ± 16 years old)<sup>1,18-20</sup> and rare occurrence in the youngest to 40 years.

In Spain, eyelid BCC showed a similar distribution for men and women, independently of age, most likely a result of similar lifestyles in both genders. In Ireland, the incidence of BCC is higher in men after the 60 s<sup>7</sup>; however, women experienced a higher average annual incidence increase compared to men.<sup>3,6</sup>

In our population, both sides of the periocular area are similarly affected (left side [53.1%]). Nevertheless, a previous study proved that BCC affects the side of the face exposed to sun

**Table 3: Relation between periocular basal cell carcinoma recurrence and surgical margin commitment, location, and histological type**

	BCC (n=337) Recurrence, n (%)		P
	Yes (5.6%)	No (94.4%)	
Margins			
Affected	<b>11 (15.9)</b>	58 (84.1)	<b>&lt;0.001</b>
Free	8 (3)	259 (97)	
Total	19	317	
Location			
Upper eyelid	1 (3.1)	31 (96.9)	<b>0.003</b>
Lower eyelid	4 (3.2)	122 (96.8)	
Inner canthus	<b>12 (7.8)</b>	142 (92.2)	
Lateral canthus	1 (5.9)	16 (94.1)	
Overlapping two sides	1 (20)	5 (80)	
Total	19	316	
Histological type			
Nodular	10 (4.7)	205 (95.3)	<b>0.274</b>
Micronodular	1 (11.1)	8 (88.9)	
Superficial multifocal	1 (12.5)	7 (87.5)	
Sclerosing	1 (16.7)	5 (83.3)	
Infiltrating	5 (10.4)	43 (89.6)	
Others*	1 (8.3)	11 (91.7)	
Mixture	0	39	

In bold higher recurrence by variable. \*Others: Adenoid, pigmented, keratotic, infundibulocystic, fibroepithelioma, cystic, basosquamous. BCC: Basal cell carcinoma

radiation during driving more.<sup>21</sup> These differences may be explained because the Spanish population, especially in the central region, is very exposed to sunlight.

White and fair skinned are well-known risk factors for BCC lesion.<sup>22</sup> BCC carriers, in Central Spain, are mainly Type II and III Fitzpatrick skin phenotype.<sup>12</sup> However, this is just one of the involved risk factors, often associated with aging and history of chronic exposure to ultraviolet (UV) radiation.<sup>23</sup> Even though sun protector is very important to prevent skin lesions, long-term sun exposure implies an increased risk, particularly in individuals with skin photosensitivity.

BCC is a slow-growing lesion. Early detection and treatment are closely related to better prognosis, favoring the majority of our patients who had lesions of <1/3 of the eyelid horizontal length, allowing direct closure of the wound after resection for the majority of BCC in our population (68%). This observation indicates that patients are proactive in seeking timely medical care in Spain.<sup>1,24,25</sup>

In the current study, the inner canthus and lower eyelids were the most common anatomical location of BCC, similar to previous reports.<sup>18,21,26,27</sup>

We confirmed the high chance of accurate clinical diagnosis and the strong agreement with histological diagnosis for BCC lesions. However, clinical aspect is not pathognomonic, and histological evaluation is mandatory.



In our series of patients, nodular BCC was the most common type (63.8%), similar to other studies.<sup>1,20,21,26,28</sup>

Complete surgical removal of BCC results in lower recurrence rate,<sup>29</sup> whereas incomplete excision should be considered the risk of local recurrence.<sup>30</sup>

Adopting our pathologist criteria, incomplete resection (positive margins) occurred in 20.9% of BCC cases. However, overall recurrence was observed in only 19 (5.6%) BCC cases. Compared to other authors, affected margins can experience recurrence in 25.6%,<sup>31</sup> 35%,<sup>32</sup> 37%,<sup>33</sup> and up to 67% of patients.<sup>34</sup> These differences may be due to a different histopathological definition of the affected margin.<sup>35</sup> Nevertheless, we observed recurrence with positive margin (11.19–57.9%) and also recurrence with free margins (8.19–42.1%), similarly reported by others.<sup>31</sup> These indicate that factors other than just affected margins are responsible for recurrence, including location, tumor size, definition of clear margins, growth pattern, histological subtype, recurrent tumor, inflammation or devitalization of the residual tumor tissue, and the immune status of the patient.<sup>35-39</sup>

