

## **Clinical Studies**



## Cryosurgery for Advanced Malignant Melanoma of the Facial Skin. A Case Report

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**Abstract.** *Background:* Cryosurgery is safely employed for the treatment of skin precancerous and malignant lesions of the head and neck in selected patients. The case of a 101-year-old female patient with advanced malignant melanoma of the facial skin, undergoing cryosurgery, is reported in order to assess the feasibility and tolerability of the technique, as well as the biological implications of cryosurgical treatment in this specific neoplasm. *Case Report:* A 101-year-old woman, with a large (pT4b N0 M0) cutaneous melanoma of the facial skin on the right cheek, was treated at the Division of Surgical Oncology of the National Cancer Research Institute, Italy, from June to August 2003. The treatment was accomplished by means of serial cryosurgical applications which were performed within three months; the bulk of the lesion was cryotreated with a liquid nitrogen cryoprobe, while the residual disease was treated with a nitrous protoxide cryoprobe, by means of the insertion technique. The treatment was well tolerated, with a good aesthetic result, and the patient is recurrence- and distant-disease-free two years after the initial cryosurgical application. *Conclusion:* Cryosurgery is feasible in the treatment of head and neck melanoma, mostly for mucosal melanomas and cutaneous lesions in anatomically critical sites, as well as in high-risk surgical patients. Here, a good aesthetic result was obtained in a very elderly patient with a large cutaneous melanoma of the facial skin, avoiding skin flap transposition for tissue repair and postoperative complications (e.g., serious bleeding or postoperative pain), with a satisfactory functional and oncological outcome at two years.

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The surgical decision in elderly patients with advanced cutaneous melanoma must be balanced between the immediate risk of an adverse event (operative mortality within 30 days, or serious postoperative complications) and utility, defined as the outcome of the treatment and the patient's perception of the same outcome. In the older age group, the operative risk is frequently increased due to comorbidity factors which increase with advancing age, whilst the utility may be reduced due to life expectancy and any possible associated disability. The assessment of the operative risk should take into account different aspects such as: the stage of the disease, side-effects related to previous or concomitant treatments, the patient's physical status, the presence of comorbidity factors (cardiovascular, respiratory, metabolic, urological, cognitive and incontinence), the type of operation as well as the surgeon's experience (1).

In recent years, surgery has become increasingly less aggressive and invasive, with a great emphasis on function-sparing treatments, particularly in the elderly, where surgery is primarily to enhance the quality of life rather than to prolong survival. Thus, cryosurgery is currently employed for the treatment of many benign and precancerous lesions of the head and neck, mostly of the oral cavity, as well as in selected patients with advanced disease, due to the easy access to many oral cavity neoplasms using different types of probes; the possibility of using local or regional anaesthetic procedures; the treatment of high-risk surgical patients, with clotting deficit, and/or with large lesions with an improved functional outcome and rehabilitation; the relatively painless postoperative course; and, finally, the direct visual inspection of the area of cryonecrosis, allowing repeat freezing cycles on residual disease (2).

A case report of a 101-year-old female patient with advanced malignant melanoma of the facial skin, who was treated with cryosurgery, is reported in order to assess the feasibility and tolerability of the technique, as well as the

biological implications of cryosurgical treatment in this specific neoplasm.

### Case Report

A 101-year-old woman, with a large (4 cm maximal diameter) malignant melanoma of the facial skin on the right cheek (Figure 1) was treated at the Division of Surgical Oncology of the National Cancer Research Institute, Genoa, Italy, from June to August 2003. Advanced age notwithstanding, the patient was in fairly good clinical condition, was not undergoing any specific pharmacological treatment and no regional lymph node metastasis or distant metastasis had been detected. An incisional biopsy was performed with a definitive histological diagnosis of nodular ulcerated melanoma (pT4b). The treatment was accomplished by means of serial cryosurgical applications which were performed within three months (Figures 2, 3); the bulk of the lesion was treated with a liquid nitrogen cryoprobe, and the residual disease with a nitrous protoxide cryoprobe, employing the insertion technique. The treatment was well tolerated, with a good aesthetic result, and the patient is recurrence- and distant-disease-free two years following the initial cryosurgical treatment (Figure 4).

