Articles, Views and Comments

To join the European or the International Society of Cryosurgery or if you would like to contribute to the next issue, your articles, views and comments would be most welcome.

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CRYOSURGERY

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Section 7 Board Meetings

Board of Directors meeting ISC/ESC 5-7 October 2001 Lisbon, Portugal

The Board of Directors congratulated J.C Gonçalves and M.O Maiwand for organising the Lisbon Congress. Excellent work has been done and gratitude was expressed to the organising committee.Both societies Board of Directors appreciate the continuous and longstanding hardwork by the cryoresearch department at Harefield Hospital

Based on the success of Lisbon meeting It was agreed by both societies Board of directors that the next combined meeting would be held in London in Autumn 2003.

There have been changes to the Board of Directors. Dr Gloria Graham and Dr Franco Lugnani have been elected as Vice Presidents for the I.S.C. Nikolai Korpan will continue as ESC Vice President and Dr Buckley has been proposed as second Vice-President of the ESC. MO Maiwand has been elected President of the International Society of Cryosurgery.

The board of directors congratulate the society for continuous and regular publication of Cryosurgery twice a year.

To improve the economical position of society the following suggestions were given, all efforts should be made to collect the membership fee of $50 arrears per year. It was suggested to look at possibilities of how Cryotechnological Companies can assist the society - and the Patronage idea was proposed.

It was suggested that each Cryopractitioner should advance and popularise cryosurgery, by publishing scientific papers and presenting to their own specialities cryosurgical papers. In addition Cryopractitioners should attempt to organise randomized trials.

Section 1 Conference Review

International and European Congress of Cryosurgery

Oct. 5-7, 2001 Lisbon Portugal

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The first combined meeting of the International and European Societies of Cryosurgery was held in Lisbon, Portugal. The meeting was organised by J.C. d'Almeida Gonçalves in Lisbon, and MO Maiwand and his team at Harefield. Participants were all very grateful to the organisers for the smooth running of the conference, the excellent dinners and high quality abstract book. The meeting was a big success with over 100 participants (cryo-users) from 30 countries all over the world and in many different specialities of medicine.

Safety and efficacy of cryosurgery in almost all disciplines of medicine were the issue. In around 80 lectures and poster presentations the successful use of cryosurgery in the treatment of both benign and malignant lesions, in curative as well as palliative settings was reviewed and lead to very interesting open discussions with many specialists in the audience. Cryoablation has become a safe tissue sparing alternative for many surgical indications and has proven to be able to achieve a cure conserving the organ in areas where conventional surgery cannot reach.

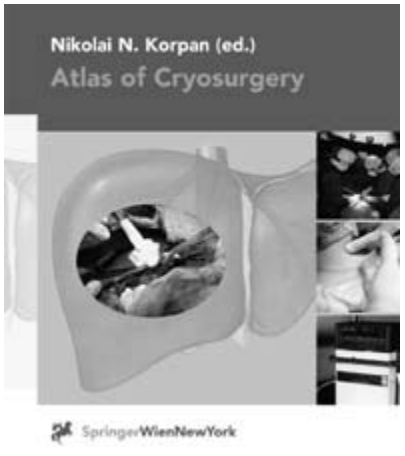
The success of cryosurgery is based mainly on the minimally invasive techniques that result in organ sparing " surgery ", the aim being to offer quality medicine according to ruling standards with respect to the quality of life of the patient, both in curative and palliative settings. The goal is to achieve equal or better results - often in places that cannot be reached by conventional surgery - with a minimal invasive organ sparing treatment modality.

We will try to give a short overview of the varied papers in different fields of medicine. You can find the entire program on the Cryosurgery website: www.rbh.nthames.nhs.uk/cryosurgery and on the Cryoforum website www.cryoforum.org. You can contact the ESC for e-mail printouts of the abstracts on cryotherapy@rbh.nthames.nhs.uk
In the cryobiology session the backgrounds and physics of freezing were

reviewed by Dr's. Baust, Sumida and Augustynowicz. The possible stimulation of the immune system, by the use of cryoablation, in malignant lesions was shown in several papers. A stimulation of the CD4 (T-helpercells), CD25 (Il.2 expressing cells) and CD8 (T-suppression cells) and elevation of CD4/CD8 was clearly demonstrated by Dr. Weshahy as proof of this immune stimulation. Although cancer patients have a " damaged " immune system, stimulation of the remaining intact immune system might be helpful in the killing of vital cancer cells remaining after cryoablation as in metastases (Dr. Ablin).

