**Review Article**

# Cryosurgery: A Therapeutic Modality for Oro-Facial Lesions

Neetu Aggarwal[1] Kapil Ahuja[2] Neha Pal[3] Rohit Pannu[3]Vikas Berwal[4]Neeraj[4]
[1] MDS (Oral And Maxillofacial Surgery) Goa Dental College And Hospital Bambolim, Goa, [2]MDS Oral Surgery M S Ramaiah Dental College And Hospital, [3]M.D.S. (Conservative Dentistry And Endodontics). Consultant, Bhiwani (Haryana), India,[4]Department of Oral And Maxillofacial Surgery, PGI Rohtak

**Abstract**

Cryosurgery is an effective treatment method for a variety of lesions of head and neck region. Modern cryosurgery uses an apparatus that employs liquid nitrogen in a closed system that permits continous and rapid extraction of heat from tissue.It has particular advantages over surgery and is much more readily accepted by patients. It may therefore be the treatment of choice in infants, anxious patients for whom other treatments are contraindicated. Bearing in mind the limitations, there is no doubt that pain relief, reduction in the bulk and infection from fungating tumours makes cryosurgery a worthwhile procedure.
**Keywords:**Contraindicated; Cryosurgery; Tumors

**Corresponding author**: Dr.Neetu Aggarwal, MDS (Oral And Maxillofacial Surgery) Goa Dental College And Hospital Bambolim
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## INTRODUCTION

Cryotherapy is derived from the greek word ‘’kryos’’ means frost hence cryosurgery is local destruction of tissue by freezing.[1]Cryo-freeze-or cold surgery is the operative cutting of tissue or the targeted destruction of pathological tissue by induced cold necrosis at temperatures down to -196$^0$C.[2] The objective of cryosurgery is to cause selective necrosis of tissue, the extent of which depends on the type of lesion and the volume of freezing required. Modern cryosurgery uses an apparatus that employs liquid nitrogen in a closed system that permits continous and rapid extraction of heat from tissue.Currently, cryotherapy is an effective treatment method for a variety of lesions of head and neck region. Cryotherapy has particular advantages over surgery and is much more readily accepted by patients. It may therefore be the treatment of choice in infants, anxious patients for whom other treatments are contraindicated.

### History

A review of the history of cryosurgery shows that it has progressed in leaps and that each leap has usually been triggered by technological innovations which immediately preceded it.

**Ancient Egypt:** Already in 2500 BC, the use of cold compresses to treat compound skull fractures and infected wounds is mentioned in the Edwin Smith Surgical Papyrus (Breasted translation 1930).

**Antiquity:** In 460 BC, Greek medicine was concerned with the prevention and cure of illness caused by cold. In 25 AD Celsus described the appearance of the skin after cold injury and noted that if the injury was severe, dry gangrene supervened (Shepherd and Dawber 1982).

**Eleventh Century:** An unknown Anglo-Saxon monk (1050 AD) employed cold as a local anesthetic (Grafton and Singer 1952).

**Sixteenth Century:** Refrigeration anesthesia was known to Italian physicians by 1570 (Davison 1959).

**Seventeenth Century:** In 1661 Thomas Bartholin of Co-penhagen described the use of cold as a therapeutic for a variety of everyday illnesses (Bracco 1980).

**Eighteenth Century:** The effects a temperature of -24°C had on insects, fish, amphibians, reptiles, birds and mammals was investigated by Spallanzani in 1787. He also established the existence of water at subzero temperatures without it becoming ice a physical state later called "supercooling" (Walder 1966). In the Napoleonic Wars, Napoleon's Surgeon General Von Larrey (1766-1842), made detailed observations of the effects of cold on his patients. Tissue cooling by surface application of snow and ice was used to facilitate amputation in Napoleon's Grand Army (Schechter and Sarot 1968).

**Nineteenth Century:** The therapeutic effects of low temperatures have been known for many years. The first successful treatment of malignant disease in England was reported between 1845 and 1851 by Dr. James Arnott (1797-1883). Although he did not cure them, he considerably reduced the morbidity of cancer, especially the pain, which is still sometimes a considerable problem.[3]

## Indications of cryosurgery in oral and maxillofacial surgery

Cryosurgery is used as a therapeutic modality for a variety of oro-facial lesions.

