

# Applications of Cryotherapy in Oral and Maxillofacial Surgery: A Review

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**Abstract:** Cryotherapy is a therapeutical freezing method that is used to obtain a tissue inflammation and/or a destructive response. It is well accepted by patients due to lack of discomfort, absence of bleeding and minimal or no scarring after healing. It has been used for several conditions in oral cavity. Oral cavity is both humid and smooth, which is ideal site for this technique. It shows a very good aesthetic result and it may be either the first or an alternative choice to conventional surgery. This article reviews various indications, limitations and advantages of cryotherapy in oral and maxillofacial surgery.

**Keywords:** Cryotherapy, Cryosurgery, Freezing, Thawing, Cryogens

## 1. Introduction

Cryotherapy is derived from the Greek word “kryos” means frost <sup>[1]</sup> thus, it is local destruction by freezing. Local application of low temperature was first used by Egyptians for pain relief, then during Franco-American war for amputated limbs <sup>[2]</sup>. James Arnott(1851) was the first one to report and demonstrate this freezing therapy by using a mixture of salt and ice in malignant disease <sup>[3]</sup>. Initially, its use was limited to oral cavity and cancer of lip but now its use has expanded to head and neck regions <sup>[4]</sup>. Also, cryotherapy can be recommended after physical injuries and various surgical procedures.

### Cryogens:<sup>[5]</sup>

Cryogenic liquids or cryogens are liquified gases that are kept in their liquid state at a very low temperature. The word “cryogenic” means producing or related to very low temperatures. They have a boiling point below -150° C. All cryogenic liquids are gases at normal temperatures and pressures. These gases must be cooled below room temperature before an increase in pressure can liquefy them. Different cryogens become liquids under different conditions of temperature and pressure, but all have two properties in common: they are extremely cold, and small amounts of liquid can expand into very large volumes of gas. The commonly used cryogens include liquid nitrogen(-196° C), nitrous oxide(-89° C), solidified CO<sub>2</sub>(-78° C), chlorodifluoromethane(-41° C), dimethyl ether and propane(-24° C, -42° C) <sup>[5]</sup>.

### Principles of Cryotherapy:<sup>[4]</sup>

The basic technique of cryotherapy stresses rapid cooling, slow thawing and repetition of the freezing process to maximize tissue destruction. Two methods are recognized, they are as follows:

- 1) A closed system- This is based on three principles mainly: thermoelectric, evaporative and Joule-Thompson effect. It uses probes and nitrous oxide, when depth orientation is required<sup>[2]</sup>.
- 2) An open system- It is the direct application of liquid nitrogen spray or by cotton pellets, the heat is released by vaporization due to drop in temperature. Used when no control over depth is required<sup>[6,7]</sup>.

The physical principle behind cryotherapy is based on Joule-Thompson expansion which enables substances to undergo a drop in temperature when moved from high pressure area to lower pressure area <sup>[4,6,7,8]</sup>. When nitrous oxide is released from the high pressure to lower pressure cryotip, there will be drop in temperature which results in freezing of tissues<sup>[7]</sup>. The biophysical changes in tissue due to cooling are vasoconstriction, which reduces bleeding, decreases secondary hypoxic injury, inflammation, fluid retention due to inflammation thereby reducing oedema and increases pain threshold. When tissue temperature is reduced and maintained in the same temperature for more than 15 minutes it causes cold induced vasodilatation followed by initial vasoconstriction. The vasodilation is due to release of substance “H” a substance similar to histamine this again followed by vasoconstriction which attributed to low the warm blood in this area. This cycle keeps repeating continuously and is known as “hunting response”. The peripheral nerves will undergo an impeded or blocked synaptic transmission due to altered transmembrane ionic flow which results in altered conduction of velocity and synaptic activity. Cold facilitates alpha motor neuron activity and decreases gamma motor neuron firing, thus this property reduces spasticity temporarily<sup>[4]</sup>.

