ADVANCES IN THE DESIGN OF SPECIAL CRYOSURGICAL APPARATUS IN CHINA*

Q. S. SHU, S. S. HU,[1] AND A. F. XIE[2]
Cryogenic Lab, Zhejiang University, Hangzhou, China

Advances in the design of special cryobiomedical apparatus and a review of the trend of developments in the field of cryosurgery in China are discussed. The typical structure of two special cryoprobes for treatment deep in the body and the technology of designing these probes are presented in detail. Some cases which are treated successfully with the above cryoprobes will also be discussed. The experimental aspects of heat transfer in frozen tissue and of the temperature profiles both of a human brain during surgery and of the cryoprobe are described. Other improvements in the field of cryosurgical devices, e.g.. four main ways of attaching freezing tips to cryoprobes during surgery and an LN_2 transfer tube with his dexterity are also presented. Finally, the development of commcreial cryosurgical apparatus in China is also discussed.

During the last 10 years, applications of cryogenics in the cryobiomedical field have grown rapidly in China (2,11, 14, 15). Although these applications also include primarily cryotherapeutics and cryopreservation, this paper will deal mainly with cryotherapeutics. As low temperature physicists, the authors will focus the discussion on the aspects of advances and on the trend of developments in the design of special cryosurgical apparatus. We will cite some clinical cases, as simple examples, which may be interesting to people who would like to know about the application in China.

Cryotherapy is mainly used in treatment of several types of malignant and nonmalignant tumors (2, 5), which may be situated on accessible areas or within the body. Cryotherapy apparatus for treating defects on the surface and on exposed areas of the body are commercially available. Briefly, the subjects of interest in the design of cryosurgical apparatus can be listed as follows:

1. Design of special cryoprobes that can be used in deep tissue.
2. Improved technologies to make apparatus more effective.
3. Study of heat transfer in frozen tissues and control of the temperature distribution on the surface of the tip of cryoprobes.
4. Development of quality commercial products.

IMPROVEMENTS OF TECHNOLOGY

1. The Typical Structure of Special Cryoprobes

Continuous improvements of cryosurgical apparatus have been made by many institutes, universities, and hospitals in order to promote the performances of the apparatus.

Some tumors are located in deep tissue and are surrounded by healthy tissues. It is necessary both to kill tumorous cells and to protect healthy cells from injury. Special cryoprobes differ from general probes for treating deep in the body. The have both special shapes (usually fine and long) and special performance properties (1, 12). The temperature in different regions of the surface of the cryoprobe not only must be variable, but also must be controlled, displayed, and recorded. To meet these requirements, several problems must be solved satisfactorily. There must be a reliable vacuum insulation in the narrow space between the vacuum jacket and the tube transferring the cryogen, a rapid cooling capacity, a high-power microheater, wireless electrical connections, and reliable soldering of all the seams in the vacuum space. A successful example of such a special cryoprobe is shown in Fig. 1. Figure 1 also shows two methods of construction for the tips of cryoprobes. Only one edge of tip can be cooled to about -196℃: the whole cryoprobe is thermally well insulated. Only the small middle part of tip B of the cryoprobe can be cooled to about - 196℃; all other parts are well insulated. Originally, the leading edge of tip B was typically made from metal construction and high vacuum insulation. Later, Teflon or Padauk (a special wood used by us) was used to make the insulation because of their lower thermal

