BOOK OF ABSTRACTS

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A11 Historical Background of Cryosurgery

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The use of cold in medicine dates back over 4000 years to the ancient Egyptians when it was noted that the application of cold minimised the pain of trauma and decreased inflammation. The father of medicine, the Greek physician Hippocrates, recommended hypothermia to reduce swelling, haemorrhage and pain, he observed that it had local anaesthetic properties. In London in 1777, John Hunter also recognised the value of low-temperature when applied to animal tissues, observing local necrosis, vascular inhibition and considerable healing properties. Half a century later, during the retreat of the armies of Napoleon from Moscow in the disastrous winter campaign of 1812, Baron Dominique Jean Larrey, the military surgeon of Napoleon's army, noted that a limb could be amputated almost painlessly and without haemorrhage if the part concerned was covered with ice or snow before the operation took place.

James Arnott of England was the first physician to use the destructive effect of cold for the treatment of advanced carcinomas of the uterus between 1845 and 1851. He designed special equipment for applying a mixture of ice and salt that achieved a local temperature of between -18 and-24ºC at the tumour site.

In the early 1900's Campbell-White demonstrated that liquid air could be used to treat dermatological lesions and currently about 90% of skin tumours are treated with cryotherapy. Around 1907, Whitehouse, a New York dermatologist, devised a method to spray the refrigerant. Whitehouse had shown that liquid air could be used in a swab form or spray to treat a vast array of benign skin lesions; Pusey (1907) proposed the use of carbon dioxide snow to be used in a similar way. In the early 1960's a number of cryoprobes were developed, the most important of which used the adiabatic expansion of compressed gas, the Joule-Thomson effect, to achieve low temperature at the tip.

In 1963 Irving Cooper of New York produced a unit in which liquid nitrogen was circulated through a hollow metal probe that was vacuum-insulated except for its tip. With this equipment it was possible, by interrupting the flow of liquid nitrogen, to control the temperature of the tip down to -196ºC, the boiling point of liquid nitrogen. Cooper's initial equipment has had a major impact in the treatment of many internal diseases, particularly in neurosurgery. Neurosurgeons were the first to use cryosurgery in Parkinson's disease. Later this method was used extensively in skin disease. The technique has also been used during maxillofacial; ear, nose, and throat, gynaecological and general surgery.

Cryosurgery is widely used in dermatology and in the treatment of malignant tumours with an approximate 90% cure rate, also for malignant tumours of the head and neck and offers the physician an added modality to combat cancer. It is a modality which, when applied skilfully and selectively, will either cure malignancy, with comparable cosmetic results, or be used as an adjuvant for inoperable patients to achieve palliation and control of their advancing neoplasms.

Cryosurgery has been used to treat unresectable liver metastases from colorectal cancer in over 1000 patients world-wide, and its safety and efficacy are well established. The American FDA in 1998 approved cryosurgery as the treatment of choice for metastatic liver lesions, commonly from carcinoma of rectum and colon in a five year survival of 48%. Advances in cryotechnology made cryosurgical treatment for prostate cancer possible and this method has been recognised by the American Urological Society. Over the past six years, more than 8000 patients have been treated with cryosurgery with very compelling results. Cryosurgery for prostatic cancer is now an accepted treatment of the US FDA and HCFA the negative biopsy from the site of treatment has been reported to be 76% after 4 years.

Treatment of advanced carcinoma of trachea and bronchi by cryosurgery was made possible by the design of long rigid probes to fit the anatomical shape of the trachea and bronchi, first reported in 1986 by Maiwand et al. Harefield Hospital has the largest number of patients treated for endobronchial lesions, over 1000 with approximately 70% showing improvements in symptoms, performance status or respiratory function tests. Similar results have been reported in France.

A12 Cryosurgery – The Search for the Optimal Technique

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Cryosurgery must be performed in a manner that produces a predictable response in an appropriate volume of tissue. In present-day clinical practice, that goal is not always achieved. Concerns with cryosurgical techniques in cancer therapy focus in part on the incidence of recurrent disease in the treated site, which is commonly ~20-40% in metastatic liver tumors and prostate cancers. Whether the cause of this failure is disease-based or technique related, cryosurgery for cancer commonly needs the support of adjunctive therapy in the form of anti-cancer drugs or radiotherapy to increase the rate of cell death in the peripheral zone of the therapeutic lesion where cell survival is in balance for several days post-treatment.

Recent evidence has identified a third mechanism of cell death associated with cryosurgery. This mechanism, apoptosis or gene regulated cell death, is additive with both the direct ice-related cell damage that occurs during the operative freeze-thaw intervals and coagulative necrosis that occurs over days post-treatment. We report on the combined roles of these distinct modes of cell death in a prostate cancer model. Data is presented suggesting that sub-freezing temperatures when sequentially applied with low dose chemotherapy provide improved cancer cell death in the freeze zone periphery. Since the mechanism of action of most common chemotherapeutic agents is to initiate apoptosis in cancer cells, the observation that sub-freezing exposures yields a like effect provides a possible route toward improved therapeutic outcome.

In summary, we conclude that (1) the combination of cryosurgery with a chemotherapeutic agent increases cell death, (2) there is a molecular-based cellular response to freezing, and (3) the molecular response of a cancer cell to cryotherapy can be modulated in such a manner as to increase level of cell death at elevated subfreezing temperatures and improved clinical results.

A13 Ice Crystals in Cells and Tissues

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Since 1965 until today, blood cells, tissues and organs have been frozen using four primary temperature of -20°C, -80°C, -196°C and -269°C (tentatively). Thawed blood and marrow cells and tissues frozen at -80°C and -196°C have been transfused or transplanted into 2,326 patients under a variety of medical conditions.

Biological Products	Number of Units Used	Number of Recipient Patients
Blood: Red Cells	18,713	1,845
Platelets	896	99
Stem Cells: Marrow	338	266*
Tissues: Bone	165	98
Skin	28	16
Vein	15	2

* Advanced malignant solid tumors.

Recently I have been wondering for how many years cryopreserved could be stored. Based on the many transfusion and transplantations performed, a regression equation was derived with the cryopreservation storage period for the X-axis and the recovery rate after freeze-thawing as the Y-axis. From this regression equation, we calculated the time until complete destruction of red cells at different temperatures of storage. The results indicate that successful storage is possible for about less than two weeks at -20°C, about 500 years at –80ºC and about 10,000 years at –196ºC!! Storage of stem cells, such as marrow, peripheral blood and cord blood, was also calculated by the same method and the results indicate about 150 years of storage at -196ºC before the cells are completely destroyed. Cryobiophysically, cells are destroyed due to the ice crystal growth, and ice nuclear formation inside and outside of cells. Crack formation of vitrified cells and tissues will be an important mechanism of cryodestruction. Pathologically, there are two mechanisms of cryodestruction, necrosis and apoptosis, which might be manipulated by immunomodulation, but still in controversy.

Our data indicate that the lower the storage temperature, the longer the blood cells can be cryopreserved. The reason for this is that frozen water molecules take a longer time to convert to hexagonal ice crystals, which are destructive to living cells, as the molecular movement of water is slowed as temperature decreases.

If living cells are constantly preserved using liquid helium (-269ºC), it appears possible to cryopreserve them for even longer times. I am very much enjoying the speculation that cells could be indefinitely preserved and never destroyed if they maintained at absolute zero!! So be it!

A14 Immune Modulation in Cryosurgery

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The Immune Medical Research Foundation has specialised in immune-based research and the development of Immune Modulation. One particular aspect has highlighted the induction of specific T-cell responses for the treatment of compromised immune systems, autoimmune disorders and cancer. In addition, the Foundation is developing targeted delivery regimes for Immune Modulation Protocols that are designed to address specific immune disorders. In 1987, over 40% of Europeans and Americans were identified as living with one or more chronic conditions (a term that includes chronic diseases and impairments). In 1935, the proportion was 22%, so chronic conditions needing treatment have approximately doubled during the last 60 years. The majority of people with chronic conditions are not disabled, nor are they elderly. Chronic conditions can often be "managed" (helping people to live with the condition), but they usually cannot be cured.

The cost of chronic conditions in 1990 in the US alone was estimated to be $659 billion - nearly three quarters of all U.S. health care costs. With these ever increasing numbers moving into the new Millennium, there has been an ever increasing force to seriously look at prevention as an approach to chronic conditions. Humans and other vertebrates come equipped with a complicated "immune system" which PREVENTS diseases that might be caused by pathogens (bacteria, viruses, fungi, and parasites) or cancerous cells.

Our living tissues and particularly skin, is the principal protective layer of the body and the first line of defence in our ongoing effort to protect the body from invasion. A consequence of any type of surgery, (including laser and cryosurgery), is a compromised organ in or near the surgical site. Our immune system is the mechanism needed to fight invading pathogens, but it is that same system which may be suppressed prior to surgery. A surgical procedure preformed on a patient with a suppressed immune system could result in unanticipated problems while also some surgical procedure may stimulate a positive immune response providing that the immune system is in as positive a condition as possible at the time of surgical intervention.

In addition, the immune system can enhance the reparation of nonlymphoid tissues and perform self-regulation. T-cell antigen receptor (TCR) structure is the key involved in signal transduction in T cells. Normally functioning cells do not proliferate unless they are stimulated by chemical signals from other nearby cells, typically located in adjoining tissue. Cell signal transduction via chemical pathways through which this mechanism occurs, is one of the keys to understanding this process. Immune modulation is key to the healing process. Lymphoid stem cells (immature CD2) mature to undifferentiated CD3. These further mature to 20% B cells (CD20 specific target Memory cells) and 80% T cells CD4.

In a compromised situation when the body is under attack from Antigens or Pathogens and when there are abnormal diseased protein codes present some particular diseased protein codes will travel into the T-cell and in so doing the normal pathogenic signals identifying it as a non-self protein are suppressed. As a result, during the regular RNA/DNA Reverse Transcription process the diseased protein codes are disguised as a self-protein and as a result there will be no stimulation of the CD8 and CD56 cells to seek and destroy and they will not be removed from the body, thus there will be the classic onset of immune suppression.

One particular problem is that when there are some outward signs of illness or immune compromise, many of the standard tests may not be as indicative of condition as would be hoped. For example, the Immune Panel Assay measuring CD4, CD8 and CD56 could show perhaps lower than normal but not seriously limited numbers. In reality the situation could be dramatically different. While the assay test will show a particular population level of CD4, it cannot distinguish those that are active from those that are Immune Suppressed all are recorded as self-protein and so the seriousness and functionally effective level of CD4 and the true degree of Immune suppression can be difficult to determine. It is in specific regard to this relationship between the CD4, the ability of the diseased protein code to disguise its presence as a self-protein within the CD4 cell and the timing of the Reverse Transcription process that Immune Modulation protocols such as ITAC ™ and Probiotin™ come in to play.

