



Experimental study on a cryosurgery apparatus^{*}

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Abstract: Cryosurgery is an effective way of curing many diseases including tumors and cancers. It can be applied using a variety of systems and cryogens. Cheap, convenient, reliable equipment still needs to be developed so that cryotherapy may be accepted by surgeons and hospitals. This paper presents a cryosurgery apparatus that utilizes an auto-cascade refrigeration system. Refrigerant mixture R50/R23/R600a was selected as the working fluid. The mixture composition was altered to achieve lower temperatures and higher capacity. The lowest temperature at the cryoprobe could be as low as $-100\text{ }^{\circ}\text{C}$, and 8 W refrigeration capacity could be obtained at $-80\text{ }^{\circ}\text{C}$. An ice ball of 11.6 mm diameter could be formed when the cryoprobe was immersed in a water bath at $37\text{ }^{\circ}\text{C}$.

Key words: Cryosurgery, Cryoprobe, Auto-cascade refrigeration system, Refrigerant mixture

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1 Introduction

Cryosurgery is a clinical method of treating disease using low temperatures. It is an effective therapy for many types of tumor including prostate cancer (Klossner *et al.*, 2007; Langenhuisen *et al.*, 2009), liver tumor (Mala, 2006; Hinshaw and Lee, 2007), renal tumor (Pareek and Nakada, 2005; Davol *et al.*, 2006), lung cancer (Maiwand M.O. *et al.*, 2004; Maiwand O. *et al.*, 2006) and others. Its advantages include less side effects, relatively high security, minimal operative bleeding, incidental anaesthetic effect and good repeatability (Fredrickson *et al.*, 2006). Also, cryosurgery can prevent cancer cells from diffusing after treatment (Zhang *et al.*, 1994). So far, cryosurgery is considered an important method of treating massive tumors that are drug-fast (Gowardhan *et al.*, 2007).

To date, commercial cryosurgery instruments have tended to rely on either liquid nitrogen (LN) or

Joule-Thomson (J-T) expansion of Ar or nitrous oxide as the means of cooling. Instruments utilizing the Peltier thermoelectric phenomena and pulse tube refrigerator were also tried (Holman and Rowland, 1997; Zhong and Mai, 2000). LN cooling is rapid and controllable but does require the supply and storage of LN. Besides, the difficulty of acquiring LN means that cryosurgery cannot be carried out in many areas of China. Ar cooling requires the handling of high pressure gas and also has the problem of supply. Also, the price of the relevant instruments is very high. In the mainland of China, only a very few hospitals in big cities like Beijing and Shanghai possess this kind of instrument. In order that cryosurgery can be undertaken in any location of medical infrastructure, the development of new cryosurgery instruments is very important.

Auto-cascade refrigeration was proposed as an alternative way to reach cryogenic and ultra-low temperatures (Luo *et al.*, 2000). An auto-cascade refrigeration system employs a refrigerant mixture in a closed cycle to achieve a multilevel cascade using a single or multistage compressor, which greatly simplifies the system and makes it easy to maintain. Compared with the established J-T devices that have

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been used in cryosurgery, the auto-cascade refrigeration system does not require the storage and handling of high pressure gases. Thus, it can be carried out conveniently in many areas. The auto-cascade refrigeration system can produce cooling over a wide range of temperatures from -180 to -40 °C. The system can be used in many applications, such as cryopreservation of cells and tissues, cryotrap and providing cooling for materials and component tests (Missimer, 1997). In this paper, we present an experimental cryosurgery apparatus using auto-cascade refrigeration cycle with a rectifying column (Cao et al., 2003).

