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CRIOCIRURGIA NO TRATAMENTO DE CANCRO CUTÂNEO NÃO-MELANOMA PALPEBRAL E PERIOCULAR – ANÁLISE RETROSPETIVA DE 78 CASOS

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RESUMO – **Introdução**: A criocirurgia é um método seguro e eficaz no tratamento do cancro cutâneo não-melanoma das pálpebras e áreas perioculares, com uma taxa de cura aos 5 anos superior a 95%. **Objetivo**: Caracterização retrospetiva dos casos de cancro cutâneo não-melanoma palpebrais e perioculares diagnosticados e tratados com a criocirurgia no nosso Serviço, entre 1988 e 2004. **Material e Métodos**: Revisão dos processos clínicos e análise estatística das seguintes variáveis: idade, sexo, profissão, fototipo, características do tumor, modalidades de tratamento, resultados estéticos e funcionais e seguimento. **Resultados**: Foram tratados 78 neoplasias malignas primárias, em 78 pacientes, sendo 30 homens e 48 mulheres, com idade média de 75,5 anos. Setenta e seis dos tumores (97,4%) eram carcinoma de basocelular e dois (2,6%) carcinomas espinocelular. Mais de metade dos tumores localizava-se no canto interno do olho. A Criocirurgia fracionada foi usada em 52 casos (66,7%), a criocirurgia convencional em 17 (21,8%) e a criocirurgia segmentada em nove (11,5%). A média de seguimento foi de 5 anos, tendo ocorrido com duas recidivas locais. Não houve complicações funcionais e os resultados estéticos foram excelentes. A taxa de cura global foi de 97,4%. **Conclusões**: A criocirurgia fracionada foi o procedimento mais utilizado. Obtivemos excelentes resultados estéticos e funcionais e uma taxa de cura aos 5 anos de 97% cinco anos.

PALAVRAS-CHAVE – Neoplasias das pálpebras; Criocirurgia; Carcinoma basocelular; Carcinoma espinocelular.

CRYOSURGERY IN THE TREATMENT OF NON-MELANOMA SKIN CANCER OF THE EYELID AND PERIOCULAR AREA - RETROSPECTIVE ANALYSIS OF 78 CASES

ABSTRACT – ***Introduction:*** *Cryosurgery is a safe and effective treatment modality for non-melanoma skin cancers of the eyelids and periocular area, with a reported 5-year overall cure rate above 95%.* ***Aim:*** *Retrospective characterization of patients with non-melanoma skin cancer of eyelids and periocular regions diagnosed and treated with cryosurgery at our Department, between 1988 and 2004.* ***Material and Methods:*** *Review of the clinical records and statistical analysis of the following variables: age, sex, occupation, skin type, tumour characteristics, treatment modalities, aesthetic and functional outcomes and follow-up.* ***Results:*** *We treated 78 primary malignant neoplasms, in 78 Caucasian patients, 30 men and 48 women with a mean age of 75.5 years. Seventy-six of the seventy-eight tumours (97.4%) were nodular basal cell carcinoma (BCCs) and two were (2.6%) squamous cell carcinomas. More than half of the tumours were located in the inner canthus. Fractional cryosurgery was used in 52 cases (66.7%), conventional cryosurgery in 17 (21.8%) and segmental cryosurgery in nine (11.5%). The mean follow-up was 5 years with two relapses observed. There were*

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no functional complications and the cosmetic results were excellent. The overall cure rate was of 97.4%. ***Conclusions:*** *Fractional cryosurgery was the most used procedure. We achieved excellent functional and aesthetic results and a 97% five-year cure rate.*

KEY-WORDS – *Eyelid neoplasms; Cryosurgery; Carcinoma, Basal cell; Carcinoma, Squamous cell; Skin neoplasms.*

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INTRODUCTION

Basal cell carcinoma (BCC) is the most common non-melanoma epithelial skin cancer of the eyelids and periocular area, accounting for 80-95% of all cases[1]. Fair skin and chronic sun exposure appear to be the most important risk factors[1]. The mainly affected regions are the inner canthus and lower eyelid[1,2]. Squamous cell carcinoma (SCC) represents approximately 5% of eyelid tumours, located on the lower eyelid, but also the upper eyelid and outer canthus and mainly affecting fair skinned elderly individuals with chronic ultraviolet exposure[1].