Most protein molecules work within tight and constrained environmental parameters. Each of the case specific protocol regimes influence the CD4 cells to emit the normal pathogenic signals

from the cell to effect the stimulation of CD56 'killer cells' and CD8 (cytotoxic killer T suppressor cells). Once effected, this action will be the precursor to the continued recognition of these codes as a non-self protein. During Reverse Transcription there is ongoing further locating and identifying of the diseased protein codes within the body which can no longer hide behind the self-protein curtain within the CD4 cell which was initially created by the presence of the diseased protein code.

For example, following clinical initiation of the ITAC protocol, the following results become apparent. Generally there is a marked proliferation of healthy cell activity evidenced by Interleukin 2 (IL-2 white cell) as increased populations without recombinant intervention; (IL-2 population increases are tracked with the Immune Panel Assay.) It is further determined by the total CD4 cell count reducing rapidly to start with then later increasing, an increase in the CD2 & CD3 complex (the precursors to CD4) and the CD56 and CD8 count increasing. Blood oxygen levels increase by as much as 18% after treatment. Evidence and observation of cell necrosis is determined by increased protein presence in the Urine and Faeces and the positive results determined through interim markers such as MRI scans, tumour specific markers and symptom reversal.

Both Probiotin ™ and ITAC ™ protocols, as treatment modalities have been observed to continue to be successfully used to modulate and maintain the body immune system and hasten the healing process. It is expected that the protocols used pre and post Cryosurgical intervention would prove very positive in an overall modality.

A15 Cryoimmunotherapy: O Grande Segredo.

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Cryosurgery is well established and when compared to other therapeutic modalities for cancer, has specific advantages. A major, but little acknowledged, advantage of cryosurgery and a factor to its successful application is that as a consequence of freezing, an immunological response may occur. Characterized by local and systemic immunity and associated cytokines, the immunogenicity of the cryolesion, as related to the freezing regimen, manner of cell death, i.e., apoptosis vs. necrosis, and balance between pro- and anti-inflammatory cytokines (Ablin. First Central Eur. Congr. Cryosurgery, Plzen, Czech Republic, 1996), for a number of tissues and eradication of experimentally-induced animal tumours and subsequent tumour challenge, is well established. The systemic immunity is critical to destruction of tumour cells beyond the freezing site. This property and that the specificity of the initial immune response to destroy affected vs. normal cells, which may leave behind a long-term memory serving to protect from subsequent disease distinguishes cryosurgery from conventional forms of therapy. In sharp contrast to data in laboratory animals, evidence that the cryoimmune response in man has a therapeutic value and is striking is statistically limited because of small numbers. Observations that (i) the immune response in cryosurgically-treated patients has for the most part not been evaluated and (ii) endeavors to demonstrate efficacy of newly designed cryosurgical equipment by evaluation of animal models employing nonimmunogenic tumours have contributed to the paucity of data in man. In aligned areas of investigation, maximization of the synergistic effect of cryosurgery and selective cytotoxic agents via cryoimmunochemotherapy (Mouraviev et al. Int. J. Molec. Med., 6 (Suppl 1): S30, 2000) has provided evidence of a further efficacious approach to the treatment of metastatic disease.

A16 Thermal Performance of Biological Substance Systems, In Vitro, under Static and Dynamic Conditions.

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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. The main goal was to develop a new soft vacuum system (from 1 torr to 10 torr) that provides an intermediate level of performance (k-value below 4.8 mW/m-K). Liquid nitrogen boil off methods were used to test conventional materials, novel materials, and certain combinations. The test articles included combinations of aluminum foil, fiberglass paper, polyester fabric, silica aerogel composite blanket, fumed silica, silica aerogel powder, and syntactic foam. A new-layered composite insulation (LCI) system has been developed at the Cryogenic Test Laboratory. This system performs exceptionally well at soft vacuum levels and nearly as good as a MLI at high vacuum levels. Apparent thermal conductivities for the LCI range from 2 mW/m-K at soft vacuum to 0.1 mW/m-K at high vacuum.

Several cryostats were designed, constructed, and calibrated by the Cryogenic Test Laboratory at KSC NASA as part of this research program. The cryostat test apparatus is a liquid nitrogen boil off calorimeter system for direct measurement of the apparent thermal conductivity at a fixed vacuum level between $5x10^{-5}$ and 760 torr. The apparatus is also used for transient measurements of temperature profiles.

The development of efficient, robust cryogenic insulation systems has been a targeted area of research for a number of years. Improved methods of characterization, testing, and evaluation of complex biological substance systems for cryosurgery and cryobiology is the focus of this paper.

A17 The Imunological Role of Cryosurgery in the Treatment of Viral Warts

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Cryosurgery is a rapid, easy and safe therapeutic modality given on an outpatient basis. It lies among the best methods for treating skin viral warts. Clinical assessment of treated subjects demonstrated a high cure rate, low rate of complications and an accepted cosmetic outcome for almost all patients.

The Immune System had been evaluated by estimation of both T-helper and T-suppresser cells (CD4, CR8, CD19 AND CD25), before and 2 weeks after the cryosurgical operation.

A comparison between the effects of the three cryosurgical techniques, i.e. (spray, probe and intralesional techniques) on the Immune System had been done.

The immunological study showed post-cryosurgical stimulation of the Immune System. This might be attributed to its ability of generating an antigenic stimulus capable of inducing a specific immunological response to antigens of frozen tissues.

The stimulation of the humoral limb of the Immune System has not been manifested, but stimulation of cell-mediated Immune System, which is more significant in the course and outcome of HPV infection was clearly proven.

Thus cryosurgery might help patients with viral warts directly by eradicating these warts in an easy, safe and commercially accepted system against the infection especially in the extensive or recalcitrant lesions or whenever the Immune System is suppressed.

Further studies are recommended to further clarify the important role of cryosurgery and its exact relation and effect upon the Immune System.

A18 The Role and Biology of Cryosurgery in the Treatment of Bone Tumors: A Review

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The application of liquid nitrogen as a local adjuvant to curettage in the treatment of bone tumors was introduced three decades ago. This technique, termed cryosurgery, was shown to achieve excellent local control in a variety of benign-aggressive and malignant bone tumors. However, early reports showed that cryosurgery was associated with a significant injury to the adjacent rim of bone and soft-tissue, resulting in high rates of fractures and infections. These results reflected an initial failure to appreciate the potentially destructive effects of liquid nitrogen and establish appropriate guidelines for its use. We review the biological effect of cryosurgery on bone, surgical technique, and current indications for its use.

A87 Cryoimmunological Responses of Advanced Malignant Solid Tumor (AMST) Patients

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Immune responses, humoral and cellular, of the AMST patients who had cryosurgery have been given the designation “cryoimmunology” by Shulman et al (1966). Patients should possess enough energy, which induces immune responses to the peptides of cryo-destroyed tissue and cell debris. Energy of the AMST patients is scanty, as they are associated of malnutrition due to increase of energy demands and failure to adapt energy expenditure. They immunologically belong to low responder, which are incompetent patients. Judgment based on those immune responses of AMST patients has confused us that “cryoimmunology” is a myth (Sumida 1983). To assess the therapeutic results of AMST, I have used three parameters, NK (natural kicker cell) activity, PWM (pokeweed mitogen) test, and PPD (purified protein derivative of tuberculin) skin test by the standard Mantaux procedure before and after cryosurgery (Sumida 1993). On this occasion, I carefully re-evaluated the results of cryomedical treatments of 318 ABST patients. Although the statistical difference was not clear, PWM titer increased in several high responder cases who had positive PPD reaction before cryosurgery. When PPD reaction was anergic-negative, so any anticancer treatments including cryosurgery would not be effective. To establish cryoimmunology, patients should be immunocompetent. Otherwise, helper T cells would not fully recognize the autologous peptides, released by cryodestruction.

References: 1. Shulman, S.: Cryo-immunology: the production of antibody by the freezing of tissue. *In* Cryosurgery, ed. Rand, RW, Rinfret, AP, and von Leden, H., Charles C Thomas Publ. 1968. 2. Sumida, S., et al: Re-canalization by cryosurgery of the anal and esophageal stenosis. *In* Congress Proceedings of the 5th World Congress of Cryosurgery, edit. Padilla-Cruz, A., and Sumida, S. University Press, Univ. of Philippines System, Diliman, Quezon City, 1983.

A19 Cryosurgical Ablation Modalities for Hepatic Metastases from Colorectal Cancer. The Hellenic Experience

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Introduction: Management of hepatic metastases from colorectal cancer is a significant challenge, since surgical resection is possible only in 20% of cases. For the remaining 80%, cryosurgery is a method that has gained wide acceptance.

Methodology: Nine patients with multiple hepatic metastatic lesions not suitable for surgical resection, underwent cryodestruction over a 12 month period. Cryoablation was performed by liquid nitrogen flow within metallic probes under ultrasound (IOUS) guidance and monitoring. Two 30 min cycles of freezing–thawing were applied in every lesion. Simultaneous treatment was applied in up to three metastases. Patients temperature was monitored by an esophageal thermocouple.

Results: No major postoperative complications or operation-related deaths were observed. Complications included bile leak (4 pts), pleural effusion (6 pts), mild, reversible thrombocytopenia (8 pts). Cryoablation led to a postoperative reduction in the level of tumor markers in all patients. Serum CEA levels returned to normal values after the procedure. Eight patients are disease-free until now (negative findings on CT or MRI, normal CEA levels), while the ninth developed local recurrence of the tumor and underwent a second cryodestruction procedure. During a 4-month follow-up the patient is free of disease.

Discussion: Cryotherapy should be considered only for unresectable tumors, as resection still remains the treatment of choice. Cryosurgery is suitable for patients with bilobar or multiple lesions, high risk comorbidity that makes resection unfavorable, functional insufficiency of the liver, or involved resection margin. Its advantages include precision in lesion destruction with adequate tumor clearance, safe destruction of any recurrent lesions, prevention of tumor cell dissemination, and the development of an autoimmune reaction against tumor antigens. Nevertheless, it is not suitable for patients with more than 6 lesions or with lesions larger than 6 cm or with diffuse infiltrating disease. Thermal injury of the biliary tree and the so called ‘heat sink’ phenomenon require a cautious approach. Hepatic cryosurgery is a relatively safe procedure with transient intraoperative hypothermia, elevation of liver enzymes, right pleural effusions, thrombocytopenia and myoglobinuria being the most common side effects. The disease-free and overall survival rates seem to be similar when compared with conventional surgical techniques.

