Review on Methodology of Cryosurgery and Different Types of Cryosurgical Techniques

Gaurang K Dabhi

Master in Thermal Engineering, Mechanical Engineering Department, A D Patel Institute Of Technology, Gujarat, India

ABSTRACT

Cryosurgery dates back to the 19th century, with the description of the benefits of local application of cooling for conditions such as pain control. Once commercial liquefied gases became available, more progress was made in the use of cryotherapy for localized lesions. As understanding of disease response to freezing increased, safer techniques for performing freezing procedures helped prepare its clinical application in different clinical situations, such as prostate disease and bronchial cancers. Cryosurgical techniques are less invasive and have lower morbidity compared with surgical resection. However, the use of cryosurgery has been limited by a lack of good understanding of the underlying mechanisms of tissue destruction. To apply cryosurgery clinically, and to extend its use, it is important to understand the mechanisms of freeze injury on cells, and to control the thermal parameters.

Keyword: *Cryosurgery treatment, Cryobiology, Cryoprobe, Heat Transfer, Freezing*

1. INTRODUCTION:

Cryosurgery is a form of surgical treatment that utilizes biological freezing phenomena to remove undesirable tissue. The advantages of cryosurgery include less invasiveness, minimal blood loss, and fast recovery times. The cryoprobe was first invented by cooper et al. in 1964 and has since played an important role in cryosurgery. Currently, cryoprobes are cooled by the Joule-Thomson effect of high-pressure gases. Cryosurgery (also known as cryotherapy or cryoablation) is an elegant method that has become an important form of medical surgery. It utilizes extreme cold temperature to destroy diseased tissues in the body. The first use of cryosurgery is started in year 1840 by Arnott using iced saline solution at -20°C temperature to treat uterine and breast cancers. When cryogens are applied on to the tumor skin by various cryosurgical methods extracellular ice formation starts followed by the intracellular ice formation. Cryosurgery or cryoablation is widely used in various medical fields like oncology, dermatology, urology, gynecology, neurosurgery etc. Using cooling as the means to destroy cancerous tissues, modern cryosurgical method represents many remarkable advantages over its competitive modalities. The purpose of this cryoprobe is to treat relatively large cancers as liver, prostate, and kidney cancers; therefore, they require high cooling power. However several drawbacks of such cryoprobes exist, including the temperature controllability, flexibility, and the size of the cooling section.

1.1 Cryosurgical Cooling Technique

The acceptance of cryosurgical technique has extraordinarily increased with the superior understanding and expansion of the procedure. Cryosurgery has been utilized as new strategy to treat skin variations like angiomas, keloids, boils, carbuncles, keratosis etc. using cold temperatures. These cryosurgical systems can be comprehensively arranged under three heads:

1. Cotton swab method
2. Cryogenic spray

3. Cryoprobe

1.2 Mechanisam

1. Effects of cooling

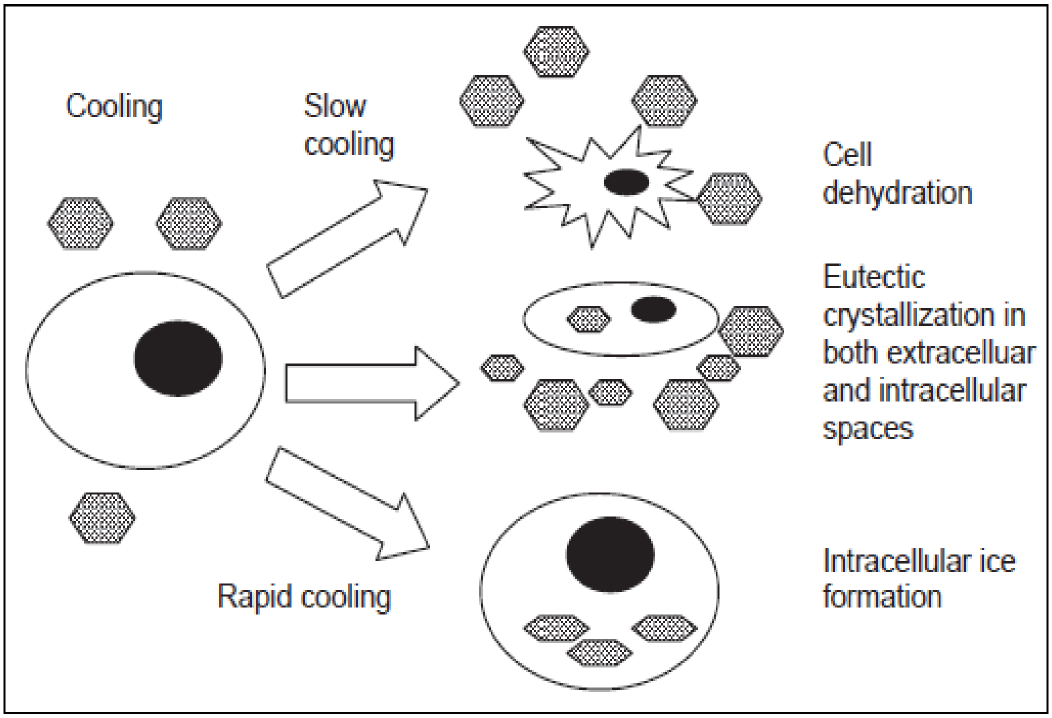
In general, most mammalian cells can withstand low, non-freezing temperatures. However, these conditions can affect several aspects of cell function. The cell membrane is a lipid bilayer structure with proteins spanning across it. The cell membrane, in general, is impermeable except where membrane proteins allow mass transfer to occur. At low temperatures, the lipid transforms into a gel phase, or a structure with low free energy. During this process, the membrane proteins become separated and lose their ability to control mass transfer. The membrane becomes more permeable and allows ions to transfer in and out of cells more easily. As a result, the ionic composition of the cells changes and damage occurs. Meiotic spindles are known to be sensitive to hypothermia, resulting in tubulin depolymerization. In a study using human oocytes cooled to 0°C for 2 min to 3 min, the meiotic spindle shortened and disappeared after 10 min (1).

2. Effects of freezing

Extensive studies have been performed to understand the effect of freezing on biological tissue. One hypothesis is directcellular injury from the extracellular space (Figure 1). The cell injury that occurs after freezing is thought to result from a high solute concentration causing cell dehydration (2). Intracellular ice formation causing intracellular organelle and cell membrane disruption has also been implicated (3). Another theory is that freezing may stimulate immunological injury. It is believed that the immune system becomes sensitized to the destroyed frozen tissue, and any tissue left behind is attacked by the host's own immune system after cryosurgery. However, the relevance of immunological injury is still controversial (4,5). Finally, it has been theorized that freezing involves vascular injury (6). The hypothesis is that freezing results in stasis of blood flow, particularly in the capillaries. The resulting ischemia leads to tissue necrosis. It is important to bear in mind that, unlike cryopreservation, where cells are frozen in vitro under uniform conditions and then stored frozen for long periods of time, tissue subjected to cryosurgery is frozen in vivo and its cells experience a wide temperature gradient.

3. Effects of thawing

The effects of thawing depend on the previous cooling rate. It is known that slow thawing allows solute effects and maximum ice growth during recrystallization to take place. Because solute effects and ice growth are deleterious to cells, complete thawing before the start of another cycle is important in determining the success of cryosurgery for oncological conditions (7). However, rapid cooling followed by rapid thawing can also be beneficial. During rapid cooling, the ice crystals tend to be small, with high surface energies. The longer the time of thawing, the easier it is for the ice to recrystallize, especially for crystals with high surface energies. The larger ice crystals can be more destructive than the smaller ones, because of the size of the crystals or the forces generated during recrystallization. This is shown by the fact that red blood cells tend to have higher survival rates when cooled and warmed faster, or vice versa (8).



[Diagram of the mechanisms of freezing injury. During slow cooling, ice forms in the extracellular space because of the elevated solute concentration in the unfrozen fraction. This leads to cell shrinkage. When the temperature is further decreased, allowing the initiation of eutectic crystallization in the extracellular space, the temperature and concentration of the intracellular space may allow eutectic crystallization to occur in the intracellular space. Alternatively, if the cooling rate is rapid, the cells are not able to lose water fast enough to maintain equilibrium, resulting in intracellular water becoming supercooled and eventually frozen. Hexagons represent ice crystals(7,8)]

1.3 Heat Transfer During Surgery

Cryosurgical methods are stranded on well recognized scientific principles for demolition of clinically-localized tumor. Cryoablation is a thermal therapy in which heat (thermal energy) will be extracted from the targeted tissue resulting in a series of destruction of cells. The rate of heat transfer decides the rate of tissue cooling. There will be an increase in heat transfer if one can have a high temperature gap between cryogen and tissues. For e.g. when the temperature of liquid nitrogen (−196 °C) contacts the skin at (35 °C).

