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A CRYOGENIC CATHETER FOR TREATING HEART ARRHYTHMIA*

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ABSTRACT

Progress in the development of a cryogenic catheter to treat heart arrhythmia is discussed. This system uses a mixed-gas Joule-Thomson (J-T) refrigerator to cool the tip of a catheter that can be inserted into the body through the large veins leading into the heart. The cryogenic catheter is intended to treat heart arrhythmia characterized by an abnormally rapid heart rate, although the system has a wide variety of other medical applications. Approximately 2 million people in the U.S. suffer from rapid-rate heart arrhythmia. Catheter therapy has proven to be a more effective and less expensive method of treatment than alternatives such as drugs or surgery. A cryogenic catheter has significant advantages over existing catheters used in this form of therapy. The catheter has coaxial tubes for the high and low pressure streams with a miniature heat exchanger and J-T orifice at the catheter tip. The high pressure is maintained at 2.5 MPa. The largest diameter is 3 mm, the length is 90 cm, and all but the last 10-20 mm is flexible. The gas mixture has been optimized for the required operating conditions using non-flammable and low ozone depletion gases. Low cost techniques have been incorporated into the fabrication of the cold tip so that each catheter can be disposable. Several prototype catheters have been built. No-load temperatures down to 85 K were achieved with the cold tip exposed to ambient air. Using room temperature gelatin to simulate tissue heat loads, catheter tip temperatures of 160 to 175 K have been achieved, and ice balls about 26 mm in diameter weighing 11 g were created. We estimate that ice balls about 10 mm in diameter weighing 1.5 to 2.0 g are required to treat ventricular arrhythmia. Although the heat load in our experiments was less than the *in vivo* load, we think the current refrigeration power is sufficient to meet the clinical requirement.

INTRODUCTION

Heart arrhythmia is a problem for over 2 million Americans. To date, such patients have been difficult to treat with conventional drugs or surgery. Catheter therapy has proven to be a more effective and less expensive method of treatment, but the electrosurgical catheters currently used are not very effective for heart arrhythmia treatment. They have limited destructive capability and are difficult to keep in contact with the heart. Lesions created with electrosurgical catheters are 3-4 mm diameter spheres, and lines of these spheres must be connected in order to perform some of the treatment. A cryogenic catheter has the potential to deliver greater destructive power to the tip, allowing larger lesions to be formed. Linear lesions are possible, and the catheter tip will adhere to the tissue during the cooling process.

To treat heart arrhythmia the cryogenic catheter must reach temperatures between 100 and 150 K. To be inserted through veins, it must be 3 mm in diameter or smaller and must be able to make a bend with a 10-15 mm radius. It must be about 1 meter in length and must have a surface temperature above 0 °C along its length. For safety reasons the maximum pressure should not exceed 3 MPa. It is estimated that 10 watts of cooling will be required. The refrigerant should be benign, nonflammable, and nontoxic, and have a low ozone depletion potential. The catheter also needs to be disposable for safety and sterilization reasons. These requirements have led us to choose a mixed-gas Joule-Thomson (J-T) refrigerator as the most practical solution.

The difficulty with existing J-T systems is that they are too large in size to be used for catheter therapy, the cold head is too expensive to be disposable, and the units require too high a pressure for catheter use. The cryogenic catheter we have designed is based upon the Joule-Thomson cycle shown in Figure 1. This is a closed-cycle system that does not require make-up gas at any time. The catheter has coaxial tubes for the high and low pressure streams with a miniature heat exchanger and J-T orifice at the catheter tip. The high pressure is 2.5 MPa. The largest diameter is 3 mm, the length is 90 cm, and all but the last 10-20 mm is flexible. The gas mixture has been optimized for the required operating conditions using non-flammable and low ozone depletion gases. Low cost techniques have been incorporated into the fabrication of the cold tip so that each catheter can be disposable.

