**Comparative analysis of the cryogens used in cryomedical applications**

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Low temperature medicine or cryomedicine is becoming a wide appreciated therapy method in rheumatology, dermatology, gynecology, surgery and sport medicine. Cryomedicine can be divided into cryotherapy and cryosurgery. The paper gives the overview of the methods, equipment and cryogens used in cryotherapy and cryosurgery. The cryosurgical apparatuses are usually supplied with liquid nitrogen $LN_2$ or compressed nitrous oxide $N_2O$. We have experimentally investigated the thermal interactions of both cryogens with a tissue during a simulated cryosurgical intervention. The conclusions concerning the applicability of both cryogens and related equipment used in specific cryosurgical interventions have been formulated.

## INTRODUCTION

Low temperatures are used in many different branches of science, technology and medicine. It has been known for a long time that low temperatures alleviate pain, decrease swelling and bleeding. The effect of low temperatures does not encumber the blood circulatory system and does not cause side-effects. Low temperatures can be applied with ice, cold compress or sprays both in the first aid and in an ambulatory treatment. The use of low temperatures in medicine can be in treatment (cryosurgery), rehabilitation (cryotherapy) and diagnostics (magnetoresonance tomography – cooling of superconducting magnets by liquid helium). Biological specimens can be kept for a long time in liquid nitrogen or in solid carbon dioxide.

To provide sufficient heat transfer intensity for medical treatment of the tissue, the temperatures lower than 200 K should be applied. The cryoliquids have boiling temperatures lower than 200 K but not all of them are convenient for medical applications. The temperatures of liquid helium, hydrogen and neon are too low for precise control of heat exchange during cryo-treatments. Besides helium, neon, argon and xenon are very expensive. Liquid hydrogen and methane can generate explosive mixture with air. Oxygen is chemically active and it is a powerful oxidizer. Therefore for medical application only nitrogen, nitrous oxide and carbon dioxide are commonly used in practice.

## CRYOTHERAPY

Cryotherapy is a stimulating therapy (cryostimulation), where a patient body is subjected to an effect of low temperature (as a rule below 150 K) within less than 3 – 4 minutes, in order to activate defensive reactions. These reactions are therapeutically beneficial and very effective in restoring the natural balance of the organism. There are two main ways of cryotherapy specified in medical nomenclature: whole body cryotherapy and local cryotherapy.

### Local cryotherapy

During local treatment (Figure 1) only a part of the body, like a joint or a muscle, is affected by low temperature. Cryotherapy is an effective way to support physiotherapy of moving organs.
The most important therapeutic effects are:

1. Raise of pain level threshold,

2. Muscle's tension decrease,
3. Muscles strength and joints mobility increase,
4. Shortening of convalescence time after contusions.

Besides nitrogen, carbon dioxide and nitrous oxide, the cryotherapy apparatuses can be supplied with cold air (cooled down in a compressor refrigerating system). A small group of cryotherapy equipment presents thermoelectric modules based on the Peltiere effect.

Whole body cryotherapy

Whole body cryotherapy treatments are carried out in cryochambers (figure 2a). A cryochamber consists of two rooms, vestibule and main cabin (figure 2b). The vestibule is a transitional room where temperature level is of about 210 K (- 60ºC). It is a place where the patients can get used to much more extreme thermal conditions. After about 30 seconds spent in the vestibule the patients proceed into the main cabin. In cryochamber main cabin the temperature is maintained from 150 K (-120ºC) to 110 K (-160ºC) [4]. One session of the whole body cryotherapy can last no more than 3 minutes. The heat exchangers in cryochambers are supplied with liquid nitrogen. One working hour of a cryochamber requires of about 90-100 $dm^3$ of $LN_2$. The air vented into both cabins is purified, dried and cooled down in a dedicated installation located outside the cryochamber.

Figure 1. Local cryotherapy (courtesy Kriosystem Ltd.)

Figure 2a. Cryochamber view (courtesy Creator Ltd.)

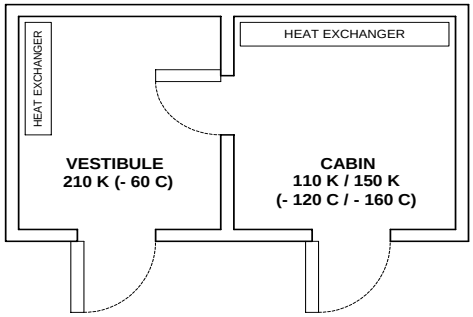


Figure 2b. Cryochamber scheme

CRYOSURGERY

The necrosis temperature of the majority of human cells is 250 K, on the condition that the fall of the temperature is fast, about 1 K/s. When the decrease of the temperature is significantly slower, the cells die in the temperature below 235 K. Therefore this effect has found the application in cryosurgery, which is the therapeutic use of cold to induce tissue necrosis with ablative intent. The first report of the use of local freezing as a treatment modality is attributed to Dr James Arnott [1], who described in 1850 the direct application of a salt-ice mixture to various skin lesions. For almost a century, cryosurgery was practiced by a handful of surgeons. Thanks to the development of cryogenics, easily available liquid gases have replaced the salt-ice mixture. Cryosurgery is now used in many medical fields e.g. dermatology, neurosurgery, gynecology, urology, ophthalmology and oncology. There are three methods of cryosurgery treatment: direct evaporating, spray and contact method [3].