Heat transfer during cryosurgery basically occurs by two methods:

1. Boiling heat transfer:
   In this method Cryogenic fluid gets in touch directly with tissue. Tissue loses their heat, while the cryogenic fluid heats up and evaporates. This is the process which occurs during spraying a cryogenic fluid on a tissue (cryospray freezing technique).
2. Conduction heat transfer:
   In this method direct contact with tissue is made by using a cryoprobe, molecules of solid body transfer heat in the form of kinetic energy to molecules of additional body.

- **Qi et al., 2005** [9] proposed a novel LN_2 cryoprobe in which the inlet handle and heat transfer segment can be detached. This adjustable construction provides many varying features, such as good maneuverability and high safety. The wall temperatures of the cryoprobe at different locations are measured in the gel, air and brine solution. The effect of various driven pressure ranging from 0.3 to 0.6 MPa had studied and results are shown in Fig. 2.1. It is found that precooling time of the probe operating at 0.6 MPa is reduced significantly. The heat flux transfer from the atmospheric air or brine solution to the cryoprobe is evaluated and it is found that the boiling pattern in the cryoprobe is film boiling. He also suggested some of the possible heat transfer enhancement technique like use of the helical coiled wire inserts, micro-fin and the swirl generators. He also found that the temperature at the tip cryoprobe is higher than that of wall temperature of the cryogenic section in the gel, opposite to what he had expected. The temperature at the tip of cryoprobe can decrease to –40°C in the gel, but the temperature at the location of 25 mm in cryogenic section can reach up to –140°C as shown in Figure 2.1. The dominant reason for this phenomenon will be formation of gas layer at the tip of cryoprobe which act as a thermal resistance.

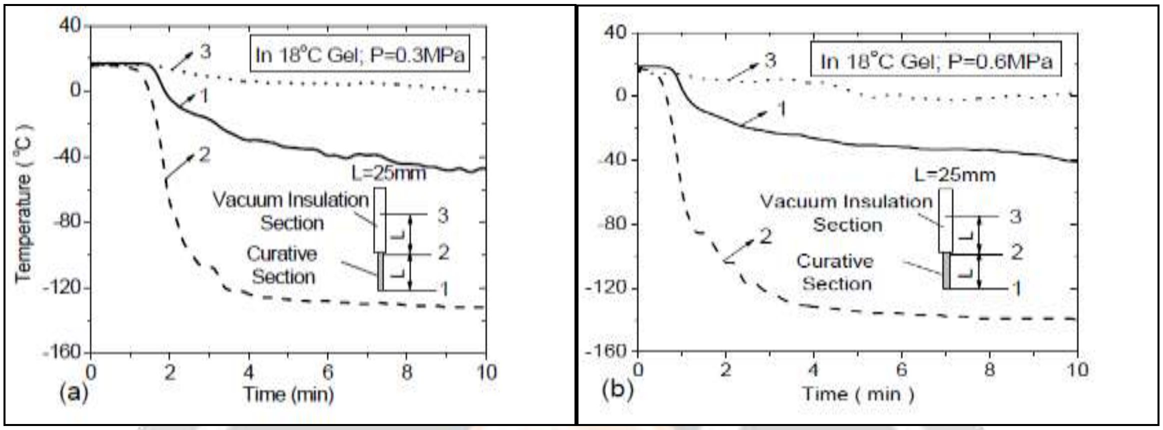


Figure 2.1: The temperature history of the wall of the cryoprobe in the 18°C gel with different driven pressure: (a) P=0.3 MPa; (b) P=0.6 MPa [9]