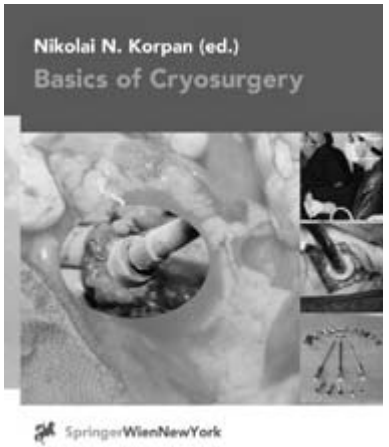
A number of papers presented successful organ sparing palliative treatment in primary liver tumors as well as in liver metastases with excellent outcome in QuOL and in recurrence / disease free survival rates.Cryoablation can be performed in open and in lapaproscopic surgery (Zoras, Mala, Pistorius, Hegenauer, et al.).
In gynaecology cryotherapy can be used in the successful curative treatment of fibromata (Lugnani), menorrhagia (Bodle), breast tumours (Korpan, Amaro).

In Urology excellent curative success rates have been reported in the treatment of localized prostate cancer, both for primary treatment and in second line treatment after failed EBRT or recurrence after radical prostatectomy (C. D'Hont, M. Verghese, B. Donnelly, P. Sofer, F. Lugnani) J.C. Rewcastle developed a practical 3D computer model to simulate TCAP (Targeted Cryo-Ablation of the Prostate) in prostate cancer (for training purposes and pre-treatment probe placement planning) and showed that ischemia due to TCAP plays a major role in cell damage by TCAP in vivo where as in vitro ice related rupturing of cells (lower temp), necrosis and apoptosis were thought to be the main players (Baust, Sumida).
C. D'Hont tried to place cryosurgery amongst the currently available treatment options in 2001 for curing localized prostate cancer.TCAP has many advantages over the other possible choices (Radical Prostatectomy, External Beam Radiotherapy, Brachytherapy), particularly because it is minimal invasive organ sparing and can be repeated in case of recurrence, leaving all other treatment options still open in second or third line. In trying to lift the veil of the future he showed his own and European very competitive results with HIFU (High Intensity Focused Ultrasound) giving the same good results, the same advantages (one day treatment, no operation, repeatable, first or second line treatment, minimal morbidity) as TCAP, all being less expensive and even less invasive since the energy is delivered through a rectal ultrasound probe and no puncturing of the prostate is necessary.
I am quite confident that both Minimally Invasive treatment options for PCA (TCAP and HIFU) will gain considerable importance in the next decade,



Atlas of Cryosurgery
Korpan N

2001. XIX, 524 pages.
Over 1200 figures, mostly in colour.



Basics of Cryosurgery
Korpan N

2001. XXII, 325 pages. Numerous figures and illustrations, mostly in colour .
For more details check the website: www.springer.at

Other Recent Publications

In Situ ablation of hepatic tumors. Cuschierei A,
Semin Laparosc Surg 2001 Mar; 8(1): 25-41

Fibrous Dysplasia of Bone: Management and Outcome of 20 cases
Schreuder HW et al. J Surg Oncol 2001 Mar;76 (3) : 157-66;

The History of Cryosurgery Cooper SM, Dawber RP
J R Soc Med 2001 Apr; 94 (4); 196-201

Cryosurgery in the management of Cutaneous Malagnancies
Graham GF. Clin Dermatol 2001 May-Jun; 19 (3):321-7

An Immune response; a possible Caveat to Endoscopic Cryotherapy
Ablin RJ. Gastrointest Endosc 2001 Jun; 53 (7) : 840

Effects of cryoanalgesia on post-thoracotomy pain and on the structure of intercostal nerves: a human prospective randomized trial and a histological study.
Moorjani N, Zhao F, Tian Y, Liang C, Kaluba J, Maiwand MO
Eur J Cardiothorac Surg. 2001 Sep;20(3):502-7

