Cryogenic Freezing of Brain Tumors for Excision or Destruction in Situ*

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The first report of the local application of cold in the treatment of neoplasms was published in England by James Arnott in 1851. Since that time, there have been many investigations that indicated the potential usefulness of cooling or freezing of biologic tissues in order to destroy malignancies. Smith and Fay reported intensive investigations of generalized lowering of body temperature in an attempt to inhibit neoplastic growth. Most students of this problem, however, concluded that the method of generalized hypothermia was too hazardous and too uncertain in its effects to be employed consistently for the purpose of inhibition of tumor cells.

The local application of cold has been employed more successfully. However, the lack of adequate instrumentation has prevented the realization of the potential value of extreme cold as a surgical tool. Nevertheless, the studies of Rowbotham et al., Hass and Taylor, Bory, Ries and Tytus, and others, have indicated that local application of extreme cold might facilitate the destruction or removal of certain types of brain tumor.

It is the purpose of this report to describe our use of a cryogenic surgical system to freeze various types of brain tumors for the purpose of producing local necrosis of the tumor in situ, or to facilitate the removal of the tumor as a solid frozen mass.

**Instrumentation**

During this investigation we have employed the cryogenic surgical system developed at St. Barnabas Hospital for physiologic studies in animals and humans, as well as for creation of lesions for physiologic surgery within the nervous system. The same system may be employed for congelation and necrosis of tumors in the nervous system and other parts of the body. A series of graduated, vacuum-insulated freezing cannulae has been developed. These are capable of producing variously sized and variously shaped areas of freezing in biologic tissue (Figs. 1 and 2).

Employment of this system provides for the rapid selection of any temperature between +37°C and −196°C, the temperature of the liquid nitrogen which refrigerates the system. Only the tip of the cooling cannula is not insulated. Thus, the freezing temperatures are applied only to the precise area selected. A more complete description of the entire system has been published in an earlier report in this Journal.

**The Biologic Effects of Freezing**

Ordinarily, during the rapid reduction of temperature of biologic tissue, the temperature will fall to as low as −15° or −20°C before ice crystals begin to form within the tissue. This period of extreme coldness below the freezing point but prior to formation of ice crystals is referred to as supercooling.

Following the period of supercooling, there is a rise in temperature or recrystallization, back up to the freezing level of −2.2°C. During this period of time the transfer of energy which occurs during the removal of heat from cells is being used to form crystals rather than to lower the local temperature of the tissue fiber. This use of the energy of heat transfer to form crystals is referred to as the latent heat of crystallization. This prior supercooling results from the fact that there are very few nuclei in biologic tissue on which crystals may start. However, once formation of nuclei and crystallization begin, a heat-jump back up to the freezing level will occur. As crystallization proceeds, further application of cold will be followed by additional lowering of the temperature. The eventual
Fig. 1. Variously sized and shaped vacuum-insulated cannulae which form part of the cryogenic surgical system.

depth to which the temperature of the tissue may be taken will depend on the original temperature of the freezing agent.

Five mechanisms through which extreme cold produces chemical and morphologic destructive changes in tissue have been described thus far.\textsuperscript{15,18,22} These are: dehydration and toxic concentration of electrolytes caused by removal of water from solution; crystallization with rupture of cellular membranes; denaturation of liquid-protein molecules within the cell membrane; thermal shock; and vascular stasis.

The potential usefulness of a cryogenic system for controlled freezing and necrosis of primary or metastatic tumors is demonstrated readily by an examination of the lesions produced consistently by this method in the laboratory animal. The cryogenic vacuum-insulated cannula placed within the liver, kidney, brain, or any other biologic tissue produces a spherical frozen lesion, the diameter of which is directly proportional to the size of the freezing surface and the temperature of the tip of the cannula. The edge of the frozen lesion is demarcated sharply from adjacent tissue. When the lesion is allowed to thaw, the cannula may be lifted from its center without adherence of any tissue to the tip of the cannula. There is no visible bleeding from the site of the lesion. Within a few minutes after thawing, the lesion becomes a very dark blue, indicating deoxygenization, but retains its sharply demarcated spherical character. Subsequent to thawing the frozen lesion may be incised without production of any significant hemorrhage. A control incision in an adjacent non-frozen tissue invariably will produce continuous hemorrhage.\textsuperscript{22} These characteristics of the cryobiologic lesion, which make it an extremely useful instrument for the surgery of tumors within the brain, are illustrated in Fig. 3.

Further indication of the possible usefulness of extreme cold to congeal and subsequently produce necrosis of malignant tissue, both primary and metastatic, in various parts of the body has been demonstrated by biopsy of various tumors before and after the application of extreme cold. Such a case is illustrated in Fig. 4, which demonstrates the effect of freezing the center of a large ependymoma, located within the third ventricle of the brain. In this case the specimen taken from the center of the tumor which was frozen was found at autopsy to be totally

Fig. 2. Lesions frozen in gelatin by 2 vacuum-insulated cannulae $2'$ and $3'$ respectively in diameter. The former produced a frozen ice ball $1'$ in diameter, the latter an ice ball $2'$ in diameter.