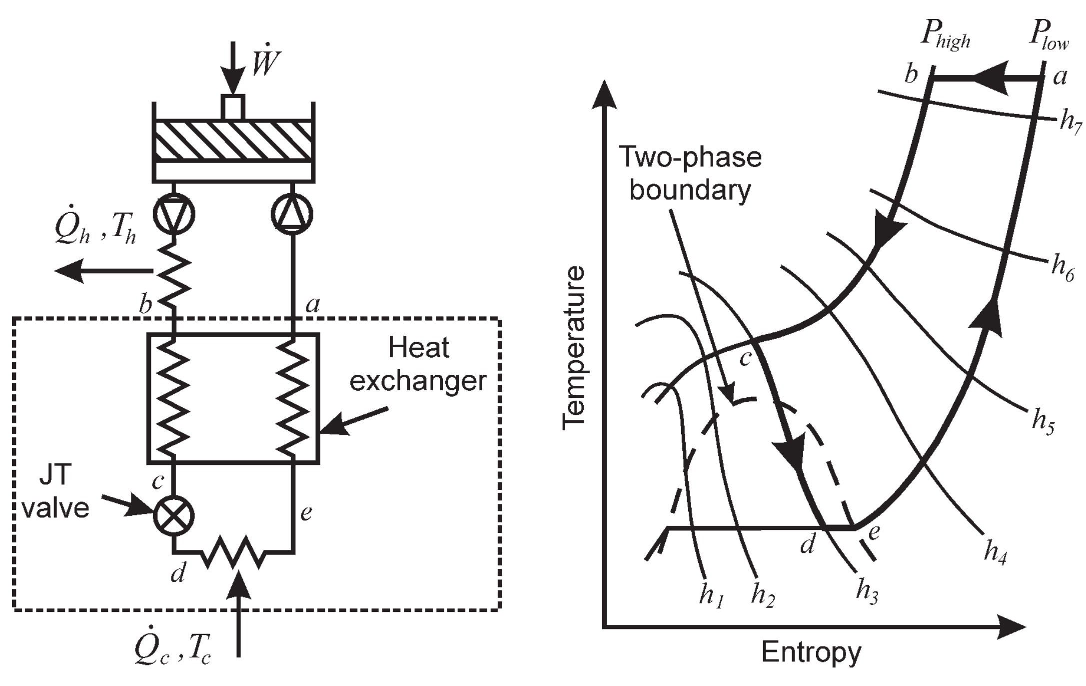

Figure 1. Schematic diagram of a Joule-Thomson system with temperature-entropy diagram.

MIXED GAS REFRIGERANTS

Mixed-gas Joule-Thomson (J-T) refrigerators have been used since the mid-1930's when Podbielniak[1] received a U.S. patent on the first use of mixed gases in a single flow stream using a series of heat exchangers and phase separators. The phase separators allow only the liquid phase to be expanded at each stage, thus maintaining a high efficiency in the expansion process. Kleemenko,[2] Missimer,[3] and Little[4] have made subsequent improvements to this mixed refrigerant cascade cycle that uses phase separators. In 1969 Fuderer and Andrija[5] first used mixed gases in a Joule-Thomson cooler with no phase separators. In this simplified cooler the entire gas mixture flows through the heat exchanger and expands at the J-T valve or orifice. Fuderer and Andrija pointed out that because the mixture is in the two-phase region in most of the heat exchanger, much greater heat transfer coefficients are possible compared with pure gas streams. The mixture is usually 100% liquid at the cold end just prior to expansion. Alfeev et al.,[6] Little,[7] and Longsworth[8,9] have described subsequent improvements to this type of mixed-gas J-T system. We decided to use the mixed-gas J-T system without phase separators for the cryogenic catheter because the extreme space limitations at the cold tip would not allow for the use of phase separators.

Mixed-gas refrigerants allow for higher cycle efficiency by maintaining a more uniform enthalpy difference between the high and low pressure streams. Traditional J-T systems have used a pure fluid for the refrigerant. This results in a very inefficient system. J-T systems rely on the fact that there is a reduction in enthalpy with increasing pressure. An ideal gas has no change in enthalpy with pressure; therefore we must use a nonideal working fluid. Fluids are most nonideal in the liquid or near-liquid state. The vapor-compression cycle works well because the fluids are nonideal over the limited temperature range of operation. Cryogenic systems must operate over a very large temperature range, making the fluids very close to ideal over most of the temperature range, as can be seen in Figure 2 by the enthalpy of nitrogen.