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probably becoming first choice therapies for localized PCA.
During the cryoresearch session new experimental settings and innovative changes to equipment and techniques were discussed (Herzog, Dohi, Popken, Lugnani, Asimakopoulos).
The successful use of cryoablation in endobronchial tumors (palliative and for removal of obstruction) and other tracheobronchial lesions (curative) through rigid and flexible bronchoscopes was widely discussed in presentations by Mathur, Maiwand, Luna Sabate, Moorjani, Gad, Asimakopoulos, Nair, Flandes, Jean-François, Peralta, and Kochenov).
Surface cryoablation is widely used - with very good outcomes in cure and aesthetic result in dermatology. Dr. Graham set the guidelines for cryo in dermatology for the start of the 21st century. It is most commonly used in the successful treatment of Actinic Keratosis, Warts and a multiplicity of other skin cancers (Buckley, Claro, Nordin, Gonçalves).
In two " mixed " sessions the use of cryosurgery in a variety of other indications was discussed. Venous Ulceration (Czajkowski), Bone tumors (Schreuder), Skincancer of the extremities (Moura), Tonsil pathology (Lopez), Snoring and Sleep-apnoea (Dorochov), Proctology (Delbello), Urethral Caruncule and prolapse (Dessai), Trigeminal neuralgia (Pradel), Cryoanalgesia (Fengrui). Prof. Prokhorov gave a lecture on the role of cryosurgery in Russia and Dr. Lagarde showed spectacular successes in the treatment of invasive Feline Facial Carcinoma.
During breaks participants were able to visit the Cryotechnology exhibition stands. The exhibitors were; Brymill Cryogenic Systems (UK) Cryoflex (Poland), Cryotechnological (Ukraine) Erbe (Germany), Galil Medical (Israel) and Spembley Medical (UK)
In conclusion, cryosurgery is being used successfully in a big variety of benign and malignant lesions in almost all fields of medicine and more are being explored.
Different techniques (liquid nitrogen spray, contact applications with N2O probes of all sizes and shapes, "internal" application by inserting needle shaped probes as small as 1.5 mm using Argon-Helium gas based systems) are being used in curative and palliative settings. The primary goal has always been: how to improve QuOL and outcome for the patient with less invasive but more effective techniques, organ sparing if possible and with less morbidity than other currently available treatment options.
For more details : contact ESC/ISC
Chris D'Hont

Fundamental Aspects of Cryosurgery

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Three technological developments during the 1990's led to a rebirth of interest in cryosurgery. These included the improvement in cryosurgical instrumentation, the use of intra-operative ultrasound to view the formation of ice crystals within the tissue in real time and the development of minimally invasive surgical techniques. More importantly, there has been a renewed interest in defining the mechanisms of cell death following cryosurgery.

The Mechanism of Injury: It has been widely recognized for many years that two major mechanisms of injury contribute to cryosurgical-effect of cell death. These mechanisms include direct injury to cells due to ice crystal formation, especially intracellular damage, and microcirculatory failure due to capillary destruction. A comprehensive review of these mechanisms has been provided by Gage and Baust (1998). More recent advances have linked the fundamentals of cryosurgery and cryopreservation of tissues and organs to stimulate new interest in direct cell injury.

Cell, tissue and organ preservation and cryosurgery share the same problem with ice crystal formation. The cell membrane functions as a barrier to extracellular ice penetration, so the manner in which ice enters the cell is of interest and the topic of recent research (Karlson, et al. 1993). The membrane - ice interface and the dynamics of these two components have proven to be a factor critical to cell survival. The freeze concentration of solutes in the liquid barrier between the crystalline ice (pure water) and the hydrophobic cell membrane results in a hyperosmotic solution thought to stress the cell in a manner that might either injure the cell membrane sufficiently to permit the entry of ice (Muldrew and McGann, 1994) or provoke cell death through a signal transduction process. The latter would result in the initiation of the apoptotic cell death cascade (Clarke, et al. 2001). Additional issues of cryosurgical-dependent injury relate to the role of ice propagation through cell-to-cell contacts and the physical disruption to tissue structure cause by ice propagation.

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Contributed papers are invited on all aspects of low temperature biology and its' applications in medicine, veterinary practice, agriculture and conservation.