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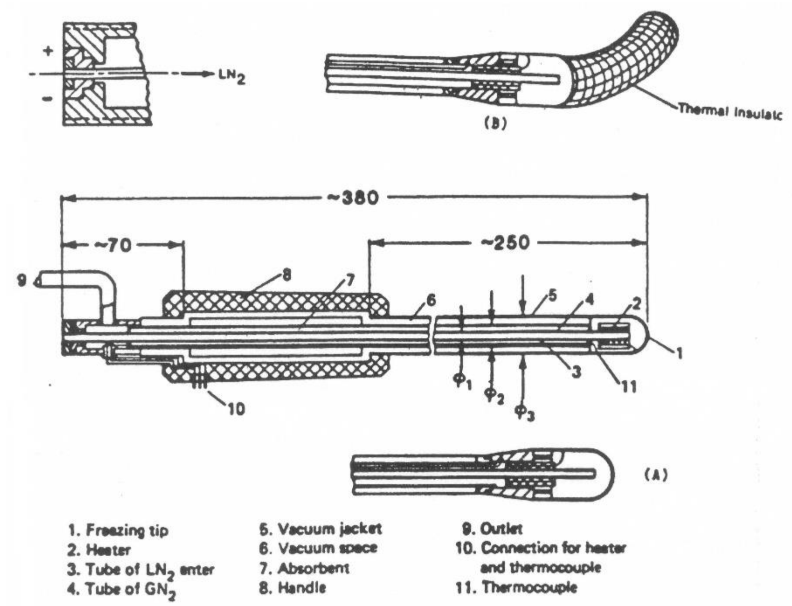
[1] Hangzhou Institute of Oxygen Plant.
[2] Hangzhou Eighth Radio Manufactory.

conductivities.

The diameters of the liquid nitrogen(LN_2) feed tube. vapor return tube. And outer jacket tube in Fig. 1 are 1, 1.8, and 2.4 mm, respectively. Because the volume of the vacuum space is very small, the liberated gas will cause the vacuum to fail; therefore, the hollow inner space of the handle of the probe was made into an enlarged vacuum space connected to the original small vacuum space, and a charcoal absorbent was placed around the cold gas return tube. The metal wall of the tube, while being evacuated, can be heated to above 300℃. A pressure of 5×10^{-6} mm Hg can be attained, and a high vacuum can be maintained for more than 2 years.

Since the space between the tubes is quite small, it is almost impossible to fix the four leads for heating elements and for thermocouples without increasing the flow resistance. Therefore we designed return and feed tubes for the liquid nitrogen as two special leads. A very thin layer of polyamide (0.05 mm) was centered around the outer surface of the liquid nitrogen feed tube for electrical insulation. For this reason there is a special shaped Teflon collar at the inlet for the liquid N_2, as shown in Fig. 1. There is a high-powered microheater in the probe tip. This heater can withstand frequent temperature cycles between - 195 and 20℃ that occur in less than 25 sec. In order to obtain a good vacuum seal, all the seams of the cryoprobe were soldered under vacuum in a single operation.



	O.D. (mm)		
Type	ϕ_1	ϕ_2	ϕ_3
1	1	1.6	2.4
2	1.2	1.8	3
3	1.6	3	5
4	1.6	4	7.6

Fig. 1. The typical structure of a special cryoprobe.

Many modified cryoprobes have been made by this method of construction, which have proven clinically successful in treating many cases in many different hospitals.

