

## Cryosurgery As A Treatment of Basal Cell Cancer

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### Abstract

Basal cell carcinoma constitutes the malignant neoplasm with the highest rates of cases worldwide. Over the years, science and technology have pioneered innovation in order to implement adequate and effective treatments against this pathology. Cryosurgery is an avant-garde procedure implemented in recent times, with which by freezing the tumor by applying liquid nitrogen on it, gratifying results have been evidenced in terms of tumor elimination, recurrence rates and aesthetics. Therefore, a review of the current bibliography is carried out in order to define its effectiveness as the main method of treatment of basal cell cancer.

**Key Words:** Cryosurgery, Basal Cell Carcinoma, Bcc, Treatment

### Introduction

Basal cell carcinoma (BCC) is the most common skin malignancy worldwide [1]. According to the American Cancer Society, more than 2 million people were treated for non-melanoma skin cancer (NSCLC) in 2006, mostly BCC [2]. A population-based study conducted in Rochester, Minnesota, estimated the age-standardized annual incidence of BCC in Caucasian men and women to be 146 cases per 100,000 people [3]. Another study conducted in Hawaii estimated the combined incidence in Caucasian residents at 422 cases per 100,000 people, the highest incidence documented in the United States at the time of publication in 1993 [4]. Both studies showed that the rate increased with age and men had a significantly higher incidence of BCC than women. The incidence among Americans under the age of 40 appears to be increasing, especially among women [5].

Sun exposure is the most important environmental cause of BCC. Several studies showed a positive association between BCB and light skin color, severe sunburn and freckles in childhood, and northern European ethnicity [6]. There is also a geographic variation in the incidence of BCC with a positive correlation between frequency and proximity to the equator. The use of tanning beds has been associated with a significantly higher risk [7]. Other factors such as ionizing radiation in the form of radiation therapy, consumption of arsenic-contaminated water and arsenic-containing drugs, immunosuppression in organ transplant recipients, etc [8]. (Table 1)

<b>TABLE 1. Risk Factors for The Development of BCC.</b>
<b>Risk factors associated with increased environmental or artificial UV exposure</b>
Intermittent, intense sun exposure (especially in childhood and adolescence)
Northern European ethnic origin
Light skin color
Tendency to burn rather than tan proximity to the equator
History of blistering sunburns in childhood
Use of tanning beds
Other risk factors
Exposure to therapeutic ionizing radiation
Immunosuppression in organ transplant recipients
HIV seropositivity
Genetic syndromes: nevoid basal cell carcinoma, xeroderma pigmentosum, Bazex

The main clinical subtypes of BCC are nodular, superficial, and morpheaform. Nodular BCC is the most common clinical subtype, accounting for 50% to 70% of all BCCs. The lesions consist of shiny, pearly quality papules or nodules and small arborizing telangiectasias. The tumor may enlarge and crusts may appear over a central depression. Bleeding with minor trauma is common. Over time, the lesion may ulcerate (rodent ulcer), but usually a rolled edge remains that serves as a clue to the diagnosis. Nodular BCC predominate on the head, especially on the cheeks, nasolabial folds, forehead, and eyelids. In one study, 90 percent of nodular BCCs occurred in the head. The differential diagnosis of a nonulcerated lesion includes molluscum contagiosum, sebaceous hyperplasia, amelanotic melanoma, intradermal melanocytic ne-

vus, Merkel cell carcinoma, fibrous papule of the nose, trichoepithelioma, and other adnexal neoplasms. Ulcerated lesions can be difficult to distinguish from squamous cell carcinomas and keratoacanthomas [9].

Superficial BCC is the second most common clinical subtype, accounting for up to 15% of cases. A lesion usually appears as a macula, patch, fine papule, or well-defined, scaly, pink to red plaque. It may show a scab or a thin rolled edge consisting of small fine translucent papules. Areas of spontaneous regression can occur, leaving behind atrophic and hypopigmented areas. Varying amounts of melanin pigment may be present. Superficial BCCs favor the trunk and extremities, unlike the other subtypes, which favor the head and neck. It usually occurs in patients younger than the other subtypes, with a mean age at diagnosis of 57 years. The differential diagnosis includes inflammatory dermatoses, such as psoriasis and nummular dermatitis, as well as lichenoid keratosis, actinic keratosis, Bowen's disease (SCC in situ), and early amelanotic melanoma [10].

