Practical Problems in Cryosurgical Techniques

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LIQUID nitrogen-cooled cryosurgical apparatus for the treatment of human tumors was first developed by Cooper,[1] and thereafter slowly found limited use in a variety of medical specialties. My experience[2,3] with over 200 patients in the past eight years has revealed several problems. One is the difficulty in evaluating the extent of freezing, especially when treatment is given via endoscopy. Determining depth of freezing is a problem even when vision is good. Another problem is the difficulty in freezing large volumes of tissue even though liquid nitrogen is used as the cryogenic agent. The purpose of this Note is to define these problems which merit the attention of the engineering community.

Three types of cryosurgical equipment were available. Choice depended upon the site and size of the tumor. One system functioned only as a closed system with freezing done via cryoprobes, so that LN_2 was never released on the tissues but rather the gas was returned to the equipment cabinet for venting (Linde CE-4 cryosurgical apparatus, Frigitronics Inc., 770 River Rd., Shelton, Conn.). The flexible feed shaft was vacuum insulated. Controls on the console made possible reasonably accurate control of the temperature of the probe tips. The other two types of equipment (Linde CE-8 cryosurgical equipment, Frigitronics Inc., and Brymill Model SP-5, Brymill Corp., Vernon, Conn.) could be used as either closed systems with cryoprobes or as open systems spraying LN_2 directly on the tissues. The feed cables of these types were not vacuum insulated. The probes lacked controls for temperature and they could not be heated. Details regarding various types of cryoinstrumentation have been described by Garamy.[4]

Technique

When cryoprobes were used in closed systems, as the frozen tissues turned white and hard, the extent of freezing was judged by inspection and palpation. Roughly, a hemispherical frozen area was produced, so depth of freezing was judged to be the same as the distance of surface freezing from the probe. When the depth of freezing was important to control, thermocouples mounted in 18 gage needles were inserted into the tissue to monitor temperatures and increase the certainty of achieving lethal temperatures deep in the tissues. They also were used at the periphery of lesions to prevent unwanted destruction of normal tissues.

Specific details of treatment varied with the part of the body being frozen. Easily accessible tumors, such as skin and oral cancer, were possible to treat with good observation of the progress of freezing so treatment was rather simple to give. Farther within the body orifices, as for tumors in the larynx, esophagus and rectum, freezing was done with long cryoprobes via endoscopy and visual control was difficult at times. In some applications, as for bone tumors, cryosurgery was used in combination with surgical exposure and curettage of the lesion. Usually only surface contact freezing techniques were used, but when the tumor was soft and bulky, the cryoprobe was pushed into the tumor to increase its freezing capability by increasing the area of contact between tumor and freezing surface.

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Spraying systems were used to freeze tumors which were very accessible and of considerable size. However, these systems were more difficult to control. Commonly the spray became droplets, resulting in runoff on the tissues and freezing in undesired areas.

The goal of cryosurgery has been the production of freezing of a predictable area of tissue necrosis. Therefore it was important to develop techniques to achieve maximal lethal effect. Rapid freezing and slow thawing are more lethal than slow freezing and rapid thawing. Repetition of freezing has been accepted as standard good practice also. The exact lethal temperature is not certain. Ice crystals form in tissues at −2.2°C, but not consistently; under certain conditions temperatures as low as −20°C may be reached before ice crystals appear. Since this temperature is close to the eutectic point of sodium chloride solution, it is commonly cited as that which must be achieved in order to be certain of cell death.[5] Our animal experimentation has shown that this is not true under usual cryosurgical conditions. Experiments with freezing the canine palate, conducted at different time-temperature freezing schedules, showed that at temperatures warmer than −50°C, single freezing episodes were uncertainly destructive. Tissue cells occasionally survived at temperature of −60°C for three minutes. At temperatures of −60°C and colder, even single freezing episodes produced predictable areas of necrosis, and increased destruction by repetitive freezing was obviously not demonstrable.

Under clinical conditions, these considerations become important. There are enormous gradients in temperature in the frozen area. The tissue next to the cryoprobe may be at −160°C, while at the border of the frozen zone the temperature may be close to zero. Therefore, at the edge of the frozen zone tissue survival is possible. With existing equipment, it is difficult to achieve the certainly lethal −60°C in a large volume of tissue. Fortunately repetition of freezing greatly increases the lethality of the freezing process and under this condition there appears to be no survival even at −20°C. To the cryosurgeon, good technique means that everything that he sees visibly frozen will die.

Limitations of Equipment

In areas where endoscopy must be used, such as in the larynx, esophagus or rectum, vision is difficult and evaluation of depth of freezing is almost impossible. Some knowledge of the depth of freezing can be obtained by experimental use of the cryoprobe system to determine how large a frozen lesion will form from a cryoprobe under a given time-temperature cycle. Formulas have been produced to predict the thermodynamic growth of ice balls around cryoprobes,[6] but they cannot be used for general clinical application. Though osmolality and thermal characteristics of various tissues show only minimal differences and only minimal variation of the cryolesion can usually be expected under fixed freezing conditions, still variations occur in certain tissues. Skin and fat have insulating qualities and resist freezing. Variations in blood supply, especially the proximity of a major blood vessel, may profoundly alter the size and shape of the frozen area. Even more often, freezing tissue under apparently identical situations still may yield great variations in tissue temperature.