Conclusion: Advances in the technology of cryosurgery make it a safe method for the treatment of unresectable hepatic malignancies that may extend survival in carefully selected patients.

A20 Cryoablation of Liver Tumours Monitored by MRI

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Introduction: Cryoablation is used for local destruction of primary and secondary liver tumours, but recurrence at the site of ablation is reported at rates of 5-44%. Inadequate monitoring of the procedures, tumour location close to major vascular structures and the limited capacity of currently available cryosurgical equipment are plausible explanations for these recurrences.
Materials and methods: Causes of inadequate monitoring and improvements introduced by MRI are discussed. Clinical experience with cryoablation of colorectal metastases and MRI assisted estimation of cryolesion temperature in pig cryolesions form the basis of this discussion. A 0.5 T interventional magnet (GE, Milwaukee, WI) was used to monitor the procedures. The numerical calculation of temperature distribution in the cryolesions was done using a simplified bio-heat equation as described by Hong et al. Cryoablation was performed under general anaesthesia using MRI compatible cryoprobes and pressurised Argon gas (Cryohit, Galil Medical, Yokneam, Israel).
Results: MR provided excellent 3D information of the cryolesion extension. The frozen tissue appeared dark on MR images due to signal void caused by the very short T2 of frozen tissue. 3D temperature maps calculated based on the MR data gave important information on the ablation by demonstrating temperature distribution in the cryolesions. Suggested monitoring improvements include temperature maps superimposed on the cryolesion and visualisation of the tumour volume within the cryolesion volume i.e. the region of signal void on MRI.
Conclusion: MRI improves monitoring of liver cryoablation in many ways; primarily, MRI provides good 3D data of the cryolesion extension. Based on these data the cryolesion temperature distribution may be calculated. Visualising the tumour volume within the region of signal void provides information of the temperature distribution in the tumour.

A21 Laparoscopic Cryosurgery of Fibromas

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Uterine fibromas, as regards frequency, are the principal gynecological pathology of surgical interest as they represent the major indication for hysterectomy. A study in northern Italy has shown that uterine fibromatosis is the cause of 75 % of hysterectomies, and that about 15% of women aged between 50 and 60 need this kind of surgery. Though hysterectomy is the most frequently used procedure in case of uterine fibromatosis not responding to medical therapy, the conservative surgical approach, when possible, is preferred despite an estimated recurrency risk of 20 % in 1 year and 51 % in 5 years. For this particular indication laparoscopy shows important limits that are basically due to the length of surgery connected with the removal of fibroma from the abdominal cavity through a posterior colpotomy with subsequent risk of adhesions. Besides we must consider the difficulty connected with bleeding control and uterine suture.

We have adopted cryosurgery for myology procedures, in a pilot study in order to determine the feasibility and efficacy of endoscopic surgical approach to cryomiolisys. This technique permits the "in situ freezing destruction" without removal of the miomatosys lesions therefore causing a true cryoablation still preserving uterine wall integrity. Since 1998, 40 women candidate for conservative surgery for miomatosys, have been recruited.
Inclusion criteria: age 30-45; 1 to 5 or multiple nodular uterine fibromatosis; diameter of miomas inferior to 10 cm (measured by transvaginal or abdominal ultrasound); written informed consent.
Exclusion criteria: indication to open surgery; previous uterine surgery; previous medical treatment for fibromatosis; abnormal creatininemia; contraindications to laparoscopic procedure and LH-RH analogous; unwillingness to co-operate in the follow-up.

Cryosurgical steps are as follows: exploration of uterus and identification of all lesions and creation of a tunnel along their major axis using a monopolar hook, insertion of an "adquate to size" cryoprobe in the tunnel, 2 freeze-thaw cycles using the argon-driven Cryocare system, probe removal and packing of the tunnel with tabo-tamp or surgicel for bleeding control. There were no major laparoscopic complications needing conversion to open surgery except for one case where a uterine fracture with consequent bleeding occurred due to inadequate manipulation of 2 cryoprobes during the freezing of a large fundical lesion.

As regards symptoms 23/40 patients reported menometrorrhagia, 7/40 were asymptomatic with incidental diagnosis, 6/40 reported dismenorrhea and 4/40 pelvic pain. Of this cohort 12/40 were treated with LH-RH analogous to obtain downsizing before surgery. In the immediate postsurgical follow-up there were no important complications. Only 2/40 patients had pelvic pain. There where no cases of temperature above 38°C and major hematic losses through abdominal drainage. Median hospital stay was 2 days (range 1-4).

Median follow-up of the 40 patients is 6 months and 17 had a follow-up period >12 months. During follow-up, an ultrasound scan was performed at 5 and 12 months, all patients were asked to report symptom variations. 39/40 patients reported complete resolution of symptoms, in 1 case the persistence and increase of menometrorrhagia required isterectomy that was performed in another site. Diameter and volume of the 50 treated fibromas, after the procedure are summarized below.

	Diameter fibromas (cm)			**Volume Fibromas (cm^3)**		
	Time 0	6 month	12 month	Time 0	6 month	12 month
Average	4,26	2,47	1,64	70,94	22,5	13,77
Median	4,25	2,50	1,40	39,57	2,97	1,12
S.D.	2,13	1,93	1,80	101,42	44,56	27,04
Average % Reduction		42	61,5		79,10	87,82
Median of % Reduction		51,43	85		83,87	99,02
S.D. of % Reduction		28,83	29,68		21,40	17,53

Though cryomiolisys is still an experimental procedure, these preliminary results are excellent when compared to the normal laparoscopic technique and traditional open isterectomy. Four important problems are still to be explored: the eventuality of adherences, possible long term reappearance of clinical symptoms and regrowth of the myomas in the long run (10 years) and behaviour of uterus in pregnancy.

A22 Is There Long-Term Survival after Cryotherapy of Liver Malignancies?

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There is no doubt that resection is the gold standard in the therapy of hepatic malignancies. Locally ablative procedures – performed alone or in addition to resection – gain increasing interest in the treatment of irresectable hepatic tumors.

Patients: Between 8/93 and 01/2001 135 patients underwent cryotherapy at our center (43 x cryotherapy and resection; 9 x cryodestruction of the resection margin; 67 x cryotherapy alone via laparotomy; 16 x percutaneous cryotherapy). 66.9% had colorectal metastatic disease, 12.4% had primary liver tumors. Their mean age was 62±0.8 years. The mean number of lesions treated was 1.65±0.1 and the mean volume of destroyed tissue 5±0.8 cm. Gayowski stage of metastatic disease was IVa in the mean (mT4).

Results: Therapy specific complications were observed in 13.1%, general complications in 11% of patients. Therapy related letality was 2.8%. According to radiological findings the primary destruction rate was 90.4% and the recurrence rate at the treatment site 7.3%.

The mean overall survival time was 36.9±2.9 months (median 34.9 months). The three year survival rate of the patients treated until 12/97 was 24%. If stratified by intention to treat the mean survival-time of patients treated with curative intent was 43.5±3.7 months (median 43.9 months), and that of patients with a palliative approach 19.3±3.6 months (median 16.8 months).

Conclusion: Cryotherapy is a supplementary treatment to resection of liver malignancies and may result in good survival times if performed with curative intent together with complete tumor destruction. A merely palliative approach, however, produces no relevant profit for patient survival compared to chemotherapy only. The results of percutaneous application are considerably worse compared to those of open cryosurgery due to the restricted possibilities of monitoring and restaging during treatment.

These results have to be evaluated by further prospective studies.

A23 Characterisation of the Microcirculation of Tumor-Bearing Rat Liver upon Cryotherapy

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Background: Although cryotherapy of malignant liver tumors has gained wide-spread interest, the mechanism of tumor destruction and impairment of microcirculation has not been clarified yet. The aim of the present study was to set up a rat liver tumor model allowing for examination of the microcirculation by intravital microscopy before and after cryotherapy.

Material and methods: Under ether anaesthesia, $1x10^6$ tumor cells of a syngeneic colon carcinoma were implanted beneath the surface of the left liver lobe in WAG-Rij-rats (n=14). 14 days later, relaparotomy was performed and the left liver lobe was exteriorised for cryotherapy of the tumor by freezing with a liquid nitrogen-cooled cryoprobe. A single-freeze mode (n=7, end of freezing when 0°C in 3mm distance to the tumor was reached) was compared to a repetitive freeze mode (n=7, freezing to 0°C in 3mm distance to the tumor, thawing to 0°C at the tumor's edge and freezing to 0°C in 3mm distance to the tumor for a second time). Intravital microscopy of the tumor and the surrounding liver tissue was performed before cryothermia, directly after as well as 1 hour and 2 hours after cryotherapy.

Results: 14 days after implantation of the tumor, relaparotomy revealed liver tumors with an average size of $25.1\pm0.5mm^2$. Intravital microscopy of the tumors before cryothermia showed significantly higher values of venular diameter and venular tortuosity as well as reduced capillary density and absence of Ito-cells when compared with normal liver tissue. Repetitive cryothermia nearly doubled the freezing time (162.3±13.2 s) vs single freezing (93.8±11.4s). Single cryotherapy demonstrated a significant venular dilatation in the marginal zone of the tumor (77±7µm vs venular diameter before cryotherapy: 60±3µm), which did not occur after repetitive freezing. In each of the experimental groups, several venules within the tumor were perfused directly after freezing, but showed cessation of perfusion at 2 hours after cryothermia.

Conclusion: Directly after cryotherapy -even applying the repetitive mode- some venules in the marginal zone of the tumor showed reperfusion with, however, complete microvascular shutdown of the tumor after 2 hours. Therefore, repetitive application of cryothermia does not reveal an advantage vs single freezing in terms of shutdown of the tumor microcirculation.

A23 Local Platelet Trapping as the Cause of Thrombocytopenia after Hepatic Cryotherapy

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Introduction: Thrombocytopenia is a well known systemic side-effect of cryodestruction of hepatic primaries and secondaries. The degree of the decrease in platelet count clearly correlates with the degree of hepatocellular injury, however, the etiology of thrombocytopenia is still unknown.

Patients and methods: In 6 patients undergoing cryotherapy of liver lesions 18.5 Mbq In-111-labeled platelets were injected immediately before cryotherapy. Platelet count was determined 1h as well as on 1, 2, 3, 4, 5 and 10 days after cryotherapy. To measure half-time and mean platelet life-span blood sampling was performed 1, 2, 3, 24 and 48 h after injection and whole body scintigraphy was performed 48 h after cryointervention.