Morpheaformed BCC represents a low proportion of cases, estimated between 5 and 10 percent. It is called a morpheaform or sclerosant because of its clinical similarity to an indurated plaque of morphea or localized scleroderma. Lesions present as pink to ivory-white, shiny, smooth, scar-shaped plaques or depressions, indurated with ill-defined borders. Often there is associated atrophy. Sometimes telangiectasias, erosions, or small scabs can develop. Lesions are known for their subtlety. Also known as infiltrative BCC, morpheaform BCC is usually more aggressive than nodular and superficial BCC, as it tends to exhibit subclinical spread with the potential for extensive local destruction. Morpheaformed BCC can be confused with scarring, morphea (localized scleroderma), dermatofibrosarcoma protuberans, Merkel cell carcinoma, amelanotic melanoma, microcystic adnexal carcinoma, and other adnexal neoplasms [11]. (Table 2)

**TABLE 2: Clinical Variants of Basal Cell Carcinoma**

<b>Clinical subtypes</b>	<b>Percent of cases</b>	<b>Clinical characteristics</b>	<b>Predominate</b>	<b>Differential diagnosis</b>
Nodular	50 to 79%	- Lesions consist of papules or nodules with a pearly, shiny quality and small arborizing telangiectasias. - the lesion may ulcerate (rodent ulcer).	Predominate on the head, especially the cheeks, nasolabial folds, forehead and eyelids	- Molluscum contagiosum - sebaceous hyperplasia - amelanotic melanoma - intradermal melanocytic nevus - Merkel cell carcinoma - fibrous papule of the nose - trichoepithelioma - adnexal neoplasms
Superficial	up to 15%	- A lesion typically appears as a well-circumscribed, scaly, pink-to-red macule, patch, thin papule, or thin plaque. - It may demonstrate crust or a thin rolled border consisting of fine translucent small papules	Head and neck	- inflammatory dermatoses such as psoriasis and nummular dermatitis. - lichenoid keratosis - actinic keratosis - Bowen's disease - amelanotic melanoma

morpheaform	5 to 10%	<ul style="list-style-type: none"> <li>- Lesions present as pink-to-ivory-white, shiny, smooth, scar-like, indurated plaques or depressions with ill-defined borders.</li> <li>- Telangiectasias, erosions, or small crusts may sometimes develop.</li> </ul>	Undefined	<ul style="list-style-type: none"> <li>- Scar</li> <li>- morphea</li> <li>- dermatofibrosarcoma protuberans</li> <li>- Merkel cell carcinoma</li> <li>- amelanotic melanoma</li> <li>- microcystic adnexal carcinoma</li> <li>- adnexal neoplasms</li> </ul>
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The current mainstay of BCC treatment includes surgical modalities such as excision, electrodesiccation and curettage (EDC), cryosurgery, and Mohs micrographic surgery. These methods are generally reserved for localized BCC and offer high 5-year cure rates, generally more than 95%. Cryosurgery is a low-risk treatment option for BCCs. It involves the controlled application of liquid nitrogen to the clinically visible tumor and a small surrounding margin of normal-appearing skin for margin control. A temperature probe can be used that is inserted into the lateral margin of the tumor, and the tip is positioned just below the tumor by pushing it obliquely. Liquid nitrogen is then applied and continued until a temperature of -60 degrees C is reached. In practice, a temperature is rarely used during this procedure. The procedure is advantageous for those who wish to avoid invasive surgery and it is also relatively quick. The treated area may hurt and swell after thawing. Cryosurgery can also cause hypertrophic scars and permanent pigmentation alteration [12].

