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Investigation on Performance of a Cryosurgical Probe in Various Feeding and Environmental Conditions

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Abstract

Cryosurgery is a procedure in which diseased tissue is destroyed by freezing. During a strictly controlled process, low temperature is used to separate diseased from healthy tissue with minimal bleeding. It is an effective method that has been applied in many areas of medicine for a number of years, especially in dermatology, oncology, laryngology, gynecology, vascular surgery and ophthalmology. There are many technical solutions—different probes—for applying low temperature to tissue. The detailed construction of the probes are trade secrets and will not be discussed here. In the paper the authors present the results of research on a chosen type of cryosurgical probe for various conditions: feeding gases, flow rates and external conditions. The results are illustrated in the form of graphs showing the temperature of the tip of the probes in changing conditions.

Keywords: Cryosurgery, N_2O, CO_2, Cryosurgical probe, Joule-Thomson effect

1. Introduction

The first to describe the benefits of local application of cold in his work [1] was the doctor James Arnott in 1850. The first clinical application of liquid air was reported in 1899 [2]. Since then various techniques have been reported e.g. [3–5] but the real milestone was the invention of the cryoprobe for treating neural diseases in 1961 by Copper and Lee [6]. After a short time of widespread application of cryosurgery, it began to fall from favor in the 1970s due to the development of new drugs, alternative methods and other drawbacks e.g. the inability to define the freezing region in light of the range of effects on various tissues. Recent developments in the apparatus (PolarCath, small diameter vacuum insulated probes) have renewed the interest in cryosurgery. Technically, cryosurgery is a procedure in which diseased tissue is destroyed by freezing [7]. To achieve cryodestruction of tissue, controlled local hypothermia is required [8]. Very low temperatures are delivered to the tissue by special cryosurgical probes. The surface of the probe in the working area keeps retains low temperature and may damage the cell following different mechanisms such as hypothermia, hyperosmotic environment created by water crystallization in extrcellular spaces (solution-effect damage), ice crystal formation inside the cells, and cellular anoxia [9]. It depends on the temperature and freezing rate. After the freeze-thaw cycle(s) cell metabolism is stopped and consequently the separation of frozen tissue (mostly diseased) from healthy tissue is performed. The working principle of the cryosurgical probe used by the authors is based on the Joule-Thomson effect [10] which describes how most gases cool during expansion. The tip of the probe is cooled by heat transfer between the probe and the working gas. The effect varies depending on the gas involved and can be described by the Joule-Thomson coefficient [11]:

$$\mu_{JT} = \left(\frac{\partial T}{\partial P}\right)_H = \frac{V}{C_P}(\alpha T - 1) \tag{1}$$

where: V—gas volume; Cp—heat capacity at constant pressure; T—gas temperature; P—gas pressure; α—coefficient of thermal expansion

The values of μ_{JT} coefficients vary from gas to gas and also depend on temperature prior to expansion. The coefficient can be either positive when the gas is cooled during expansion, or negative when the gas warms up while expanding, and the sign can also change after reaching the Joule-Thomson inversion temperature. This is illustrated in Fig. 1.

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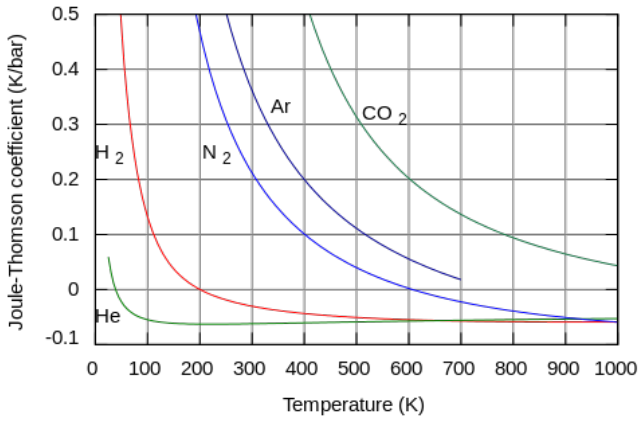


Figure 1: Joule Thomson coefficient for different gases [12]