The value of cryosurgery in the treatment of small (up to 1.0 cm) non-melanoma skin cancer of the eyelids and periocular region (BCC and SCC) is well established (according to its reported high overall cure rate and magnificent aesthetical and functional outcomes)[3-5], its effectiveness depending, in large part, on the cryosurgeon's degree of experience. Poor cosmetic and functional results in lesions larger than 1.0cm resulted in the abandonment of cryosurgery as first therapeutic option by some cryosurgeons[3]. However, this situation was reversed with the introduction of specialized cryosurgical techniques, such as Zacarian's segmental cryosurgery[6] and Gonçalves's fractional cryosurgery[3].

The aim of this study was to report the experience of our Department in the treatment of non-melanoma skin cancer of the eyelids and periocular region by cryosurgery.

MATERIAL AND METHODS

Patients

Data were obtained after review of the clinical records of patients with skin cancer of the eyelids and periocular region, confirmed by histological examination and treated by cryosurgery at our Department, between the 1 January 1988 and the 31 December 2004. All patients who had discontinued the 5-year follow-up visits were contacted by telephone to ascertain and verify their recurrence-free status.

The parameters studied were: patient's age and sex, risk factors (occupation and skin type), tumour characteristics, treatment modalities, cosmetic (hypertrophic scar, milia, hypopigmentation and depigmentation) and functional (ectropion, entropion) results and follow-up. Tumour features included location (inner canthus, outer

canthus, lower eyelid and upper eyelid), size (longest axis), duration (since the probable onset of symptoms to date of presentation), clinical type (nodular and nodulo--ulcerated) and staging. We used the TNM (American Joint Committee on Cancer)[7] and the Thomas B. Fitzpatrick classifications, respectively, for staging and skin types.

Exclusion criteria were: invasion of adjacent structures (muscles, fat and bones of the orbit); morpheaform BCCs; recurrent tumours; SCCs larger than 1.0cm in diameter; and adnexal cancers. A total of 78 patients were identified and included in this retrospective study.

Surgical modalities

The treatment modalities (Figs. 1 and 2) used were:

1. Conventional cryosurgery (CC): a simple technique, based on two freeze-thaw cycles which was used in the treatment of BCCs and SCCs with diameter equal to or smaller than 1.0cm.
2. Segmental cryosurgery (SC)[6]: a technique developed for tumours that, due to their large size, cannot be treated in a single session. The lesion is segmented and each area is treated in successive sessions 3-4 weeks apart, using two freeze-thaw cycles, with a safety margin. With SC, freezing always starts at the periphery of the tumour and advances toward its centre. While offering excellent results in elongated lesions, SC has limited application in rounded carcinomas located in the periocular region.
3. Fractional cryosurgery (FC)[3] is an innovative technique, in which the main purpose is to reduce the tumour area until it reaches a size that allows its complete eradication without risk of retraction or deforming scar. Therefore, FC is indicated for round carcinomas larger than 1.0cm in diameter adjacent to important physiognomic structures, such as the periocular area. Particularly for tumours located in the periocular region, during the first cryosurgical session only the centre is frozen. One month later, the size of the tumour is reduced. If it still measures more than 1.0cm the procedure is repeated.