For further details contact
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http://www.societyforcryobiology.org then click on Annual Meeting

1st Mediterranean Melanoma Meeting

2 - 5 May, 2003

1ST Melanoma Meeting

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Useful Links
Cryoforum www.cryoforum.org
Int.Eur Society www.rbh.nthames.nhs.uk/cryosurgery

ASSOCIATION OF BRITISH AND IRISH CRYOSURGERY

The next ABIC meeting will be held in Autumn 2002 in Ireland. Further details can be shortly found on the internet website

www.rbh.nthames.uk/cryosurgery

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Arguably, the most important advance in basic research related to cryosurgery is the recognition that apoptosis, gene regulated cell death, is a mechanism of injury following tissue freezing. While the necrotic boundary is sharply circumscribed in a cryogenic lesion, the periphery of the lesion, the border zone, does not experience sufficiently low temperatures to be lethal to all cells. In this margin of the cryolesion, some cells survive, linger for a few days and then die through a process defined as apoptosis (Hollister, et al. 1998). Cells in this region show evidence of non-random DNA cleavage, membrane blebbing, membrane phospholipid inversion and caspase activation (Clarke et al., 1999, 2000). Cells exposed to lower temperatures consistent with the central lesion mass demonstrate cell death characteristics common to necrosis.
The observation of a complex molecular biological event (apoptosis) occurring in the region of likely cryosurgical failure, and therefore possible disease recurrence, has clinical implications since most chemotherapeutic agents also work through this same destructive pathway. In recent studies on human prostate cancer cells (PC-3) it was noted that cells exposed to -25° to -80°C yielded 1 - 10% survival and only when cells were exposed to -100°C was complete mortality realized. However, if PC-3 cells were first exposed to a sub-clinical dose of 5-fluorouracil or other cytotoxic agents, complete loss of viability was obtained between -5° and -25°C. These result show both are remarkable resistance of these cancer cells to freezing and suggest that combination chemo-cryotherapy is of potential therapeutic benefit. Similar observations have been made using a human colon carcinoma cell line (Hanai et al., 2001).

Clinical applications: However the practice of cryosurgery in the clinical setting must follow the advances that have been achieved in the understanding of the mechanism of cryosurgery and cell death. To put this knowledge into practice we must accept there are shortcomings in the practice of cryosurgery, in terms of delivery of the lethal temperature to the whole of the lesion and monitoring of the temperature. Delivery of a lethal temperature of around -30°C to the periphery of the abnormal tissue must be the goal for cryosurgeons. In order to achieve this measurement of temperature at the lesion should become routine. Attention must also be given to the protection of the surrounding tissue and selection of the most appropriate cryogen for the particular clinical use. These goals are only achievable by the close cooperation of cryobiologists, clinicians and cryotechnological organisations.
However, the achievements of cryosurgery, in a variety of pathological conditions

have been widely acknowledged. These have been particularly strong in the fields of dermatology, metastatic carcinoma of the liver, carcinoma of the prostate, bone and extremities. Cryosurgery for malignant and benign skin lesions has shown a cure rate of over 90% for 5 years and patients are treated by open spray method without the need for hospitalization or general anaesthetic .(Kuflik) Cryosurgery is also an effective option for the 80% of patients with advanced metastatic lesions of the liver with a median survival of over 2 years. Cryosurgery for prostate carcinoma has given 5 year survival rates of up to 70% with comparable morbidity to radiotherapy (Long). . Adjuvant treatment of low malignancy and benign bone tumours has allowed for preservation of more bone and less reconstructive surgery with recurrence rates less than 15% (Schreuder). The anatomical position of certain conditions makes delivering a low temperature to the site of the lesion more difficult. This is particularly true for the trachea and bronchial tree where the probe size is limited by the internal diameter of the fibreoptic or rigid bronchoscope and monitoring the temperature at the periphery of the lesion is not possible with technology available today.

The fact that the technique is easy to perform, well tolerated by patients, that the treatment can be repeated, has minimal risk to operators and also being economical compared to alternative treatments all serve to extend the popularity of cryosurgery as a treatment option. To promote the wider use of cryosurgery, it is important that all cryopractitioners publish their work in the literature of their specialty, particularly since cryosurgery is used in so many different areas. Randomized controlled trials are essential in convincing the medical establishment of the efficacy of cryosurgery. This will help to speed up the expansion in the use of cryosurgery and ensure its role in the future as a treatment for malignancies and benign conditions.

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viability of tumours in short term follow up. The serum level of ALT, AST, LDH and CRP were elevated but they returned to normal within 2 or 3 weeks. The common adverse reaction was mild fever. In one case, temporary pleuritis occurred.