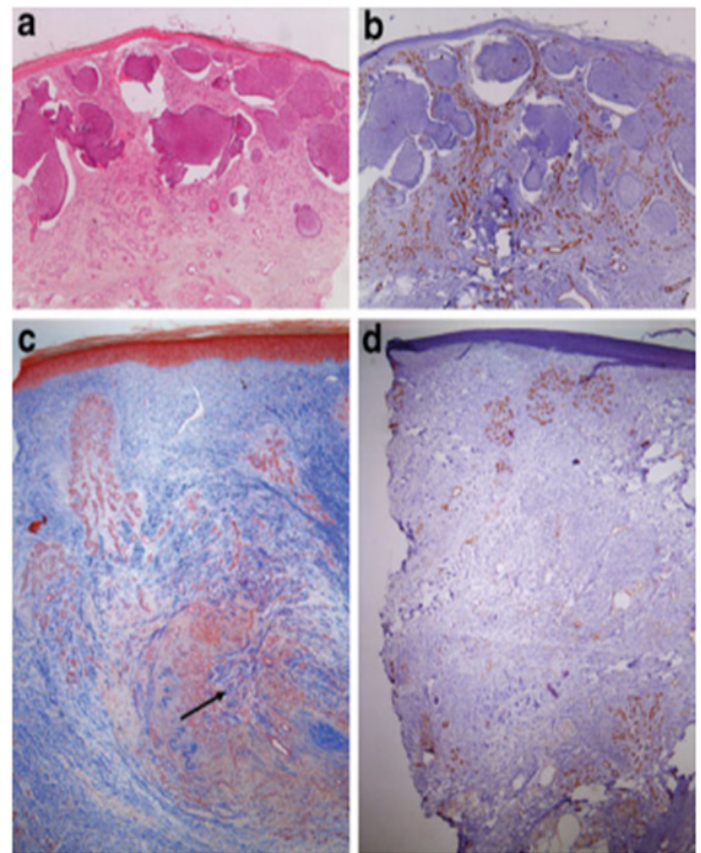
### Materials and Methods

In this review article, a detailed bibliographic search of information published since 2011 was carried out, in the databases PubMed, Elsevier, Scielo, national and international libraries. We used the following descriptors: Cryosurgery, basal cell carcinoma, CCB, treatment. The data obtained ranged from 2 to 15 records after using the keywords. The search for articles was carried out in Spanish and English, limited by year of publication, and studies published since 2011 were used.

### Results

Yaron Har-Shai & et al. They report a case report of an 80-year-old Caucasian woman with hypertension and hypothyroidism referred to her clinic with two skin lesions that have been increasing for a year in the lower third of her right leg. On examination, skin lesions 1 cm in diameter were clinically diagnosed as nodular BCC. A punch biopsy of the lesions diagnosed BCC (Figure 1a, b) but the distinct subtype of BCC could not be specified. The patient refused surgical removal of the tumors due to her fear of wound healing difficulties and infection due to her varicose veins. Therefore, the intralesional cryosurgery method was proposed and performed under local anesthesia according to the pain control protocol. After inserting the cryo-needle at the base of the tumors, the cryo-needle was connected to a cryo gun (CryoPro Maxi, Cortex Technology, Hadsund) filled with liquid nitrogen which is introduced into the cryoprobe thereby freezing the contiguous tumor. Once a complete freezing of the tumor is evident, the cryoprobe is thawed and it is removed. The duration of said treatment was 10 min respectively for each lesion. The patient was told that the area should be washed and an antibiotic ointment applied. After 2 months the patient was cured. No wound complications were

reported. After 3 months, punch biopsies of healed scars revealed no signs of malignancy (Figure 1c, d) [13].

