BIOMEDICAL APPLICATIONS OF CRYOGENICS IN CHINA

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INTRODUCTION

Cryogenics is widely used in the life sciences in today's world. In China, biomedical applications of cryogenics have grown to become an important branch of science and a series of encouraging results has been produced.[1-3] Cryogenic techniques deserve emphasis as excellent alternatives for certain problems which are especially difficult to manage by other methods. The future is promising and activities are on going in diverse institutions, laboratories and hospitals belonging to universities,industries and the Chinese Medical Academy of Sciences. The national conference on cryobiomedicine is held in China each year, and it draws several hundred technical reports. Biomedical applications of cryogenics in China cover a wide range of activities which are summed up here for brief discussion as follows:
1) Cryotherapy and cryoequipment for cancers and tumors, 2) artificial insemination employing cryogenics, 3) cryoprotection and cryopreservation, 4) cryobiology, 5) study of heat transfer in living tissue and organs at cryogenic temperature, and 6) therapeutic effects of high magnetic field and studies of the magnetic field of the human body.

This article will be limited mainly to discussion of examples of cryogenic technical approaches and results, not medical aspects.

CRYOTHERAPY AND CRYOEQUIPMENT FOR CANCERS AND TUMORS

Cryotherapy is mainly used in the treatment of malignant and nonmalignant tumors situated in all parts of the human body, either surface or deep tissue. Cryotherapy is remarkably advantageous over other therapeutics in treating some tumors and cancers. Startling successes have been achieved in various medical fields in China treating leukoplakia, hypertrophic rhinitis, chronic tonsillitis, gynecological diseases, chronic cervicitis, carcinoma in situ, disease of the vulva, pilonidal disease, rectal disease, neurological disease and prostate, liver and lung diseases.

Commercial cryoequipment for treating disorders of the skin or exposed parts are readily available in China to meet the diverse needs of physicians in various specialties. Also, many types of cryoequipments for treating the more complicated problems of disorders in deep organs are being developed. There are many kinds of cryosurgical apparatus manufactured in China, using various cryogens including liquid nitrogen (-196℃), nitrous oxide (-89℃), solid carbon dioxide (-78.5℃), and several fluorinated hydrocarbons. 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 (LN_2).

General Cryotherapy equipment and results

There are about ten factories currently producing various cryosurgical equipment which can be classified as stationary or portable.[5-7] The stationary type meets the needs of treating some complicated diseases, usually in large hospitals. The portable type is less expensive and so can readily be used in outpatients' clinics, in small towns, or in rural areas.

Shown in Fig. 1 is 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 cryo-probe 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.

Fig. 2 is another portable apparatus in which a new method for LN_2 transfer is adopted. Here, a polyethelene tube using a vapor film adiabatic insulation technique provides greater flexibility than flexible stainless steel tubes. In this case, operation is limited to lower pressure, to meet the boundary condition for heat transfer. This apparatus is inexpensive and convenient.

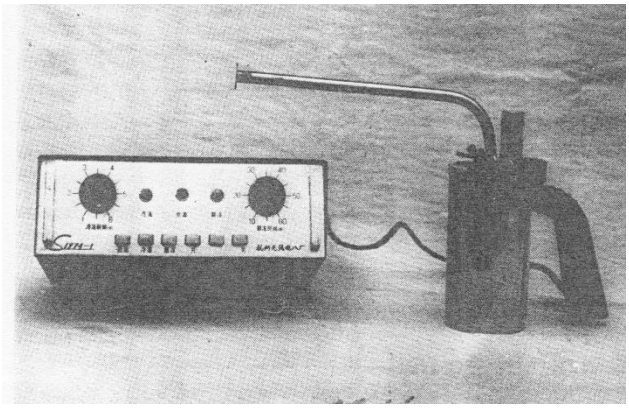


Fig.1. A portable automatic cryosurgical apparatus.