Results: The platelet count droped from $224 \pm 32 \times 10^9$/l to $94 \pm 14 \times 10^9$/l. The half-time was 1.5 ± 0.3 days (normal 3.5 – 6.0 d) and the mean platelet life-span was 2.9 ± 0.4 days (normal 7 – 11 d). The calculation of organ activities as percent injected dose gave 43.8 ± 5.8% in the liver vs. 22.8 ± 4.5% in the spleen. Comparison to MRI identified the cryolesion as the predominant site of platelet accumulation and destruction. Additional histomorpho-logical examination confirmed platelet trapping in the region of the cryo-margin.

Conclusion: We can demonstrate at first that local platelet trapping is a major cause of systemic thrombocytopenia after cryodestruction of liver lesions.

A24 Development of Cryosurgery for the Surgical Management of Menorrhagia using an In-Vitro Perfusion Model

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Hypothesis: A uterine perfusion model is a useful tool for the development of safe and effective cryoablation of the endometrium.

Background: The surgical management of menstrual disorders has altered in recent years with the emergence of minimal access technology. Intra-uterine surgery using laser or electrocautery to ablate or ressect the endometrium have proved satisfactory conservative surgical alternatives to hysterectomy . However, these procedures are difficult to learn, require expensive equipment and specialist support staff. Cryoablation is simple to perform, does not require expensive equipment and therefore should allow more widespread access for patients to conservative surgery.

In vitro investigation by Kremer et al in the 1990's determined the median temperature to produce 4mm of cell death, which is necessary to prevent endometrial regeneration. However, the in vitro protocol used was found to be ineffective in vivo as it had not taken into account the effects of tissue temperature, blood circulation or cavity shape.

Aims: To set up a uterine perfusion model to overcome the problems cited above and develop an effective clinical protocol for cryoablation.

Methods: The model was designed to mimic in-vivo conditions of temperature, humidity and perfusion. Cell death was quantified using a histochemical technique based on the presence of NADH diaphorase. Depth of cell death was measured in different areas of the uterus to assess efficacy and safety. Using the experimental data a clinical protocol was developed and tested in the perfusion model.

Results: The model is capable of perfusing a uterus at a steady temperature of 37^{o}C, whilst maintaining tissue viability. Temperature changes during perfusion and in-vivo cryoablation were not statistically different. There was no statistically significant difference between depth of cell death produced by perfusion and in-vivo experiments. The mean temperature which produced cell death in the uterine body was –9.3^{o}C (SD 7.2). Using this and safety data, a temperature of -14^{o}C at 4mm should produce cell death at 4mm in 77.7% of uteri. This clinical protocol is currently under assessment.

Conclusions: Building a uterine perfusion model which is representative of in vivo conditions is feasible. The model is a useful tool for developing safe and effective endometrial cryoablation and has implications for investigation of other methods of intrauterine surgical techniques.

A25 Cryosurgical Ablation as a way to Improve the Treatment Results of Patients with Unresectable Liver Cancer.

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Background. Surgical resection remains the treatment of choice for the treatment of liver cancer. But only 10 to 20 per cent of these tumors are found to be resectable. Cryosurgery seems to lead to a feasible alternative for patients with unresectable hepatic malignancies.

Patients and Methods. From January 1997 to January 2001, 17 patients with liver cancer in whom we used cryosurgery were treated in our institution: 5 patients with hepatocellular carcinoma, 12 patients with metastatic liver cancer. In patients with metastatic liver cancer primary tumor was in the colon and rectum in 8 patients, in kidney in 2 patients, in pancreas in 2 patients. The sizes of tumors were from 1.5 to 15 cm. Seven patients underwent a synchronous liver resection. Ten patients had cryoablation alone.

Results. During a mean follow-up of 27 months (range, 1-47), tumors recurred at the site of cryosurgery in one patient (5.9%), in the remaining liver in 5 patients (29.4%) and elsewhere in 3 patients (17.6%). There was no intraoperative death. The rate of postoperative complications was 17.6%. All patients were discharged home in stable condition with a mean hospital stay of nine days (range 5-19 days).

Conclusion. Cryosurgery can be considered safe and effective method of treatment of unresectable hepatic malignancies.

A28 The Place of Cryosurgery in the Treatment of Prostate Cancer in 2001

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At the beginning of the 21st Century, a lot of treatment possibilities are commonly available to patients suffering from prostate cancer. The choice is not always easy and should be driven by objective patient information. The urologist plays the most important role in helping and guiding his patient towards a correct and consented decision.

In order to be able to offer his patient the objective information he is entitled to, the urologist should keep pace with all the new developments in the field of prostate cancer. He should be eager to discover and explore the alternative new choices that offer the patient minimally invasive curative treatment with minimal interference in his quality of life.

The different treatment options for localized prostate cancer will be openly discussed and critically reviewed by the author. Starting from the watchful waiting policy, over radiotherapy in all its ancient and modern trends, to radical surgery via cryosurgery and hifu treatment, the different choices will be evaluated in regard to risks, success, age, quality of life and patients preferences.

The supposed place of cryosurgery in this supermarket of opportunities and possibilities will be clearly marked, open for discussion.

Cryosurgery is one of the least invasive and best tolerated treatment options for localized prostate cancer. Its success rate and possible future treatment indications in other urological tumors make it a first choice alternative treatment option that is capable of curing prostate cancer.

A29 Temperature Evolution and Direct Cell Damage During Prostate Cryosurgery.

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A mathematical model was developed to calculate and display temperature changes around multiple cryoprobes in a thermally realistic environment. Phantom studies established the model's accuracy to be within experimental error. As a theoretical case study temperature changes were calculated about six cryoprobes placed within a typical 24g prostate. The probe configuration and protocol of operation for this simulated treatment was specified by an experienced cryosurgeon. Probes were angled, in a clinically realistic manner, to conform the iceball to the prostate. The anatomy of the bladder and urethra were specified and were treated as heat reservoirs maintained at 37^{o}C. The timing of probe operation reflected the clinical sequencing of anterior to posterior utilized to maximize ultrasound visualization. Isotherm locations were rendered in 3-dimensions and were overlaid on the anatomy. A time-temperature-volume histogram was also generated. The images created with the model allow, for the first time, the user to visualize the complete 3-dimensional iceball shape and the distribution of isotherms within the iceball. This allows for objective evaluation of the procedure. The time-temperature-volume histogram available from the model plots the percentage of target volume enclosed by any specified isotherm. After 12min freezing (a typical duration of a freeze cycle during prostate cryosurgery) 97.8%, 94.0% and 86.3% of the prostate volume was enclosed by the -20^{o}C, -30^{o}C and -40^{o}C isotherms, respectively. The thermal model developed generates 3-dimensional isotherm evolution maps of temperatures around multiple cryoprobes and will be combined with anatomical contours to permit complex preop planning for prostate cryosurgery. These contours may be specified from images of the patient using any one, or combination, of several imaging modalities (ie, X-Ray CT, MRI and Ultrasound).

The *in vivo* freezing and thawing of tissue that occurs during cryosurgery leads to a region of necrosis within the iceball. Injury mechanisms that result from exposure to a freeze-thaw cycle are complicated and not yet fully understood. Cryomicroscopy has been used to evaluate cellular survival for different freezing rates, thawing rates, end temperatures and hold times. However, the utility of the results has been limited by the use of constant freezing and thawing rates to approximate the actual thermal histories that occur within a cryosurgical iceball. We report a series of cryomicroscopy experiments using cooling rates generated by a mathematical model of temperature evolution about a single cryoprobe and thawing rates observed during an *in vivo* single cryoprobe study to assess *in vitro* cell damage. An exponential relationship was observed between end temperature and survival for cells experiencing both single and double freeze thaw cycles. There was no statistical difference between the square of the fractional survival after one freeze and the fractional survival after a double freeze. Using this relationship it was possible to create an in vitro cell survival map after a double freeze thaw cycle in the clinical we have modeled. These can be considered maps of the maximum survival since post treatment ischemic injury will greatly decrease cell survival throughout an *in vivo* iceball.

A30 Targeted Cryoablation for Localized Prostate Cancer: The Washington Cancer Institute Experience.

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Purpose: The management of early stage (TI-2NOMO) and locally advanced T3NoMo includes radical surgery, radiation therapy and cryosurgery. Cryosurgery for stages T I to T3 should be considered as an option when counseling patients diagnosed with localized prostate cancer.

Methods: Cryosurgery was performed in 14 patients with early stage prostate cancer under Transrectal ultrasound guidance and thermal monitoring after appropriate counseling.

Results: In nine of fourteen patients not pretreated with LH-RH agonists, PSA was undetectable at a mean follow up of three months with minimal morbidity. Two patients failed therapy as evidenced by PSA failure.

Conclusions: Cryosurgery should be considered as a treatment option when counseling patients with early stage prostate cancer based on our own and other peer reviewed data. Indications, techniques, morbidity, and results will be presented in detail

A31 Cryosurgery for Localized Prostate Cancer.

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Introduction and Objectives: From 1994 –98, a prospective study of cryosurgery (CS) in T1-3, N0, M0 prostate cancer patients was conducted at a single institution. The objectives were to evaluate potential theraputic efficacy, to establish complication rates and to determine the feasibility for a randomized comparative trial with alternate local treatments.

Methods: 76 consecutive patients with baseline PSA < 30ng/L were entered and had the following prognostic characteristics: Stage T1-2: 67 (88%), T3: 9 (12%); Gleason score 5-6: 34 (45%), Gleason 7: 29 (38%), Gleason 8-9: 13 (17%); PSA<10: 47 (62%), >10: 29 (38%). In 326 patients with glands > 45 gms, neoadjuvant androgen deprivation was used to achieve cytoreduction. A single freeze cycle was used in pts. 1-10 and a two freeze cycle in all remaining pts. Follow up for all patients included MRI scan, prostate biopsy 5mos. post op., in addition to clinical, PSA and Quality of life assessment (QoL) every 3 months.

Results: The procedure was well tolerated. There were no deaths. Hospital stay was 1 night for 71 pts. 3 pts. required TURP for sloughing, 1 pt. had an orchidectomy for testicular abscess 6 wks post op. and 1 pt developed incontinence. Impotence occurred in all patients initially, but at 2 years complete recovery occurred in 23%, and partial recovery in 26%. QoL assessments returned to baseline within 12 months in 100%, except for potency. Follow up biopsy was done in 73 of 76 cases. 72/73 (98%) are biopsy (-) after one or more treatments (10 pts. - 2 treatments, 4 pts. - 3 treatments). 5 year overall survival is 89%(68 pts); 5 year cancer specific survival is 98%.PSA is <0.3 in 54% at 5 years, and < 1.0 in 76% of all patients.

