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Cryosurgery: state of the art and perspectives in 2001

by

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I. INTRODUCTION

Medical use of cold has existed since ancient times. It started out as an empirical technique, then in the 19th and early 20th centuries progressed thanks to breakthroughs in the fields of physics and gas liquefaction. Two modes of use exist; they can be contradictory or complementary. The two modes can be defined as preservation or destructive modes. Cryobiology covers preservation using cold (cryopreservation of blood, bone marrow and gametes, etc.), while cold used for destructive purposes is cryosurgery. In between these two extremes, cryotherapy makes use of cold as an anti-inflammatory treatment in the fields of rheumatology and functional re-education. However, the terms cryotherapy and cryosurgery are often perceived as being one and the same. Modern cryosurgery is only 40 years old. In 1961, I. Cooper¹, a neurosurgeon, was the first to use automated cryosurgical equipment with a liquid-nitrogen-cooled probe. Up until then, cold was used only to treat readily accessible areas (skin, and genital and rectal mucous membranes); the advent of new probes has made it possible to treat deeper lesions and has paved the way to cryosurgical treatment in cancerology. Over the past 40 years, equipment has been perfected and miniaturized, and knowledge has expanded constantly. Among publications illustrating this rapid progress are those describing the work of P. Mazur,^{2,3} that of B. Rubinsky^{4,5} on various organs, and in-depth studies by J. Baust⁶ and A. Gage.⁷ Recently developed predictive methods have led to a more scientific approach to the freezing process: an impedance-based measurement method developed by P. Le Pivert,⁸ and above all ultrasound imaging.

Unfortunately, cryosurgery is not taught in medical schools as part of the traditional syllabus. It is generally considered as rather obscure and tends to be overshadowed by other therapeutic approaches. It is thus used to widely differing extents in different medical fields and in various countries: in some contexts it is rarely used, while in others it has increasingly become part of the therapeutic arsenal or is declining. In some countries, cryosurgery is considered as being a new discovery while in others it is being readopted following years of non-use. In the US, cryosurgery was formerly used to treat benign and malignant endobronchial lesions as early as 1968,⁹ with peak use between 1977 and 1983¹⁰⁻¹¹ before being abandoned in favour of Nd:YAG laser treatment, then reappearing around 1996.¹² In some countries, cryosurgery is widely adopted in the dermatological field but not in other domains, whereas in other countries such as France, a veritable "school of cryosurgery" has been established in the field of chest medicine, leading to renewed worldwide interest in this technique that has now been codified and has

gained recognition as having a role to play along with classic therapeutic bronchial endoscopic techniques. The efficacy of cryosurgery is not its only positive feature — it is also easy to use, non-traumatic and complication-free. The equipment required is relatively low-cost to purchase (3900 euros) and inexpensive to maintain.

Overall, cryosurgery is expanding slowly, but in certain fields and in some countries, fast expansion is occurring. Eastern-European countries have advocated cryosurgery for many years and are in this respect well ahead of the West where cryosurgery remained relatively obscure until more recently. In certain developing countries, obtaining supplies of refrigerating gases can prove to be a major obstacle to the use of cryosurgery.

In medical applications, the most commonly used cryogenes are liquid nitrogen and nitrous oxide.

This discipline has now progressed far beyond the stage of dipping cotton wool in liquid nitrogen then treating warts with it. Liquid nitrogen can now be used in spray form but is above all used to cool probes of various diameters and lengths according to the intended applications.

II. KEY CLINICAL APPLICATIONS

I. Dermatology

Skin lesions are readily accessible and have thus been the application of predilection for cryosurgery for many years worldwide. Most benign skin lesions, including epithelial lesions (warts, papillomatous tumours, etc.), vascular lesions (senile angiomas or infantile tuberous angiomas...) or mesenchymal (fibrous histiocytomas, keloids...) tumours, respond to cold treatment. Aesthetic considerations govern perception of results. Healing usually takes place with little scarring following cryotherapy and this explains why this technique is extremely acceptable. Certain malignant lesions, particularly superficial basal cell carcinomas, can also be effectively treated using cryotherapy. Well-differentiated spinocellular carcinomas can also be treated using cryotherapy, with almost no contraindications, and this applies to the seat of lesions. Thus, carcinomas of the nose, the oculonasal angle, and the ears and the lips, which are difficult to treat using classic surgery and sometimes require skin grafts,¹³⁻¹⁵ can be successfully treated using cryosurgery.

II. Chest medicine

The use of cold in the field of chest medicine began relatively recently. The diameter of the operating canal of the bronchoscopes used was the limiting factor in the past and probe miniaturization was an initial challenge to be met. Following initial trials in the US, this cryotherapeutic technique lost ground in favour of Nd:YAG laser but was relaunched in Europe by J.P. Homasson¹⁶ (in France), M. O. Maiwand¹⁷ (in England) and A. Astesiano¹⁸ (in Italy). Its use expanded particularly rapidly in France and was readopted in the US¹² as of 1996 thanks to the development of highly improved European equipment featuring flexible probes. Today, bronchoscopic cryotherapy is a clearly codified technique.^{19,20} As it involves deferred destruction, this technique cannot be used in emergency clinical contexts involving acute respiratory distress due to tumoral obstruction of the trachea. However, it is an alternative to other techniques in all other situations, whether used as sole therapy or in combination with other bronchial carcinoma therapies (radiotherapy and chemotherapy), and appears to exert potentiating effects.^{21,22} Already used as palliative treatment of bronchial carcinomas, bronchoscopic cryotherapy could soon become the first-line treatment of severe dysplastic precancerous lesions and in-situ carcinomas detected during screening performed using new autofluorescent endobronchial techniques. It is also a useful tool enabling extraction of foreign bodies in the bronchial tree.²³