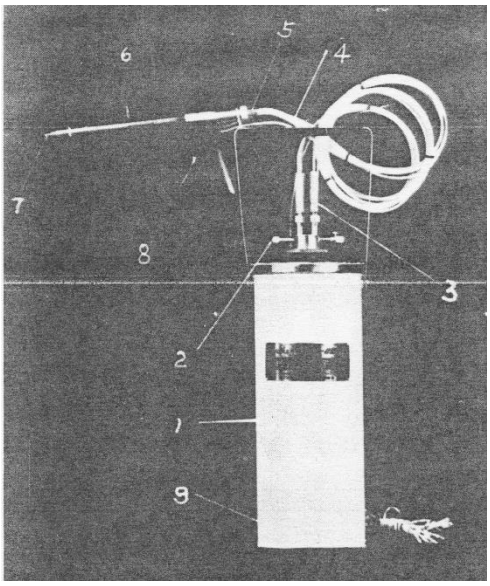


Fig.2. A cryosurgical equipment adopting adiabatic vapor film insulation.

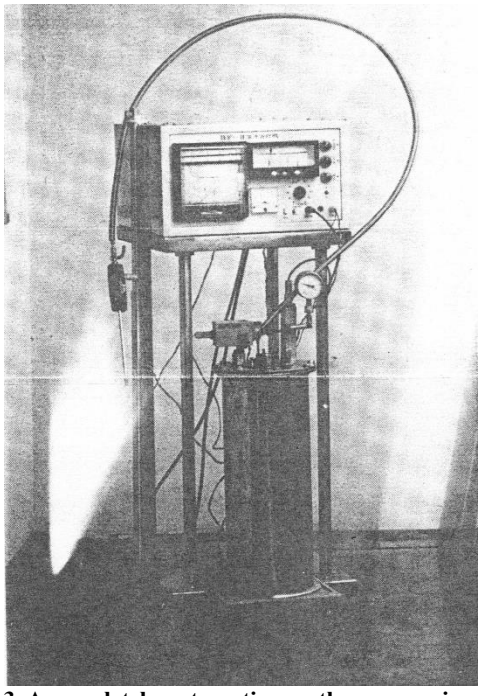


Fig.3. A completely automatic cryotherapy equipment.

Fig. 3 presents a more complete cryotherapy equipment designed and tested by us. It has a set of cryo-probes with hundreds of differently shaped freezing tips. The temperature both of 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.

The number of cases treated by cryotherapy in China has now exceeded 10 thousand. A few examples of the results are presented here as follows.

Oral cancers and precancers in hospitals such as Stomatological Hospital in Beijing have been treated by cryotherapy with cure rates of 83.3% and 94.4% respectively. One example is shown in Fig. 4. Lung cancer is treated successfully with cryotherapy in the cancer hospital of Shanghai, First Medical College, as shown in Fig.

5.[4] The patients in this case can not be treated by either radiation therapy or pulmonary reserve. Some of the patients have poor pulmonary or cardiac functions, or large tumors with cavitation; others have metastatic lung cancer including multiple dilateral lesions. It is found that cryosurgery combined with cornebacterium anacrobic vaccine is more effective than cryosurgery alone n the cases with multiple lesions and pleural effusion.

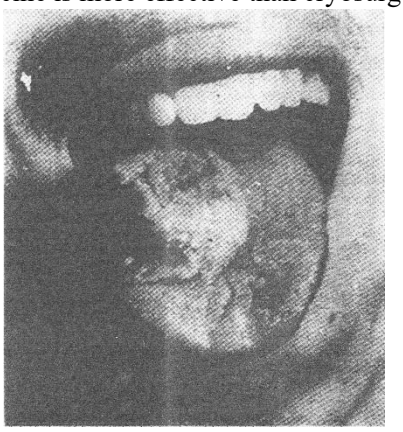


Fig.4a. Cancer of the tongue; before cryotherapy.

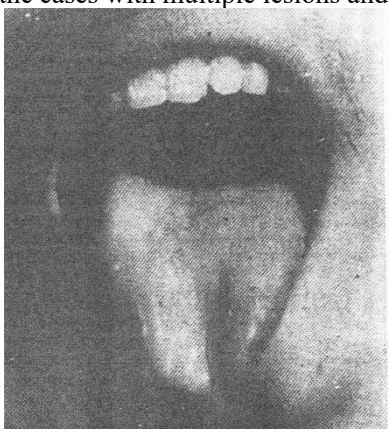


Fig.4b. Cancer of the tongue; after cryotherapy.