Conclusions: Our findings demonstrate that cryosurgery is technically feasible, has acceptable complication rates and appears to be effective in prostatic ablation. Consequently, we are evaluating cryosurgery further in a prospective, randomized trial of cryosurgery and radiation therapy.

A32 Initial Experience of MRI Guided Percutaneous Cryosurgery for the Liver and Renal Tumors

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Purpose: To present our initial clinical experience using percutaneous cryoablation with MRI guidance in treating liver and renal cancers.

Materials and Methods: Criteria for the candidate are as follows:

1. Good performance status.
2. Tumors are limited in the liver or the kidney.
3. No other serious disease.
4. Number of tumor is less than or equal 3.
5. Maximum diameter of the tumor is less than 10 cm when it is solitary. And the diameters are less than or equal 3 cm when tumors are 2 or 3.

MRI is open type, low magnetic field (Airis II, HITACHI: 0.3T, permanent magnet).

Cryo-system is Cryo-Hit (Galil Medical) which uses high-pressure argon gas for freezing and helium gas for thawing.

Results: Four cases of hepatocellular carcinoma (HCC) and 1 case of renal cell cancer (RCC) were treated. In all cases, cryoprobes were located safely and accurately using MRI guidance. SPIO was administrated to 3 cases of HCC for delineating the tumor clearly. Five tumors were ablated whole area and there was no residual viability of tumors in short term follow up. One RCC was ablated partially because it was very close to jejunum. Mild fever was the only adverse reaction.

Conclusion: MRI guided percutaneous cryoablation for the liver and renal cancer is a safe and accurate modality.

A33 Efficacy and Complications of Salvage Cryosurgery for Recurrent Prostate Carcinoma after Radiotherapy

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Despite improvements in the treatment of clinically localized prostate cancer, local recurrence remains a significant problem after radiotherapy. Cryosurgical ablation (CSAP) of the prostate is a potentially curative treatment for locally radio-recurrent prostate carcinoma yet its clinical application continues to be defined. As a prospective trial, CSAP was performed with in 31 men with biopsy proven radio-recurrent carcinoma of the prostate. Follow-up included serial prostate specific antigen (PSA) levels, a digital rectal exam (DRE), self-reported standardized questionnaires, and other evaluations as clinically indicated.

Persistent complications included incontinence (2), retention (3), and impotence (6). Nineteen patients (64%) displayed a PSA nadir < 0.3 ng/m, six (19%) showed a PSA nadir less or equal to 1 ng/mL, and 4 (13%) had a PSA nadir less than or equal to 4 ng/mL. Using the PSA definitions for biochemical failure as PSA >= 0.3 ng/mL, the Kaplan-Meier plots showed the incidence of patients to be free of biochemical recurrence at 54% and 47% at 1 and 2 years respectively. For a PSA >= 1.0, the values at 1 and 2 years were 74% and 54% with a flattening curve thereafter.

This prospective evaluation shows that salvage cryosurgery after failed radiotherapy is safe and can rescue many patients to biochemical freedom from disease.

A35 Experimental In-Vivo Tests of Cryosurgical Procedures and Determination of the Thermal Response in Tissue While Cryolesion by Means of Ex-Vivo Organ Perfusion.

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The basic features of cryosurgical procedures were established in the mid 1960s. Nevertheless since then, the correlation between the biophysical effects of cold application on organic tissue and the engineering aspects of such cold application has been investigated in wide field of experimental cryobiological and clinical works. Gage and Baust (1998) presented a review about the mechanisms of tissue injury in cryosurgery. Many investigators have performed in vitro experiments of cell freezing to establish the typical temperature conditions of cell death.

To increase the effectiveness of the cryolesion for the cell destruction in the tissue depth needs a very high cooling power of the cryoprobe. This cooling power Q/t is necessary to reject the heat out from the tissue depth. The total heat rejection Q_{total} while the freezing process of biological tissue is given by the terms of Q_c - heat capacity of the tissue, Q_L- latent heat of water-ionic solution and Q_{blood} , Q_{meta} – heat sources caused by blood flow and metabolic processes.

The targets for our interdisciplinary basic research activities are placed in the medical domain of Oral and Maxillofacial Surgery (OMS) with the following tasks (Herzog *et al.* 1998):

(1) Engineering design and development of different minimal invasive cryodevices for high power freezing, (2) Validation of the cryosurgical devices and procedures in model tissue substances and in real organic tissue, (3) Cryobiological and histological investigations of enhanced cryodestruction.

The evaluation tests in tissue-like substances are necessary for the determination of thermophysical process parameters of cell destruction. The cooling behaviour and the thermal response in real perfused tissue structures was investigated.

Validation experiments of cryodevices and cryosurgical procedures on real organic tissue were carried out by using a special apparatus for organ perfusion in correlation with histological investigations. The cooling and freezing behaviour were determined in perfused pig paw on the skin or on muscle tissue under real and various blood flow densities Vp and metabolic conditions (Vpnormal=105ml/min). The thermal response in the tissue depth by cryolesion of pig paw muscle is strongly dependant on the thermal loads caused by the blood flow. Initial experimental results demonstrate here an influence of the real blood flow density on the cooling behaviour within the tissue, particularly the increase of cold penetration depending on the reduction of perfusion blood flow.

Further studies will concentrate on reproducibility of results, and obtaining reliable histological results with long-term experiments.

A36 Initial Experiences of MR Guided Percutaneous Cryosurgery under Horizontal Magnetic System.

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Purpose:MR is able to guide and monitor the procedure of cryosurgery, which is known as minimal invasive therapy. The purpose of this study is to evaluate the clinical feasibility of percutaneous cryosurgery using horizontal magnetic system and to determine the efficacy of this procedure in our initial experiences.

Materials and Methods: Materials were two cases with renal cell carcinoma, less than or equal to 3cm in size. Both were male with mean age of 65.5 years old. A MR-compatible cryotherapy system (CryoHit, Galil Medical Ltd, Yokneam, Israel) was used. Following local anaesthesia, two 2mm diameter probes were inserted percutaneously into the mass under 0.3T open type MR system (AIRIS II, Hitachi) guidance. MR fluoroscopy was performed with GrE sequence (TR/TE/FA: 35/11.5/35 up date 4sec. or 25/11.8/30 up date 2sec.). Three freeze/thaw cycles were performed, basing upon the size and morphology of each mass targeted. Both patients were hospitalized overnight.

Follow up CT, with and without contrast, was performed on the following day, and 2 weeks and 6 weeks after the procedure.

This study was approved by an ethics committee in our institution.

Results: All procedures were safely and accurately performed under MRI guidance. Size of ice ball reached to entire tumour and 1cm of tissue peripheral to the tumour. No major complications were encountered. Follow up CT showed no contrast enhancement of these masses.

Conclusions: Although our experience is limited, percutaneous cryosurgery for renal call carcinoma appears to be a safe and effective treatment.

A37 Successful Treatment of Locally Confined Prostate Cancer with the SeedNet™ System - Preliminary Multicenter Results

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Introduction: Prostate cancer, most commonly diagnosed during the sixth decade of life, is the second most common malignancy found in men, and the second most common cause of cancer deaths in men after lung cancer (Landis 1998). Currently, a patient diagnosed with early stage prostate cancer is basically offered two options - Radical Prostatectomy [RP] and various types of Radiation Therapy [RT] (implanting internal radioactive seeds, external beam irradiation, or a combination of the two). Both RP and RT carry a risk for acute or chronic residual morbidity, early or late recurrence of disease and even direct or indirect risk of mortality (Fowler 1993).

Methods and Materials: SeedNet™ developed by Galil Medical (Yokneam, Israel), is an innovative system that further advances cryotherapy by reducing the probe diameter to that of a 17-gauge (1.47 mm) needle. These ultra-thin needles, inserted percutaneously in a method identical to brachytherapy, provide high-resolution freezing and even temperature distribution for accurate yet very controlled destruction of prostatic tissue. Using the SeedNet™ system, and guided by a bi-plane transrectal ultrasound (TRUS), an array of ultra-thin SeedNet™ needles were inserted through a template, similar to that used in brachytherapy. Prior to performing the SeedNet™ procedure volumetric measurements of the prostate were taken. Under general or regional anesthesia, the SeedNet™ needles were inserted through the template in accordance with the physician's pre-treatment plan. A closed system urethral warming catheter has been used to protect the urethra from the extreme temperatures. Two freeze/thaw cycles were generally employed in order to ensure complete cell death.

Results: Over 100 cases, in the USA, Europe, and Israel, have been performed with the SeedNet™ system during the past year. The first 33 cases have follow-up of at least 3 months. The patients were divided into two groups, favorable and unfavorable according to their PSA levels, TNM staging and combined Gleason score (CGS).

Conclusion: The SeedNet™ system is an innovative, minimally invasive technology for the treatment of locally confined prostate cancer. Incorporating the use of ultra-thin SeedNet™ needles and transrectal ultrasound, the procedure is simple to perform, easy to control and has a short learning curve, especially for physicians familiar with brachytherapy. The SeedNet™ system has proven to be a safe and effective modality for treating localized prostate cancer with promising preliminary results that exhibit almost no adverse effects. With a rapidly developing trend towards minimally invasive procedures, SeedNet™ is an optimal choice due to its ease of use, basically same day surgery and fast recovery time.

A38 Perioperative Complications in Cryosurgical Treatment of Bone Tissue in Sheep with a New Type of Miniature Cryoprobe.

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In-vitro studies indicate that new miniature cryoprobes are suitable for cryoablation of bone tissue. Probes of this kind are already used for tumours in liver and prostate tissue. Besides wound infection, bone marrow embolism due to intramedullar expansion of the freezing zone and consecutive increase in pressure is a well-known complication of conventional cryoablation. Purpose of this experiment was to examine the perioperative complications; in particular the danger of embolism; of cryoablation with miniature cryoprobes.

Method: 24 sheep were put under general anesthesia, holes were drilled into the epiphysis of the right tibia and the left femur metaphysis, one cryoablation with 2 freeze-thaw-cycles each was carried out with new cryoprobes. The femoral ablation was performed mono-cortically to ensure postoperative stability. In contrast to that, in freezing of the tibia epiphysis the probe was pushed to the opposite cortical. In order to detect possible pulmonary embolism and resulting pulmonary arterial hypertension, pulmonary artery pressure (PAP), wedge pressure (PAWP) and central venous pressure (CVP) were measured with a Swan-Ganz pulmonary artery catheter. Throughout the intra- and perioperative phase heart rate and oxygen saturation by pulse oxymetry, blood gas and electrolytes were monitored regularly. Postoperative complications were examined.