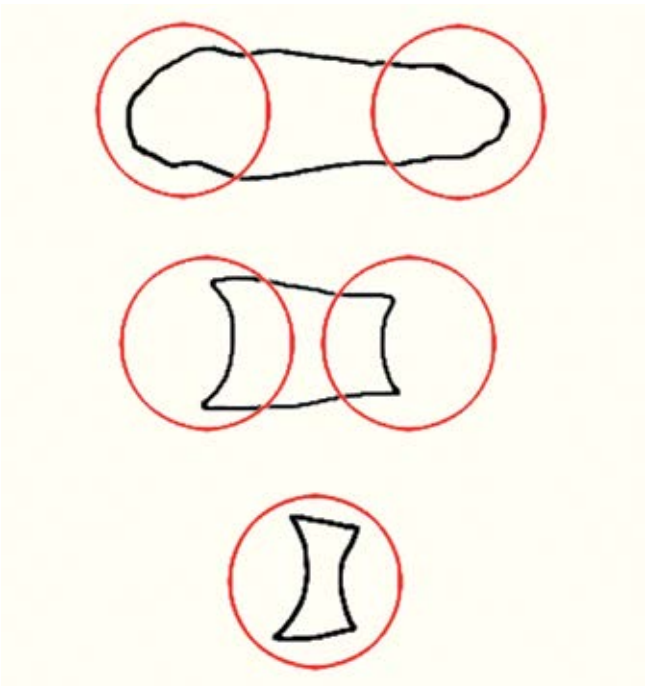

Fig 1 - Segmental cryosurgery. The technique starts at the periphery of the tumour and advances toward the center (centripetally).

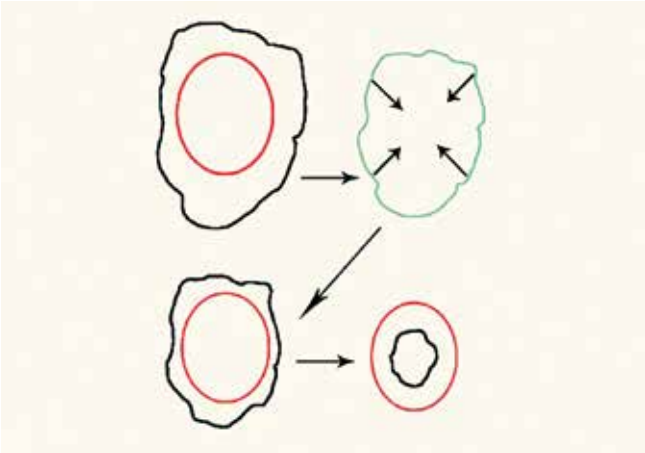

Fig 2 - Fractional cryosurgery. The procedure begins in the center of the carcinoma and advances centrifugally outwards.

For thin eyelid tumours, the first treatment consists of only one freeze-thaw cycle; for thick eyelid tumours, two cycles are carried out. Over the following 3-4 weeks, the resulting ulceration has healed and the remaining lesion has reduced in diameter or in thickness. If the newly obtained size indicates no risk of retraction, the second session is performed with a safety margin. If not, the first procedure is repeated, as many times as necessary until achieving a diameter (smaller than 1.0cm) that allows complete freezing without danger of retraction or deforming scar.

Neoplasms measuring approximately 1.0 cm often appear clinically cured one month after treatment; however, a second cryosurgical procedure is mandatory, in order to treat the safety margin.

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For all these procedures, the thawing time was at least double the freezing time, and the safety margin was 2-3mm around the apparent limit of the lesion. The thawing time was determined when the safety margin was achieved. Temperature monitoring with thermocouples was not executed because the large experience with the technique at our Department.

RESULTS

Between 1988 and 2004 we treated 78 primary malignant neoplasms, in 78 Caucasian patients [48 (61.5%) females and 30 (38.5%) males (a *ratio* of 1.6:1)]. Among men, the mean age was 68.7 years (range: 49-93 years) and 71.3 years in women (range: 50-94 years); the global mean age was 75.5 years. The highest incidence of tumours was noted between 70 and 76 years in both sexes (Fig. 3). Seventy-seven patients (98.7%) reported a history of chronic sun exposure: 74 farmers (96.1%), two construction workers (2.6%) and one driver of industrial machines (1.3%). Fifty-three (68%) were skin type 2 and 25 (32%) skin type 3.