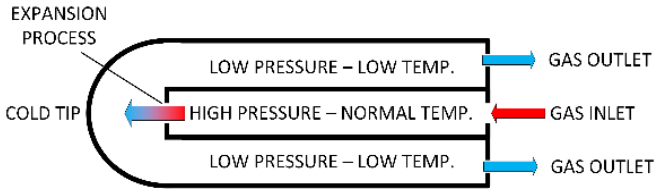


Figure 2: The principle of operation of a cryosurgical probe

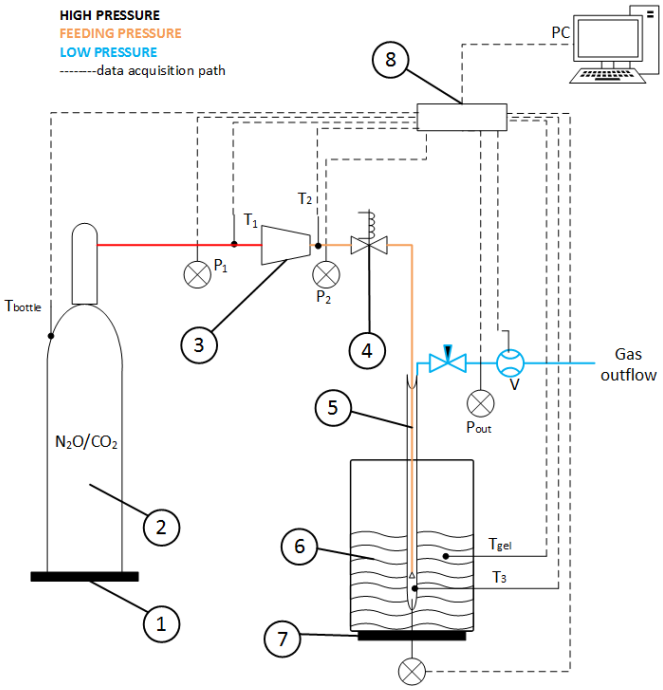


Figure 3: Research stand scheme: 1-bottle heater; 2-feeding bottle; 3-gas regulator; 4-electromagnetic valve; 5-medical probe; 6-tissue simulator; 7-simulator heater; 8-measurement card

Using this effect it is possible to obtain the cooling effect of a probe tip just by the expansion process inside. The most commonly used working medium for medical probes are nitrous oxide (N_2O), carbon dioxide (CO_2), Argon (Ar) and liquid nitrogen. During the research the authors used N_2O and CO_2 due to their low price and ready availability and for safety reasons. Both gases are also characterized by high vapor pressure. This means that when those substances are stored in liquid form at room temperature (290K), the pressure of gases above the liquid surface in the bottle is about 50 bars. Hence the gases can be delivered through pressure regulator into the probe without needing to use pumps, for instance, to increase the pressure. There are many technical solutions—different probes—to apply low temperature to the tissue. The detailed construction of the probes are trade secrets and will not be discussed here, but the general principle of operation is set out in Fig. 2. The working gas is delivered to the probe at high pressure. Inside the probe there is a nozzle which ensures the expansion process goes ahead with a high pressure ratio. During expansion the gas is cooled and due to heat transfer the probe tip becomes cold. As the mass flow rate of a gas is very low, it can be released into the atmosphere with no harm to the environment. Inlet pressure can be adjusted to control the expansion rate and so the temperature of the probe. The mechanical construction of a probe is very simple, but the processes inside the probe—during expansion, cooling and heat transfer—are complicated, so temperature evaluation is problematic. Only a full understanding of the freezing effect on cells and precise control over the thermal parameters can lead to extended clinical application of cryosurgery This work is dedicated to research into the temperature of tips under different inlet conditions.

2. Research stand

The research stand consists of a probe placed in a tissue simulator, feeding and measurement systems and data acquisition. The tissue simulator was composed of a 50-50 mixture of ultrasound gel and water. To obtain more realistic results, the simulator was heated to 36°C by a heater placed inside the tank. The feeding line delivers the working gas from the bottle through a pressure regulator and electromagnetic valve to the probe. After expansion the gas is released into the atmosphere. The pressure inside the gas bottle is controlled by the temperature of the bottle using an ultra-thermostat or heating blanket. Many different sensors and measurement devices are used to measure the required parameters. K-type thermocouples are used to measure the temperatures of the bottle (T_{bottle}), before (T_1) and after (T_2) the pressure regulator, temperature of the tissue simulator (T_{gel}) and the probe (T_3). Piezoelectric transducers are used to measure three pressures: before (P_1) and after (P_2) the pressure regulator and at the gas outlet (P_{out}). Information about the flow rate is obtained from a flow-meter placed in the outlet region. All measurement data are delivered to an acquisition system based on the NI-PXI system and in-house software. The software handles the acquisition, processing and archiving of data and delivers fully automatic control of the stand. It provides relative certainty of common conditions for all experiments and improves the qual-