- Premalignant lesions
- Benign oral and orofacial lesions
- Malignant soft tissue lesions of oral cavity, pharynx, face and scalp
- Bone lesions
- Cryosurgery of nerve
- Cryosurgery of blood vessels
- Cryosurgery of salivary glands
- Cryoneurotomy for intractable temporomandibular joint pain

Cryoneurotomy of peripheral branches of the trigeminal nerve has been shown to be of benefit for patients with trigeminal neuralgia (Barnard et al., 1978; Goss, 1984). This is particularly so for patients who do not respond to or cannot tolerate carbamezapine and who are sufficiently medically compromised to contraindicate neurosurgical procedures.[4]

- Cryosurgical treatment of melanin-pigmented gingiva

Cryosurgery is a simple and effective technique to eliminate the pigmentation of gingiva. It requires no anesthesia or sophisticated equipment. The treated gingiva appeared normal within 1 to 2 weeks after cryosurgical treatment.[5]

**Contraindications for cryosurgical interventions are not known at present.**[2]

## The advantages to the patient of modern cryosurgery in comparison to conventional surgical methods

- Short duration of surgery
- Minimal operative and anesthesia trauma
- Surgery without bleeding
- Surgery without scar formation
- Prevention of metastasis at time of excision of tumour
- Surgically uncomplicated results, the high rate of curative success, short hospital stays, lower hospital costs, as well as increased quality of life for the patient
- Anesthesia is usually unnecessary, as the cold itself functions as an anesthetic
- The period of convalescence is a fraction of that usual for stationary hospital admissions
- No local complications stemming from the area of surgery
- Quick and technically simple method of tumour removal
- Both benign and malignant tumours are easily extirpated
- Improved subjective state of the patient through palliative cryosurgical methods, lessening of pain and fetor, as well as improvement in the general condition of the patient by containment of tumour growth.[2]

## Physical & biochemical effects of cryosurgery

The mechanisms of injury in cryosurgery can be attributed to the direct effects of freezing tissue and to vascular stasis. This damage is enhanced during subsequent thawing of the tissue by the development of vascular stasis, which leads to failure of local microcirculation. With repeated freeze-thaw cycles, maximum destructive effects are produced.

## Physical events during freezing

Lowering the temperature of biological systems depresses molecular motion and slows physical and chemical processes in production to the loss of heat. This obeys the **Arrhenius Relationship**[6] which states that the log of reaction rate is proportional to the reciprocal of absolute

temperature. Hence, for every 10°C reduction in temperature, the rate of these reactions decreases by 50%.Freezing of solution cause formation of ice crystals that removes water from the system and since dissolved solutes cannot be incorporated in the crystalline structure, the concentration of solutes continues to rise in the remaining liquid phase.[7]

**Immediate biochemical effects**

The damaging effects of low temperature on cells begin as temperature falls into the hypothermic range. At around -15°C, ice crystals begin to form, initially in the extracellular spaces. As ice crystals form from pure water the extracellular spaces become hypertonic relative to the cell interior resulting in net movement of water from the intracellular to the extracellular space causing intracellular shrinkage and increasing intracellular solute concentration. A reduction of the intracellular pH to a value of 4 or below will cause further damage impairing enzyme systems and affect the lipoprotein components of the plasma membrane containing the cell and its organelles. This biochemical effect possibly has more destructive consequences than the physical effects.[7]

**Immediate physical effects**

With further cooling, ice crystals may form within the cells. Once ice crystals form within the cell, cell death is almost certain. Continuous intracellular cooling eventually reaches the eutectic temperature immediately below which the remaining solvent and solute crystallize simultaneously. Further physical damage ensues as the cryolesion is allowed to thaw. Slow thawing leads to recrystallization with larger, stable crystals, which are highly destructive over the longer time period.[7]

**Delayed effects**

The delayed effects of freezing are caused by vascular changes, in particular platelet aggregation and deposition of microthrombi on the vessel wall resulting in narrowing and obstruction of the vascular lumen. This process increases permeability of the vessel wall and edema of the tissues. The loss of blood supply deprives the cell of any possibility of survival. These changes explain the therapeutic value of cryosurgery for the control of surface bleeding.