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**Stages of Cryotherapy (Hocutt et al. 1982) <sup>[9]</sup>**

**Stage 1** -Sensation of cold 1-3 min

**Stage 2** -Aching or burning 2-7 min

**Stage 3** -Local numbness 5-12 min

**Stage 4** - Deep dilation >12 min

It has been suggested that after an injury >12 min should be used to attain stage 3.

**Cryolesion Dimensions**

Cryolesion dimensions are dependent upon three variables: the temperature of the cryotip, the period of contact and the area of contact between the tip and tissue<sup>[6]</sup>. Temperature of the probe tip contributes to the size of the freeze ball and the velocity of freezing within cells.

**Mechanism of Tissue Death:<sup>[10,11]</sup>**

There are various distinct mechanisms by which tissues may be damaged by freezing. These mechanisms co-exist at the time of a single cryosurgical treatment, and since the preponderance of each varies according to the apparatus used, the physical nature of the tissues being treated, the distance from the cryoprobe, and the rate and degree of cooling, an understanding of these mechanisms enables one to vary the technique according to the nature, site and depth of the lesion to be treated<sup>[10]</sup>.

Effects on the tissue following cryosurgery are as follows:

**Direct effects**

- 1) Ice crystal formation - Rapid cooling causes formation of ice crystals from intracellular and extracellular fluid resulting in physical disruption of cell<sup>[10,11]</sup>.
- 2) Cellular dehydration and electrolyte disruption - Initially during freezing the extracellular fluid alone forms ice which is limited by intracellular fluid and there is increase concentration of electrolyte in the extracellular fluid this causes movement of intracellular fluid to extracellular spaces where they again form ice crystals. This results in dehydration of cell, cell shrinkage, intracellular increase in electrolyte which is toxic to the cell and all together causes cell death.
- 3) Thermal shock - Damage to the cell membrane due to freezing occurs and this alters cell permeability leading to cell death.
- 4) Inhibition of enzymes - Each enzyme requires particular temperature for their functioning which when altered prevents their function.
- 5) Effect on proteins - During the phase after cooling when the cells return to normal temperature imbibes more water as it has high concentration of electrolyte which result in swelling and rupture<sup>[12]</sup>.
- 6) Effects of Thawing - When the freezing process stops and the tissues are allowed to rewarm, further damaging effects may take place. If the intracellular water was supercooled, then on thawing, ice crystals form leading to damage from crystallization. Also, because of raised concentrations of intracellular electrolytes, there is water intake in the cells, which then vacuolate, swell and rupture<sup>[12]</sup>. A slow thaw prolongs these damaging effects.

**Indirect effects**

- 1) Vascular effects - Ischemic necrosis results due to vascular thrombus and micro-thrombus formation<sup>[13]</sup>.

- 2) Immunological effect -Massive release of pathological cell antigen occurs making them susceptible for host surveillance mechanism.

**2. Instrumentation**

The application of cryotherapy to the mouth requires equipment with following capabilities:

- 1) The cold source must be small and sufficiently maneuverable to reach the various parts of mouth.
- 2) It must be controllable to the extent that selected areas can be frozen without damaging the nearby structures.
- 3) Should maintain the required temperature for as long as required.
- 4) Temperature of the cold source should be variable.
- 5) Rate of thawing should be controllable.
- 6) Should be fitted with thermocouple so that temperature at the tissue surface can be easily read by surgeon<sup>[14]</sup>. (Figure: 1)