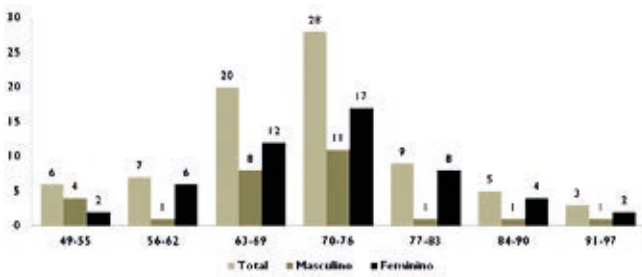

Fig. 3 - Tumour distribution according to sex and age.

Clinically, 78 tumours (97.4%) were BCCs and two (2.6%) were ulcerated SCCs. Among the former, 43 (55.1%) were nodular BCCs and 33 (42.3%) nodulo-ulcerated BCCs. Neoplasm locations were: 43 (55.1%) in the inner canthus, four of which included part of the adjacent lateral nose, 24 (30.8%) in the lower eyelid, seven (9%) in the upper eyelid, three (3.8%) in the outer canthus and one (1.3%) involving, simultaneously, both the lower eyelid and the inner canthus. The mean duration of carcinomas on presentation was 5.1 years (with a minimum of 2 months and a maximum of 20 years); their mean diameter was 1.3cm (range: 0.3-2.5cm). In 26 cases the duration was undetermined. According to TNM classification, 67 tumours (86%) were stage I (T1N0M0), seven (9%) stage II (T2N0M0) and four (5%) unknown. Head lymph node palpation in the SCC cases was negative.

Fractional cryosurgery was the treatment modality performed in 52 BCCs (66.7%), in which the mean axis was 1.3cm (range: 0.9-2.5cm). Of the tumours that have benefited from this technique, 21 were located in the inner canthus and 22 in the lower eyelid. Conventional cryosurgery was used in 17 cases (21.8%) (12 BCC and two SCC), with a mean diameter of 0.6 cm (range: 0.3-1.0cm). The remaining nine BCCs (11.5%) [with a mean diameter of 1.8 cm (range: 1.4-2.5cm)] were treated by segmental cryosurgery (Table 1).

Five patients (6.4%) developed permanent hypopigmentation, four (5.1%) developed hypertrophic scars and three (3.8%) developed milia. In the sixty-six remaining cases, the aesthetic results were excellent; within nine to twelve months after treatment, only in a few patients was it possible to distinguish the treated area, due to very slight hypopigmentation. The skin was thin and smooth (Figs. 4-8) with no functional complications, namely ectropion or entropion.

The follow-up ranged between 5 months to 10 years (mean: 5 years) and the median follow-up time was 6.5 years. Six patients were followed for a period of less than 1 year (all of whom died of unrelated diseases), 24 between 1 and 4 years, 25 for 5 years and 23 for more than 5 years. All patients in the second group were contacted by telephone to ascertain their recurrence-free status. Four patients (5.1%) died of unrelated diseases

Table 1 - Cryosurgery modalities according to diameter, types and location of lesions

CRYOSURGERY	n	%	DIAMETER (CM)			CLINICAL TYPES	
			Maximum	Mean	Minimum	BCC	SCC
Conventional	17	21.8%	1.0	0.6	0.3	15	2
Fractional	52	66.7%	2.5	1.3	0.9	52	-
Segmental	9	11.5%	2.5	1.8	1.4	9	-