The shape of the cryolesion will depend on the shape of the probe and on the proximity of blood vessels traversing the tumour. Studies have shown using thermography that the ice ball is rarely hemispherical. Hence, the radius of the visible surface will not necessarily provide an accurate guide to the depth of the lesion. As a rough guide, the depth is likely to be about two thirds the radius of the surface ice ball if the probe or spray is applied at one point only. Liquid nitrogen is the only cryogen which can possibly meet all the demands.[7]

**Cryogens**

Cryogen is a term used for materials used specifically for the purpose of generating low temperatures. The choice of cryogen in cryosurgery is very important, as the result of the procedure is directly related to the lowest temperature delivered to the whole of the abnormal tissue. Freezing to -30°Cor below at the rate of 100°C per minute will cause over 90% cell death. Most cryogens used are in the liquid phase and remove heat (via heat of vaporization) while maintaining a constant temperature, during the transition to the gaseous state. There are a number of cryogens, which have been used in cryosurgery including nitrous oxide, liquid nitrogen, carbon dioxide and argon (Table 1).

**Table 1: The commonly used cryogens**

| Cryogen | Boiling Point |
|---|---|
| **Liquid nitrogen (most commonly used)** | **-196°C** |
| **Nitrous oxide** | **-89°C** |
| **Solidified $CO_2$** | **-78°C** |
| **Chlorodifluoromethane** | **-41°C** |
| **Dimethyl ether and propane** | **-24°C, -42°C** |

**Cryosurgical apparatus**

**A. Liquid Nitrogen Cryoprobes**

In liquid nitrogen cryoprobes the liquified gas is allowed to boil within the tip of the instrument and in doing so absorbs its latent heat of boiling from this region. It is an efficient method of cooling, because for every gram of liquid nitrogen that boils in the tip, 209 J of heat is

absorbed in turning the nitrogen from liquid to gas at the boiling point.

### B. High Pressure Cryoprobes

High pressure cryoprobes utilize controlled expansion of a high pressure gas or liquid to cool the cryoprobe. A high pressure fluid is allowed to escape through a narrow orifice and expand into the tip cavity. This process is known as a **Joule-Thomson expansion**.
Table 2 summarizes the temperatures achieved for different fluids, assuming they are expanded through an orifice from their bottle pressure to atmospheric pressure. Nitrous oxide is a widely available gas in hospitals and also is an excellent refrigerant.[2, 7]

**Table 2 : Thermodynamic Properties of some of the fluids used in high pressure cryoprobes**

| | Freon 12 | Freon 22 | $CO_2$ | $N_2O$ |
|---|---|---|---|---|
| **Cylinder pressure at 20°C (atm)** | **5.8** | **9.3** | **57.2** | **51.6** |
| **Temperature after Joule-Thompson expansion (°C)** | **-29.8** | **-40.8** | **-78.5** | **-88.5** |
| **Latent heat of boiling (J/g)** | **167** | **234** | **574** | **376** |

### C. Liquid Nitrogen Sprays

A potent method of cryosurgery is to use liquid nitrogen in the form of a spray. The liquid again cools by absorbing its latent heat of boiling from the tissues, but in this case, the boiling takes place on the tissue surface rather than inside a cryoprobe tip.[2, 7]

## 8. Cryosurgery of benign oro-facial lesions

Cryosurgery may be used for the local destruction of most of the benign soft tissue lesions found in the oral cavity and has shown cost effectiveness with low morbidity.

### Vascular lesions

Some dramatic results have been achieved in the treatment of recurrent hemorrhagic pyogenic granuloma, haemangioma, fibroangioma and lymphangioma by cryotherapy. When these lesions are treated by two applications of a suitable high pressure nitrous oxide Amoils cry probe, excellent final results have been obtained.[8]The specific advantages of cryosurgical treatment of vascular lesions are the relatively few recurrences, generally low morbidity, relative freedom from scarring after healing and the facility to treat recurrences with ease and little or no resistance on the part of the patient. In addition to direct cellular damage by freezing, cryosurgery stimulates the thromboembolic phenomenon in the tissue surrounding the treatment area, generating a tissue slough effect that is highly desirable in the treatment of vascular lesions.[9]

### Diffuse epithelial lesions

Irregular irritative hyperplastic lesions of the sulcus, associated with chronic irritation from denture flanges, can be managed simply and effectively by cryosurgery. This modality is especially indicated in medically compromised patients where postsurgical haemorrhage and infection must be avoided at all costs.

### Cryotherapy for the Treatment of Verrucous Epidermal Naevi

Cryosurgery is an extremely effective therapeutic modality for the treatment of epidermal naevi. The low cost, the simplicity of the technique and the good cosmetic result makes cryosurgery an excellent therapeutic modality for the treatment of epidermal naevus.[10]

### Intraoral erythroplakia and lichenoid lesions

Until the development of oral cryotherapy, there was no simple and generally effective method of treatment for these potentially malignant or premalignant lesions.