In case of RCC, the patient was a 35-year-old female, von Hippel-Lindau disease. Two RCCs were in the left kidney and three in the right. The maximum diameters of tumours ranged from 1.5 to 4.1 cm (average 2.4 cm). Cryoablation was performed twice. The first treatment was to the left kidney and the second to the right, after a 6-week interval. The number of cryoprobes was 1 or 2 depending on the size of tumour. In 4 out of 5 tumours, cryoprobes were placed accurately with the MRI guidance. In one tumor, accurate placement was impossible, because of a distortion of the renal parenchyma and because the MR image of the tumor showed poor contrast. Only partial cryoablation of one tumour in the upper pole region of the left kidney was possible due to close proximity of the tumour to the jejunum. And we were not able to successfully freeze the largest tumor in the right kidney because the tumour was in partial contact with the colon. The other three tumours were ablated completely. In all cryoablations, frozen areas were detected clearly as asignal areas on the MRI. The follow up periods were 24 weeks and 18 weeks. The serum level of AST, ALT, LDH and CRP were elevated; but returned to normal within 3 weeks.

Conclusion: MRI guided percutaneous cryoablation is a safe, accurate and effective modality for HCC and RCC. However, it's use is limited when tumours are in contact with adjacent organs.

Initial Experience of MRI-Guided Percutaneous Cryosurgery for Hepatocellular Carcinoma and Renal Cell Cancer

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Purpose: To introduce our initial experience of MRI-guided percutaneous cryosurgery for hepatocellular carcinoma(HCC) and renal cell cancer(RCC).

Materials and methods: Using an MR-compatible, high pressure argon-based cryoablation system (CryoHit; Galil Medical, Israel) with 2 and 3mm diameter probes, MRI-guided percutaneous cryoablation is performed. Treatments are guided and monitored with a low magnetic field (0.3T) horizontal type open MRI (Airis II; HITACHI Medico, Japan). Criteria for the candidates were as follows.

1. Good performance status.
2. Tumors limited to the liver or the kidney.
3. No other serious disease.
4. Number of tumours less than or equal to 3.
5. Maximum diameter of a single tumour is less than 10 cm, or less than or equal to 3cm where there are 2 or 3 tumours.

Two freezing cycles are used. The freezing time depends on the size and shape of the ice ball.

Results: From April to September 2001, 6 HCCs in 6 patients and 5 RCCs in one patient were treated. For patients with HCC, ages ranged from 46 to 65 years (average 57.8). The maximum diameters of tumours ranged from 1.2 to 4.0 cm (average 2.3 cm). All HCCs were confirmed by CT, MRI and tumour markers (AFP or PIVKA-II). Superparamagnetic iron oxide (SPIO) was administered intravenously in 5 cases out of 6 for delineating the tumour clearly. The numbers of probes were 1 in 3 cases, 2 in 2 cases and 3 in one case. The follow up periods were from 2 weeks to 23 weeks (mean 13.3 weeks). In all cases, cryoprobes were located safely and accurately using MRI and all tumours were contained inside ice balls on the MR images. The entire area of all tumors was ablated and there was no residual

Basic Concepts And Future Use Of Cryoimmunology: A Brief Commentary

Richard J. Ablin
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In addition to the physical and vascular effects of cryodestruction, a major, but little recognized property of cryosurgery is that, as a consequence of freezing, a cryoimmune response may occur. Characterized by local and systemic immunity and associated cytokines, the immunogenicity of the cryolesion and, therefore, the intensity of the immune response is related to the freezing regimen, manner of cell death, i.e., apoptosis vs. necrosis, and balance between pro- and anti-inflammatory cytokines. Likened in many respects to an autoimmune response and associated immunopathology, the systemic immunity is critical to the destruction of tumour cells beyond the freezing site, i.e., metastases. This property and the specificity of the initial immune response to destroy malignant vs. normal cells, which may leave behind a long-term memory serving to protect the patient from subsequent disease, distinguishes cryosurgery from other conventional therapeutic modalities for cancer. The ability to cryogenically ablate tumour and also induce antitumour immunity forms the basis of the concept of cryoimmunotherapy, which adds a "double-edged sword" to our armamentarium.Within the course of the recognition of the potential therapeutic application of the principles of cryoimmunology, several concerns have arisen. Well beyond the limits of this brief commentary, several of these concerns have been considered in depth elsewhere (Ablin. In: Onik et al. Percutaneous Prostate Cryoablation. QMP, Inc., St. Louis, 1995, p. 136).