The traditional analysis of a J-T system is very simple. We can draw a control volume, shown as the dashed line in Figure 1, around the cold end of the system. With the assumption of an ideal heat exchanger, the first law energy balance around the control volume can be written to find the refrigeration power, $\dot{Q}_c$, given by

$$\dot{Q}_c = \dot{n}(h_a - h_b) = \dot{n}\Delta h, \tag{1}$$

where $\dot{n}$ is the molar flow rate and the molar enthalpy, h, is evaluated at points a and b shown in Figure 1. From this simple expression, the refrigeration power can be maximized by simply

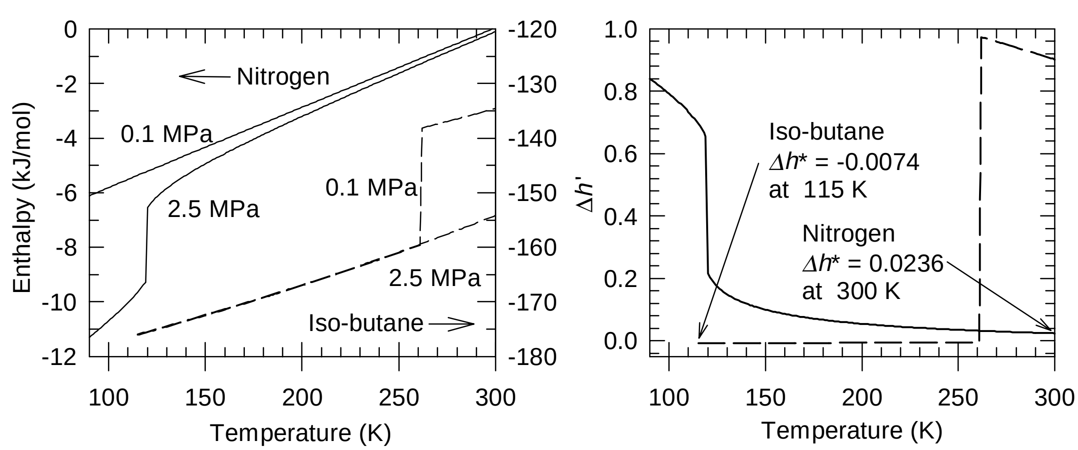

Figure 2. Enthalpy and normalized enthalpy for nitrogen and iso-butane.

maximizing the enthalpy difference at the warm end. Customarily these warm end enthalpies are evaluated at the same temperature when assuming a perfect heat exchanger. The problem with this analysis is that it also makes the assumption that the minimum enthalpy difference of the refrigerant occurs at the warm temperature; this assumption is rarely stated or even recognized. This traditional analysis works fine for a single fluid refrigerant, like nitrogen shown in Figure 2, but for a mixed gas we must recognize that the Δh in Eq. (1) should be the minimum enthalpy difference over the entire operating temperature range.

Molar flow rate is used instead of mass flow rate because a constant volume compressor will give a constant molar flow rate but the mass flow rate will vary. Using molar flow rate makes it easier to compare gas mixtures with different compositions.

The enthalpy difference, Δh, needs to be normalized in order to compare different gas mixtures. The enthalpy difference can be normalized in a number of ways depending on what is critical for effective operation of the system. For the cryogenic catheter, the heat exchanger is the most difficult component to make effective due to the small size. The enthalpy difference should then be normalized by using the amount of heat transferred in the heat exchanger. Therefore, the normalized enthalpy difference, $\Delta h'$, is defined as

$$\Delta h'(T) = [h(T, P_{low}) - h(T, P_{high})] / [h(T_{high}, P) - h(T_{low}, P)]_{min}, \qquad (2)$$

where $[h(T_{high},P)-h(T_{low},P)]_{min}$ is evaluated at either the high pressure or low pressure, whichever gives the smaller enthalpy difference. We now define Δh^* as the minimum value of $\Delta h'$ over the operating temperature range.