Results: Compared with the initial data prior to freezing, no significant increase of PAP, PAWP, CVP or heart rate was measured in any of the sheep. Merely a temporary increase of PAP and CVP was observed which was not of pathologic genesis; this was due to the right lateral position of the animal, i.e. compression of the pericordial blood vessels by the rumen. During the entire operation the results of the blood gas analyses were inconspicuous; pO2 and pCO2 were constant; for pH, standard bicarbonate and base excess an isolated insignificant change to slight acidosis was noted. The average decrease of HB was 1.1 g/dl. In one animal postoperative wound infection and wound edge necrosis was observed; after surgical revision and administration of antibiotics the wound healed.

Conclusion: Occurrence of major perioperative complications of cryosurgical treatment of bone tissue, especially regarding clinically relevant pulmonary embolism, were not confirmed in experiments with sheep. Using new types of miniature cryoprobes, cryosurgery appears to be a safe alternative or addition to resectional procedures for treating abnormal bone tissue.

A39 Cryosurgery of the Prostate: Changing Technique and Technology without Forgetting the Past.

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Spreading of cryosurgery in prostatic neoplastic pathology during the decades have brought a progressive improvement of technology and surgical technique with improved results and a reduction of morbidity. In the early 60's and 70's cryosurgery was applied to the prostate transurethrally with a special probe inserted under digital control and length of freezing was determined in a rather empirical way by palpation. An important attempt to get better visual monitorization was introduced by Reuter who attempted to verify freezing with a soprapubic cistoscopy. In the last 10 years the reintroduction of cryosurgery was led by ultrasound control, multiprobe devices and the use of thermocouples to monitor temperatures as refined by Lee and Bahn. More recently Onik introduced the systematic use of instillation of liquid in the Denonvilliers fascia to easily obtain a lower temperature outside the gland during the procedure.

We have compared results and complications in patients who received surgery with different methods of reducing the risk of rectal injury, using a larger volume of liquid injected in the Denionvillier's, 60 ml for 30 pts, 30ml for 20 pts or none in 50 pts (as with the initial group). The cryo technique used multiple probes (4-8), urethral warming, thermocouple monitoring at both bases, apex and external sphincter, double freeze-thaw cycle. Indications to cryosurgery were cancer of the prostate, not treatable with open surgery due to previous surgery or rx therapies, age, patient condition, local advanced stage, high PSA or Gleason, patient choice.

Results: with the new technique it is possible to obtain temperatures <–30°C in all cases and –40°C in at least one of the cycles. Temperatures recorded at external sphincteral level kept higher than 0°C. Freezing maintained time was >7 mins (mean 10 mins). We stopped injecting warm water in the rectum as protection when we started using 60ml liquid in the fascia. Post surgical morbidity seems to be identical to that when using the Lee and Bahn technique. We observed that this technique which does not consider the artificial shifting away of the rectal wall, makes it more difficult to maintain a lower temperature outside the gland and to hold it low for several minutes as we easily do with the Onik method. This is due to the fact that the –40°C isotherm lies somewhere around 8 mm inside the ice-ball external limit and this distance is seldom present in the normal anatomy between prostate and rectum.

Conclusions: achieving temperatures <–40°C outside the prostatic gland causes destruction of all neoplastic cells. Recent technical improvements have made prostate cryoablation easier, safer and more effective also in high-risk patients. All the above considerations clarify why using the old transurethral techniques the 60's and 70's cryosurgery pioneers had so bad time in controlling the limit of the ice-ball at the level of the bladder neck, sphincter and rectum. This was the reason of the abandonment of the technique and not its failure in terms of neoplastic control that, on the contrary, was always excellent!

A40 Randomised Phase II Trial Comparing the Outcome of External Beam Radiotherapy alone Versus Cryosurgery plus External Beam Radiotherapy in Patients with Malignant Endobronchial Obstruction.

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Objective; Endobronchial carcinoma is the commonest tumour in humans with an appalling prognosis causing distressing symptoms including dyspnoea, cough and haemoptysis. Unfortunately 85% of patients do not present until the disease is well advanced and only palliative treatment is possible. Endobronchial cryosurgery was pioneered in the UK at Harefield Hospital in 1986 and since then over 2000 applications have been carried out resulting in median survival of 12.9 months. The standard treatment of patients with inoperable, non small cell lung cancer in the UK is radiotherapy.
External beam radiotherapy is the treatment most often used in patients afflicted with non-small cell lung cancer and which has a median survival of 11.4 months. Radiotherapy and Cryosurgery are often used in combination. No randomised trials comparing the results of combination therapy to radiotherapy alone however, have been reported. This trial has been established to compare the use of radiotherapy alone with cryosurgery followed by radiotherapy.

Patients and Methods; Patients attending the Thoracic surgical outpatients department with inoperable non-small cell endobronchial carcinoma will be considered for the study. Patients who are unfit for general anaesthetic or who have had previous radiotherapy will be excluded from the study.
Using two-sample comparison of proportion at the 5% significance level with 90% power and if we assume that cryosurgery and radiotherapy together will lead to an improvement of at least one dyspnoea score in 61% of patients (based on previous studies in this institution) and that radiotherapy alone will lead to an improvement of at least one dyspnoea score in 30% of patients, 60 patients will be required in each group. Giving a total of 120 patients in the trial. Based on our current workload, these patients will be recruited over 24 months.
Patients will be recruited into the trial after their informed consent has been obtained and will be randomised to group 1 or group2.
Group 1 will undergo radiotherapy.
Group 2 will undergo two sessions of cryosurgery at approximately 2 week intervals followed by radiotherapy.
Outcome measures will include relief of breathlessness, palliation of cough, haemoptysis and chest pain. Quality of life as assessed by the Rotterdam symptom checklist. Secondary outcome measures will include lung function tests and survival

Conclusion;The main hypothesis of this study is that the combination of cryosurgery plus radiotherapy improves outcome of lung cancer patients with central endobronchial lesions in comparison to radiotherapy alone.
This trial is in its early stages and only a small number of patients have been recruited. We hope that this will be the first randomised controlled trial to demonstrate the benefit of the combination of cryosurgery plus radiotherapy over radiotherapy alone.

A41 Investigation of the Ice Formation Process Around a Cryosurgical Probe

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Understanding ice crystal formation mechanisms in tissue and organ cells is important for the development of new efficient cryosurgical methods. The aim of the work is cryomicroscopic study of ice crystal formation during the liquid medium freezing around a standard cryosurgical probe. The Accu Probe System (Cryomedical Sciences, Inc.,USA) with standard probe (diam 3.4 mm, freezing zone 40 mm) located in a cryochamber was used. The instrument has an original construction with a high-capacity freezing system (Subcooled L N_2) and is used in many US and European centers. Normal (FREEZE) and maximum (MAX FREEZE) freezing were used. Thawing was at maximum probe heating. Temperature was measured by thermocouple and microprocessor thermometer.

For cryomicroscopic experiments the probe was submerged in a liquid drop. Aqueous medium saline and gelatinous solution, located on a lower side of cryochamber were used. Visual and photographic control of the freezing process was carried-out by means of the cryochamber and microscope with photocamera. Morphometrical analysis of an ice crystal width was conducted by means of Morpho Tools computer system, developed by the authors.

Visual cryomicroscopic analysis of the whole formation process of an ice sphere around probe allowed us to distinguish 3 phases, 1 & 2 correspond to the beginning of freezing process (probe activation) and 3 to an ice sphere. To study the mechanism of initial ice formation around probe, slow cooling to the temperatures of crystallization was used. In phase 2 the distance from the probe to the ice front varies, depending on N_2 entering the probe and the ice front moves forward and back. Phase2 may be considered as "non-stable freezing". With a further temperature drop, Phase 3, the ice sphere increases. During FREEZE regime down to moderate low temperatures, the front shows polycrystalline character with spicule-like crystals, directed radially from probe. Frozen phase is a bulk of long crystals, growing in the direction of temperature gradient, forming a "teeth-like" crystallization front. Sometimes elongated gas bubbles, captured by an ice front and orientated radially are seen. At a sharp decrease of probe temperature (moderate to low, "Jump Freeze") a dark line, from a layer of smaller crystals which can grow, can bee seen in the ice front. During probe thawing the outer side of the ice front shows rounding of spicule-like surface and gas bubble isolation. Thawing around probe with liquid between probe and ice, preserving even at positive temperatures occurs at probe heating. When freezing in the MAX FREEZE regime phases 1&2 are not seen, but a sharp growth of an ice front with structure described earlier is observed. Morphometrical sizes of crystals are close to the FREEZE regime. With the ice front increases, cracking can be seen inner side in a radial direction. Dynamics of cracking process is significantly falls behind from the beginning of forming and occurs actively only in the second half of freezing and especially has linear dependence on freezing time. When thawing after the MAX FREEZE regimen an outer side rounding of an ice front crystals is observed and the ice front loses its regular structure, cracking is revealed on outside and liquid phase penetration is observed. Ice directly in contact with probe thaws.

In a gelatinous medium,the crystal formation process under the FREEZE and MAX FREEZE regimens in whole remains freezing process of an aqueous and salt medium. At the same time the structure of an ice front in gelatinous medium keeps its morphological characteristics for a long time even after the absolute thawing. Such state limits the study of the possibility of an ice crystal structural reconstructions during thawing, but allows to preserve for a long time the photo of crystalline structures of an ice sphere surface, that could be used in further deep investigations. Application of the following experimental cryochamber model with the cryoprobe and with the system of temperature registration as well as the microscope with a large depth of sharpness allowed to obtain for the first time the real data about the structure and character of ice crystals, forming in a liquid medium at probe freezing of cryosurgical instrument. The presence of a powerful probe cooling system conditions the appearance of high temperature gradients between probe surface and liquid medium the explains the presence of ice crystals, radially directed from a probe center. The character of these crystals in FREEZE and MAX FREEZE regimes approaches to spicule-like model of ice crystals at freezing, according with data. The outer surface of an ice front has sharp crystal sticking-out, revealed not only in horizontal plane, but in volume (3D),

determined at microscope refocusing on lower sections of an ice sphere. Conducted cryomicroscopic investigation allowed to fix the dynamics growth of an ice front during freezing. The presence of gas bubbles in an ice front structure, as well as the character of their connection with polycrystalline structure supplements our ideas about the process, proceeded during frozen zone structure formation. Gas emission, revealed at thawing of ice crystals, allows to suppose the gas presence in cryoeffect zone after frozen medium thawing, that also may affect the viability (or damage) of thawed tissue cells. Visual analysis of the cracking process in an ice sphere structure (the character of their redistribution, time of appearance) gives an opportunity to conclude, that their appearance, obviously, is connected with recrystallizational processes, taking place in the last phase of an ice sphere formation and may be controlled, for example, by means of a rate direction and (or) frezing time. Considering the revealed "toothed" character of crystallization front in freezing zone, it may be supposed, that the presence of expressed destructive effect during the interactions between ice and tissue under the conditions of tissue cells real freezing by means of cryosurgical instrument.