For the present, a major step toward the long overdue acceptance of cryoimmunotherapy in man, for which evidence has been referred to by some in recent years as anecdotal and even "mythical," has been the increasing realization that the absence or low level of an immune response in the majority of patients following cryosurgery has been due to their generally poor, if not anergic state, of immunological competence. Fundamental as this observation is, it has been virtually ignored even though the author has explained it on numerous occasions over the past 30+ years.

Age and/or disease-related reduced immunocompetence, as well as that induced by prior therapies, has important implications for the application of immunotherapeutic strategies, inclusive of cryoimmunotherapy. Therefore, as with traditional staging and grading of a patient's malignancy, it is critical to evaluate their level or stage, hence, "immunostage," of immunological competence. Immunostaging provides the necessary criteria for determining a

patient's suitability for cryoimmunotherapy and for monitoring their postoperative responsiveness. Monitoring the cryoimmune response has shown it may be biphasic (bidirectional), exerting temporally favourable (tumouricidal) vs. unfavorable (tumour enhancing) effects. Therefore, successful implementation of cryoimmunotherapy lies not merely in inducing an antitumour response, but in directing (modulating) the response toward that which will be tumouricidal.

Further related to immunocompetence is the effect of cryoablation on immunologically competent cells (immunocytes) within the target tissue and its microenvironment. Just as the immunocompetence of the systemic immune system is critical to the development of an immune response following freezing, it is axiomatic that the thermotolerance (cryoprotection) of the immunological integrity of the host and its modulation are paramount. A candidate to protect this integrity is molecular chaperones, also known as heat shock or stress proteins (HSPs). A highly conserved, constitutively expressed and stress-induced family of proteins, HSPs possess the ability to suppress the aggregation of nascent and altered cellular proteins under normal and stress conditions. Central to immune responsiveness, HSPs are involved in signal transduction pathways, wherein they may provide cryoprotection to immunocytes within the microenvironment of the cryolesion and be involved in the translocation and presentation of antigens.In looking at ways in which to increase the tumouricidal effectiveness of the cryoimmune response, re-attention to earlier observations of changes in the microcirculation following freezing have provided a means to maximize the synergistic effect of cryosurgery and selective cytotoxic agents via cryoimmunochemotherapy. By way of example of this approach, recent observations in a small group of prostate cancer patients with advanced disease disclosed increases in select parameters of immune responsiveness in association with regression of metastases in some (Mouraviev et al. Int. J. Molec. Med., 6(Suppl. 1): S30, 2000). An increased understanding and appreciation of the uniqueness of cryosurgery has witnessed its increased application from the prostate to a variety of tissues, which include breast, kidney, liver and lung. There from, in this author's opinion, it is only a matter of time, before the immunotherapeutic aspects of cryosurgery are fully realized. In fact, presentations at the recent XIth World Congress of Cryosurgery (Lisbon, 5-7 October, 2001) attest to the beginnings of this realization. Given this interest, it may be useful to consider reorganization of an earlier international collaborative Cryoimmunotherapeutic Study Group (Ablin et al. J. Nat'l. Cancer Inst., 67:1173, 1981) to reassess guidelines for the implementation of cryoimmunotherapy.

Cryosurgery in the Treatment of Venous Ulceration

Dr Konrad Czajowski,
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Venous Ulceration is thought to affect about 1% of the population and 3% of people over 65. Treatment can be divided into conservative and surgical. Conservative treatments include elevation of the limb, compression therapy, local antiseptic and antibiotic treatment. Surgical treatments include excision with skin grafts or ligation and cutting of anastomising veins.

Cryosurgical treatment involves removing the anastomising veins with the cryosurgical probe in the suprafascial layer. After removing the varices the probe is inserted in an area of healthy skin, as close as possible to the ulceration. Incisions in the region of lipodermatosclerosis should be avoided. The perforators, which have been inserted during doppler tests and palpitation, are removed. The whole region of ulceration is then separated from the fascia together with a margin of a few centimetres of skin. On some occasions the procedure will require an additional incision from another site.

Since 1994 I have treated over 1200 cases with varices of the lower limb, including 52 with chronic tibial venous ulceration at clinics in Warsaw. Of these 52 patients, 69.3% of results were classified as very good (full healing, without recurrence) and 13.4% good (one recurrence, healed with conservative therapy, compression and elevation).