In our study, periocular BCC of the inner canthus was significantly associated with recurrence. The inner canthus BCC can be easier associated with incompletely excised tumors, reaching as high as 86%<sup>1,39</sup> probably due to the wrong attempt to preserve the lacrimal drainage system.<sup>39</sup> To avoid inner canthus tumor recurrence, our approach is to re-excise an affected margin and have a close follow-up.

The risk of orbital involvement with necessity to adopt drastic measures as exenteration was observed in only 2 of our cases, periocular BCC being the most common indication for exenteration.<sup>40</sup>

In our sample, the most common recurrence according to histologic type was sclerosing (16.7%), then superficial multinodular (12.5%), and infiltrating (10.4%) although we did not find a significant difference according to histological type. It is reported that infiltrative BCC had a more common recurrence.<sup>41</sup> We may explain this discordance due to shortage of infiltrating subtype sample size.

Finally, even accepting that our study is not a population-based epidemiological study and no inferences on true incidence can be made, our retrospective study represents a complete description of eyelid BCC in a Spanish region and can help in informing policy. We recognize that eyelid BCC frequency of occurrence can be influenced by referral bias to our tertiary care hospital despite the fact that special tumors located in the eyelids are not frequently managed by referring physicians. However, our data may well serve as a platform for future population-based epidemiological studies in Spain.

The authors strongly recommend a prospective randomized study with a defined zone of scope to achieve more definitive results. Improvement of public health initiatives needs to

be implemented as a country skin register of cases, and measures specifically target at reducing the number of BCC cases such as adopting preventive protection, including seeking shade, the use of physical agents (clothing, hat, sunglasses), and application of sunscreens on exposed areas to UV radiation.

In conclusion, our study showed that the eyelid BCC in Central Spain has an estimated mean annual frequency of occurrence lower than the estimated crude incidence for skin tumors involving all areas of the body in Spain, other European countries, the USA, and Australia. Our study provides novel demographic information and histological features of eyelid tumors in this region. Eyelid BCC affects more individuals in the seventh decade of life, with no predilection for gender, mainly located in the inner canthus and nodular histological type. The recurrence rate was related to site and affected margins, even though clear free margins can also have recurrence. Incomplete removal can predispose to recurrence and may define the follow-up.

### **Financial support and sponsorship**

Nil.

### **Conflicts of interest**

There are no conflicts of interest.