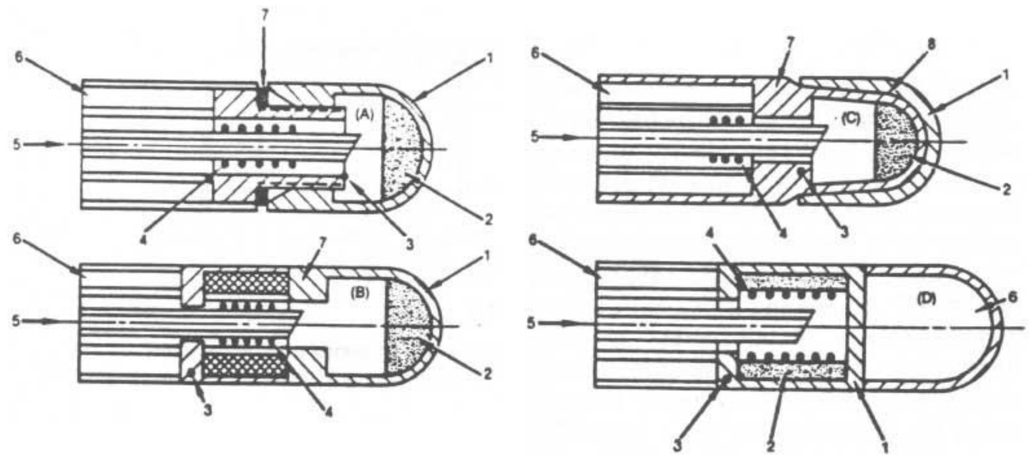


Fig.2. Four main ways of fixing freezing tips into cryoprobes. (A) Screw joint with oblique planar shape. (B) sleeve joint with a Teflon collar, (C) sleeve joint. (D) a tip soldered to cryoprobe as a unit. (1) Top of freezing tip. (2) microexchanger. (3) thermocouple head. (4) microheater. (5) liquid N_2 enter. (6) vacuum insulated. (7) seal washer. (8) oil.

2. Technique for Fixing Freezing Tip to Cryoprobe

The freezing tip which experiences cryogenic temperatures may be manufactured in various shapes and sizes to meet the clinical requirements for freezing tissues. However, the method of changing the freezing tips of cryoprobes rapidly during operations to treat different patients or different problems must also be anticipated.

Four main techniques (Fig. 2) (13), by which the tips can be fixed to the cryoprobes, have been developed. Figure 2A shows a screw joint. When connected, part 1 is pressed against part 7, a Teflon washer. Owing to the oblique planar shape of the sealing surface the tip can be rotated within 360° easily to meet the defect's position after attachment. If the shape of the sealing surface is rectangular, the tip will not rotate easily after being connected. Figure 2B shows a sleeve joint. This joint is more convenient to operate. As soon as the tip is inserted into the cryoprobe, the Teflon collar will press the tip to seal the joint. Figure 2C is another sleeve joint which is mainly used in outpatient clinics, where changing tips frequently and rapidly is routine. A medical oil may be used between part 1 and part 7 to enlarge the heat contact area. Figure 2D is a complex tip used to treat disorders in deep tissue. It is usually sold with the cryoprobe as a unit.

In order to enhance the freezing capacity of the tips, copper fins or copper powders are sintered to the internal surface of the tip. The temperature sensor must be fixed lightly under the surface of the tip contacting the defect. Only in this way can the temperature be measured accurately and sensitively. It is necessary to equip the freezing tip with a microheater.

3. Transfer of LN_2

In order to transfer LN_2 from the Dewar vessel to the freezing tip during a clinical operation, high vacuum insulated flexible stainless-steel tubes are quite useful.

The use of polyethylene tubes to transfer LN_2 is usually difficult because this material becomes brittle at low temperatures and is easily broken. However, use of the vapor film adiabatic technique makes it possible to retain flexibility (16). The polyethylene tube incorporating a vapor film adiabatic technique provides a flexible transfer line especially in the lower pressure case. The method is used to the transferring of liquid N_2 drops in infrared technology. It is also used in cryosurgery successfully. The principle is shown in Fig. 3. Even though the pressure is limited to meet the boundary condition for heat transfer, this is acceptable to doctors because it is inexpensive and convenient.

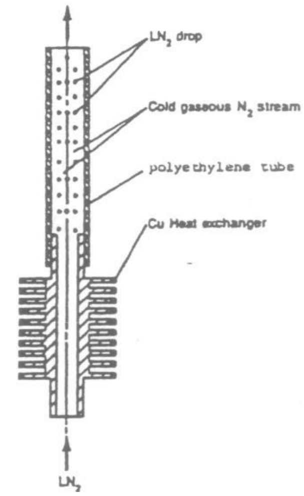


Fig. 3. The principle of the polyethylene tube adopting a vapor film adiabatic technique.