Conclusion Cryotreatment of venous ulceration is cheap, precise, minimally invasive and gives good results for a large number of patients. Patients do not require hospitalisation, or general anaesthesia, it produces small scars (2-3mm) and is easy to carry out.

months after the first cryosurgery treatment and 71% showed improvement in FEV1 and FVC and 43% in PO2. Mortality and morbidity were 3.5% and 28.5% respectively. Mean survivals were 7.5 months for lung cancer, 9.3 months for endobronchial metastasis and benign lesions showed no recurrence after 18 months follow up.

Discussion; The results of this study showed an improvement in RFTs in 71% of patients and resolution of obstruction in 80% of cases after 2 applications.

Our results confirm the utility of cryotherapy obtaining improvement in FEV1 and FVC two months after initial treatment in 71% of patients and complete resolution of bronchial obstruction after two applications in 80% of patients. This contrasts with studies by Mathur who suggested that more than two applications are needed before results can be shown. In our study the mean survival for patients with lung cancer was 7.5 months and for patients with metastases 9.3 months. These results compare to median survival with Nd-YAG laser of 5.5months, brachytherapy 9 months and photodynamic therapy 40 days.

A large proportion of the patients (46%) presented with a tumour in the main bronchus which can be easily managed with a rigid probe. The tumour is frozen for one minute and the bronchus recanalised with biopsy forceps. Cryotherapy is then carried out for a further 3 minutes. This can achieve 100% recanalisation in one treatment for some patients. We have also successfully used cryotherapy to treat granulation tissue after lung transplantation and a critical stenosis secondary to invasion of a stent wall by an endotracheal tumour resulting in 100% tracheal patency.

Conclusion; Cryotherapy offers an effective method of palliation, either singly or in combination with external irradiation, brachytherapy or chemotherapy for bronchial carcinoma or metastasis. For benign tumours it may avoid resective surgery or be curative. Coupled with its cost effectiveness and the symptomatic, functional and visible endoscopic improvement strongly supports its increased use. Results for survival and quality of life may indicate better local control of the disease and the use of combined modalities of treatment.

KENNEDY SPACE CENTER

Thermal Performance of Biological Substance systems in Vitro undUnder Static and Dynamic Conditions at the NASA Kennedy Space Center, USA

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In principle, cryosurgery is a thermodynamic process where tissue at body temperature is frozen with a specific cooling rate. In most cases the cooling/freezing rate and, after that, the thawing rate are unknown. There is no readily applicable method to indicate the temperature inside the tissue at specific distances from the probe. Using direct liquid nitrogen spray onto the tissue does not mean, in many cases, that this method is the fastest method of cooling and freezing. The nitrogen gas film isolates part of the tissue; therefore, cooling rates at the beginning and after the freezing process can be different. The most important need is to develop a practical system to measure and predict, in advance, the temperatures inside a given tissue for a specific geometry of the probe. The Cryosurgery Modular Unit System1 for different applications like dermatology, gynecology, urology, etc. should be developed and marketed for widespread use.

From the thermodynamic viewpoint the analysis of tissue temperature and heat distribution can be similar to the analysis of heat transfer for composite thermal insulation systems including multilayer insulation (MLI). A unique research program, including a comprehensive study of the thermal performance at cryogenic vacuum insulation systems, was performed at the NASA Kennedy Space Center, Cryogenics Test Laboratory. Liquid nitrogen boil-off methods were used to test conventional materials, novel materials, and certain combinations. A new

Layered Composite Insulation (LCI) system was developed to perform exceptionally well at soft vacuum levels and nearly as good as a standard MLI at high vacuum levels. The Cryogenics Test Laboratory has experience with all practical aspects of thermometry, measurement procedure, data acquisition systems, instrumentation, and experimental set-up. We are familiar with control and monitoring system development including concept, hardware, software, packaging, and the use of "building blocks" approach with commercial-off-the-shelf equipment.

We can improve the methods and methodologies for cryosurgery and cryobiology applications in two ways: 1) characterization of substances, and 2) testing and evaluation of complex substance systems. The heat transfer studies are based on experimental approaches. We can also develop and build Cryosurgery Cryostat System (CCS) for both static and dynamic studies of substance systems. Static studies, or steady state methods, would be used to determine apparent thermal conductivities of specimens, overall heat flux rates, and temperature profile measurements. Dynamic studies, or transient methods, would be employed to determine cooling, freezing, and thawing rates; heat flux ratio mapping for elemental surface areas; and time-temperature profiles.