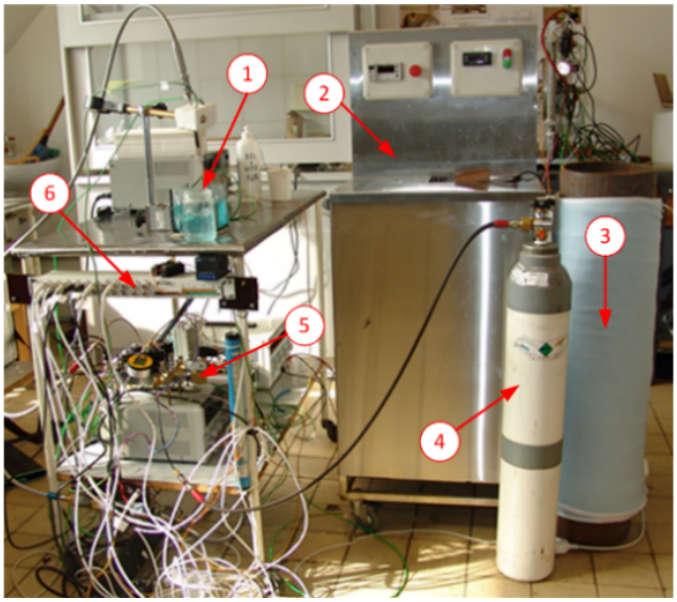


Figure 4: Complete research stand: 1-medical probe in a tissue simulator; 2-ultra-thermostat; 3-cylindrical tank with heating blanket 4-feeding bottle; 5-valves and pressure regulator; 6-Data acquisition bus

ity of results. A schematic diagram of the research stand is shown in Fig. 3. The complete research stand is presented in Fig. 4 with a closer look at the tank with the tissue simulator in Fig. 5 and the probe in Fig. 6.

3. Experimental research

The research was divided into phases that differed in terms of the feeding gas and outlet conditions.

3.1. Temperature of a probe

3.1.1. Nitrogen oxide (N_2O)

In the first phase, research using nitrogen oxide under steady pressure inside the bottle was conducted. In this phase the pressure is 52 bar and corresponds to ambient normal temperature (ab. 290 K). Since the bottle was not thermally stabilized during the research, maintaining a steady pressure was problematic due to the dropping temperature in the bottle during the expansion process. Nevertheless, pressure was maintained to an accuracy of 1 bar. The research was aimed at studying the temperature of the probe tip at different pressures after the pressure regulator (P_2)—so for different mass flow rates. To improve the quality of results 5 experiments were conducted for every batch of settings. Every experiment took 180 s. Data acquisition started 3 seconds before the valve was opened to collect the initial data, with a frequency of 100 Hz. The most important parameters derived during the experiments were: pressure before and after the pressure regulator, temperature of the probe tip and the volumetric flow rate. An exemplary result for a single experiment is shown in Fig. 7. Since the experimental data were taken in time, only mean values from a single second (at the end of the experiment) were taken

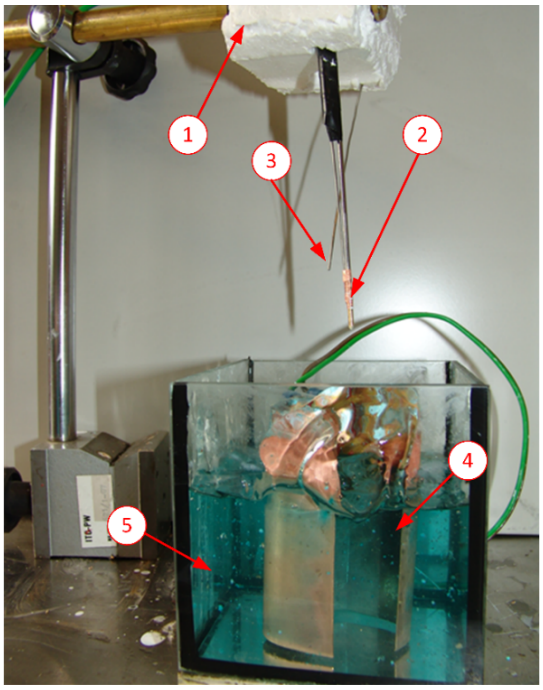


Figure 5: Research stand: 1-probe holder; 2-probe with thermocouple T3; 3-thermocouple Tgel; 4-tissue simulator heater; 5-tissue simulator

into account for the aggregated results. The most valuable outcome are the characteristics of temperature of the probe tip versus the flow rate, as presented below in Fig. 8. A sudden temperature drop is noticeable when the flow rate rises above 300 dm^3/h. The lowest temperatures are obtained for a range of 500-700 dm^3/h of flow rate and are equal to about minus 47°C (226K). The second phase of the research focused on investigating the influence of pressure changes in the feeding bottle. Gas pressure (vapor phase) in a bottle is strongly related to the temperature of the liquid phase, so to control the pressure inside the tank the temperature of the bottle has to be controlled. The temperature of the feeding tank was controlled by placing it in a cylindrical tank filled with water. Water circulated in a closed system between the