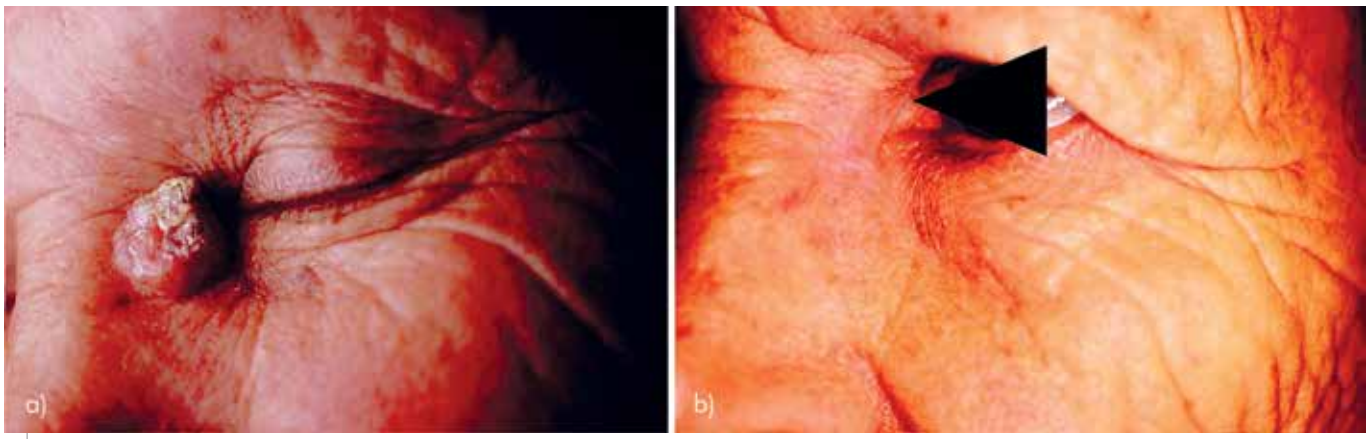

Fig 4 - Inner canthus nodular BCC (a) treated with fractional cryosurgery. The aesthetical and functional results were notable (b).

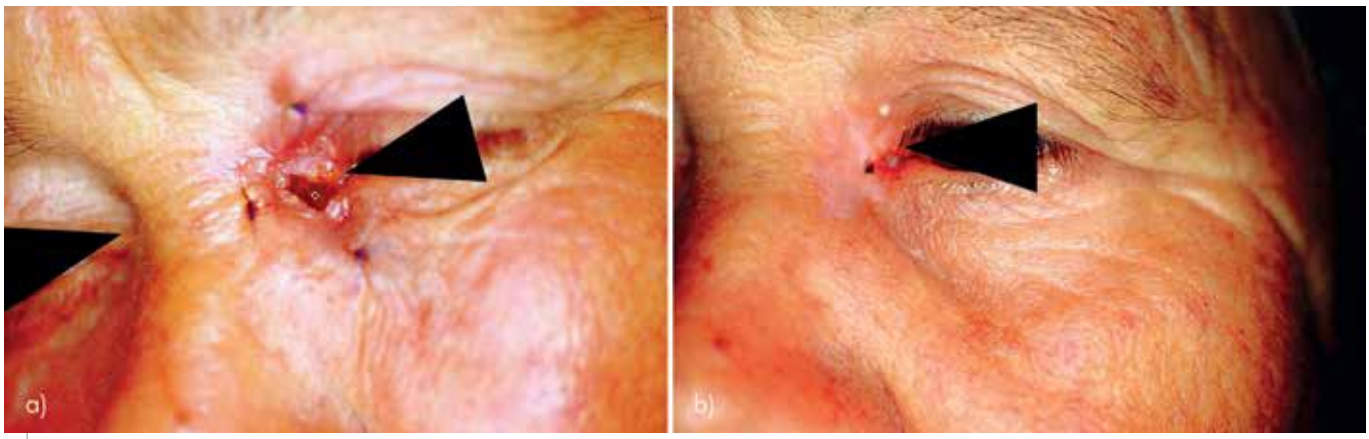

Fig 5 - Nodular-ulcerated BCC (a). Milia and slight hypopigmentation (b) were observed six months after fractional cryosurgery.