## **REFERENCES**

1. Abbas OL, Borman H. Basal cell carcinoma: A single-center experience. *ISRN Dermatol* 2012;2012:246542.
2. Auw-Haedrich C, Frick S, Boehringer D, Mittlvielfhaus H. Histologic safety margin in basal cell carcinoma of the eyelid: Correlation with recurrence rate. *Ophthalmology* 2009;116:802-6.
3. Quigley C, Deady S, Hughes E, McElnea E, Zgaga L, Chetty S. National incidence of eyelid cancer in Ireland (2005-2015). *Eye (Lond)* 2019;33:1534-9.
4. Kaliki S, Bothra N, Bejjanki KM, Nayak A, Ramappa G, Mohamed A, *et al.* Malignant eyelid tumors in India: A study of 536 Asian Indian patients. *Ocul Oncol Pathol* 2019;5:210-9.
5. Deprez M, Uffer S. Clinicopathological features of eyelid skin tumors. A retrospective study of 5504 cases and review of literature. *Am J Dermatopathol* 2009;31:256-62.
6. Birch-Johansen F, Jensen A, Mortensen L, Olesen AB, Kjær SK. Trends in the incidence of nonmelanoma skin cancer in Denmark 1978-2007: Rapid incidence increase among young Danish women. *Int J Cancer* 2010;127:2190-8.
7. Carsin AE, Sharp L, Comber H. Geographical, urban/rural and socioeconomic variations in nonmelanoma skin cancer incidence: A population-based study in Ireland. *Br J Dermatol* 2011;164:822-9.
8. Tejera-Vaquero A, Descalzo-Gallego MA, Otero-Rivas MM, Posada-García C, Rodríguez-Pazos L, Pastushenko I, *et al.* Skin cancer incidence and mortality in Spain: A systematic review and meta-analysis. *Actas Dermosifiliogr* 2016;107:318-28.
9. Boulinguez S, Grison-Tabone C, Lamant L, Valmary S, Viraben R, Bonnetblanc JM, *et al.* Histological evolution of recurrent basal cell carcinoma and therapeutic implications for incompletely excised lesions. *Br J Dermatol* 2004;151:623-6.
10. Jankovic I, Kovacevic P, Visnjic M, Jankovic D, Binic I, Jankovic A. Does incomplete excision of basal cell carcinoma of the eyelid mean tumor recurrence? *An Bras Dermatol* 2010;85:872-7.
11. Ho SF, Brown L, Bamford M, Sampath R, Burns J. 5 years review of periocular basal cell carcinoma and proposed follow-up protocol. *Eye (Lond)* 2013;27:78-83.
12. MelanomaEspaña. Spanish Melanoma. Skin Types and Risk Factors