The development of high performance cryogenic thermal insulation systems using novel materials has been a targeted area of research for a number of years. This research at the Cryogenic Test Laboratory can be applied to improve methods of characterization, testing, and evaluation of complex biological substance systems for cryosurgery and cryobiology under static and dynamic conditions.

1Cryosurgery Modular Unit System is the name of the system developed by the authors.

Section 2 Original Articles

Tracheobronchial Cryotherapy. The Chilean Experience

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Introduction; Around 20 - 30% of patients with lung cancer will develop atelectasis or pneumonia secondary to obstructive endobronchial tumours development, endobronchial metastasis or benign lesions. A number of treatments have been used palliatively to recanalise the tracheobronchial tree, including Nd-YAG laser, Cryotherapy, brachytherapy and photodynamic therapy. The object of this paper is to our initial experience in the management of tracheobronchial obstruction with cryotherapy.

Materials and Methods; Cryoequipment consisted of a Spembly 142 Cryomachine with a rigid, semi rigid or flexible probe (nitrous oxide cryogen) passed through a Storz rigid bronchoscope. The tumour is frozen for 3 mins with the possibility of a second freeze thaw cycle. Patients are admitted as day cases and chest radiograph, lung function tests, thoracic CT, blood gases, coagulation time and liver and urine tests are carried out. Cryosurgery is carried out under general anaesthesia. For lesions in the trachea, main bronchus and lobar superior or apical inferior lobes a rigid probe is recommended; segmental lesions normally require a flexible probe. The location of the probe tip must be within the tumour area or within the immediate vicinity. After treatment, the patient is checked with a fibreoptic , any secretions or effusions are aspirated, and bleeding controlled if present. A post-operative radiograph is taken six hours prior to discharge. Ten days later, the patient attends the Outpatient Clinic and lung function tests, quality of life and symptom improvement, are evaluated by personal interview by a specialised nurse, using scoring systems previously described by Walsh et al. A second treatment and a third if required, are carried out two and six weeks after the first treatment. After the last session, the patient is evaluated with respect to continuation of cryotreatment, and to the possibility of combination with other appropriate therapies (e.g. external-beam radio therapy or brachytherapy).

This study included 28 patients (mean age 61, range 23-83, 17 male) with histologically proven malignant or benign lesions. Their main presenting symptoms were dyspnoea 57%, cough 43%, and haemoptysis 29% and 51% of patients had lung or lobar atelectasis.

Results ;Radiographs after cryosurgery showed resolution of lung and lobar atelectasis in 70% of patients after two sessions of cryosurgery. Significant improvements ($P < 0.01$) were found for cough, dyspnoea, and haemoptysis 2

Welcome

I hope you had a pleasant year.

Welcome to the sixth issue of CRYOSURGERY, we are pleased to be sending out the current issue.
Both the European and International Societies of Cryosurgery are deeply saddened at the tragic September 11th incident. In spite of this devastation, I am pleased to report that the combined meeting of International and European Societies of Cryosurgery, held on 5-7 October in Lisbon, Portugal was a success. Over 100 delegates were present, representing 30 different countries, with a total of 20 Cryosurgical specialities. Because of the situation following the events of September 11th, a few well known faces,were not able to attend at the last minute. Nevertheless there was a full programme and delegates enjoyed the combination of a fascinating city and interesting presentations. All the abstracts from the meeting will be put on the cryosurgery website. A summary and self observation of the conference by Dr D'Hont can be seen on pages 3-5

The Board of Directors of both societies (ISC ESC) decided that the next combined meeting of International and European society of Cryosurgery will be scheduled for 2003 and will be held in the city of London. Please look out for further details which will be published shortly. The International and European Society of Cryosurgery encourage and welcome the active participation of Cryotechnological companies in the next meeting.

We are pleased to invite you to the next Association of British and Irish Cryosurgery meeting to be held in Ireland Autumn 2002. Details about this meeting will be available shortly.

There have been changes in the Board of Directors Committee, details of which can be seen on page 22 & 23.

The Board of Directors of both societies wish you all a very happy and prosperous New Year.
MO Maiwand President ISC/ESC

Section 5 Board of Directors

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