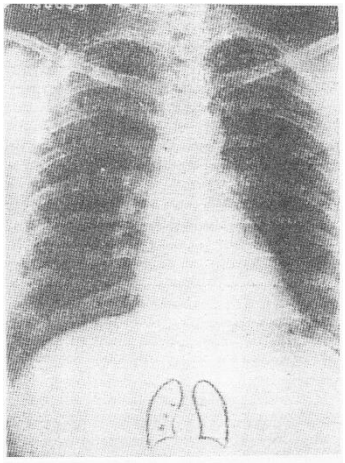


Fig. 5. Chest X-ray film of a case where 32 metastatic lesions of the left lung have been removed cryosurgically.

Special Cryo-probes for Disorders in Deep Organs

There are many cancers and tumors located in deep tissues,e.g. in the brain, stomach, prostate,etc. If doctors are to treat them without injuring normal tissue around the disorders they need special apparatus. Several special cryo-probes have been developed, some of which are shown in Fig. 6 designed and tested by us.

There must be a "cool region" and "warm region" on the surface of some special tips which are inserted into deep tissue. At the tip of a neurosurgery cryo-probe, only a small area is cooled. In the prostate cryo-probe, only a small middle part of the tip is cooled, and the temperature of both ends of the tip must be more than 0℃. Some special cryo-probes are quite refined and small, with an outer diameter of only 2.4 mm.There is an LN_2 entry tube, a gaseous N_2 return tube, a high vacuum space, a thermocouple and a heater, all inside the 2.4 mm diameter tube. These technical problems have been met with success.

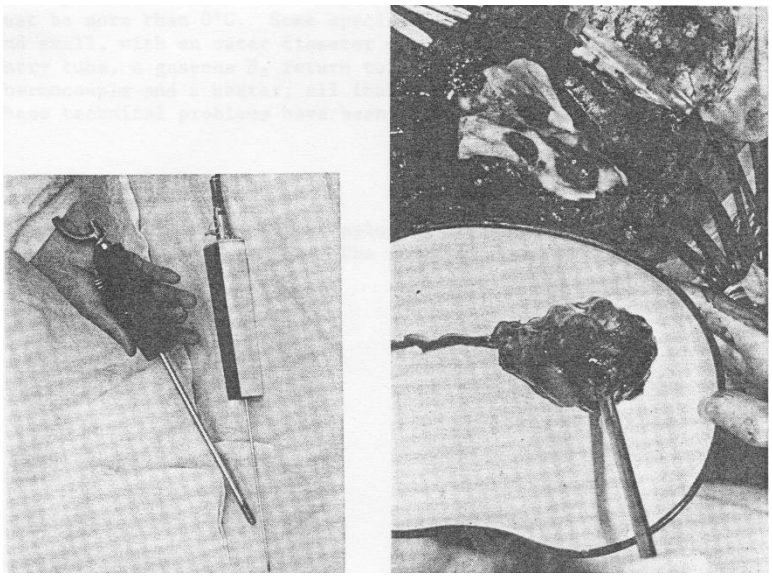


Fig. 6. (a) special cryo-probe (b) brain cancer removed

ARTIFICIAL INSEMINATION

Artificial insemination employing cryogenic techniques is expanding steadily in China. The semen of cows, sheeps, pigs,horses, etc., can be stored in special Dewars for many years and then later thawed to be used for artificial insemination.Today, this kind of apparatus is manufactured in China and sold abroad.

CRYOPROTECTION AND CRYOPRESERVATION

It is an important facet of biomedical applications of cryogenics in China that human blood, skin, and bone, etc., have been preserved for long periods by cryogenic techniques. [8-9] Many hospitals and biomedical institutes have this kind of special Dewar. In Shanghai Second Medical College and Shanghai Biological Products Research Institute, scientists use this kind of equipment successfully to preserve bones. Irradiated freeze-dried homogeneous bone grafts have been used in many patients and virtually all have healed without infection. Initial clinical successes suggest that freeze-dried homogeneous bone is suitable for use in bone banks. Figure 7 illustrates a use of freeze-dried bone.