- **Aihara et al., 1993** [10] introduced flexible long slender cryoprobe with a vacuum insulation of outermost diameter 3.1 mm having length 1m. The tip of the cryoprobe was cooled by a micro impingement jet of LN_2. He investigated boiling heat transfer of the micro-impinging jet in three types of probe tips: hemispherical surface, flat surfaces and flat surface without needle. He founds that probe tip with the hemispherical surface finished shows the best freezing performance for cryosurgical treatment. He obtains the maximum cooling heat flux of $1.5MW/m^2$. The effect of mass flow rate was carried out by experimentation and concludes that as the mass flow rate is increased, the heat transfer coefficient increases and the critical heat flux also becomes high. He also studied the effect of jet mouth-to-tip distance and surface roughness on boiling heat transfer. As the distance between jet mouth and probe tip will decreased the heat transfer coefficient increase because the impinged layer of liquid nitrogen breaks the vapor layer halted at the tip of cryoprobe.
- **Qi et al., 2006** [11] experimentally studied the effect of cryoprobe with HTEC (heat transfer enhancement configuration) and evaluates its freezing performance. He has taken total two types of heat transfer enhancement configurations: (1) coiled wire insert and (2) helical mesh insert.

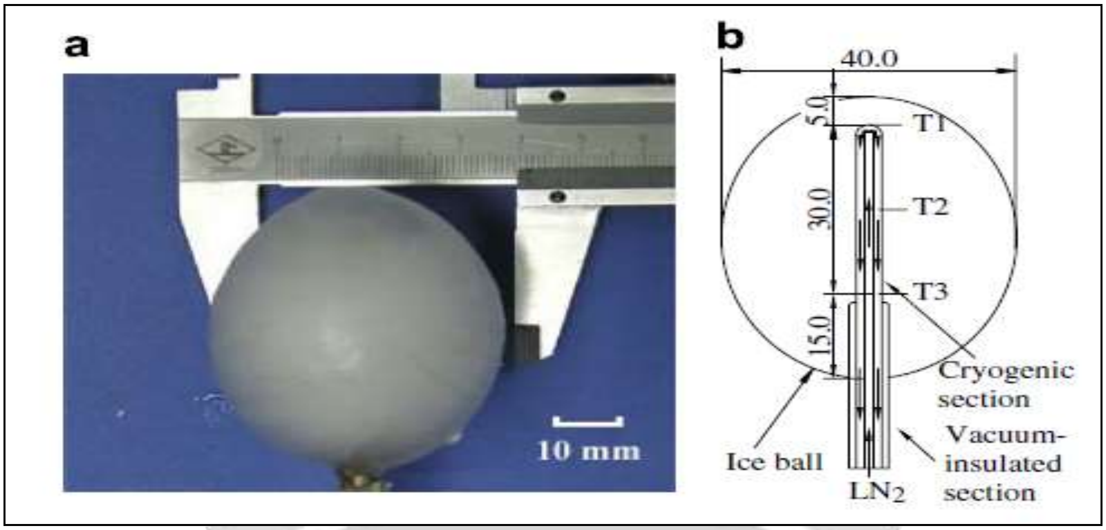


Figure 2.2: The ice ball forms around the cryogenic section in 290 K brine solution in 30 min with pressure of 0.6 MPa for cryoprobe without HTEC [11]

He founds that the enhancement of the freezing capacity with the coiled wire insert is less superior to that with the helical mesh insert. The cooling capacity of the cryoprobe can be increased by 41% with heat transfer enhancement configuration. He suggests that the cryoprobe with heat transfer enhancement configuration has comparable freezing performance to that cooled by subcooled liquid nitrogen. He had taken the Outer probe diameter of cryogenic section as 2.5mm and that of vacuum insulated section diameter as 5mm. The length of cryogenic section is taken as 30mm. He founds under working pressure of 0.6 MPa, there will be an ellipsoidal ice ball will be forms in 290 K brine solution within 30 min for the cryoprobe without heat transfer enhancement configuration. The lengths of the minor and major axis of the ice ball are about 40 mm and 50 mm respectively.

- **Lam et al., 1998** [12] studied the size, shape and temperature zones within the cryolesion and evaluation of single versus repeated freeze–thaw cycles. He has taken a needle cryoprobe having diameter of 3mm. carried out an ex vivo analysis on porcine liver tissue equilibrated to 37°C in a water bath. Experimentally he founds that after 15-20 minutes of freezing shape of cryolesion will be cylindrical. He suggested that single continuous freeze produces a large amount of cryolesion than two freeze–thaw cycles of the same freezing duration. Also concludes that ex vivo experiment does not provide actual diameter and volume of cryolesion due to absence of blood flow while performing cryosurgery on porcine liver.