### Lichen Planus and Lichenoid-Like Lesions

These lesions respond quickly to 2 x 30 sec freeze-thaw applications of the cryoprobe given to initiate healing of the lesion. While cryotherapy, in such cases, is regarded as palliative, not curative, it has had a place in the relief of pain even though the course of the dermatological disorder has not been significantly altered in the long term.[7]

### Oral leukoplakia

Cryotherapy has frequently been reported to be an effective therapy for oral white lesions which can be identified by no other description than leukoplakia. The advantages of cryosurgery by comparison with excision or electrocautery are simplicity, the relative absence of peri and postoperative pain and bleeding, the steady, infection free period of repair and the absence of scarring in the healed tissues.[7] When leukoplakia involves the gingiva, cryosurgery should be considered the treatment of choice. In addition, cryosurgery can potentially be used in the treatment of other gingival conditions.[11]Cryosurgical treatment of mucosal carcinoma should only be applied if the chances for an operation are restricted by certain factors, for instance poor general condition of the patient or haemorrhagic diathesis. The advantages of cryotherapy as applied to the oral mucosa rest in the bloodless application of this technique and in the possibility to heal with tender scar formation.[12]High-risk lesions should be treated similarly except that the freeze cycle should be extended to 3 min and repeated three times rather than twice. Marked erythema and local swelling may follow this treatment. The slough separates within a week leaving a clean granulating surface that quickly heals by epithelialization. The treated area may exhibit variable paresthesia for weeks or months, depending on the relationship of the ice ball to major sensory nerves in the peripheral tissues. This regimen has been reported to produce excellent clinical results in many studies from different parts of the world.[13]

**Extravasation Cysts of Minor Salivary Glands**

These lesions may be treated more successfully by electrodesiccation, but this technique demands the local infiltration of an anesthetic agent and is also accompanied by most offensive odors of charring which may upset nervous, young patients. Simple application of the cryoprobe to the centre of the mucous cyst, without prior application of a local aneshtetic and freezing of the mucus in the cyst with a 1.5 min freeze are sufficient to destroy the cyst lining and associated secretory gland.[7]

**Oral Inflammatory Hyperplasia**

It is possible to conclude that cryosurgery is an effective therapy for up to 12 mm long pedunculated hyperplasias and can be considered an alternative, useful, fast and painless method for treatment of inflammatory hyperplasia.[14]

**Verrucous hyperplasia and verrucous carcinoma**

Treatment of verrucous hyperplasia and verrucous carcinoma by shave excision and simple cryosurgery is a simple and effective treatment method. Surgery has been used widely however those with wide involvement often make the total excision difficult. Shave excision and simple cryosurgery offers satisfactory results without resorting to complicated surgery and / or use of sophisticated equipment.[15]

**Healing after Cryo-application:**Normal healing is seen between second to fourth weeks post-operatively after last cryo-application.[16]

**Oral cancer**

Cryosurgery may represent an alternative modality of treatment in oral cancer, as palliation in high surgical risk patients and after failure of conventional surgery, radiation therapy or chemotherapy. In selected patients, cryosurgery may even represent the treatment of choice. In an advanced stage of the disease cryosurgery may interrupt sensitive neural fibers thus reducing the pain as well as the need for analgesics; the tumour burden is reduced as well as local invaliding symptoms, thus allowing for a transient but almost normal lifestyle. The selection of patients for primary cryosurgery should be restricted to patients without lymph node metastasis and with the following co-morbidity factors:

• Patients with inoperable malignant tumours at other sites
• High-surgical-risk patients due to cardiac or pulmonary insufficiency or with serious clotting deficits
• AIDS patients with a high morbidity rate

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 occurs. Post-operative edema is rather serious and a post-operative tracheostomy may be required in some patients with large tumours or with tumours in the posterior part of the oral cavity.

**Head and neck mucosal melanoma**

Cryosurgery can be effective in the treatment of mucosal melanoma of the head and neck.

Cryosurgery is a good palliative procedure for inoperable or recurrent disease; the peculiar features of this neoplasm make it particularly freezesensitive so that the application of the cold temperature very selectively destroys the neoplastic tissue as compared to other tumours.