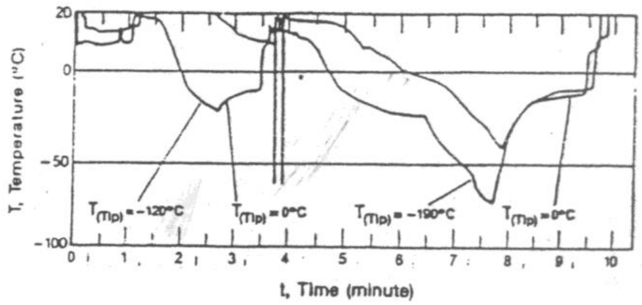


Fig. 4. Temperature-time curves recorded during a clinical operation in the brain. The lower curve is the temperature of a point 10 mm from the surface of the tip of the cryoprobe, upper is 15 mm.

HEAT TRANSFER IN FROZEN TISSUE AND TEMPERATURE DISTRIBUTION OF CRYOPROBES

It is known that the survival of cells (both tumor cells and normal cells) is closely related to the temperature and rate of change of temperature during operations (4, 6, 9, 10). So one of the focuses in the field of cryosurgery is the problem of how the temperature profile is measured in the tissue and what kind of temperature profile will benefit to kill tumor cells and protect normal cells from injury, and how to make the temperature distribution on the surface of the probe (which is dependent on its construction and design) meet the required temperature profile in tissue. Figure 4 shows recorded temperature-time curves at various depths in a male brain tissue during a clinical operation. Up to now, experimental measurements of the temperature profile are still important because a perfect and complete theoretical model has never been available. The experimental results can roughly indicate what tip temperature is needed and how long the temperature should be maintained during an operation.

Because the process of heat transfer in large organs and live tissue is very complicated, no adequate mathematical model for heat transfer during the freezing process of organs is presently available, although several models have been made. Heat transfer in freezing organs depends on the blood circulations, the heat produced during metabolism, the heat transfer media, the thermal conductivity of tissue, the heat exchange with environment, etc. A simplified heat transfer equation is

$$\nabla \cdot (K \nabla T) + M_b C_b (T_b - T) + S_m = \rho_c \frac{\partial T}{\partial t} \qquad (1)$$

$\nabla \cdot (K \nabla T)$ indicates the portion of heat transferred by conduction through the tissue: $M_b\ C_b\ (T_b - T)$ indicates the portion of beat transferred due to blood flow: S_m is the portion of heat transferred due to metabolism, which may be a function of temperature, time, and position; and $\rho_c\ (\partial T / \partial t)$ represents the increase (or decrease) of internal energy of a small region of tissue. If a steady state is reached , $\rho_c\ (\partial T / \partial t) = 0$.

In most biological substances water is the major component; when cooled below 0°C, ice forms, usually in the vicinity of -1°C, dependent on the molar concentration of the soluble cell components. Besides the latent heat, the thermal conductivity also changes considerably. All of these factors will make heat transfer calculations more complicated.

In view of the requirements mentioned above, there needs to be a "cold region"and "warm region" on the surface of some special freezing tips for deep tissue operations. For the tip (Fig. 5A) of a prostate cryosurgical probe, the small middle part of the tip is cooled to about -196°C, while the temperature of both ends of the tip needs to be more than 0°C during operating. Figure 5B shows the "cold region" and "warm region" on the surface of a cryoneurosurgical probe. At the tip of neurosurgery cryoprobes, only a small area is cooled. The temperature of all the other parts is more than 0℃. It turns out that the line of demarcation between the "cold region" and "warm region" is very clear, and that the freezing capacity of the tip is powerful.

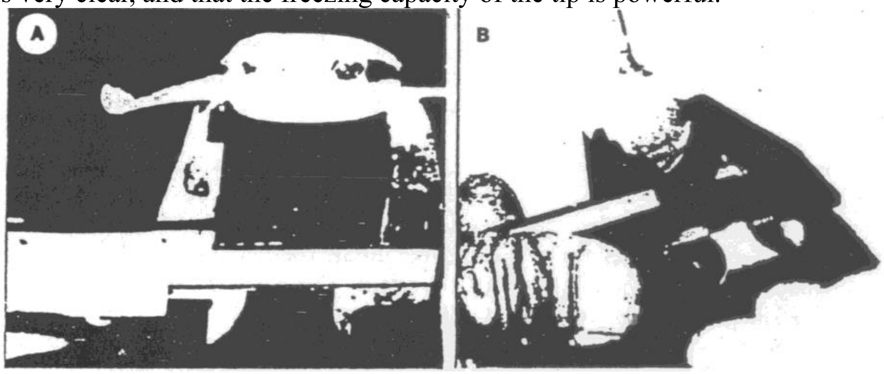


Fig.5.(A) Ice ball on prostale cryoprobe.(B) Ice ball on neurosurgery cryoprobe.