- **Young et al., 2009** [13] made cryosurgery in ex vivo porcine kidney, using in vitro gel and in vivo porcine kidney models. He suggested that by using multi-point temperature sensing probe one can improve the accuracy of the procedure. Since, Cryosurgery account as a minimally invasive surgery for treatment of various types of skin diseases and cancers. Surprisingly, regardless of increasing demands for cryosurgery, there has been limited innovation has been made in the design of cryoprobes.

- **Tanaka et al., 1982** [14] had studied immunological aspects of cryosurgery. During experimental studies on animal found that cryotherapy augments cryoimmunologic reaction. The use of proper immunopotentiators with cryotherapy brings strong antitumor process, yields increase in life span of the animals. To achieve most benefits of cryosurgery, the immunological background of patient should be studied. The most effective form in which to evoke cryoimmunologic reaction is still not known.

- **Har-Shai et al., 2007** [15] evaluate the effect of skin pigmentation during intralesional and contact cryotherapy of keloids. The temperature on the surface of skin was measured by using Ni/Cd thermocouple. The thermal history of both method was evaluated by measuring cooling rate, end temperature, hold time and thawing rate. The slower cooling rate and thawing rate was obtained while performing intralesional cryosurgery. The 91.7% of keloids have a significant hypopigmentation while using contact type cryosurgical method. There will be a no mark of hypopigmentation was noticed in intralesional cryosurgical treatment. They concludes that intralesional cryosurgery provides better survival rate for melanocytes compare to that of contact cryosurgical method.

- **Scala et al., 2006** [16] performed a cryosurgery on advanced malignant melanoma for facial skin. He had studied biological implication of cryosurgery in specific neoplasm and reported a feasibility and tolerability of technique. He founds that treatment was well tolerated and have a good aesthetic results. The patient was disease and recurrence free after two years of cryosurgical treatment. They concludes that cryosurgical treatment is feasible for neck and head melanoma.

2. APPLICATION OF CRYOSURGERY

There are most important and wide areas of medical science in which cryosurgical treatment are applied:

1. General surgery
2. Dermatology
3. Oncology, including surgery of the breast
4. Urology
5. Neurosurgery
6. Plastic (including cosmetic) surgery
7. Thorax surgery
8. Orthopedics
9. Gynecology

The cryosurgery is used in treatment of both surface lesions, benign tissue lesions and malignant tumor. The cryospray method has been widely used by dermatologist for the treatment of skin tumor like warts and actinic keratosis. Shockingly, there has been limited advancement in the design of cryoprobe particularly in solid tumors (e.g., breast, prostate, and lung cancers). The current work of developing liquid nitrogen cryoprobe offer potential for future preclinical and clinical testing in solid cancers.

3. BENEFITS OF CRYOSURGERY

1. Surgery without bleeding.
2. Surgery without the scalpel.
3. Prevention of metastasis at time of excision of tumor - there is no "cutting".
4. There are no scars formation and have a good cosmetic results.
5. There will be a short duration of surgery.
6. There will be a high rate of curative success, short hospital stays, lower hospital costs, as well as increased quality of life for the patient.

4. CONCLUSIONS

Various investigators have studied the mechanism of cryosurgery and the effect associated with it. The cryosurgical method is investigated experimentally in which parameters investigated are freezing rate, thawing rate, effect of LN_2 pressure, effect of tip of cryoprobe, effect of mass flow rate and effect of jet mouth to tip distance. Prediction of formation of cryolesion while performing cryosurgery is very difficult task. The depth of cooling is increased while performing second cycle of in vivo study and thawing rate should be as slow as possible for effective cryosurgery. The following points are concluded from the literature review for cryosurgical phenomenon:

- This study shows that cryoprobe performance mainly depends upon inlet fluid (cryogen) and the contact surface area with biopsy.

- A formation of vapor layer at tip reduce the performance of LN_2 cryoprobe.

- Hemispherical tip will be more advantageous compare to that of flat surface.
- An intracellular ice formation will be more lethal compare to extracellular ice formation.
- A healthy tissue resist the freezing formation compare to that of neoplastic tissue.

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