**Epidemic kaposi's sarcoma**

Epidemic Kaposi's Sarcoma is associated with AIDS. Cryosurgery has been proposed as a palliative measure in localized disease due to the possibility of performing the treatment under local anesthesia, the easiness of subsequent cryosurgical applications and the limited postoperative pain or bleeding complications.[2]

**Cryosurgery of bone tumors**

In benign and low-grade malignant stage skeletal tumors it is used as an adjuvant treatment to intra-lesion resection. The advantage of this kind of treatment, as compared to local resection, is that as much as possible of the supportive function of bone is preserved and reconstructive surgery can be limited.

**Clinical Results:** In general following bone tumors are suitable for cryosurgery:

- Simple bone cyst
- Aneurysmal bone cyst
- Giant cell tumor
- Eosinophilic granuloma
- Enchondroma and chondrosarcoma grade 1
- Fibrous dysplasia
- Odontogenic Keratocyst

**The use of Liquid Nitrogen Cryotherapy in the Management of Locally Aggressive Bone Lesions**

Cryosurgery is an acceptable method for locally aggressive bone lesions that fall short of true malignancy but have a high incidence of local recurrence following local enucleation or curettage only.

A wide spectrum of surgical treatment has been used for the odontogenic keratocyst. The more aggressive approach to this lesion has been advocated because of its known high rate of recurrence. Combinations of enucleations and liquid nitrogen cryotherapy may offer patients improved therapy in the management of odontogenic keratocysts. Advantage of liquid nitrogen is that it maintains the osseous architecture and facilitates new bone formation.[18]For locally aggressive lesions larger than 4.0 cm in greatest diameter, simultaneous cancellous bone grafting following enucleation and liquid nitrogen cryosurgery will decrease the risk of complications and result in greater residual bone height and a better ability to place endosseous dental implants.[19]

**Complications of cryosurgery**

**Immediate and common**

- Pain during the freezing and thawing period
- Blister formation
- Intradermal hemorrhage
- Edema

**Immediate and less common**

- Headache affecting forehead, temples and scalp
- Syncope

**Delayed and rare**

- Postoperative infections
- Hemorrhage from the wound site
- Pyogenic granuloma

**Prolonged and rare**

- Hyperpigmentation
- Milia
- Hypertrophic scars
- Neuropathy

**Permanent**

- Hypopigmentation (common)
- Ectropion and notching of eyelids
- Notching and atrophy of tumors overlying cartilage
- Tenting or notching of the vermilion border of the upper lip
- Atrophy
- Alopecia

Nerve conduction can be affected by cryotherapy its advantage has been taken in the management of trigeminal neuralgia and other painful conditions.[20]

**Acute Total Body Hypothermia in Cryosurgery**

When performing large volume cryoablation, however, there is a real threat of severe complications due to acute total body overcooling of the patient, which is clinically termed cryogenic shock (Morris 1998) which is typical response of the human body to acute total body hypothermia (ATBH).[2]

**Future of cryosurgery**

Computer treatment planning for cryosurgery is an area of research and development that will greatly assist the practicing physician and will promote improved quality assurance for clinical procedures.Additional studies are needed to determine the effectiveness of cryosurgery in controlling cancer and improving survival. Data from these studies will allow physicians to compare cryosurgery with standard treatment options such as surgery, chemotherapy, and radiation. Moreover, physicians continue to examine the possibility of using cryosurgery in combination with other treatments[21]Good planning and precision image-guided treatment delivery are complementary in achieving an optimal treatment outcome. State-of-the-art cryosurgery treatment planning systems are at an early stage of development in comparison with radiation treatment planning systems for external beams.[19]Fractional cryosurgery is the new technique which has the ability to measure skin surface temperature during cryotherapy.[7]

## CONCLUSIONS

Cryosurgery is a safe and effective method of treatment for many benign soft tissue lesions in the oral cavity. Vascular lesions, viral warts, leukoplakic lesions and cysts of the minor salivary glands have all been treated with convenience to the operator and minimal morbidity for the patient by cryosurgery. Under certain conditions and for specially responsive lesions cryosurgery is at least as effective as the surgical scalpel in the oral cavity. Treatment may be applied on a simple outpatient basis, on repeated occasions, over long intervals and with few severe side effects and minimal complications. Frail and anxious patients may be treated. Bearing in mind the limitations, there is no doubt that pain relief, reduction in the bulk and infection from fungating tumours makes cryosurgery a worthwhile procedure.

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