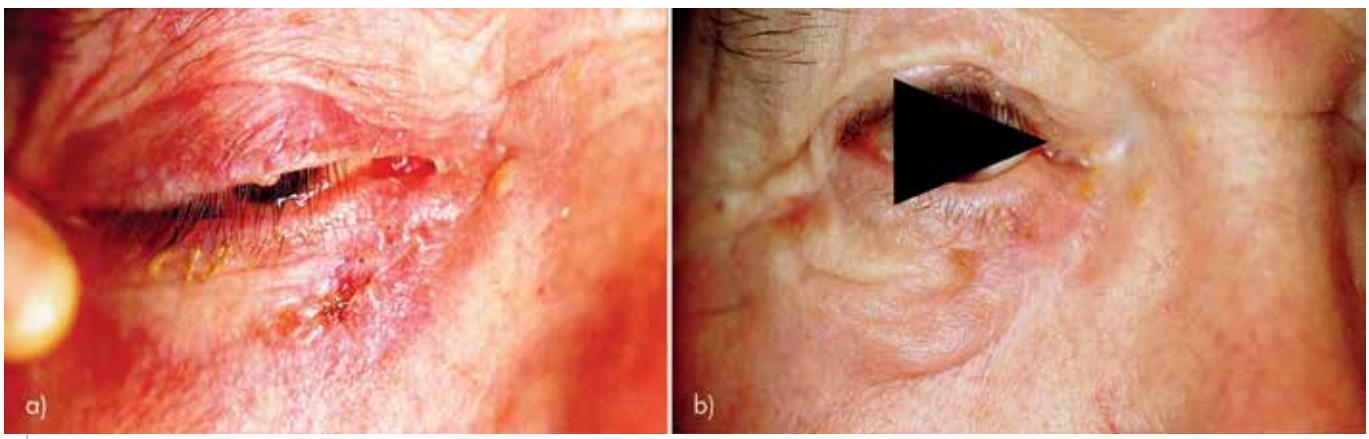

Fig 6 - Nodulo-ulcerated BCC (a). One year after segmental cryosurgery there was no lagophthalmos and the treated area was quite imperceptible (b).