**Figure 1:** Armamentarium. (A): Cryosurgery using liquid nitrogen, (B): Cryogun

**Variables in Cryotherapeutic Technique: <sup>[1,2]</sup>**

- 1) Type of apparatus -For most superficial oro-facial lesions, probes operating on the Joule-Thompson or evaporative principles are satisfactory. For papilliferous or invasive lesions, liquid nitrogen sprays may be preferred since it is difficult to obtain uniform contact with a probe.
- 2) The rate of cooling -This is the most important factor in efficient cryonecrosis. Below,  $-30^{\circ}\text{C}/\text{sec}$ , it has been shown to that tumour destruction is more efficient with rapid cooling rates, probably because of cell damage by intracellular ice crystallization is more lethal than damage by dehydration and electrolyte disturbance.
- 3) Temperature achieved - It is achieved by selecting a large probe by repeating the freeze-thaw cycle and ensuring an intimate probe-tissue contact.
- 4) The duration and repetition of freezing - Most mucosal leukoplakia respond to two freeze-thaw cycles of 45-60 seconds each. Large cavernous haemangiomas are usually frozen in about  $1-1\frac{1}{2}$  minutes. Basal cell carcinoma with raised beaded margins usually responds to two applications of  $1\frac{1}{2}$  minutes. Invasive neoplastic tissues require three freeze-thaw cycles, each of  $2\frac{1}{2}$ -3 minutes duration. During repeated freezing and thawing, tissues are frozen at successively more rapid

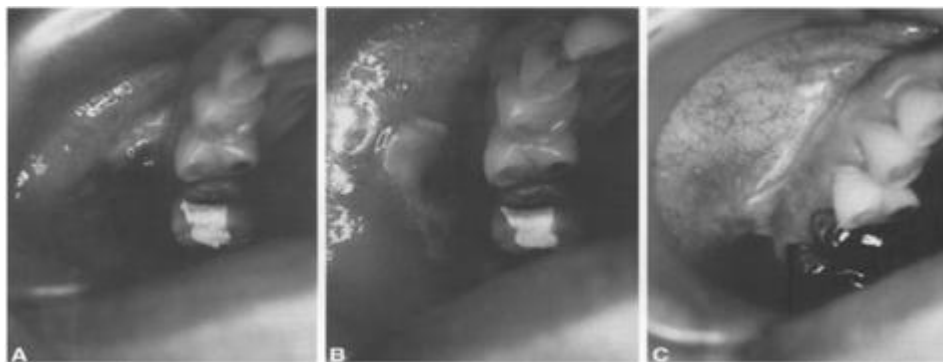
rates so that each zone is subjected to more than one mechanism of damage.

- 5) The re-warming phase -Active damaging events takes place during the thawing of frozen tissues so; a slow thaw is more effective than a rapid thaw.
- 6) Volume of tissues - This may be increased by firmly pressing the probe to invaginate the surface before freezing commences or decreased by applying traction on the probe as soon as it is adhered to the surface.
- 7) Other ancillary measures - The freezing effect may be enhanced by reducing the blood supply to the part by prior injection of vasoconstrictor agents, digital compression of afferent vessels, etc.

**Applications of Cryotherapy in Oral and Maxillofacial surgery:**<sup>[11,15]</sup>

**1) Vascular malformations:**

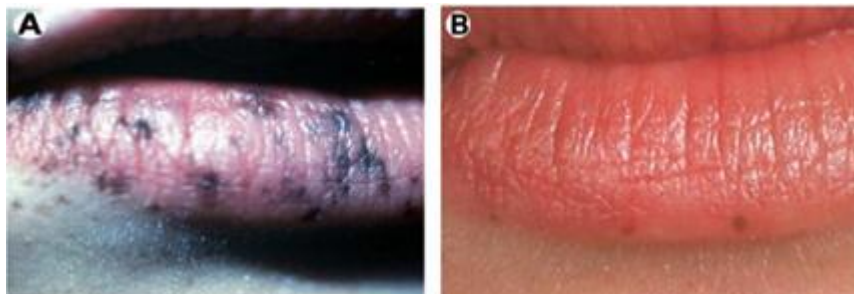
**Cavernous Hemangioma:** Cryosurgery produces complete regression of these malformations, whether of skin or of mucosa, with minimal scarring. Two freeze thaw cycles of 1½ minutes each are usually sufficient. **Nevi:** the nevi are emptied by compression with the probe before and during treatment. It is very effective in strawberry nevi where there is lot of bleeding, ulceration. Capillary nevi respond to cryosurgery<sup>[15]</sup>. The most satisfactory technique is to freeze the entire nevus site by site for 2-3 seconds only. A second freeze is applied for approximately 10 seconds. By restricting freezing duration, scarring can be avoided. **Lymphangiomas:** they are less responsive to cryosurgery so; a combined excisional and cryosurgical approach is useful sometimes. (Figure: 2, 3, 4)