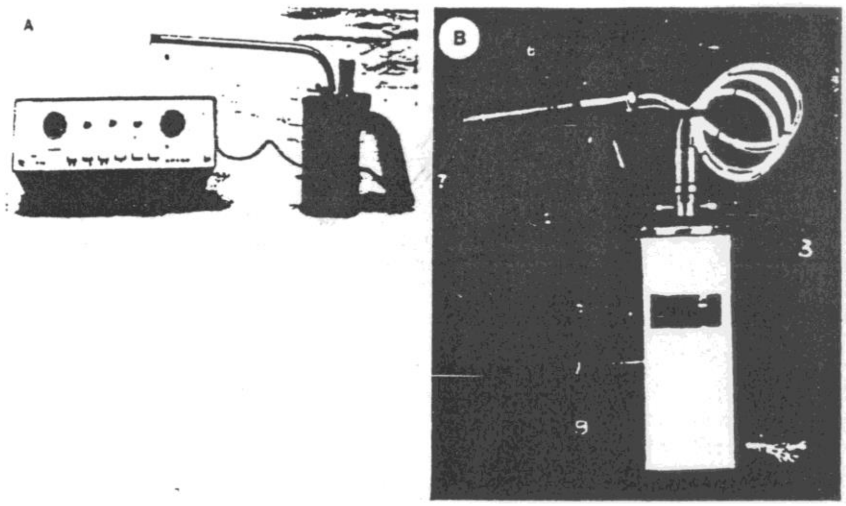


Fig. 6. (A) A portable automatic cryosurgical apparatus. (B) A portable cryosurgical apparatus adoptins adiabatic vapor film insulations.

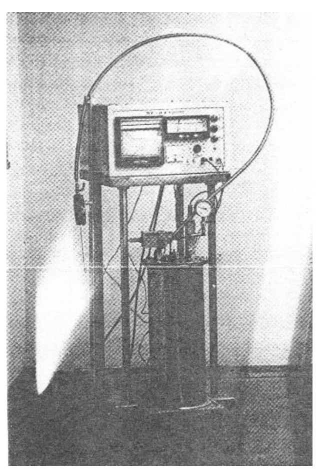


Fig.7.A completely automatic multipurpose set of cryotherapy equipment.

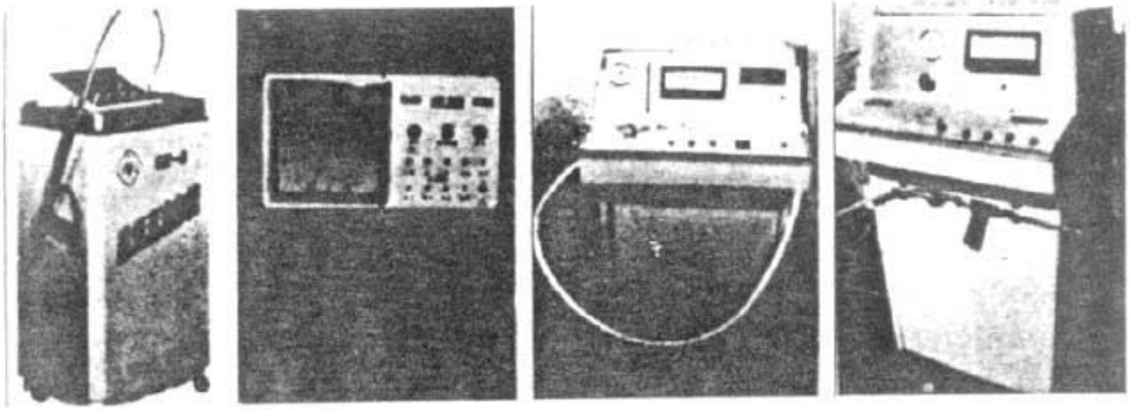


Fig.8. Configuration of cryosurgical apparatus with vacuum insulated flexible stainless-steel tube.