Some of these problems were evident in experiments made on freezing dog skin comparing spray and probe techniques, using the three commonly used types of cryosurgical apparatus. The conditions of the experiment simulated clinical freezing. A copper-constantan thermocouple mounted in an 18 gage needle was placed on the surface of the skin between the probe and the skin. A similar thermocouple was placed subcutaneously directly beneath the probe and the first thermocouple. The distance between the two thermocouples was 3 mm. Temperature readings were recorded continuously. Probe temperature was not recorded since that information cannot be obtained from some of the equipment used,

but all equipment was used in such a way as to produce maximal freezing from the probe.

Vagaries in LN_2 flow and erratic freezing were encountered in many experiments and from all apparatus, though not to an extent that would cause a problem in clinical freezing. For example with cryoprobe freezing, occasionally frozen tissue warmed as much as 20° before deeper freezing resumed. The reverse also occurred, that is, tissue temperature apparently rather stable at −110°C suddenly cooled to −175°C, apparently coincident with unexpected increase of liquid nitrogen flow through the probe. Speed of freezing was also erratic and greatly dependent upon the excellence of tissue contact. The cryoprobe almost always produced surface temperatures colder than −80°C in less than a minute and commonly produced surface temperatures as cold as −170°C in this time. Subcutaneous tissue temperatures were generally 20° warmer than the surface and the curves written on the recorder closely imitated one another. This experience indicated the merit of routine use of thermocouples to ascertain the status and progress of freezing in all clinical treatments. The most sophisticated apparatus with its vacuum insulated feedline functioned much better than the less expensive apparatus.

The open systems, using the spray to freeze tissue, produced extensive tissue freezing over a wide area, but problems in flow control resulted in wide fluctuations in tissue temperature and in runoff liquid nitrogen from the tissues if extensive freezing was attempted. Variations in temperature resulted from pulsatile increases in liquid nitrogen flow from the reservoir and commonly from partial occlusion of the aperture in the spray nozzle. When the occlusion was blown open by pressure, then greatly increased flow suddenly followed. As the apparatus cooled and the tissue froze, LN_2 droplets could form, strike the tissue without vaporizing and run off to freeze in undesirable areas. Reducing the pressure within the reservoir did not prevent this phenomenon.

With existing equipment, it is difficult to freeze sufficient volumes of tissue. For example, with a 9.5 mm diam cryoprobe used at −180°C, it is possible to create a roughly hemispheric frozen lesion 3 cm in diameter in 3 min and about 4 cm in diameter in 5 min. On continued contact, the ice ball grows very slowly until an equilibrium is established. For practical purposes, it is pointless to continue freezing more than 7 min. Instead, the cryoprobe must be moved to a new site. Moving the cryoprobe to a new site improves the width of the frozen area but only slightly increases the depth of freezing.

Cryosurgical equipment needs considerable improvement for endoscopic use. For example, in the treatment of rectal tumors, use of the 9.5 mm cryoprobe through a sigmoidoscope leaves insufficient room for good vision. As far as the rectum is concerned, the sigmoidoscope is already just about at maximum size, so advances must depend upon the construction of a smaller cryoprobe system with improved freezing capability. Another area in need of development is the application of freezing techniques to visceral cancer. Here a laparotomy must be performed in order to treat the tumor, and even under these conditions the usual bulk of such tumors requires the development of special instruments to perform the massive freezing required.

Concluding Remarks

Cryosurgery for the cure of tumors is not yet generally practiced and cannot yet be considered a standard method of treatment. However, its use is gradually expanding. Its advantages lie in simplicity of use, rather little need for anesthesia, lack of hemorrhage during freezing, and few complications in the postoperative period. Most of these advantages are due to the fact that in treatment nothing is excised but rather the tumor is allowed to become necrotic and slough.

Benign tumors are easily treated by freezing and there is little risk because treatment can be conservative and can be repeated if not successful initially. On the other hand, to treat cancer by freezing in situ demands recognition of the risks involved. Caution is justified by the realizations that tissues resist freezing injury and that the extent of cancer is always uncertain. Considerable confidence in any technique is necessary before use for cancer therapy. Present day cryosurgical apparatus is barely adequate for the task and both equipment and technique of its use need improvement. My view on the prospects of cryosurgery in the treatment of cancer is one of optimism because of the likelihood that the needed improvements can be achieved.

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Secondary Jet Interaction with Emphasis on Outflow and Jet Location

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Nomenclature

C_m	= pitching moment coefficient
d	= jet slot width
$F_{N,A}, F_{N,R}$	= jet interaction and reaction forces, respectively
h	= jet penetration height
L	= model length
M_∞	= freestream Mach number
P_3/P_∞	= total pressure above jet shock to freestream static pressure; see Fig. 2b
$P_{t,j}/P_\infty$	= jet total pressure to the freestream static pressure
α	= angle of attack
λ	= mass-flow correlating parameter
$\bar{\omega}$	= effective slot width for orifices, having same span and area as the orifices

SECONDARY jets are being considered for aerodynamic control of a variety of supersonic and hypersonic vehicles including the space shuttle. Although considerable research has been conducted on this subject,[1] uncertainties still exist in the prediction of aerodynamic forces associated with the jet-flowfield interaction. The present Note discusses some

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