**Figure 2:** Application of cryotherapy on hemangioma. (A): Hemangioma on right upper vestibule of a 45-year-old woman, (B): Appearance of lesion one week after treatment, (C): Appearance of cryosurgical site six weeks after treatment. Minimal scar could be identified.



**Figure 3:** Application of cryotherapy on hemangioma. (A): Preoperative view, (B): Application of liquid nitrogen via the utilization of large contact tip of lesion, (C): Necrotic and sloughing area at the post-operative first week, (D): the view of complete healing was observed with minimal scar formation one month after cryosurgery

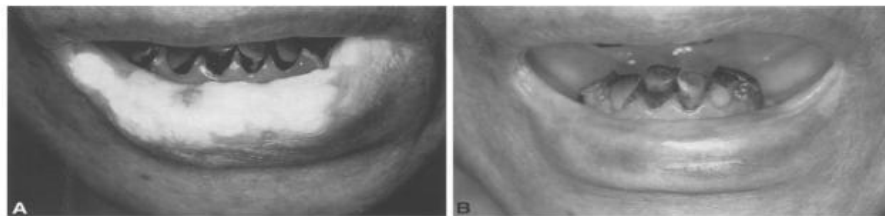


**Figure 4:** Melanotic macule of lower lip with cryotherapy. (A): Pre-operative view, (B): Post-operative view

**2) Hyperkeratosis and leukoplakia:**

Cryosurgery is a simple and effective means for fissured or granular types of leukoplakia and also for thick plaques as well as in cases in which candida are found. Following

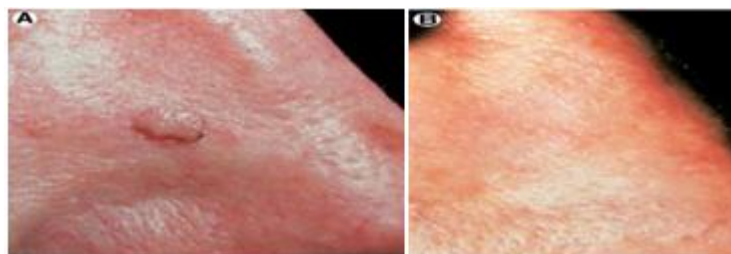
biopsies, each area is given two freeze thaw cycles of 1½ minutes depending on site and thickness of lesion<sup>[2]</sup>. (Figure: 5, 6, 7)



**Figure 5:** Application of cryotherapy on leukoplakia. (A): Leukoplakia involving whole lower lip of a 65-year-old man, (B): Six months after treatment



**Figure 6:** Application of cryotherapy on leukoplakia. (A): Leukoplakia lesion at the angle of mouth being treated using cryoprobe, (B): Frozen appearance of lesion after cryosurgery



**Figure 7:** Seborrheic keratosis treated with cryotherapy. (A): Pre-operative view, (B): Post-operative view

**3) Granulomatous and hyperplastic conditions**

It is a satisfactory alternative to excision or cautery for the treatment of papillary hyperplasia of the palate, fibrous epulis, fibroepithelial polyps, myeloid epulis and viral warts [2,11]. Denture hyperplasia: Simple excision leads to loss of sulcus depth, which results into more radical approach to the problem, such as vestibuloplasty. In elderly and debilitated, cryosurgery may be used. Necrosis of the hyperplastic tissue can be achieved by minimal alteration of sulcus depth [2].