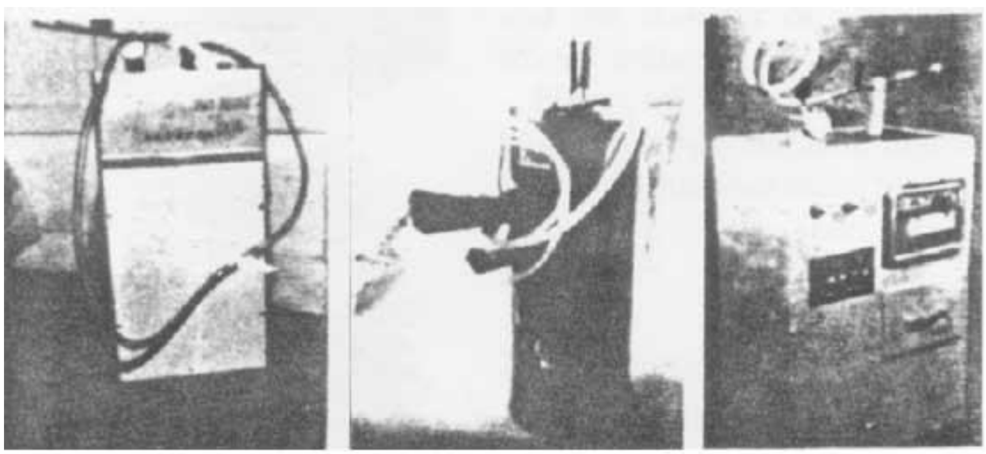


Fig.9. Configuration of cryosurgical apparatus with vapor adiabatical tube (polyethylene).

DEVELOPMENT OF COMMERCIAL CRYOSURGICAL APPARATUS

There are many companies in China that can provide various kinds of commercial cryosurgery apparatus, which use various cryogens including liquid nitrogen (-196℃), nitrous oxide (-89℃), solid carbon dioxide (-78.5℃), and several freons. of course, some semiconductor coolers are also used. but discussion in this paper will be limited to devices operating with the most common cryogen, liquid nitrogen, because these are most powerful. Although there are numerous products on the market as shown in Figs. 6, 7, 8, and 9,they can be classified in two groups.

1. Portable Cryosurgery Apparatus

The portable type is less expensive and can be readily used in outpatient clinics, in small towns, or in rural areas (8, 15). In Fig. 6A is shown a portable apparatus designed and tested by us, which includes a control console and a hand-held cryosurgical probe with liquid nitrogen coolant. A small and sensitive electromagnetic valve is mounted on the cover, and two heaters are inside the small Dewar and the cryoprobe tip. High vacuum insulated LN_2 piping is used. The temperature, the time to freeze, and the transfer of LN_2 all can be controlled automatically.

Figure 6B is another portable apparatus, in which a polyethylene tube using a vapor film adiabatic insulation technique provides greater flexibility than flexible stainless-steel tubes.

2. Multipurpose Cryotherapy Apparatus

On the other hand, many multipurpose automatic cryotherapy apparatus have been developed to meet the requirements both for treating complicated cases and for biomedical experimental purposes.

Fig. 7 presents a complete set of cryotherapy equipment designed and tested by us. It has a set of cryoprobes with hundreds of differently shaped freezing tips. The temperature of both the tip and the tissue can be displayed, recorded, and controlled automatically. There is also a system for storage and transfer of LN_2 with a complete set of instruments displaying and controlling both the pressure and the level of LN_2. The LN_2, transfer pipe is a flexible stainless-steel tube with a high vacuum insulation space. Several thousand cases have been treated.and many cryobiology tests have been performed successfully by these kinds of machines.