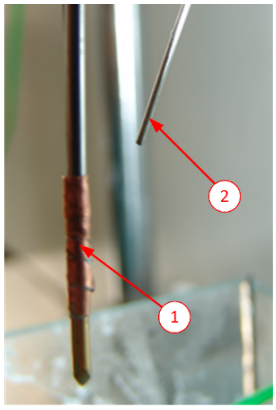


Figure 6: Close-up view of a medical probe: 1-probe with thermocouple attached; 2-thermocouple Tgel

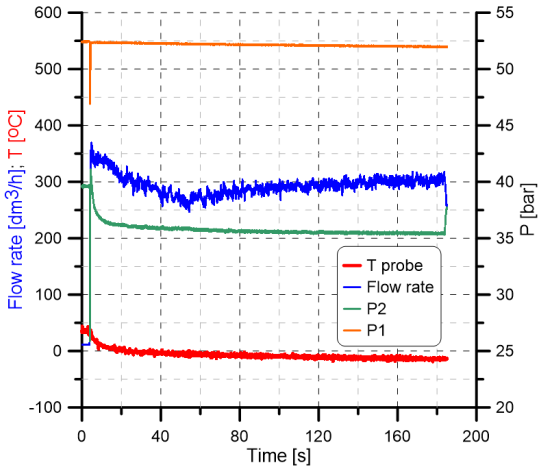


Figure 7: Time chart of different parameters in an exemplary experiment

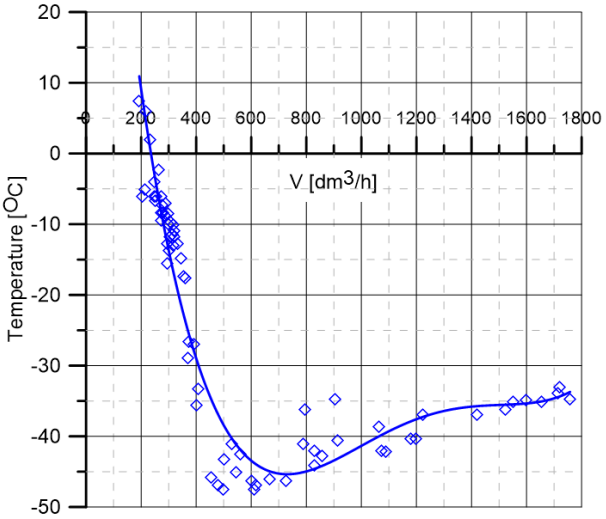


Figure 8: Experimental results for 52 bar pressure

tank and thermostat, enabling precise temperature control. To increase the temperature change rate, a heating blanket was used as well. After achieving thermal balance between the gas bottle and water, it was possible to obtain the steady, required level of temperature inside the tank. Research was conducted at three different levels of pressure in the tank: 45 bar, 52 bar and 60 bar corresponding to the following tank temperatures: 285 K, 290 K and 300K due to data from [13]. For every pressure level in the tank, the feeding pressure was changed by the pressure regulator from 30 bar to the fully opened regulator every 2 bars, to obtain different flow rates. A number of experiments (3—4) were conducted for every batch of settings to improve the quality of research. The results are presented in Fig. 9. For every pressure level inside the tank there is a strong relation between the flow rate and the temperature of the probe. At low flow rates, the temperature linearly decreases with increasing flow rate, obtaining 0°C (273K) at about 150-250 dm^3/h. At about 300 dm^3/h there is a sudden drop in temperature and extreme temperatures appear for about 500-700 dm^3/h. In this range