By maximizing Δh^* the gas mixture can be optimized for use in a cryogenic catheter.[10] Figure 2 shows the enthalpy, h, and the normalized enthalpy difference, $\Delta h'$, of nitrogen at pressures of 0.1 and 2.5 MPa between 90 K and 300 K. The figure shows that nitrogen has a very low change in enthalpy above 120 K and shows that Δh^* is only 0.0236, which occurs at the highest temperature, 300 K. The large change in enthalpy at 120 K is due to the liquefaction of the nitrogen at the high pressure. All fluid property data were calculated using the mixture property database NIST14.[11] Figure 2 shows h and $\Delta h'$ of isobutane; the liquefaction point can be seen at 261 K. The Δh^* is slightly negative for pure isobutane at temperatures below 261 K. Figure 3 shows h and $\Delta h'$ of a mixture of 80 mole% nitrogen and 20 mole% iso-butane, Δh^* has been increased to 0.0317, a 34% gain. The Δh^* occurs at a midpoint temperature of 168 K, whereas the temperature extremes have a high $\Delta h'$. Δh^* can be increased by adding a gas to the mixture that has a liquefaction range about where a higher $\Delta h'$ is required. Figure 4 shows how Δh^* is increased by adding methane (111-180 K liquefaction range) and ethane (184-275 K liquefaction range) to the mixture. Now Δh^* is 0.0365. The component amounts are next

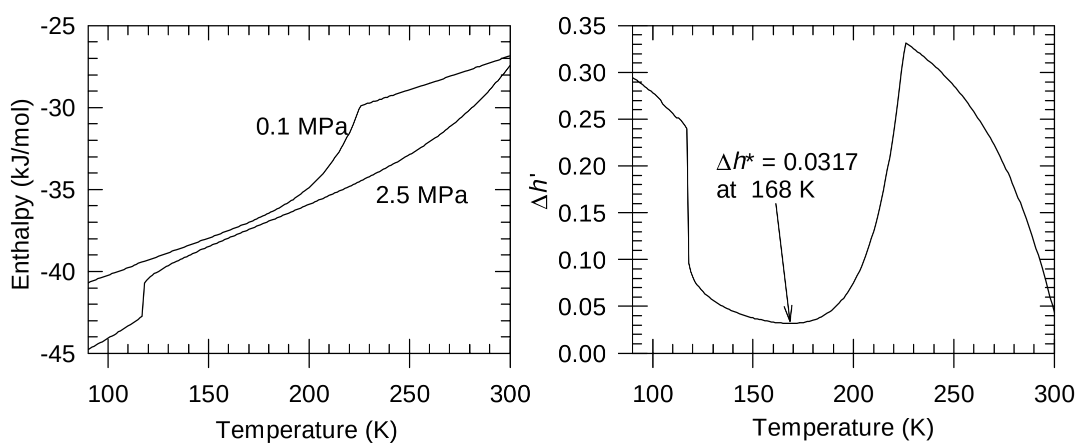

Figure 3. Enthalpy and normalized enthalpy for 80% nitrogen and 20% iso-butane.

adjusted until the maximum Δh^* of 0.0958 is achieved with a composition of 38.5% nitrogen, 27.5% methane, 10.5% ethane, and 23.5% isobutane by mole fraction shown in Figure 5. The new gas mixture has an improved Δh^* more than 4 times that of pure nitrogen. Other gases could continue to be added to the mixture until $\Delta h'$ is nearly independent of temperature.

Precooling the gas mixture before it enters the cold end heat exchanger offers the possibility of greatly enhancing the gas mixture performance at the cold end. Figure 5 shows a typical optimized gas mixture has a steep negative slope in $\Delta h'$ at the highest temperature. If the high end operating temperature is reduced a small amount, the value of Δh^* can be greatly increased by reducing the amount of the highest boiling point gas and increasing the amount of the other gases.

