REVOLUTION in ONCOLOGY

CryoSurgery - CryoTechnology
in
21st Century

Modern Cryosurgery & Cryotechnology
against Cancer
in 21st Century

Introduction

Looking at the development of the disease statistics of the past decades the enhancing rate of cancer disease and cancer deaths attracts attention, despite the exorbitantly increased financial expenditure for diagnosis and therapy (Big appliances, intensive medicine, etc.). In the last years no significant improvements could be achieved in this area, whereby the applied therapeutical methods are of limited efficiency. Among the other cancer kinds particularly breast cancer is advancing. Secondary manifestations like metastases and local recurrences due to protracting cancer cells as a result of diagnostic interventions mean a death sentence for patients with mamma carcinoma.

A new way of thinking must, thus, prevail in the future of cancer research and treatment. New disguise and treatment methods should enhance the healing rate of the cancer disease. Modern cryosurgery - a particularly gentle operation technique - experiences nowadays an international attention and dissemination. Good results can be proven through long-standing practical experience and numerous international publications. Thereby it has been shown that a successful employment of this method can only be reached through the development of effective medical-technical appliances. The existing new concept of a multimodal oncology demonstrates how modern,
cryosurgical technology for diagnosis, prevention and treatment of cancer could be developed and produced.

**What is Cryosurgery?**

Cryo-, freeze- or cold-surgery is the operative cutting of tissue or the targeted destruction of pathological tissue by induced cold necroses at temperatures down to –196°C. Tumors are usually not excised but shock-frozen. In these cases vacuum-isolated cryoinstruments (cryoprobes, cryoscalsps, cryoclamps, cryoneedles) are used. These instruments are cooled to -170°C to -190°C by the evaporation of liquid nitrogen.

The prerequisites for the art of cryosurgery include not only long experience in the use of the instruments but also experimental and clinical knowledge. In the last 22 years, Nikolai N. Korpan, MD, PhD, Professor of Surgery, and his colleagues together in co-operation with other international scientific institutions have developed and refined new cryosurgical techniques for operative procedures in patients with liver and pancreas tumors, breast cancer, lymph node metastases, and recurrent skin cancer.

Cryosurgery is established in medical practice both as a single technique as well as supplementary to other oncological treatments. The development of the cryocauterity (on the Cooper principle), which makes the destruction of large areas of tissue by extreme hypothermia possible, was the technical prerequisite for a cryosurgical method applicable in general surgery. However, the reliable destruction of tumors requires the use of high-performance devices.

**Main Mechanisms of Action**

Numerous theoretical and experimental studies in vitro and in vivo have been carried out to understand the action of low temperatures on tissue. It has been determined that the processes of ice crystallization are here of primary importance. Current opinion holds that one of the most important elements contributing to the action of subzero cold is intracellular ice formation, which damages the delicate cell structures. Also important in cryoactivity is the formation of extracellular ice, which is followed by cell and tissue dehydration as well as protein denaturation and rupture of the cell membranes. But the major effect on cell damage and cell destruction in cryoactivity is exerted by the speed of freezing and of thawing of the tissue.

The macroscopic picture resulting from the influence of cold on different organs is almost always identical. At first one notices a mild hyperemia. This is followed by a hint of a change in color of the tissue to livid, after which a snow-white area of solid ice builds around the cryoprobe, which expands as the temperature sinks and the effect of the action of cold increases. Then the ice formation decelerates and finally ceases at –196°C. After thawing, the tissue has regained its original color and consistency. In the hours immediately following the area of focus swells up with edema, and after 3-4 days a completely necrosed focus with a discolored gray surface has formed.

Several days later the process of regeneration begins with the sloughing off of the necrotic tissue. After about 4 weeks the deep necrotic crater is entirely replaced by course granulation tissue.
Microscopically the picture is similar. Total cell dissociation with interstitial bleeding can be seen – a hemorrhagic infarction immediately followed by the formation of an unstructured, homogeneous mass, i.e., a coagulation necrosis. With the sloughing off of the necrotic mass, a seam of fibroblasts appears in the border foci that initiates regeneration absent of leucocytic infiltration (aseptic necroses). Finally a hypocellular stoma rich in connective tissue fibers forms.

Under the electron microscope, swelling of the mitochondria, fragmentation of the plasma membranes, and thickening of the nuclei can be seen.

Our own experimental studies in the animal model on dog livers and pancreas showed that the cryodestruction zone of the liver parenchyma had a sharp, well defined line of demarcation clearly discernible contours. On the 5th postoperative day the liver parenchyma that had been frozen was now a pronounced necrosis of homogeneous substance. In the following weeks, granulation tissue formed. Four weeks later loose connective tissue with numerous blood vessels formed in the cryozone, after 9-10 weeks there was tight connective tissue and after 12 weeks the transformation of the cryozone of the liver parenchyma to connective tissue was complete.

Already in the works of Hippocrat, Galen, Celsus and Ibn Sina numerous indications to the treatment of various diseases through warmth deduction can be found, as in cases of haemostasis, analgesia and at feverish states and inflammations. The modern cryosurgery leans on the theoretical, clinical and experimental experiences since 1963. However, because of lacking technical-apparative prerequisites no dissemination could take place. A successful use of this method - particularly for various cancer types - is only possible through the development of efficient medical-technical appliances.