SOME CLINICAL APPLICATIONS

In this paper we could not discuss the clinical aspects in detail, which are out of our subject, but we would like to introduce several cases (3, 7, 17-19) in China with pictures which hopefully will promote the understanding of scientists of the world. Significant successes have been achieved in various medical fields in treating leuko- plakia, hypertrophic rhinitis, chronic tonsillitis, chronic cervictis, carcinoma in situ,and vulval, pilonidal, neurosurgeon and prostate, liver, and lung diseases in China.

As an example, Fig. 10A shows a male brain tumor being extracted with a cryoprobe. The temperature variation in the deep brain tissue at various distances from the tip can be monitored with two or three needle thermocouples placed close to the probe. In this case, gliomata, which ordinarily is gelatinous and difficult to manipulate, can be transformed into a solid to be more easily handled, while the line of demarcation between the tumor and normal brain tissue becomes clearer to facilitate identification and separation. A removed male brain tumor is shown in Fig. 10B. When the tumor is located in a critical area of the brain, it is better to leave a small part of residual tumor rather than to remove it completely, in order to protect normal tissue from injury. Then, repeated freezing and thawing is conducted to destroy the residual tumor cells in this area: the cryoprobe is placed close to the tumor to freeze for 2-3 min. and after thawing, it is frozen again. The operation is carried out under local anesthesia, general anesthesia, or acupuncture anesthesia, depending on the patient's condition. Hydrocortisone or mannitol were administered intravenously during this operation and after.

Figures 11, 12, 13,.and 14 show several cases in different medical fields in China.

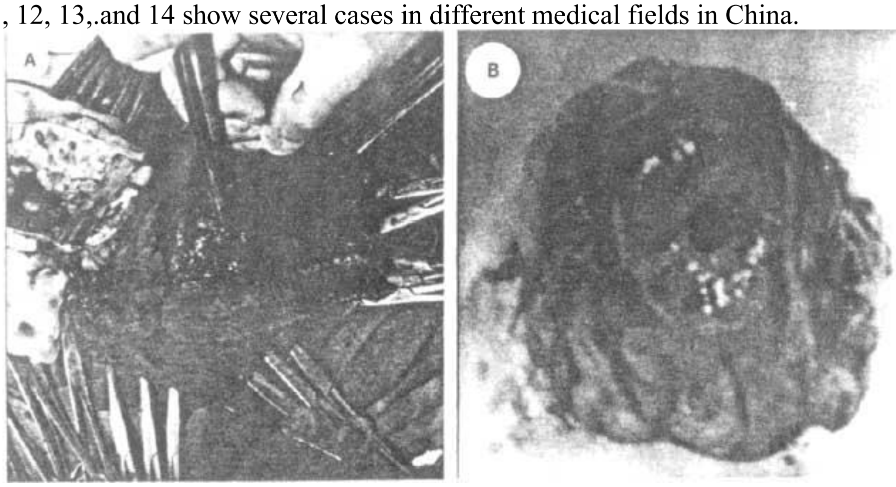


Fig.10.(A) Extracting a brain tumor with the cryoprobe.(B) The removed brain tumor.

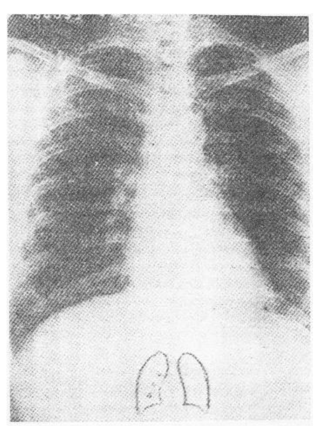


Fig. 11. Chest X-ray film of a case where 32 meta-static lesions of the left lung have been removed cryosurgically.