- 2015; 2019. Available from: <http://www.melanomaespana.es/respuestas/factores-de-riesgo/tipos-de-piel-y-riesgos/>. [Last accessed 2019 Feb 02].
13. National Statistics Institute 2019. Instituto Nacional de Estadística; 2018. Available from: <http://www.ine.es/jaxiT3/Tabla.htm?t=2904&L=0>. [Last accessed 2019 Feb 02].
  14. Griffiths RW, Suvarna SK, Stone J. Basal cell carcinoma histological clearance margins: An analysis of 1539 conventionally excised tumours. Wider still and deeper? *J Plast Reconstr Aesthet Surg* 2007;60:41-7.
  15. Lawrence CM, Haniffa M, Dahl MG. Formalin-fixed tissue Mohs surgery (slow Mohs) for basal cell carcinoma: 5-year follow-up data. *Br J Dermatol* 2009;160:573-80.
  16. Cancer TIAfRo. Keratinocytic tumours. Pathology and Genetics of Tumours of the Skin World Health Organization Classification of Tumours. 1<sup>st</sup> ed. IARC Press Lyon, 2006.
  17. Lomas A, Leonardi-Bee J, Bath-Hextall F. A systematic review of worldwide incidence of nonmelanoma skin cancer. *Br J Dermatol* 2012;166:1069-80.
  18. Bagheri A, Tavakoli M, Kanaani A, Zavareh RB, Esfandiari H, Aletaha M, *et al.* Eyelid masses: A 10-year survey from a tertiary eye hospital in Tehran. *Middle East Afr J Ophthalmol* 2013;20:187-92.
  19. Fatigato G, Capitani S, Milani D, Grassilli S, Alameen AA, Candiani M, *et al.* Risk factors associated with relapse of eyelid basal cell carcinoma: Results from a retrospective study of 142 patients. *Eur J Dermatol* 2017;27:363-8.
  20. Al Wohaib M, Al Ahmadi R, Al Essa D, Maktabbi A, Khandekar R, Al Sharif E, *et al.* Characteristics and factors related to eyelid basal cell carcinoma in Saudi Arabia. *Middle East Afr J Ophthalmol* 2018;25:96-102.
  21. Ben Simon GJ, Lukovetsky S, Lavinsky F, Rosen N, Rosner M. Histological and clinical features of primary and recurrent periocular basal cell carcinoma. *ISRN Ophthalmol* 2012;2012:354829.
  22. Modenese A, Korpinen L, Gobba F. Solar radiation exposure and outdoor work: An underestimated occupational risk. *Int J Environ Res Public Health* 2018;15. pii: E2063.
  23. Broadbent T, Bingham B, Mawn LA. Socioeconomic and ethnic disparities in periocular cutaneous malignancies. *Semin Ophthalmol* 2016;31:317-24.
  24. Lara F, Santamaría JR, Garbers LE. Recurrence rate of basal cell carcinoma with positive histopathological margins and related risk factors. *An Bras Dermatol* 2017;92:58-62.
  25. Kumar P, Orton CI, McWilliam LJ, Watson S. Incidence of incomplete excision in surgically treated basal cell carcinoma: A retrospective clinical audit. *Br J Plast Surg* 2000;53:563-6.
  26. Malhotra R, Huilgol SC, Huynh NT, Selva D. The Australian Mohs database, part II: Periocular basal cell carcinoma outcome at 5-year follow-up. *Ophthalmology* 2004;111:631-6.
  27. Gayre GS, Hybarger CP, Mannor G, Meecham W, Delfanti JB, Mizono GS, *et al.* Outcomes of excision of 1750 eyelid and periocular skin basal cell and squamous cell carcinomas by modified *en face* frozen section margin-controlled technique. *Int Ophthalmol Clin* 2009;49:97-110.
  28. Afridi RA, Ahmed E, Khan SA, Ali A. Demographics of basal cell carcinoma and its surgical management. *J Ayub Med Coll Abbottabad* 2012;24:141-3.
  29. Rustemeyer J, Bremerich A. Outcomes after surgical treatment of facial skin basal cell carcinomas. *Acta Chir Plast* 2006;48:89-92.
  30. Madan V, Lear JT, Szeimies RM. Non-melanoma skin cancer. *Lancet* 2010;375:673-85.
  31. Hauben DJ, Zirkin H, Mahler D, Sacks M. The biologic behavior of basal cell carcinoma: Analysis of recurrence in excised basal cell carcinoma: Part II. *Plast Reconstr Surg* 1982;69:110-6.
  32. Gooding CA, White G, Yatsuhashi M. Significance of marginal extension in excised basal-cell carcinoma. *N Engl J Med* 1965;273:923-4.
  33. De Silva SP, Dellon AL. Recurrence rate of positive margin basal cell carcinoma: Results of a five-year prospective study. *J Surg Oncol* 1985;28:72-4.
  34. Shanoff LB, Spira M, Hardy SB. Basal cell carcinoma: A statistical approach to rational management. *Plast Reconstr Surg* 1967;39:619-24.
  35. Patel SS, Cliff SH, Ward Booth P. Incomplete removal of basal cell carcinoma: What is the value of further surgery? *Oral Maxillofac Surg* 2013;17:115-8.
  36. Dieu T, Macleod AM. Incomplete excision of basal cell carcinomas: A retrospective audit. *ANZ J Surg* 2002;72:219-21.
  37. Bogdanov-Berezovsky A, Cohen AD, Glesinger R, Cagnano E, Krieger Y, Rosenberg L. Risk factors for incomplete excision of basal cell carcinomas. *Acta Derm Venereol* 2004;84:44-7.
  38. Hamada S, Kersey T, Thaller VT. Eyelid basal cell carcinoma: Non-Mohs excision, repair, and outcome. *Br J Ophthalmol* 2005;89:992-4.
  39. Masud D, Moustaki M, Staruch R, Dheansa B. Basal cell carcinoma: Risk factors for incomplete excision and results of re-excision. *J Plast Reconstr Aesthet Surg* 2016;69:652-6.
  40. Kasaei A, Eshraghi B, Nekoozadeh S, Ameli K, Sadeghi M, Jamshidian-Tehrani M. Orbital exenteration: A 23-year report. *Korean J Ophthalmol* 2019;33:366-70.
  41. Newlands C, Currie R, Memon A, Whitaker S, Woolford T. Non-melanoma skin cancer: United Kingdom National Multidisciplinary Guidelines. *J Laryngol Otol* 2016;130:S125-32.