**4) Mucus cysts and polyps:**

They respond to cryotherapy without recurrence and scarring, hence well accepted [16]. (Figure: 8,9)

ball formed during treatment, (D): Appearance of lesion 1 week after treatment, (E): Two months after treatment. Complete disappearance of lesion without scar formation.



**Figure 8:** Application of cryotherapy on mucocele. (A): Mucocele on the lower lip of a 17-year-old boy, (B): Application of liquid nitrogen with a cotton swab, (C): Ice



**Figure 9:** Application of cryotherapy on mucocele. (A): Mucocele on lower lip, (B): Border marked, (C): Application of cryoprobe, (D): Snowball formation, (E): Immediate postoperative view, (F): 1-day postoperative view

**5) Erosive conditions**

A few cases of long-standing erosive lichen planus have been successfully treated with cryosurgery.

**6) Intractable facial pain:**

Lloyd *et al.*<sup>[17]</sup> reported the use of cryoanalgesia in various forms of chronic facial pain. A reliable, prolonged, reversible nerve block is achieved by a simple technique which does not aggravate symptoms. Postoperative pain is minimal and there is return to normal sensation in the distribution of peripheral nerves which have become incidentally incorporated in cryolesion. Bradley *et al.* reported the return of sensory function of inferior alveolar nerve over 3-6 months following cryosurgery<sup>[18]</sup>.

**7) Intractable temporomandibular joint pain:**

AN Gross used cryoneurotomy to the TMJ capsule and/or great auricular nerve. The patients had severe pain complicated by failed previous treatment, analgesic abuse or psychiatric problems. The patients had excellent relief for 1 year following cryoneurotomy<sup>[19]</sup>.

**8) Cryotherapy and oral cancer:**

In established oral carcinoma, cryosurgery is at best a means of localized tissue destruction in superficial accessible lesions. Its use has been mainly confined to recurrent or persistent growths following surgery and/or radiotherapy. It is used as a treatment choice in recurrent nasopharyngeal carcinoma<sup>[20]</sup>. Also helps in management of radiation mucositis.

**9) Cryotherapy and basal cell carcinoma**

Although surgical excision and radiotherapy are well tried and carry a good prognosis, in certain circumstances, there is danger to surrounding structures, for example, rodent ulcers at the inner canthus. It is a sound alternative provided the tumour has not invaded deeper structures. (Figure: 10)



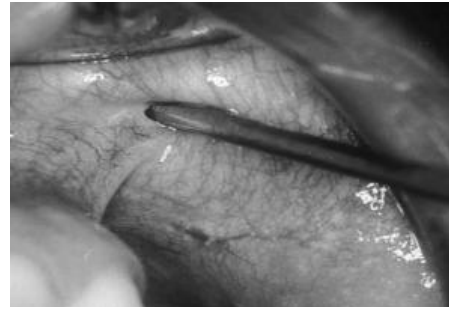
**Figure 10:** Auricular basal cell carcinoma treated with cryotherapy. (A): Preoperative view, (B): Post-operative view after 1 week of treatment, (C): 6 weeks after treatment.

**10) Cryotherapy and herpetic or aphthous ulcers:**

Used for eradication, by conversion of specific ulceration to a non-specific traumatic ulcer which heals more rapidly<sup>[21]</sup>.