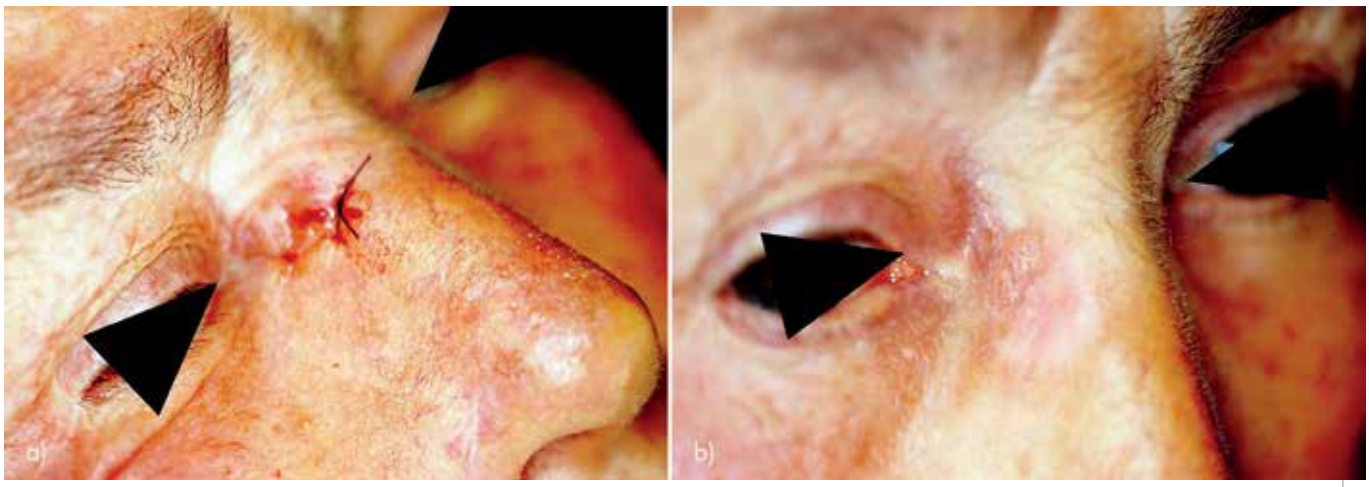

Fig. 7 - Nodular BCC evolving inner canthus and lateral wall of nose (a) treated by segmental cryosurgery with excellent results one year later (b).

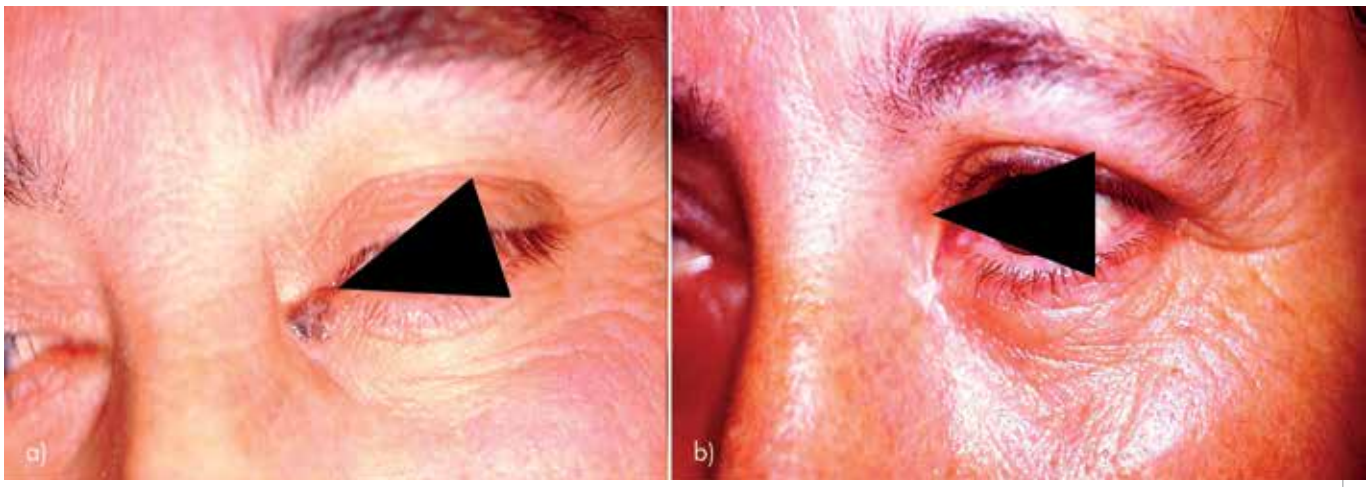

Fig. 8 - Small pigmented nodular BCC (a) in a young female. Six months after conventional cryosurgery only a slight scar was observed (b).

and up to the date of death no recurrence was documented. The remaining 20 (94.9%) reported to our department and no recurrence was observed.

There were two (2.6%) recurrences histologically confirmed. The first occurred after 2 years of follow-up and was a stage I (1.4cm) nodular BCC, treated by segmental cryosurgery. The second, who occurred after 3 years of follow-up, was a stage I (1.4cm) nodulo-ulcerated BCC, also treated by segmental cryosurgery (Table 2). Both patients were submitted to scalpel surgery, with cure and follow-up of 7 and 8 years, respectively. There were no recurrences in the conventional and fractional cryosurgery groups. The overall recurrences and cure rates were, respectively, of 2.6% and 97.4%. There was no mortality associated with the skin cancers treated.