2 Experimental system

Fig. 1 shows the schematic of the experimental system. The system uses ternary refrigerant mixture R50/R23/R600a (methane/trifluoromethane/isobutane) as the working fluid. The cycle is described as follows. A certain mass flow of refrigerant mixture R50/R23/R600a enters the compressor. After compression the refrigerant mixture is cooled in the condenser. The filter drier is used to remove water and dirt. The mixture then enters a rectifying column. Here, most of the high-boiling-point component R600a changes into a liquid and flows out of the bottom of the column. Most of the low-boiling-point components R50, R23 remain as vapor and escape from the top of the column. In the heat exchanger 2 R600a evaporates to offer cooling for R50 and R23. The mixture of R50 and R23 is further cooled in heat exchanger 1 by the returning flow and condenses finally into liquid. After throttling this mixture enters the cryoprobe and produces cooling. The returned flow from the cryoprobe mixes with R600a and then goes through heat exchangers 2 and 3. Heat exchanger 3 affords the cooling that is necessary for the running of the rectifying column. Eventually the compressor sucks the refrigerant mixture from heat exchanger 3 to form a complete cycle. Fig. 2 gives the detail of the cryoprobe. The cryoprobe is made of three concentric tubes. The inner tube and the middle tube have inner diameters of 1.6 and 3 mm, respectively. The high-pressure refrigerant mixture is delivered to the tip through a stainless steel tube. After absorption of heat, the refrigerant mixture will

return through the annular space to the exhaust line. Vacuum insulation is applied for the body of the cryoprobe. The flexible connection line between probe and system has inner diameters of 1.6 and 10 mm for supply and exhaust lines, respectively. Due to operational pressure and cryogenic temperature, the supply line uses stainless steel and the exhaust line uses stainless steel bellows.

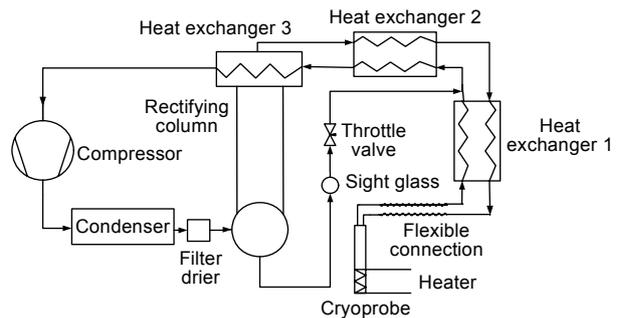


Fig. 1 Schematic of the experimental system

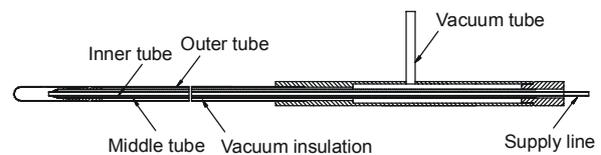


Fig. 2 Schematic of cryoprobe

The temperature at the tip of the cryoprobe was measured with copper-constantan thermocouple and recorded with data acquisition software. An electric heater was twisted at the tip of the cryoprobe to measure the refrigeration capacity and a programmable DC power supply was used to input a given heat load. The tip of the cryoprobe was sealed in thick vesicant material made of polyurethane to reduce heat leaks. The ice ball formation experiment was also carried out to observe the possible effect of the cryoprobe on real tissue. As shown in Fig. 3, the tip of the cryoprobe was immersed in a water bath maintained at 37 °C. The diameter of the final ice ball formed was measured with a vernier caliper.

3 Result and discussion

For the system shown in Fig. 1, three factors will influence the performance: the composition of the

refrigerant mixture, the quantity of the refrigerant charged and the position of throttle valve. In this work the influence of the composition was investigated. Four kinds of composition of R50/R23/R600a: 0.37/0.21/0.42, 0.46/0.14/0.40, 0.45/0.13/0.42, 0.39/0.23/0.38 (mole percentage) were tried. Fig. 4 shows the cryoprobe refrigeration capacity as a function of the tip temperature. From the four kinds of composition, 0.39/0.23/0.38 was found to be the best. The lowest temperature at the cryoprobe could reach $-100\text{ }^{\circ}\text{C}$ and the refrigeration capacity was about 8 W at $-80\text{ }^{\circ}\text{C}$. An 11.6 mm ice ball could be formed when the cryoprobe was immersed in a $37\text{ }^{\circ}\text{C}$ water bath. For clinical applications, needles shaped to cure different diseases should be mounted on the tip of the cryoprobe. To stop the freezing process the heating wire bound at the tip may be used.