**11) Cryotherapy and trigeminal neuralgia:**

Treatment of genuine trigeminal neuralgia is a step-by-step procedure. Among them in 1976, Lloyd *et al.*<sup>[22]</sup> described the use of cryotherapy to eliminate pain in peripheral nerves. Good results were achieved with open nitrogen spray, the so-called spray-freezing, of the infraorbital nerve<sup>[23]</sup>. (Figure: 11)



**Figure 11:** Cryoprobe at infraorbital foramen during performing cryotherapy.

**12) Cryotherapy and third molar surgery:**

Surgical removal of impacted third molars constitutes a large proportion of maxillofacial surgery procedures. Cryotherapy referring to local or systemic application of cold for therapeutic purposes has long used to control inflammation, pain and oedema in addition to reduction of spasticity and facilitation of movement. It leads to slowing of nerve conduction velocity resulting in analgesic response to cold and increased pain threshold, decrease in muscle spasticity, slowing in metabolism rate and control of haemorrhage<sup>[24,25]</sup>.

**13) Cryotherapy and odontogenic keratocysts:**

Cryotherapy leads to minimal amount of bleeding and scarring<sup>[7]</sup>.

**Healing after cryotherapy:**

The epithelial basal layer is severely damaged after cryotherapy, whereas the parabasal and intermediate layers of epithelium are affected less. Re-epithelization occurs within 7-12 days in the mouth and 10-20 days on the skin. Bone gets devitalized by cryotherapy and the dead bone acts as a segment for future bone growth. Only cells in cortical bone may undergo death, cells deeper in the marrow cavity may survive to promote growth<sup>[4]</sup>. Freezing to  $-30^{\circ}\text{C}$  close to a developing tooth causes death of ameloblasts and odontoblasts, but the cellular components are replaced within 2 weeks<sup>[26]</sup>.

**Advantages:**<sup>[27]</sup>

- 1) Minimal or no pain.
- 2) Less discomfort, no hospitalization is required.
- 3) Predictable, low tissue damage.
- 4) Minimal or no scarring.
- 5) Can be an adjunctive therapy with surgery or radiation therapy in malignancy.
- 6) Safe, easy to perform, inexpensive.
- 7) No need to suture.
- 8) No anaesthesia.

**Disadvantages:**<sup>[2,28,29]</sup>

- 1) Healing is slow often results in ulceration in about 3-5 days of time. Healing by secondary intention<sup>[28]</sup>.
- 2) In lesions of tongue the procedure can limit its function.
- 3) Volume of lesion can be beyond capacity<sup>[29]</sup>.
- 4) Extensive lesions are difficult to treat<sup>[29]</sup>.
- 5) Cryosurgery is non-specific in its destructive effects<sup>[2]</sup>. Because of the flow rate in larger arteries, it is virtually impossible to freeze these structures using surface contact probes.

**Complications:**<sup>[10,24,30]</sup>

- 1) After pain
- 2) Vesicle formation
- 3) Exposure of bone if probe is applied to areas with thin mucoperiosteal areas such as mucosa over lingual aspect of mandible.
- 4) Scarring of facial skin if freezing is done for more than 20-30 seconds. Healing occurs with reduction in pigmentation in such cases. After a few months, it is difficult to detect.
- 5) The late complications include pseudo epithelioma hyperplasia, post-surgical infection, fever and pyogenic granuloma. There are some permanent complications like hypopigmentation, atrophy, alopecia and ectropion when performed near eyes.

**Contraindications:**<sup>[11,15]</sup>

- 1) Cold urticarial where patient develops redness and swelling in the skin.
- 2) Cryoglobulinemia where abnormal blood protein results in formation resulting in ischemia or gangrene.
- 3) Raynaud's phenomena.
- 4) Paroxysmal cold haemoglobinuria where haemoglobin is released from lysed red cells and is excreted in urine.
- 5) Peripheral vascular disease.
- 6) Patients with platelet alterations or with multiple myeloma.

**3. Conclusion**

Cryotherapy is a very safe, easy to perform, and relatively inexpensive technique for treating various oral lesions in an out-patient clinic. It is advantageous over surgery and well accepted by patients. Many a times it is used when the conventional therapy either fails or is contraindicated. But unless the physician is confirmed of the diagnosis and volume of lesion is not advisable to use it.

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