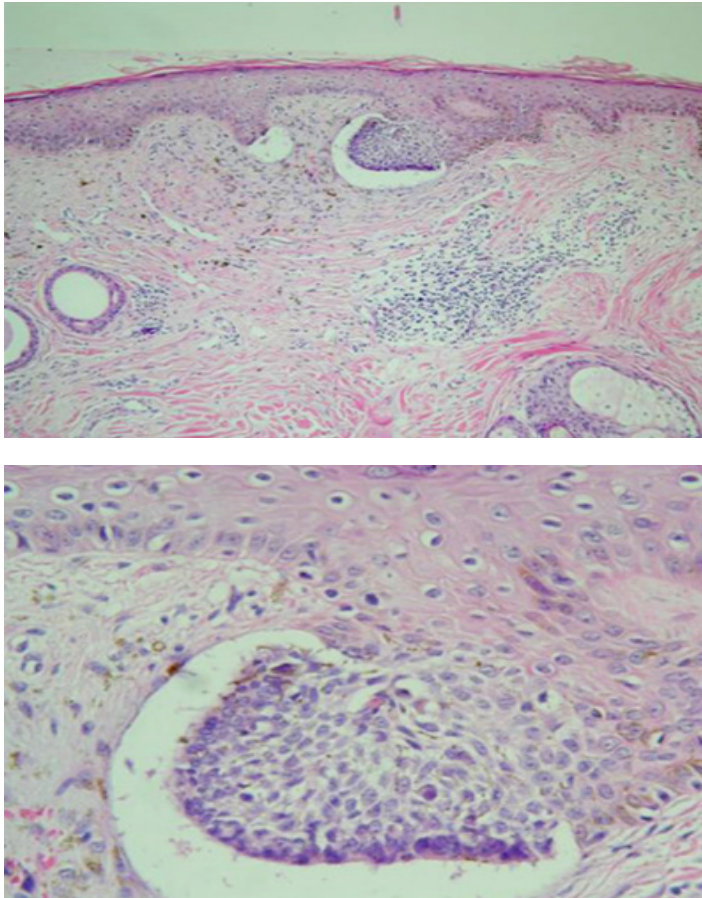


**Figure 1:** From the Har-shai, Y, Harh-shai, L, Lurie, M. Intralesional cryosurgery for the treatment of basal cell carcinoma in an elderly patient. *Eur J Plast Surg.* 2012; 35: 613-616.

a Pre-cryo-treatment biopsy which demonstrates islands of basal cell carcinoma distributed in the dermis, surrounded by proliferating capillaries and chronic inflammation (H&E,  $\times 4$ ). b Pre-cryotreatment biopsy demonstrates an immunohistochemical stain for CD31 which displays an abundant capillary network that surrounds the basal cell carcinoma islands (CD31,  $\times 4$ ). c Post-intralesional cryosurgery treatment of the previous tumor site showing the dermis and epidermis free of tumor. The epidermis is normally structured. In the deep dermis, a large and well-demarcated relatively round area of dense fibrosis, haphazardly oriented elastic fibers, and a center displaying loose fibrosis and a few capillaries (black arrow). This structure is reminiscent of an obstructed ves-

sel; however, its size, content, and anatomic location are suggestive for being the site in which the cryoneedle had been introduced (Masson trichrome,  $\times 4$ ). d Postintralesional cryosurgery view of the previous tumor site showing the dermis and few capillaries, free of tumor (CD31,  $\times 4$ )

Young Soo Heo report a case of a 54-year-old man who presented with an asymptomatic dark spot on his front scalp. The lesion had been increasing slowly for 15 years, without concern for medical care on the part of the patient. Physical examination revealed a  $6 \times 8$  cm well-defined round black spot on the frontal scalp. On closer examination, four other dark-colored macules were observed around the main lesion. A biopsy sample of the main lesion showed an irregular proliferation and budding of tumor tissue adhering to the lower surface of the epidermis. The peripheral cell layer of tumor formations generally showed palisade. In addition, a mild amount of a nonspecific chronic inflammatory infiltrate was present in the upper dermis, which is a typical feature of superficial BCC. (Figure 2a, b).



**Figure 2a:** Tumor shows buds and irregular proliferations of tumor tissue attached to the undersurface of the epidermis (H&E,  $\times 40$ ). **b:** The tumor cells have a large, uniform, oval, non-nucleolar nucleus with little cytoplasm (H&E,  $\times 100$ ). Tomado de: Soo, Y, Hee, J, Eun, J & et al. A Case of Superficial Giant Basal Cell Carcinoma with Satellite Lesions on Scalp. *Ann Dermatol*. 2011;23(1).

The giant BCC was treated with a combination of 5% imiquimod

and cryosurgery, given the reluctance of the patient to an operation and the lesion was too large to recover by skin graft. Cryosurgery consisted of 2-3 freeze-thaw cycles (15 seconds of freezing with an intermediate period of 60 seconds of thawing). Four days later, the patient topically applied 5% imiquimod once. This procedure was performed four times. Subsequently, topical treatment with imiquimod cream was continued for 4 months. Two months after the last treatment, the clinical examination revealed only atrophic and hypopigmented areas, without any sign of residual tumor [14].

## Discussion

Because during this procedure a direct application of liquid nitrogen is made on the tumor, which results in the formation of extra and intracellular ice crystals, which damage the cell phospholipid membrane and damage the surrounding vessels associated with the tumor, for as it lacks blood supply and therefore its cellular capacity to replicate and metastasize is considerably decreased, this is considered a highly effective and minimally invasive management option.