### Discussion

Cryosurgery is a relatively safe and simple technique but the proper instruments, as well as respect for codified procedures, are required. The freezing capability of nitrous protoxide ( $-89.5^{\circ}\text{C}$ ) is limited to a depth of about 5 mm, but liquid nitrogen ( $-196^{\circ}\text{C}$ ) can freeze substantially deeper. Thus, adequate treatment of bulky lesions should require two cryogenic instruments: one with liquid nitrogen for the bulky tumor, due to the more pronounced vascular supply and the depth of infiltration of surrounding tissues which require a higher freezing power, and nitrous protoxide for the superficial residual disease. In the course of cryoprobe application, an adequate pressure with the probe on the tissue is required in order to reduce the amount of blood flow within the lesion; moreover, repeated freezing cycles are requested mostly in extensive lesions. In any case, the cryosurgical treatment should be aggressive, in order to produce an "ice-ball" including at least 5 mm of apparently normal tissue surrounding the primary tumor site. The insertion technique should be used whenever deep infiltration does occur, as in our patient. In order to freeze the entire lesion, different cryoprobes can be inserted at the same time, using (preferably) liquid nitrogen with repeated freeze cycles, followed by a long thawing period to improve cryonecrosis. Although rare,

postoperative bleeding may occur due to the high vascular supply of such lesions; moreover, a slough of necrotic tissue may occur 10 to 20 days following cryosurgery, although this bleeding can be controlled by the electrocoagulation of small vessels (2).

Recently, cryosurgery has been proposed in the treatment of head and neck melanoma, mostly for mucosal melanoma in anatomically critical sites as well as for palliation in high-risk surgical patients or those with unresectable disease (3, 4). Mucosal melanoma of the upper digestive tract includes 2-27% of all mucosal melanomas. The site of origin may be normal mucosa or a pre-existing pigmented lesion; it is usually a black, soft, easily bleeding lesion of irregular shape and width. The nasal cavity, paranasal sinus, hard palate, alveolar ridge, gingival fornix, tongue and floor of the mouth are, in decreasing order, the most frequent sites of head and neck mucosal melanoma, with a 5-year survival rate of 4.5-40% (5). Cryosurgery represents a good palliative procedure for inoperable or recurrent disease due to the peculiar features of this neoplasm which makes it particularly freeze-sensitive, so that the technique selectively destroys the neoplastic tissue. Moreover, cryosurgery seems to promote an immunostimulating effect due to the unmasking action of tumor-antigens produced by tissue necrosis, as suggested by the detection of specific antineoplastic antibodies (6, 7).

Recently, in experimental models, *in vivo* destruction of tumor tissue by cryoablation inhibited secondary and metastatic tumor growth. Both in the colon 26-B tumor model and in the melanoma model (MV3) in nude mice, the treatment of primary tumor implants by cryoablation resulted in a significant inhibition of secondary tumor growth and distant metastasis as compared to animals treated by surgical excision alone ( $p < 0.01$ ). Notably, six hours after cryoablation, the plasma levels of IL-1 $\alpha$  and TNF- $\alpha$  were higher than after excision ( $p < 0.01$ ) (8).

Cryotherapy has been successful for the treatment of lentigo maligna, although amelanotic malignant melanoma following cryosurgery for atypical lentigo maligna has been reported in two patients (9, 10).

Other clinical experiences in the treatment of head and neck cancer by means of cryosurgery have been reported in patients with thyroid cancer as well as lymph node metastasis, although patients with head and neck cancer amenable to primary cryosurgery should preferably be those without lymph node metastasis, unless they are at high surgical risk due to systemic disease, such as cardiovascular and/or pulmonary insufficiency (11, 12).

### Conclusion

Cryosurgery is feasible in the treatment of head and neck melanoma, mostly for mucosal melanomas and cutaneous



Figure 1. The patient with an advanced facial cutaneous malignant melanoma.



Figure 2. Ice-ball immediately after cryosurgical treatment.



Figure 3. Necrosis ten days after the cryosurgical treatment.



Figure 4. Excellent result 1 year after cryosurgery. The patient is disease-free.

lesions in anatomically critical sites, as well as in high-risk surgical patients. Here, a good aesthetic result was obtained in a very elderly patient with a large cutaneous melanoma of the facial skin, avoiding skin flap transposition for tissue repair as well as any postoperative complications (such as serious bleeding or postoperative pain), with a satisfactory functional and oncological outcome at two years.

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