Gases other than hydrocarbons can be used and show great promise to create mixtures that perform better thermodynamically than hydrocarbons without being flammable. However, the advantage of hydrocarbon mixtures is that up to about 2% compressor oil can remain dissolved in it without freezing out at temperatures as low as 85 K.[12]

We can now write the refrigeration power $\dot{Q}_c$ of a Joule-Thomson refrigerator by

$$\dot{Q}_c = \dot{n}\Delta h_{min}, \tag{3}$$

where Δh_{min} is the minimum enthalpy difference for the gas mixture. The ideal work of compression $\dot{W}_{ideal}$ is given by

$$\dot{W}_{ideal} = \dot{n}\{h(T_0, P_{high}) - h(T_0, P_{low}) - T_0[s(T_0, P_{high}) - s(T_0, P_{low})]\} = \dot{n} / \Delta g_0, \tag{4}$$

where s is the entropy and Δg_0 is the change in the Gibbs free energy at the compression temperature T_0. The ideal coefficient of performance COP of the refrigerator is given by

$$COP = \dot{Q}_c / \dot{W}_{ideal} = \Delta h_{min} / \Delta g_0. \tag{5}$$

If system efficiency is more important, COP can be maximized by adjusting the mixture composition. The mixture discussed above which has a Δh^*=0.0958 gives a COP of 0.2443, which for a temperature of 90 K is 57% of the Carnot COP.

Further studies are needed regarding the freezing point of gas mixtures, including gases with trace amounts of water and oil. There are very little experimental data on the freezing

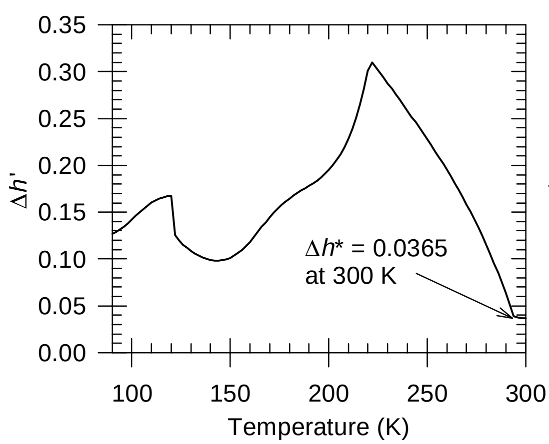

Figure 4. Normalized enthalpy for 45% nitrogen, 20% methane, 20% ethane, and 15% isobutane.

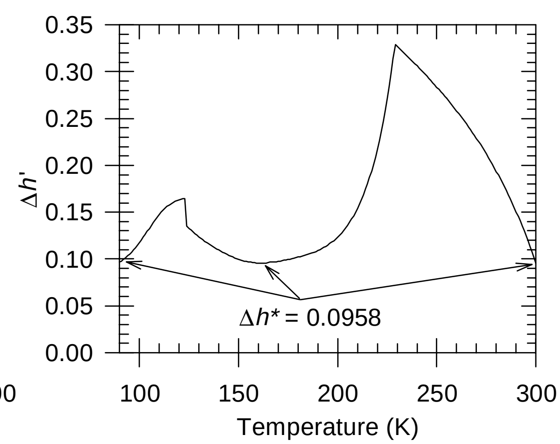

Figure 5. Normalized enthalpy for 38.5% nitrogen, 27.5% methane, 10.5% ethane, and 23.5% isobutane.