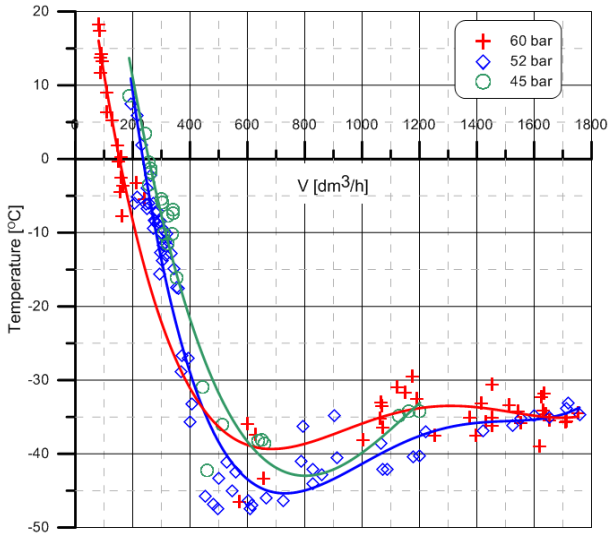


Figure 9: Influence of pressure inside the tank on the temperature of the probe tip at different flow rates (feeding pressures). Trend lines: 4th degree polynomial.

the working region of a medical probe obtains a temperature of about -45°C (228 K). Further increase of the flow rate causes an increase in probe temperature, stabilizing at a level of -35°C (238K). Irrespective of the pressure inside the tank, the character of changes in probe temperatures remains the same. Due to the limited number of experiments it was not possible to illustrate the exact extremum position, which might be useful for the purpose of finding the optimum flow rate. To do so extensive research with an increased number of experiments is advisable.

3.1.2. Carbon Dioxide (CO_2)

The next phase of research was conducted for carbon dioxide as the working gas. The research stand was modified slightly by the addition of equipment enabling photographic documentation of experiments—a digital camera Nikon 3100 with 18 .. 105 mm lens, extra lighting and 1mm grid on the tissue simulator tank, which was used as a reference grid for research on the dynamics of ice growth. The research was conducted in the same way as for N_2O. The probe was changed (to another one which was similar in design—to confirm the repeatability of parameters for various devices) so some experiments for N_2O were repeated in the first stage. For CO_2 the experiments were conducted for two levels of pressure inside the tank—40 bar and 60 bar—also obtained by the temperature control system. Feeding pressure was adjusted by the pressure regulator from 30 bar to a fully opened regulator every 2 bar as in the previous case. The research results are presented in Fig. 10.

It is noticeable that for a common range of flow rate both the character and values of temperature are common, irrespective of pressure in the feeding tank. At 60 bar there is a change in behavior visible on the graph. The “disrupted” values were obtained after a change of feeding bottle. Both bottles were sourced from the same manufacturer and both

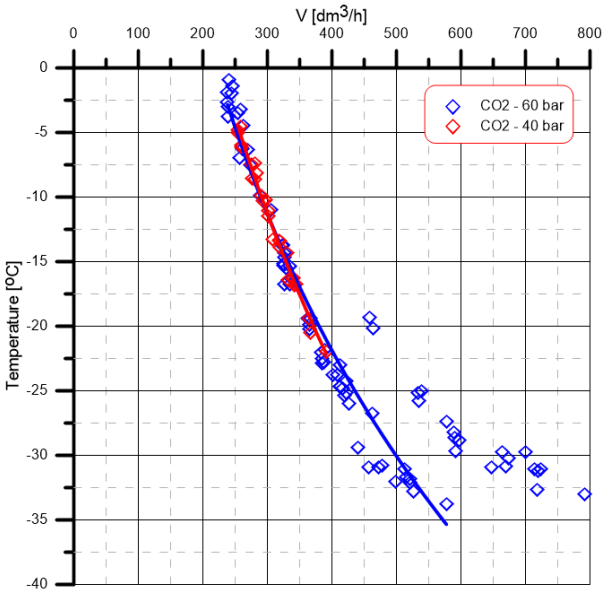


Figure 10: Dependence of probe temperature on flow rate for two pressure levels in the feeding tank. Trend lines: logarithmic ("disturbed" points for CO_2 - 60 bars, not taken into account)