Results show a sharp decrease in probe temperature (“Jump Freeze ”) is accompanied by typical changes, occured in crystalline structure of an ice sphere and the formation of small crystalline structures on outer surface of an ice sphere is observed. Such change of crystalline structure creates the “sphere-membrane” inside an ice sphere and makes possible the controlled modification of an ice structure, depending on the aims set. An ice sphere with given parameters of crystalline structure has great importance in cryosurgery to obtain an efficient cryodestruction in pathological cells and tissues.

A42 Cryosurgery of Advanced Breast Cancer

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Patients with locally advanced breast cancer experience considerable discomfort as they can easily observe the local progression of the tumour, with more or less pain, haemorrhage and malodourness. This increases the psychological distress of the patient and have a negative impact in his fammiliar and social environment.

Cryosurgery, in selected patients, may achieve the local erradication of the tumour, or even the clinical cure, thus improving the quality of life of this patients.

From 1985 to 2000, 21 female patients, with locally advanced breast cancer, were treated with cryosurgery in our department. Nineteen patients were in Stage III-B, one in Stage III-A and another in stage IV. One patient had advanced cancer in both breasts. All patients had been previously treated by conventional methods, such as radiotherapy and chemotherapy. They were referred to us as incurable cases, for local palliation. Cryosurgery was performed under general anesthesia with a strong spray of liquid nitrogen (Frigitronics CE-4) and temperature monitoring .

Careful isolation of the surgical field was mandatory to avoid the risk of accidental freezing of the surrounding skin. The most serious complication that ocurred was severe haemorrhage, in the first 48 hours after cryosurgery, in two patients. The patients were discharged from hospital about one week after the treatment. Healing was very slow and took about six to eight months. The follow-up ranged from one month to five years with an average time of 25 months. Six patients are still alive and well.

A43 Endobronchial Cryotherapy Using a Flexible Bronchoscopy, The North American Experience

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Endobronchial cryotherapy is another modality to treat endobronchial lesion that causes pneumonia, hemoptysis shortness of breath or cough. This has been an alternative to endobronchial Nd: Yag laser and electrocautery. Although endobronchial cryotherapy was initially initiated in North America, at the Mayo Clinic, however subsequent interest in endobronchial cryotherapy in North American essentially disappeared. However, the interest in endobronchial cryotherapy persistent in Europe and a significant work, refinement and number studies was conducted. Endobronchial cryotherapy was reintroduced in North America using it with the flexible bronchoscope in 1995 under topical anthesthesia and sedation performed in the bronchoscopy suites.

At Indiana University Medical Center we started performing cryotherapy using a flexible bronchoscope in 1995 after FDA approval. Since then we have now performed endobronchial cryotherapy procedures in more then 100 patients. Cryotherapy has been used for treatment in both malignant and benign endobronchial lesions. In addition we have removed foreign bodies. We have also used cryotherapy as an adjuvant therapy such as brachytherpy and argon plasma coagulation. The largest group of patient had lung cancer.

In the group of endobronchial lesions we treated three groups. In group 1, we performed endobronchial cryotherapy alone, in group 2 we performed cryotherapy and standard endobronchial brachytherapy, in group 3 we performed cryotherapy and brachytherapy on fewer occasion.

In group 1 we had good success in reopen the airway, but needed at least two or three bronchoscopes, in group 2 the use of cryotherapy was only needed on one occasion when brachytherapy was used, and in group 3 despite less radiation the result were the same. Thus tumor specific therapy was also used in the same setting.

In the group with benign tracheal endobronchial disorders we have used endobronchial cryotherapy to remove foreign bodies. We also have successfully removed cryotherapy sensitive tumor but were unable to remove cryotherapy resistant tumors. We were also successful in removing all foreign bodies.

The complications have included one death and one significant drainage of pus after removal of the endobronchial tumors.

In summary the endobronchial cryotherapy using a flexible bronchoscope performed in the bronchoscopy suite with local anesthesia and IV sedation has proved to be clinically effective and safe and has a viable valuable tool for added clinical utility for pulmonologist.

A44 Endoscopic Cryotherapy in Five Intraluminal Typical Bronchial Carcinoids.-

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Cryotherapy is a method of local destruction based on the effects of extreme cold on living tissue. We present our experience in the endoscopic treatment of intraluminal typical carcinoid tumors, using cryotherapy.

Broncho-pulmonary carcinoid tumors constitute around 5% of primary neoplasias of the lung. They are neuroendocrine tumours of relatively low malignancy, mostly arising in main bronchi. They, often, become apparent through coughing, hemoptysis (50% of cases), recurring infection or wheezing etc. In most cases, diagnosis is carried out endoscopically by way of the typical image displayed by this kind of tumour and then confirmed by biopsy, although said diagnosis must be undertaken with great care due to the possibility of sometimes major and occasionally fatal bleeding. Histologically speaking, two types of carcinoid tumour are described: typical and atypical, according to architectural organization, mytosis and necrosis etc., with the atypical ones being more serious. Surgical treatment continues to be considered the kind offered as a matter of course, with more conservative treatment (such as bronchotomy, Yag-Laser etc) being reserved for irresolvable cases of typical carcinoid tumours. Nonetheless, there do exist writers who advocate endoscopic treat using Yag-Laser with variable results.

We have treated five typical bronchial carcinoid tumours from different localizations, accesible by means of bronchoscope and with biopsies displaying typical features of this kind of tumour, with complementary normal blood tests and with thoracic scanner showing the whole wall.

Endoscopic cryotherapy proved completely effective in 4 patients, whithout scanner, histological, endoscopic relapse at **11** years, **9** years, **7** years, **6** years and **4** years, respectively. The 5th case, following cryotherapy prior to diagnostic biopsy and subsequent to various sessions, enabled us to carry out a more conservative pulmonary resection (lower left lobectomy) than that originally envisaged left pneumonectomy. After seven years the results are normal. Endoscopic therapy anables us to carry out cryodestruction not only of the endoluminal mass but also of the base of implantation on the inside of the bronchial wall practically as far as the cartilaginous lining, the aforementioned without risk of perforation. This justifies the use of said treatment in this kind of tumour (and in other benign and precancerous lesions and carcinomas in situ). From our experience, 3 carcinoid tumours initially treated using Yag-Laser suffered relapse in the control which we carried out. Treatment using cryotherapy was subsequently undertaken with the afore mentioned results.

From our experience in the endoscopic treatment of benign lesions and those of so-called low malignancy, in addition to other types of lesion (precancerous, carcinoma in situ) we believe that cryotherapy may constitute:

1. The ideal treatment in cases of typical intraluminal carcinoid tumours, on account of its destructive action even on the inside of the bronchial wall without the risk of accident which may arise from endoscopic methods.
2. Essential complementary treatment when another endoscopic technique is initially used (Yag-Laser).
3. Suggestion of cryotherapy prior to diagnostic biopsy in very hypervascularized tumours so as to avoid serious complications.

A45 The Role of Cryotherapy in the Management of Benign Tracheo-bronchial Lesions

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BACKGROUND: Although benign lesions of the tracheobrochial tree are relatively rare, they can cause distressing respiratory symptoms, including dyspnoea and stridor. The management of these benign lesions remains controversial, depending on the site and nature of the lesion. Cryotherapy has been shown to be effective in the treatment of advanced malignant bronchial tumours. There is, however, very little in the literature describing its use with benign lesions. In this study, we retrospectively assessed the effectiveness of cryotherapy in the management of benign endobronchial lesions.

METHODS: Between January 1995 and December 1999, 47 patients with benign endobronchial lesions were referred for treatment. Of these patients, 31 were men and 16 were women, ranging in age from 24 to 84 years (mean 52.2 years). Histological diagnosis of the lesions included 27 with post transplant anastomosis granulation, 4 tracheobroncheopathia-osteochondroplastica, 4 sarcoidosis, 3 polyps, 2 non-transplant granulation tissue, 2 amyloidosis and one each with haemangioma, leiomyoma, lipoma, Wegner's granulomatosis and post-intubation tracheal stenosis. Endobronchial cryotherapy was performed under general anaesthesia using a straight or angled cryoprobe, which delivered temperatures of about –70 ^{o}C to the lesion. The patients were assessed clinically, radiologically and by respiratory function tests before and after each cryotreatment.

RESULTS: Over the 5-year period, 47 patients received 98 cryo-applications, during which there were no peri-operative deaths. Good symptomatic improvement was reported post cryosurgery for cough, chest pain, dyspnoea and stridor. Overall 68.8% of patients described a subjective improvement in their symptoms. Both FEV_1 (2.02 ± 0.09 v 2.33 ± 0.17, $p<0.01$) and FVC (2.64 ± 0.12 v 3.04 ± 0.20, $p< 0.01$) showed significant improvement following surgery.

CONCLUSION: Cryosurgery is able to provide effective symptomatic control in patients with benign endobronchial lesions, the majority of who are discharged on the day of surgery. It affords an easy to perform, safe procedure, which should be considered for all patients with benign endobronchial lesions.

retrospectively assessed the effectiveness of cryotherapy in the management of benign endobronchial lesions.

A46 The Alexandria Experience of Bronchoscopic Cryotherapy in the Management of Different Tracheobronchial Lesions

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This work was designed to study the clinical uses of fiberoptic cryotherapy in the tracheobronchial lesions and the possible effects of such therapeutic modality on the pulmonary function tests, arterial gasometry, and dyspnea index (clinical parameters) as well as radiographic findings.

The study was conducted on twenty-five patients with different tracheobronchial lesions. The mean age was 55.4 (range 23 - 72 years) and the male: female ratio 4:1.The histological composition of the cases was as follows; Squamous cell carcinoma 56 %, Adenocarcinoma 24 %, Carcinoid tumor 12 %, Small cell carcinoma, 4 %, Bronchial adenoma 4 %. The sites of the lesions in the bronchial tree were as follows: Left main bronchus 52 %, Left lower lobe bronchus 20 %, Right main bronchus 12 %, Right lower lobe bronchus 8 %, Left upper lobe bronchus 4 %,Right upper lobe bronchus 4%.The total number of sessions of cryotherapy performed was 92 (range 2 - 6, mean approximately 4) performed in 500 days (range 7 - 40 days, mean 20 days).