Direct evaporating method

In this method a small amount of cryoliquid is applied directly on the surface of a pathology tissue.
Usually a sterile wooden rod with a cotton ball on its end is used as cryogen applicator. When the cotton ball contacts with a surface of the tissue the cryoliquid will evaporate and it will cool down the tissue. This method is easy to practice, but the heat capacity of the cotton ball is small and it can be used only for local, shallow and small pathologic changes. Due to its availability and low price, liquid nitrogen is used in this method.

Spray method

In this method liquid refrigerant is sprayed directly on the surface of the tissue. Cryogen evaporates very fast and cools down rapidly the tissue. The cryoliquid in spray apparatus should be under pressure to

create a jet when relieved from the vessel. Cryosurgery sprays are fed with liquid nitrogen, nitrous oxide or carbon dioxide.

Contact method

The method is similar to spray way of cryo-treatment. It can be applied by use of the same apparatus, but with different, closed applicator. The heat exchange proceeds through the wall of the applicator contact surface. In this method the liquid does not come into direct contact with the tissue.

## CRYOSURGERY EQUIPMENT

The cryosurgical apparatuses are usually supplied with liquid nitrogen $LN_2$ or compressed nitrous oxide $N_2O$. The liquid nitrogen is stored in a dewar and transferred to cryosurgical tip, where it is evaporated providing a cooling power at 78 K. The compressed nitrous oxide is stored in a gas cylinder at ambient temperature. To obtain a low temperature source it is throttled at the Joule-Thomson valve, then partly liquefied and vaporized at 185 K. In spite of much higher phase transition temperature in comparison with $LN_2$, nitrous oxide $N_2O$ is often used due to its non-limited storage time in a compressed gas cylinder.

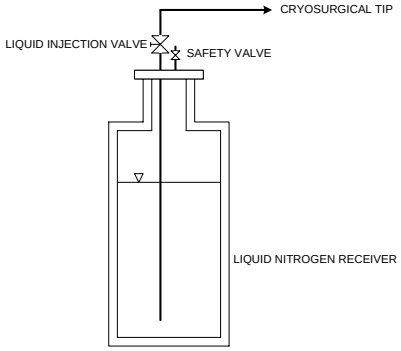


Figure 3. $LN_2$ cryosurgical apparatus

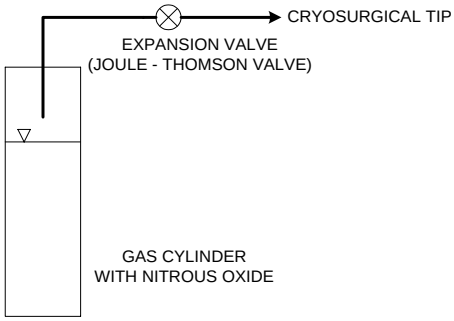


Figure 4. $N_2O$ cryosurgical apparatus

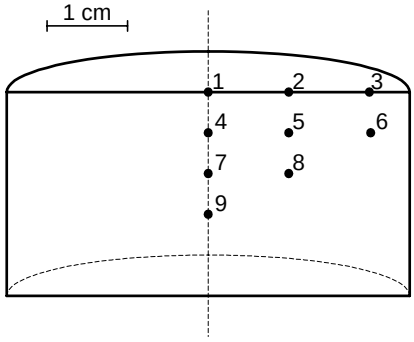


Figure 5. Location of measured points

In spite of the fact that boiling $LN_2$ and $N_2O$ differ in the temperature by about 100 K, both cryogens are commonly used in cryosurgical treatment. We have experimentally investigated the thermal interactions of both cryogens with a tissue during a simulated cryosurgical intervention.

The tissue was modeled with a water-gelatin and the heat transfer between the cryosurgical tip and the solution was measured. We have measured simultaneously the temperature at 9 points (figure 5).