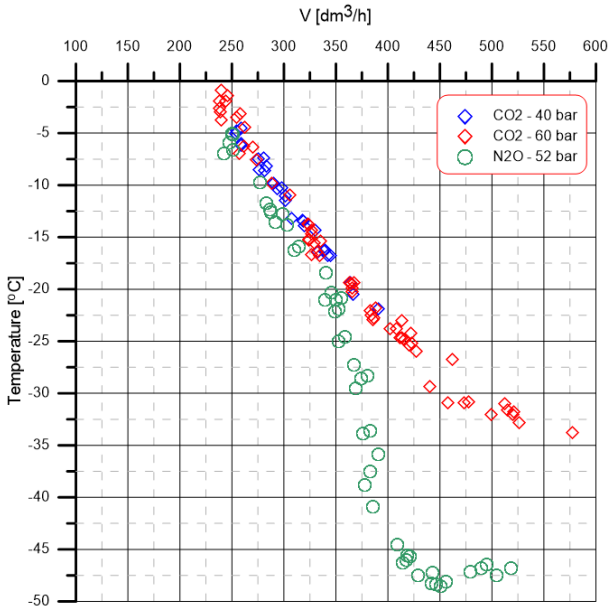


Figure 11: Comparison of the results for two different gases

had to meet the same standards. The only difference between them was the level of the liquid phase—the liquid mirror was higher in the new bottle. The results obtained suggest that the level of the liquid phase might have influenced the performance of the medical probe. Extensive research is required to prove this theory. The results presented in Fig. 11 are obtained for the same probe but for different feeding gases—the results after the change of bottle have been omitted for the purpose of this comparison. The graph shows up several differences. For low flow rates—between 250 and 350 dm^3/h—the temperature for N_2O is lower than for CO_2 and they both decrease linearly with increasing flow rate. The difference is low—about 4°C and almost constant—so it should not have any influence on actual medical use of the probe. For flow rates higher than 350 dm^3/h the temperature change for CO_2 preserves its character and still decreases linearly until it reaches about -32°C for 520 dm^3/h of flow. The temperature of the probe fed by N_2O acts in a different way. After crossing 305 dm^3/h flow the temperature drops rapidly and achieves the lowest temperature of -47°C for 450 dm^3/h flow. This sudden drop was also noticed in the previous stage of research. The difference between temperatures for CO_2 and N_2O in the 450 dm^3/h region differs by about 17°C and it might have an impact on medical procedures—for example freezing time—so it should be taken into account. It is also clear that it is impossible to obtain temperatures lower than -35^{O}C using CO_2 in the investigated range of flow rates.

3.2. Dynamics of ice growth

Some visual measurements were conducted. The data obtained was used to compare the dynamics of ice growth in different conditions. As was proved previously, the pressure inside the tank has no influence on temperatures obtained at the end of the experiment (Fig. 10). To compare the dynamics of freezing, a chart showing the temperature of a probe over time for two different pressure levels inside the tank was drawn up. Feeding pressures were similar in both cases. See Fig. 12 for a comparison of temperature change for different pressures inside the feeding tank. The comparison of the two experiments shows that the temperature drops faster at higher tank pressure, but this difference is very low and has no influence on the temperature achieved at the end of the experiment. This can be confirmed by the photographic documentation. Pictures for chosen points in the experiments are presented in Table 1. Full visual documentation is available from the authors. Ice visibly starts to grow at the tip of the probe 3 seconds after the opening the valve in the case of pressure of 60 bar in the tank. Lowering the pressure to 40 bar increases this time to 5 seconds. However, this time there is a visible difference in the amount of ice at the end of the experiment (180s). The same procedure was followed to visualize the situation of common pressure inside the tank (60 bar) but different feeding pressures (after the pressure regulator).

The dynamics of freezing and the temperatures obtained at the end of the experiment are clearly strongly dependent on feeding pressure. This is due to the different flow rates for different feeding pressures. It also has a major influence on the process of ice growth. The first sign of ice is visible after 3 seconds at feeding pressure of 52 bar, compared to 40 seconds at 34 bar. This difference also affects the amount of ice at the end of the experiment.

3.3. Influence of tissue temperature

In the last stage of research the influence of tissue simulator temperature on the freezing process was investigated.

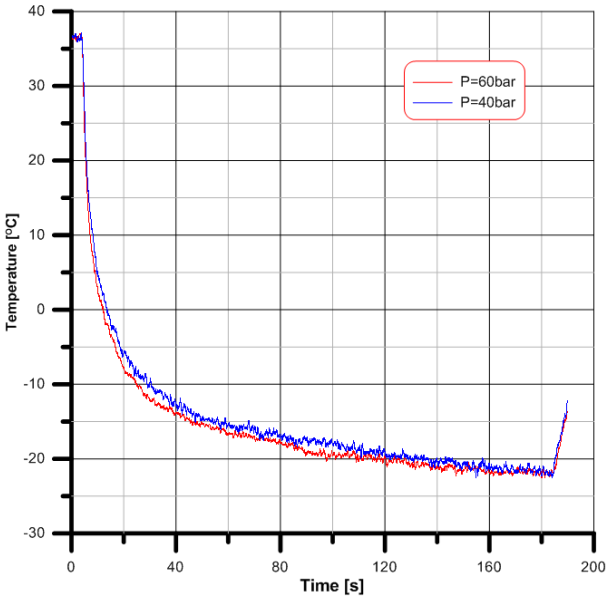
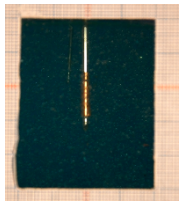
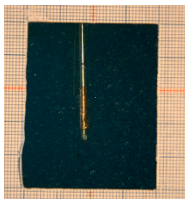
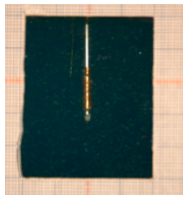
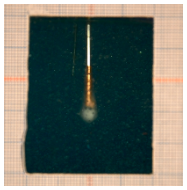
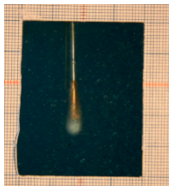