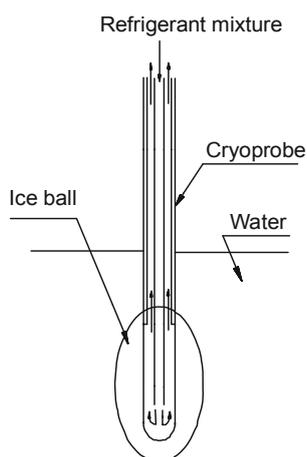


Fig. 3 Ice ball formation experiment

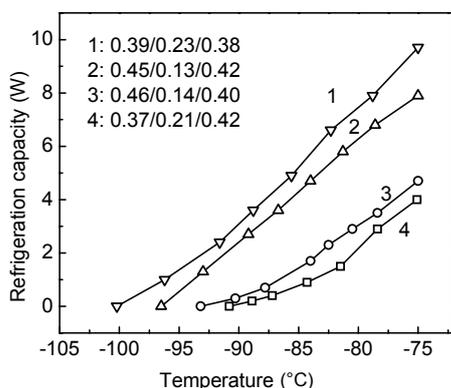


Fig. 4 Refrigeration capacity for different compositions of R50/R23/R600a

The prime factor leading to cell death in cryosurgery is the lowest temperature that can be

achieved in the tissue (Gage and Baust, 1998). Therefore, the cryoprobe temperature should be low enough to maintain a temperature gradient in the tissue. The experimental results demonstrate that the present system can reach a comparable temperature level to open J-T type apparatus using nitrogen oxide (Yu and Liu, 2004). The startup of the J-T type apparatus is much faster. The high pressure for the present system is about 1.9 MPa whereas J-T systems require gas pressure of more than 5 MPa. Nevertheless, the J-T type apparatus produces cooling only at the probe tip and does not need vacuum insulation of the supply line (Gage and Baust, 2002).

The application of a closed cycle system in cryosurgery can solve the problem of limited cryosurgical duration and eliminate ventilation issue that exists in open type apparatus. Coleman and Richardson (2005) reported a novel closed cryosurgical system with two-stage cycle, using either R23 or R508B in the low temperature stage and R404A for pre-cooling. The temperature achieved by this cycle is restricted by the compression ratio for each stage. Typically the working temperature is about $-80\text{ }^{\circ}\text{C}$. One problem for the two-stage system is the selection of a suitable compressor with specified lubricating oil working in the low temperature stage. For the system developed in this study, commercial air-conditioning compressors can be employed. The manufacturing and maintenance costs are relatively low, this makes wide applications realizable.

As to similar systems, Naer and Rozhentsev (2002) reported an auto-cascade system with refrigerant mixture R600a/R270/R50. The cryoprobe temperature could fall down to $-125\text{ }^{\circ}\text{C}$ and 15 W refrigeration capacity could be obtained at $-110\text{ }^{\circ}\text{C}$. The main difference between our system and theirs is that we use a rectifying column instead of a vapor-liquid separator. Another auto-cascade system was developed by Gong *et al.* (2000). A refrigeration capacity of 11 W at $-120\text{ }^{\circ}\text{C}$ was achieved.

As a primary study the lowest temperature obtained here is enough for killing cells, although the refrigeration capacity is small compared with apparatus using LN. For the cryoablation of a large target, such as tissue, multiple probes are needed. Due to its limitation the present apparatus is only suitable for small-scale cryotherapy. To make it feasible for

more cryotherapies, continued improvements should be made to lower the temperature, to increase the capacity and to add more cryoprobes.

4 Conclusion

Today cryosurgery can be applied to many kinds of disease. Appropriate cryosurgery instrumentation is crucial for wider applications of cryotherapy. The experimental apparatus developed here does not need LN or high pressure gas supply or expensive investment. Primary experiments have shown that it can reach low enough temperatures to treat disease. Further research is needed to make the cryosurgery apparatus applicable in more clinical practices.

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