III. Urology

After having found considerable favour in the urological field during the 1970s, cryotherapy was little used until recently. It is now being used for a specific indication: prostate cancer. Cryotherapy has been successfully employed to treat superficial bladder tumours (and does not involve any risks of perforation or haemorrhage thanks to the small endourethral probes used), and ectropions and venereal condylomas of the urethra. Use of cryotherapy as codified treatment of prostate cancer is more recent and has been made possible by ultrasound regulation of the volume of tissue that is frozen. All stages of prostate cancer are treated using cryosurgery but the best results are achieved in the case of localized glandular forms. Less satisfactory results^{25,26} are achieved in more advanced stages requiring freezing of larger volumes as these involve a higher risk of complications. Patient morbidity is low. Optimal patient selection enables good results to be obtained using cryotherapy, as demonstrated by objective follow-up (prostate biopsy and prostate-specific antigen [PSA] assay). The equipment required is expensive (90 000 euros), and this is no doubt a factor that is limiting expansion of its use.

IV. Hepatic metastases in colorectal cancers

Ablation of hepatic metastases using cryosurgical probes and echography in order to position the probe is a recently developed technique. In at least 75% of patients, traditional surgical resection can not be performed, even though the latter remains the first-line technique: where multiple metastases are present in both lobes or where metastases are located close to major vessels, surgery can not be envisaged. Cryotherapeutic probes are inserted using echographic guidance or transcutaneously via a trocar, or using an abdominal incision and direct hepatic approach. The number of probes used and their diameters depend on the size of the tumour to be ablated. When used in the right indications, complete ablation is achieved in 25% of cases.^{27,28} **For some metastases, cryosurgery and classic surgical ablation are both required, as is chemotherapy, and cryosurgery can potentiate the destructive effects of the latter.**

V. Gynaecology

Endometrial cryosurgery is no longer performed but cryosurgery does enable good results to be achieved in the treatment of benign cervical lesions: ectropions and condylomas. In the case of precancerous lesions and in-situ carcinomas, opinions diverge markedly concerning treatments of choice. Many surgeons prefer laser resection but randomized studies comparing laser treatment and cryosurgery have not demonstrated that either treatment gives rise to greater benefits than the other.²⁹

All benign vulvar lesions can be treated using cryosurgery.³⁰ Advanced stages of vulvar carcinoma can not as a general rule be treated using classic surgery. Palliative cryosurgery can sometimes produce spectacular results.³¹ This is also the case in advanced stages of breast cancer.

VI. Other indications

Cryosurgery has been used in almost all medical domains. Although its efficacy has been demonstrated, its use has often remained limited: this is the case for maxillofacial surgery,³² ophthalmology³³ and neurosurgery. One field in which cryosurgery is widely used is the treatment of haemorrhoids, an application that is rarely described in publications or papers. The treatment of varicose veins using cryosurgical ablation is still used, particularly in France. Cryosurgical treatment of pancreatic and renal tumours is rarely used but deserves further investigation. Cryosurgery appears to be attracting renewed interest in the field of treatment of certain cardiac arrhythmias. Certain bone tumours have also been successfully treated cryosurgically. Cryosurgery is used in

veterinary medicine, but to a limited extent because of the cost of cryosurgical equipment: various types of equipment are required, for instance, that used to treat a dog is not the same as that used to treat a horse.

III. CRYOSURGERY IN THE THIRD MILLENNIUM

Over the past 20 years, cryosurgery has progressed considerably thanks to the miniaturization of probes and better regulation of the freezing process in vivo provided by echographic techniques. Equipment can be improved still further and surgeons are awaiting finer, more powerful probes for endocavity surgery. The immunological effects of cryo-surgery require additional experimental research in large clinical cohorts. The synergic effects of cryosurgery, chemotherapy and radiotherapy require confirmation. Cryosurgery must be taught on a wider scale and indications must be clearly specified. Too much enthusiasm and partiality can hamper the development of this technique. The European Society of Cryosurgery was set up in 1996 in order to address these needs and everyone is aware that funding is required in order to launch and develop experimental research. Naturally, a scientific approach is far more important than data that are too subjective and publication of studies on small cohorts or individual cases.

GLOSSARY

Nd:YAG: neodymium-yttrium aluminium garnet laser. Laser rays are emitted via a flexible (quartz fibre) conductor, enabling destruction of endobronchial lesions through coagulation or vaporization.

Angioma: vascular skin tumour

Mesenchymal tumour: tumour of connective tissue

Exeresis (excision): removal/cutting out of a foreign body or harmful tissue from the human body (e.g. exeresis of a carcinoma)

Keloid: a linear cutaneous mass of hyperplastic scar tissue

Spinocellular carcinoma: a form of skin carcinoma

Dysplastic lesion: a precancerous lesion

Carcinoma: cancer

Ectropion: a rolling outward of a margin such as that of an eyelid; in gynaecology: eversion of the cervical mucosa

Condyloma: wartlike excrescence on the anus or vulva

Endometrium: mucous membrane comprising the inner layer of the uterine wall

PSA: prostate-specific antigen

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