Despite its high success rates for this procedure, in his review article, Tanese states that the reported efficacy of cryosurgery is variable and dependent on the treatment procedure based on a single institution study looking at the efficacy of deep cryosurgery for 4406 non-melanocytic skin cancers it determined a cure rate of 98.6%. Meanwhile, a review of six studies that included 796 BCC patients treated with cryosurgery found recurrence rates ranging from 3.5% to 16.5%. A non-randomized study comparing cryosurgery and radiotherapy (RT) revealed the inferiority of cryosurgery, based on 2-year recurrence rates of 39% and 4%, respectively. In a randomized trial comparing surgical excision and a combination of curettage and cryosurgery, the recurrence rate was 8.2% and 17.6%, respectively, indicating the inferiority of cryosurgery, even when combined with curettage, compared to surgical excision. Furthermore, the cosmetic result of cryosurgery is also inferior to surgical resection. For these reasons, cryosurgery should not be the first-line treatment for BCC, especially for tumors with a high risk of recurrence or if the treatment is likely to result in a poor cosmetic outcome [15].

However, various authors such as Samain and others, who conducted a retrospective study between 2005 and 2012 in which 108 patients were included with a mean age of 76.5 to 11.1 years, with a total of 144 BCCs. The mean follow-up was 40.7-15.6 months. Wound healing occurred after a median delay of 4 weeks (range 1 to 12 weeks). No serious complications were recorded. Seven recurrences (4.9%) were observed after a median of 24 months (range 4 to 36 months), which underwent cryosurgery with additional curettage, for which they concluded that initially this procedure is simple, inexpensive and profitable. In addition, it preserves the tissue, allowing the implementation of other techniques (Mohs micrographic surgery or standard surgery) in those patients who, after cryosurgery, have recurrence [16]

For their part, Soong and Keeling in their retrospective study with immunocompromised patients with basal cell carcinoma who underwent cryosurgery and were treated with 5% 5-fluorouracil 3 weeks later. In this, 30 cancers of the 34 that were evaluated showed no evidence of recurrence, four cancers showed recur-

rence, and patients with recurrence were subsequently treated with Moh's micrographic surgery. Including patients who were lost to follow-up, 30 cancers out of 41 sBCC that were treated showed no evidence of recurrence, resulting in a 73% clinical cure rate [17] therefore, cure rates are higher. 70% and recurrence rates are low.

In turn, as Martinez et al. Conclude in their retrospective case study, the percentage of tumor recurrence after cryosurgery may be reduced to the extent that patients are correctly classified with strict diagnostic criteria and cryosurgery is performed by a trained operator, with a standardized technique and with adequate peripheral margins [18]. So that even in Colombia it can be implemented as the first therapeutic option.

Therefore, taking into account the advantages of cryosurgery exposed by Tobon and others who understand that its preparation time is short and a great versatility for the treatment of different diseases, it serves as a treatment in any body area, as a palliative treatment of tumors. inoperable, excellent cosmetic results are obtained, is suitable for consultation, outpatient or outpatient care, is inexpensive, does not need general anesthesia, local anesthesia is optional, no operating room is needed, various injuries can be treated, it is a safe procedure and relatively simple, with few or slight complications, it is not necessary to leave work or sports, it is useful during pregnancy, it is useful in patients who reject surgery or with surgical risk, it is a procedure without age limit and suitable for patients in wheelchair or bedridden [19] and that this is a procedure that can be used with other techniques Innovative cases for high-risk cases such as 5% imiquimod [20] and, when performed by an expert, represents a very suitable option for the treatment of basal cell cancer, taking into account the high cure rate, low cost and aesthetic results that are obtained by means of this.

## Conclusion

Basal cell cancer is the most common malignant neoplasm in the world, that is, its epidemiological rates are high, thus representing a health problem of great importance worldwide, for which rapid diagnostic impression and its differential diagnosis is decisive at the moment to implement the correct treatment method.

It is important to take into account the diagnostic criteria for this neoplasm and the type of carcinoma in each case in particular, and in recent years cryosurgery, a procedure in which the affected tissue is basically frozen, depending on the area that is compromised. represented one of the most efficient methods to treat this pathology, due to the fact that various studies show that it has high rates of efficacy, it is ambulatory, inexpensive, non-invasive and through the follow-up of patients subjected to this it has been shown that it has its Once there is little chance of recurrence and it also provides good aesthetic results, which simultaneously contributes to the increase of the emotional stability of the patient and therefore of their quality of life, however, currently other equally effective methods are used, for which the main method of treatment is still under study.

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