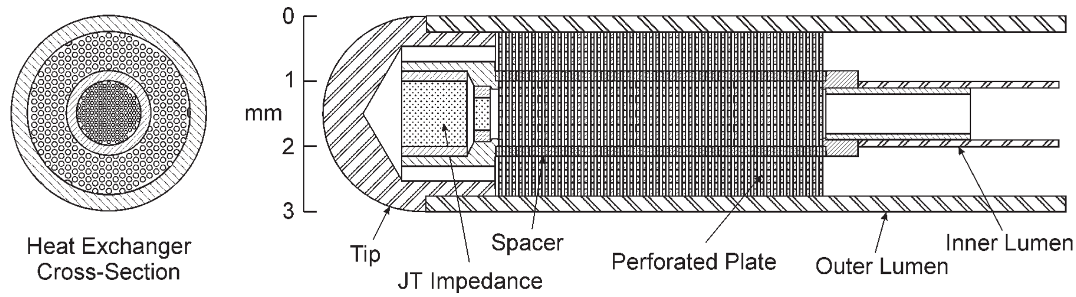

Figure 6. Schematic diagram of catheter tip.

point of gas mixtures, but it is clear that individual components that normally have a freezing point below the operating temperature may not freeze out of the mixture. Other areas that need further study include heat transfer effects of multi-component multi-phase mixtures.

CRYOGENIC CATHETER SYSTEM

The schematic diagram of the catheter tip is shown in Figure 6 and details both the heat exchanger and the expansion orifice.

Heat Exchanger

The miniature heat exchanger at the cold end is fabricated by diffusion bonding perforated plates of copper alternated with stainless steel spacers. Photos of the heat exchanger are shown in Figures 7 and 8. By diffusion bonding large metal sheets containing many individual heat exchanger layers, we are able to make large numbers of cold ends at one time, significantly reducing the cost in order to make them disposable. Prototype heat exchangers varied in length from 5 to 15 mm. The outer diameter of the heat exchangers was 2.5 mm. The enthalpy is more affected by changes in pressure at lower pressures, so the low pressure side of the heat exchanger must have a much lower pressure drop than the high pressure side.

Expansion Orifice

The J-T impedance shown in Figure 6 was fabricated of sintered copper powder. This permitted many flow channels, limited plugging problems, and provided a large area for heat transfer. Later catheters were fabricated using a single knife-edge orifice and provided similar

Figure 7. Catheter cold end. The tube on the right is only for making pressure measuments and is not part of the working catheter. The left tube is the high pressure inlet to the heat exchanger.

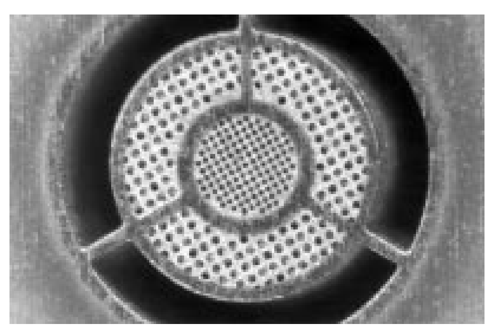

Figure 8. End view of heat exchanger. The top layer is a stainless steel spacer and the copper perforated plate can also be seen.

results with much less effort.

Lumens

A lumen is simply the tubing used for the flexible catheter pressure lines. The inner lumen was a 1 mm outer diameter polyimide tube with a stainless steel reinforcing braid. The reinforcing braid provided not only strength against the 2.5 MPa pressure but also helped to reduce the possibility of kinks in the tube. The outer lumen was a braided nylon-derivative tube with a 0.25 mm wall. For safety, the outer lumen was designed to withstand the highest pressure in the system, although a ballast volume was added to the low pressure side to reduce the average system pressure.

Compressor

The compressor was a commercial single stage oil lubricated compressor that required input powers from 300 to 500 W. Some experiments operated two compressors in parallel to increase the mass flow rate. Later experiments were performed using a custom built oil-free compressor. This simplified problems with the gas mixture since higher boiling-point components are more soluble in the oil than the lower boiling-point components.

RESULTS

Most experiments were performed with the catheter sitting on the bench top exposed to ambient air. A typical experimental result can be seen in Figure 9. The catheter is characterized by fast cool-downs and warm-ups. The lowest temperature achieved was 85 K with no load on the cold end. Typical operating conditions were 140 K with about 3 W of additional heat added to the cold end. Figure 10 shows the cryogenic catheter in operation.