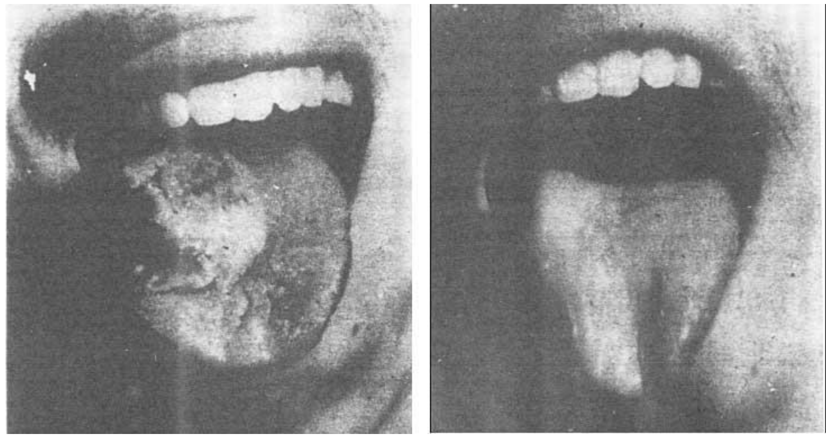


Fig.12 (A)A tumor of the tongue before operating.(B)A tumor of the tongue after operating.

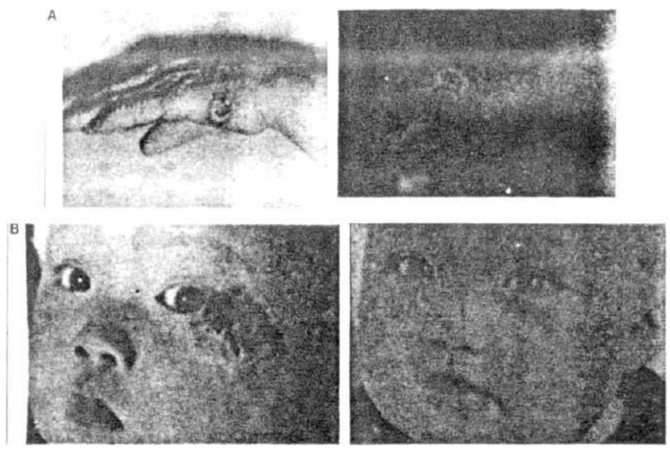


Fig.13.(A) Carcinoma of the skin before and after cryosurgery.(B) Capillary hemangioma of the outer canthus, before and after cryosurgery.

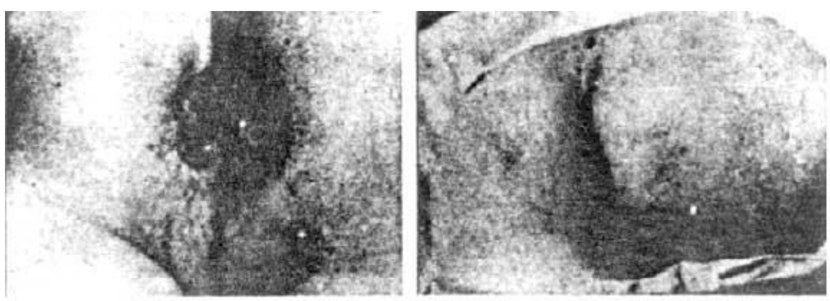


Fig.14. Internal hemorrhoids before and after cryosurgery.

APPENDIX: NOMENCLATURE

C	specific heat of unfrozen blood, cal/g • ° K
C_b	specific heat of blood, cal/g • ° K
k	thermal conductivity, cal/cm • ° K • sec
M_b	blood mass flow rate, g/cm^3
S_m	metabolic heat generation rate. cal/cm^3 • sec
T	temperature of unfrozen phase,° K
T_b	arterial system blood temperature,° K
t	time, sec
ρ	tissue density, g/cm^3

$$\nabla \bar{i}\frac{\partial}{\partial}+\bar{j}\frac{\partial}{\partial\gamma}+\bar{k}\frac{\partial}{\partial}, \mathrm{cm}^{-1}$$

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