Figure 12: Comparison of the results for two different gases

Table 1: Visual comparison of ice growth for different pressures inside the feeding tank and common feeding pressure

Time, s	P_{tank}=40 bar	P_{tank}=60 bar
3		
5		
180		

Research was conducted for CO_2 common feeding conditions—60 bar in a tank and 58 bar of feeding pressure. The tissue simulator temperature was set to 22, 36, and 42°C. These are evidently extreme temperatures—such a wide range of variance is highly improbable in the case of living organisms—but the temperatures were chosen to illustrate the influence. The temperature of the probe tip was chosen as a comparative criterion. The comparison of temperature and flow rate for different gel temperatures is presented in Fig. 14. It is visible in Fig. 14 that the freezing dynamics depend on the temperature of the tissue simulator—the probe temperature drops more rapidly for lower gel temperatures, but at the end of the experiment the temperatures are very close to each other. More experiments for the same conditions were conducted for confirmation. The results show that gel temperature has no influence on temperature and flow rate at the end of the experiment.

4. Summary

This paper reports on research into the behavior of a cryosurgical probe in various working conditions. The research was divided into a number of phases focused on different aspects. Two working gases were examined—nitrogen oxide (N_2O) and carbon dioxide (CO_2). The influence of various feeding pressures and bottle pressures on the operation of the probe was determined for both gases. The results indicate that for N_2O there is an optimum flow rate for obtaining the lowest probe temperature. For CO_2 an almost linear change in temperature with mass flow rate was noted, with no optimum value in the investigated region. Data concerning the dynamics of probe operation was also collected. Measurements indicate slight differences in dynamics in terms of bottle pressure and large differences for various feeding pressures. The results were confirmed by photographic documentation. During the last stage of research the influence of gel temperature on probe operation was examined. Initial gel temperature was set at three different levels: 22°C, 36°C and 42°C. The results show some differences in the dynamics of the probe at the initial stages of operation, but after about 160 s the temperature of the probe is equal for all cases. The unsteady heat transfer process occurring inside a medical probe that relies on the Joule–Thomson effect is very complicated. During the project, extensive documentation was collected on operation of cryosurgical probes in laboratory conditions. The differences identified provide insight for extended research in this area—for example helping to create and verify the numerical modeling of a process. It coud also be used by engineers to develop modern, effective probes that operate at their own optimum conditions.

Acknowledgments

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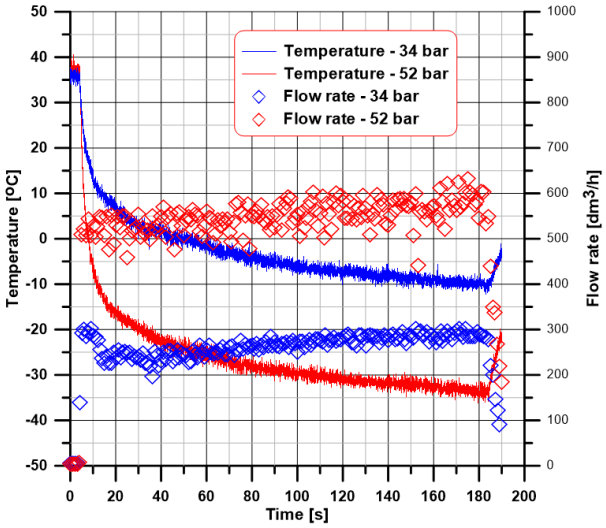

Figure 13: Comparison of temperature for common pressure in the tank but different feeding pressures