A few experiments were performed with the cold end inserted into a room temperature gelatin to simulate biological heat loads.[13] Catheter tip temperatures of 160 to 175 K have

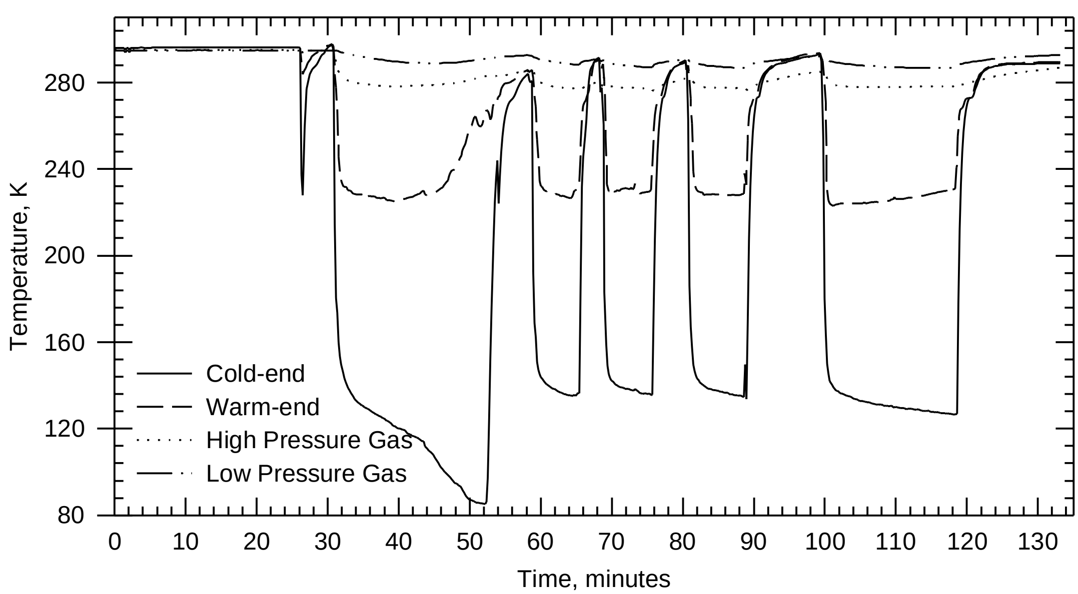

Figure 9. Catheter test results.The cold end is the catheter tip, the warm end is on the surface of the outer lumen at the warm end of the heat exchanger, high pressure gas is the gas temperature entering the inner lumen, and the low pressure gas is the gas temperature leaving the outer lumen.

been achieved and ice balls with diameters of about 26 mm and a mass of 11 g were created.

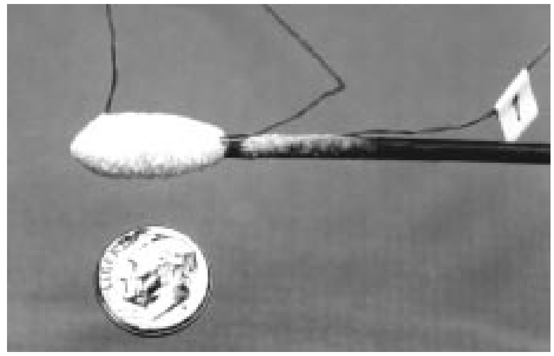

Figure 10. The cryogenic catheter in operation.

CONCLUSIONS

We have developed a cryogenic catheter to treat heart arrhythmia. The required cold end temperature has been achieved, and ice balls with diameters of 26 mm weighing 11 g were created in a gelatin. We estimate that ice balls about 10 mm in diameter and a mass of 1.5 to 2.0 g are required to treat ventricular arrhythmia. Although the heat load in our experiments was less than the *in vivo* load, we believe the current refrigeration power is sufficient to meet the clinical requirement.

A procedure to optimize gas mixtures was developed. It was shown that optimization of a gas mixture can enhance the performance of a Joule-Thomson system by at least 4 times that of pure nitrogen. Low-cost techniques for fabricating miniature heat exchangers that yielded a heat exchange effectiveness of sufficient quality to reach a low temperature of 85 K were developed.

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