DISCUSSION

Our Department has vast experience in the treatment of multiple types of tumours, in various locations, with cryosurgery, with excellent results. In line with data from the relevant literature[3,8,9], we also found BCC to be the most common non-melanoma malignancy of the eyelids and periocular area. Aligned with results

Table 2 - Characterization of the recurrences

	PRIMARY TUMOR				RECURRED TUMOR			
	Clinical type	Location	Stage/ Diameter (cm)	Therapeutic modality	Period of recurrence (years)	Therapeutic modality	*Follow-up* (years)	Evolution
1	Nodular	IC	I /1.4	Segmental	2	Classic surgery	7	Cure
2	Nodular-ulcerated	IC	I /1.4	Segmental	3	Classic surgery	8	Cure

obtained by other authors[10], a female predominance in our series was also found. This may be explained by the important role played by women in agricultural activities (growing crops, raising livestock) over the centuries in the Santarém District (Portugal). The advanced mean age, chronic ultraviolet exposure and low skin types prevalence corroborate the data from relevant literature[1,3], as major risk factors for non-melanoma skin cancer.

Regardless of the location, the predominance of nodular BCC in our patients is consistent with data observed in other studies[10]. The inner canthus and lower eyelid are the most important locations reported by many authors[2,3,11,12], a fact also observed in our series. The mean duration of carcinomas attests to the long delay in seeking medical care.

Currently, classical excision followed by repair with one of different flaps is the option used in most centres, with excellent results and reported overall cure rates between 90.5 and 96.3%[10,12,13]. Mohs micrographic surgery, although not performed in many surgical centres for several reasons (including the high cost and the length of the procedure), is considered by many physicians as the best surgical option, offering the highest cure rate (between 94.4 and 100%), particularly in tumours located in the inner canthus[2,11,14]. Our overall cure rate was within these values.

Cryosurgery has many advantages over the other treatment methods[3-5,8,15,16]: it is a cheaper and faster method; it provides better cosmetic and functional results; no risk in displacement of malignant cells and no need for interruption of anticoagulant therapy; and a very high cure rate. Additionally, cryosurgery allows greater preservation of the ocular structures and lachrymal pathway as shown by Gonçalves[9] and experimental work performed by Liu and colleagues[17].

When treating non-melanoma skin cancers of the eyelids and periocular regions larger than 1.0 cm with CC, one should not expect the excellent results reported by several authors in tumours smaller than 1.0cm; the outcome may be good in some cases, but a huge disappointment in others. Segmental and fractional cryosurgery, two specialized techniques devised by Zacarian 6 and Gonçalves[3,8], respectively, for the treatment of tumours larger than 1.0 cm, provide excellent aesthetic and functional results. In our series, tumours up to 1.0cm in diameter (BCCs and SCCs) were treated by conventional cryosurgery. Those rounded and larger than 1.0cm in diameter, located in regions where there is an increased risk of retraction or disfiguring scars (inner canthus and lower eyelid), were treated by fractional cryosurgery. We used segmental cryosurgery for elongated lesions measuring over 1.0cm in diameter.

Our overall 2.6% recurrence rate was lower than those found in several publications on cryosurgery in the treatment of skin cancer of the eyelid and periocular area[4,15,16]. Tuppurainen[4] showed that the lesion size (larger than 1.0cm) is one of the major prognostic factors for local recurrence. Additionally, according to different authors[2,11,14,15], the inner canthus is the location with the highest relapse rate. Likewise, in our series, the two tumours that recurred were larger than 1.0 cm and located in the inner canthus. These two recurrences (2 and 3 years post-treatment) demonstrate, unequivocally, the need for regular surveillance over a period not lower than 5 years.

The low number of relapses and the absence of functional complications in our patients was a notable fact, attesting, once again, to the effectiveness of cryosurgery, particularly the specialized techniques of segmental and fractional cryosurgery, in the treatment of non-melanoma skin cancer of the eyelids and periocular areas.

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