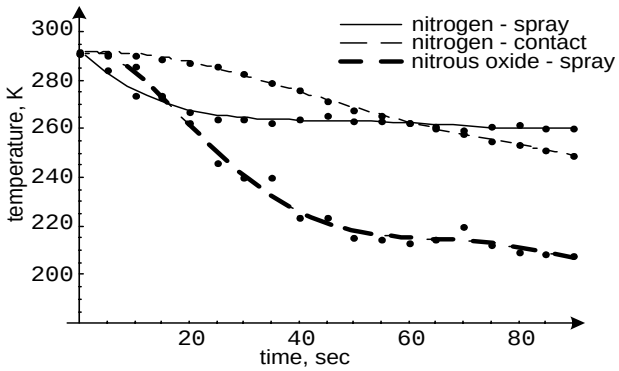


Figure 6. Dynamics of temperature in point 2

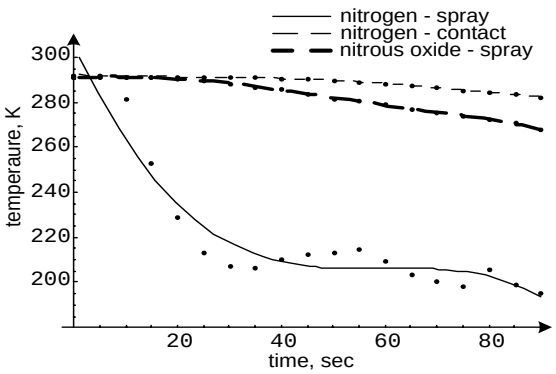


Figure 7. Dynamics of temperature in point 4

Every treatment simulation has lasted for 90 seconds. We have assumed that the cells are dying in 235 K and have tried to find out the dynamic geometry of the tissue frozen to this temperature. In the point 1 we have always measured the temperature lower than 238 K (spray $N_2$ – 158.9 K, contact $N_2$ – 222.4 K and spray $N_2O$ – 190.8 K). The temperature below 238 K has been measured in point 2 (figure 6) only with $N_2O$ spray – 207.8 K (spray $N_2$ – 260.1 K, contact $N_2$ – 248.9 K). The similar result was observed for point 3. It means that the wide pathogenic change should be destroyed with a spray method using a nitrous oxide. The development of temperature measured in points 4 (figure 7) and 7 indicated that

deep changes can be destroyed only by a spray method using liquid nitrogen. If the pathologic cells are located below 1.5 cm, the time of the treatment has to be extended.

A dynamic creation of an ice ball was observed (figure 8), giving the basis for further mathematical modeling of cryosurgical treatment of different morbid changes.

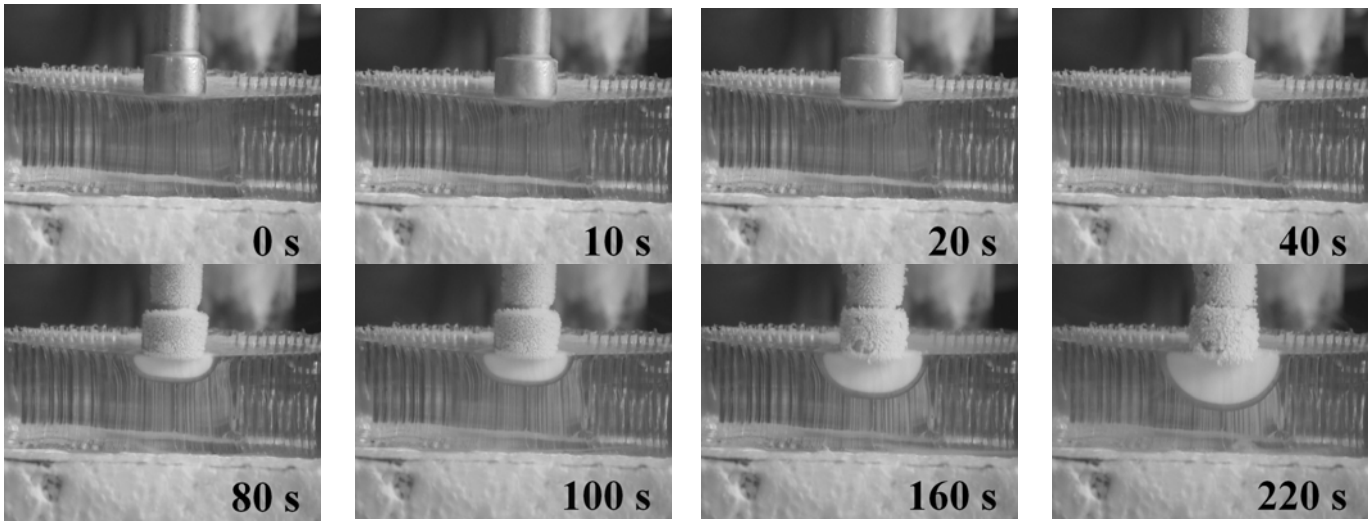

Figure 8. Dynamics of "ice ball creation"

## CONCLUSIONS

Cryosurgical treatments have been simulated using liquid nitrogen and nitrous oxide as the cooling agents. In liquid nitrogen case both spray and contact treatment methods were investigated. On the basics of the obtained results our experiments recommendations of cryosurgical methods and refrigerants suitable for the type of pathogenic changes were formulated – table 1.

Table 1. Summary of cryosurgical treatment recommendations.

| | **NITROGEN** | | **NITROUS OXIDE** |
|---|---|---|---|
| | SPRAY | CONTACT | SPRAY |
| Local surface change (radius up to 0.5 cm) | *** | * | *** |
| Surface change (radius over 0.5 cm) | * | * | *** |
| Changes up to 0.5 cm deep into tissue | *** | * | * |
| Changes up to 1.0 cm deep into tissue | ** | - | - |
| Changes up to 1.5 cm deep into tissue | * | - | - |

Symbols: *** – perfect, ** – good, * – not recommended, - – not applicable

## ACKNOWLEDGEMENTS

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