**The main points of this concept are:**

- Radical and palliative cryosurgical operations: cryoresection and cryodestruction.
- Extra- and intracorporeal tumour cell filtration by means of haemo- and lymphsorption.
- Minimal conventional tumour surgery
- Development and production of new cryosurgical technology
- International Teaching and Training

**The most important application fields are as follows:**

- General surgery
- Oncology (cancer treatment), including breast cancer surgery
- Cosmetic surgery
- Urology
- Gynecology
- ENT
- Dermatology
- Orthopedics
- Neurosurgery
- Thorax surgery

**General surgical indications:**
Benign and malign skin cancers (papillomas, birth marks, warts, basaliomas, melanomas, etc.)
Cancers of the liver, pancreas and large intestine
Inoperable liver metastases, rectum and anal cancers
Breast cancer
ENT tumors
Prostata cancer
Scar and cicatritial formations
Ulcera cruris
Noduli haemorrhoidales

**Contraindications:** are not known at this point in time.

**Positive aspects** - or what the patient gains from modern cryosurgery as opposed to the conventional surgical methods?

**Advantages:**

1. The most important advantage of cryosurgery is the impediment of the metastatic spread during tumor removal - since no "cutting" takes place.

2. Short trauma after both operation and narcosis.

3. Through direct entrance opportunity a short or no narcosis at all is possible. On many applications narcosis can be dispensed with since the cold already has an analgetic effect.

4. The convalescence reduces itself to a fraction of the usual stationary staying periods.

5. Good cosmetic result: no scar formation. When cryosurgery is applied on the skin surface (on the outside) scars are avoided (e.g: tumors in the face).

6. The resorption of this kind of frozen tissue seems to additionally carry a vaccination effect with it - however, this effect can scientifically not be explained yet.

7. No local complications deriving from the operating table.

8. Quick and technically simple tumor removal process.

9. Good removal of both benign and malign tumors.

10. Substantial subjective facilitation with cancer patients through cryosurgical palliative procedures with a pain reduction (painlessness or pain reduction) and fetor ex ore as well as improvement of the general condition through getting the tumor growth under control.

*The modern day of cryosurgery* of the present consists of the achieving efficiency and effective modality through good, uncomplicated surgical results and a high curative rate (treatment rate) as well as high life quality of the operated patients.
In order to reliably destroy the pathological tissue, especially malign tumours, thus achieve a successful cancer treatment high quality appliances need to be implemented. The new "Cryosurgical System" is universally applicable in the modern cryosurgery, especially suitable for particularly mild cryosurgical operation techniques in the medical application area. The cryosurgical system created by “Vienna International Institute for Cryosurgery” is world-wide the leading appliance in the medical field. Finally, the modern cryosurgical unit „FreezeForce1“ is a highly sophisticated Universal Cryosurgical System developed to meet the most demanding needs of today's „White Surgery“.

Ad personam

Nikolai N. Korpan, MD, Professor of Surgery, is an active member of the International Society of Surgery, International College of Surgeons, International Society of Cryosurgery, the N.Y. Academy of Sciences, Austrian Patent and Inventor Union (OPEV). He is also founder and vice president of the European Society of Cryosurgery and head of the Vienna International Institute for Cryosurgery, being additionally member of the Austrian, Ukrainian and Swiss Society for Surgery, International Association of Inventors „Perpetuus“, International Society „InterCryoMedFocus“, Research Board of Advisors, The American Biographical Institute, Lindau Nobel Alumni (Germany), etc.


The art of cryosurgery not only requires a long-standing experience with the dealing of instruments but also Professor Dr. Nikolai Korpan pioneers cryosurgery both in Europe and world-wide, being able to refer to his longstanding practical experience in thousands of cryosurgical operations. Publications in renowned international
journals as well as lectures on numerous congresses have drawn world-wide attention to this revolutionary operating technique.

On the basis of own long-standing theoretical, experimental and clinical research, experience and knowledge in the field of cryosurgery a new generation of highly efficient appliances under the market name “FreezeForce1” is intended to be developed, thus enabling cryosurgery to an international breakthrough.

**What are the Latest Developments in Cryosurgery?**

The development of unique state-of-the-art high-performance medico-technical cryoinstruments and devices (*see Table*):

- 21 national patents (Austria)
- 153 world-wide patents (EU, USA, Japan)
- The development of new operations
- Innovative cryotechnology with healing cold

**Keys to success**

The keys to success in this business are:

- Marketing: either dealing with national distributors or with well-established international companies.
- Licensing at least one technology and application to a major medical device corporation.
- Product quality.
- Product approval in Europe and USA.
- Management: products delivered on time, costs controlled, marketing budgets managed.
- There is a temptation to fix on growth at the expense of profits.

**In process**

The development of an International Antitumor City with a concentration on cryosurgery and cryotechnology and an international Training Center in Europe or other world place are intended.

**Further information on request!**