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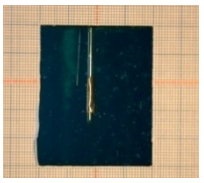
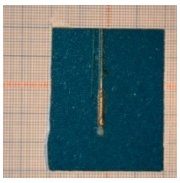
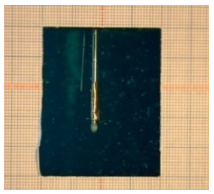
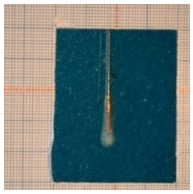
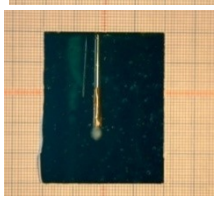
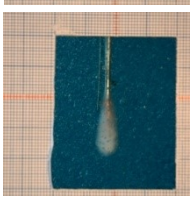
Table 2: Visual comparison of ice growth for common pressure inside the tank and different feeding pressures

Time [s]	P_{tank}=34 bar	P_{tank}=52 bar
3		
40		
180		

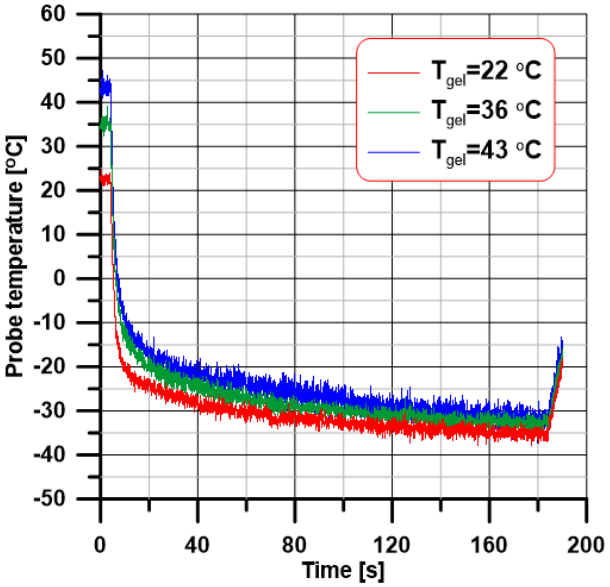


Figure 14: Comparison of temperature for different gel temperatures.

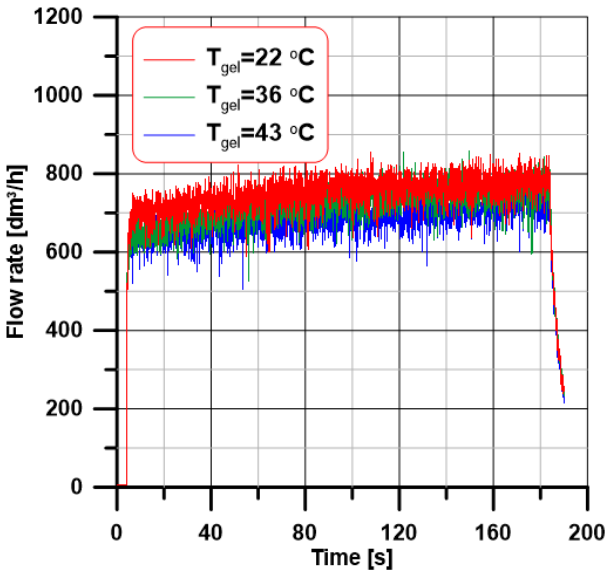


Figure 15: Comparison of flow rate for different gel temperatures.

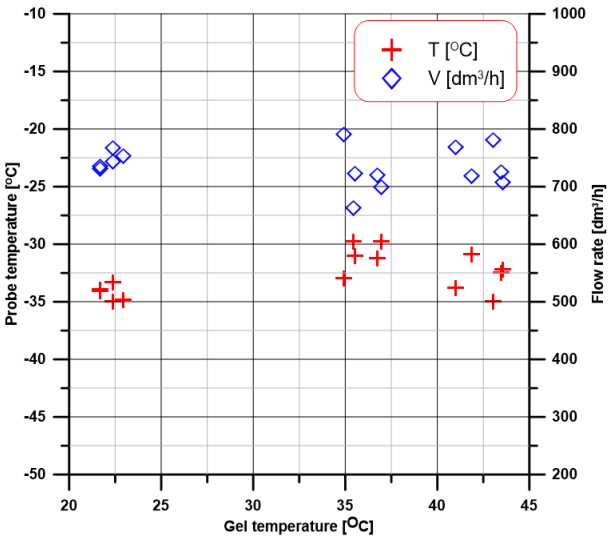


Figure 16: Flow rate and probe temperature at the end of experiment for different gel temperatures