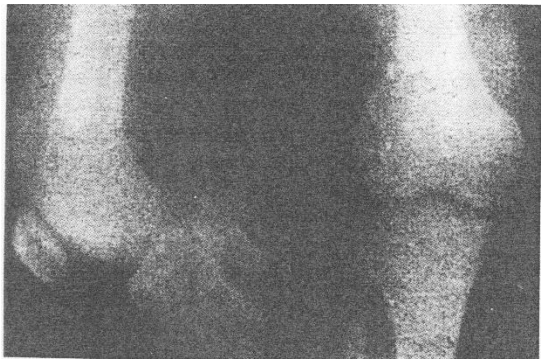
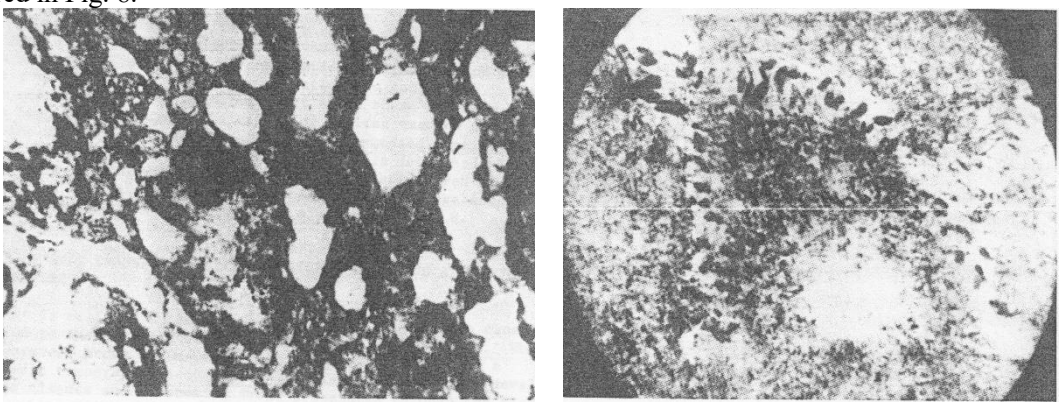


Fig. 7. Bone used freeze-dried.

CRYOBIOLOGY

Both in order to improve the effectiveness of cryotherapy and cryopreservation, and in order to research biological processes at the cellular level (e.g. molecular and electron transfer), cryobiology has begun to receive attention and has achieved some success.

The lethal effect of freezing on normal and tumorous cells has been studied. Immunologic reactions after cryosurgery have been studied. The results of observation of immunization prove that cryosurgery may restore immunizations to good order. Also, high energy phosphates of a rat heart after rapid freezing by LN_2 have been investigated.The effect of cooling rate on the viability of bone marrow hematopoitic cells has been studied, and it was shown that the viability of hematopoitic cells decreased with increasing cooling rate.The submicroscopic structures of the cancer cells of oral and maxillo-facial regions before and after cryosurgery have been researched as pictured in Fig. 8.



a. ice forming in cells. **b. after cooling**

Fig.8. Cooling of cells.

STUDY OF HEAT TRANSFER IN LIVING TISSUES AND ORGANS AT CRYOGENIC TEMPERATURE

It is well known that the survival rate of cells is closely related to the temperature and rate of temperature change. When a cryosurgical probe is inserted into tissue and brought to a cryogenic temperature suddenly, a transient thermal field develops in the tissues and a freezing front propagates through the tissue. The problem is to decide on a freezing program so that the cancer cells can be killed while the normal cells survive.

Unfortunately, because the process of heat transfer in large living organs is very complicated, no practical mathematical model for the freezing process of whole large organs is available at the present time. No existing device can preserve large organs for long periods for storage or transplantation.For this reason we and our colleagues study heat transfer mechanisms and record many measurements pertaining to various living human and animal tissues during freezing. We hope that such data will help us to develop a more precise mathematic model and help us to design special cryogenic apparatus that will lead to more effective cryotherapy and cryopreservation.

FUTURE PLANS

The research discussed above will continue. In addition, two other projects will be initiated:
1) superconductive magnets will be employed in the biomedical field, and 2) SQUID devices will be used for detecting weak magnetic fields from human as well as other living bodies.

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