The presenting symptoms of the patients in the present study were dyspnea (88%), haemoptysis (88%), chest pain (56 %) and cough (48 %). Symptom improvement following cryotherapy was found to be; 72% for haemoptysis, 68% for dyspnea, 57% for chest pain, and 41% for cough. The objective measurement of respiratory function showed improvement in forced vital capacity (FVC) for 60% of patients, in forced expiratory volume in one second (FEV1) for 72% of patients, in FEV1/FVC % for 60% of patients, in peak expiratory flow rate (PEFR) for 56% of patients and in maximum voluntary ventilation (MVV) for 72% of patients.

Conclusion For a specialist familiar with the use of endoscopy, cryotherapy will not present any particular problems. One of the main advantages of cryotherapy is that, it is simple and relatively harmless and thus the technique can be mastered easily. Cryotherapy offers an effective method to restore the patency of blocked tracheobronchial lumen and therefore improves symptoms and quality of life. Cryotherapy is not beneficial in voluminous tumors. The advantages of cryotherapy over other forms of therapy are safety of use, since there is no danger of bronchial wall perforation or endo-bronchial fire, no danger for operator's eyes, no danger of electric accidents, or radiation emission. The technique is easy to perform, economical, has minimal complications and well tolerated by the patients.

A47 Cryosurgery for Malignant Endobronchial Tumours: Analysis of Outcome

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BACKGROUND Cryosurgery, the controlled application of extreme cold**,** is effective at lysing malignant cells. Since 1986**,** we have used cryosurgery to treat malignant central endobronchial tumours in patients with lung cancer considered unsuitable for lung resection. Full treatment consists of at least two cryosurgery sessions. We analysed outcome of cryosurgery in our institution over the last five years.

METHODS Data were extracted from our prospective computerized data base.
The effect of cryosurgery on clinical parameters such as dyspnoea, cough, haemoptysis, lung function and Karnofsky performance score was evaluated with the Wilcoxon rank sum test. Univariate Cox regression and multivariate analyses were performed to assess the effect of age, sex, anatomical site, histological type, stage and additional treatment on the above clinical parameters and on survival.

RESULTS From 1995 to 1999, 356 patients underwent cryosurgery in our department. The mean age was 68$\pm$9 years while 231 (65%) patients were male. Mean survival was 52 weeks.
Overall, dyspnoea, cough, haemoptysis, FEV1, FVC and Karnofsky score improved significantly after cryosurgery ($P<0.001$).
Dyspnoea improvement was higher ($P=0.05$) in Stage IIIa tumours.
Survival was significantly prolonged in patients who received additional radiotherapy ($P<0.01$). No other patient or disease characteristic influenced the outcome.

CONCLUSIONS Cryosurgery reduces dyspnoea, cough, haemoptysis and improves lung function and Karnofsky performance score in patients with inoperable endobronchial malignancies. Combination with radiotherapy is associated with prolonged survival.

A49 Cryosurgery in the 21st Century

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The use of cryosurgery in the past has been a breakthrough in Dermatology and has been a very important cost saving device for the efficient management of many skin tumors including actinic keratosis, seborrheic keratosis, and basal and squamous cell carcinomas. The use of modern day cryosurgery has extended to full-faced cryosurgery for acne and actinically damaged skin. Hemangiomas have been treated effectively especially Dr. Castrron by using a freezing probe. Depth of lesions can be determined by ultra-sound prior to freezing, and measurement of temperatures in the skin during freezing by use of thermocouple needles and electrical monitoring devices.

Will cryosurgery remain a viable treatment in this new century? A recent study by Thissen et al[1] compared the cosmetic results looking at cryosurgery vs. excision. Ninety-six basal cell carcinoma's were treated, 48 by each technique. Clinical professionals evaluated the results after surgery as significantly better. A cost comparison was not done. Interestingly a cosmetician who evaluated the patients saw less difference in the sights than did the professionals who were aware of what the techniques were. In my own opinion, cryosurgery remains one of the most effective methods for treatment of superficial to medium depth basal and squamous cell carcinomas. Many series of published curates have shown statistics in the range of 97-98 %. This is based on selection of patients for this procedure and not on a comparison which this study was. It is very important to compare the cost of each procedure and give patients a choice when they present for treatment.

In considering the treatment another skin commonly treated by cryosurgery is lentigines with excellent cosmetic results. Studies have been done which have shown cosmetic results with cryosurgery better than that with laser, but lasers has improved. A recent stuldy by Chan[2], found that the versapulse long-pulsed 532mm laser is more effective than others that they have tried in the treatment of facial lentigines in oriental patients. Chiarella[3] shows that cryopeeling (extensive) is a highly effective method for removing actinic keratoses and preventing recurrence. He has shown statistically that the development of squamous cell carcinomas is greatly reduced.

A history of cryosurgery[4] discusses the many treatments developed over a span of a hundred years. This began with the work of Campbell White who in 1899 reported on his work treating various skin conditions including: nevi, warts, varicose leg ulcers, boils, carbuncles, herpes zoster, and epithelioma. Many of these conditions now have far superior treatments. The best example being antibiotics for treatment of boils and carbuncles. As new techniques become available and are able to prove their effectiveness those of us who pride ourselves as being cryosurgeons must open the door to the future and step aside when better methods are available. As increasing constraints on cost plague every country the cost-effective use of cryosurgery may remain a preferred alternative to certain other treatments until really superior cost effective methods are available.

1.August 2000 in Dermatologic Surgery 26:759-764 by Thissen MR, Nieman FH, Ideler AH, et al
2. Chan et al, Henry H, Fung, WKK, et al, pages 743-749
3. Chiarella in Derm Surgery 26:728-732
4. DS 26:715-722

A50 Cryosurgery in Primary Care

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While most of the literature on Cryosurgery emanates from hospital based medicine, there are more Cryosurgeons in Primary Care than in any other speciality.

Cryosurgery has many unique features that make it eminently suitable in for the treatment of a wide range of cutaneous disorders in Primary Care. Treatment times are short (usually less than five minutes), techniques are relatively easy to learn, the equipment is relatively cheap and the running costs are low. With careful patient selection and pre treatment counselling, serious side effects are exceptionally rare. However, Cryosurgery is not a panacea for all surgical problems in Primary Care and certain patients and lesions are better treated with other surgical modalities such as surgical excision, cautery, radiosurgery, etc. Combination treatments such as radiosurgery and cryosurgery can be very useful, particularly when dealing with selected cases of non - melanoma skin cancers.

This paper will present one General Practitioner's experience of using cryosurgery in Primary Care over the last twelve years.

The following recommendations are suggested to further promote and develop cryosurgery in Primary Care.

- More education and training for General Practitioners in cryosurgery.
- More funding for research and development of cryosurgery within Primary Care.
- Encouraging General Practitioners to become actively involved in the various cryosurgery societies.

Negotiating realistic payments from Insurance Companies and National Health Services for cryosurgical procedures within Primary Care.

A51 Cryosurgery, the Best Treatment for Actinic Keratosis

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The area of influence of Hospital Distrital de Faro, is the east part of the Province of Algarve, which is the most southern region of Portugal continental. Algarve is a well-known tourist destination due his sunny weather. In fact we have 300 days of sun per year. Traditional activities in Algarve population are farming and fishing.Life expectation is growing in Portuguese population, which means a very high number of senior citizens.

The combination of these facts results in a very high incidence of skin diseases related with the chronic sun exposure. Actinic Keratosis are probably the most important hallmark of sun exposure through many years. A.K. are epidermal tumours that have the potential of developing into invasive squamous cell carcinomas. Most of the people with A.K. have many lesions at the same time, on sun-exposed areas like face, hands, arms, and legs on women.

So for the treatment of A.K. it is important to have a method that permits the simultaneous treatment of many lesions. In our Department, Cryosurgery is that method. It's easy to perform, cheap, yields good results and is adequate to the use in elderly people, usually with other medical problems.

In a previous communication we reviewed the Cryosurgery use at our Department and we noticed that its foremost indication was A.K.

For the moment we report Cryosurgery use in A.K., made by one of us, during a three months period, in consultations that took place in different cities of Algarve.

A52 Cryosurgery for Skin Cancer in Patients 90 years of Age and Over

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The percentage of people 90 years of age and older is steadily increasing and cryosurgery is a useful modality for treatment of such patients. During the period between 1971 and 2001, the author treated 4515 patients with basal and squamous cell carcinomas with cryosurgery, excluding squamous cell carcinoma in-situ and keratoacanthoma. Among them 196 patients of 90 years of age and over were studied. There were 118 men and 78 women. The lesions consisted of 142 basal cell and 54 squamous cell carcinomas, of which 7 were recurrent lesions. The sizes ranged from 0.5 cm to 8 cm. The locations included the head and neck, trunk, arms and legs. Despite their advanced ages there were no medical contraindications to performing cryosurgery. Treatment is curative, safe and relatively simple to perform. It can be used in high-risk surgical patients with limited mobility, and can be performed in the office. It is useful for difficult and large tumors since cryosurgery can be carried out in stages. Healing occurs uneventfully with excellent results. Cryosurgery is ideal as a primary form of treatment for the very elderly.

A53 Curettage-Cryosurgery for Non-Melanoma Skin Cancer of the External Ear. My Way of Doing it.

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The external ear is an area where skin cancer often recurs and is one of obvious functional and cosmetic importance. In order to obtain the best treatment most of the patients were assessed in consultation with a surgeon experienced in Mohs Micrographic Surgery (MMS) at a skin tumour clinic. Diagnosis was verified on histopathological findings in one or more punch biopsies. Morphoeiform and recurrent basal cell carcinomas (BCC) with secondary sclerosis, tumours of the auditory canal, and most of the squamous cell carcinomas (SCC) were referred for MMS, while selected tumours of other types were treated by curettage cryosurgery (CC). After local anaesthesia a thorough curettage using different sized ring curettes was performed. The main purpose of the curettage is to delineate clinically ill-defined tumours, which are not suitable to be treated by cryosurgery alone. After hemostasis with a cotton stick dipped in 50% iron chloride solution, the tumour area was frozen with liquid nitrogen (-196 C) using a hand-held Cry-Ac (Brymill Corp, USA) in a double freeze-thaw cycle with a freeze zone of at least 5 mm outside the tumour area. On flat surfaces an open neoprene cone of suitable size was used to get a more concentrated spray. The auricular canal was protected with soft cotton. Exact details of my way of doing the CC in different tumours and 5-year results will be presented

A54 Protection of the Skin around Small Tumours with a Silicone Sheet, Cryosil ®

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In order to freeze a small skin cancer with thin open spray of liquid nitrogen (LN2), it must be applied intermitently until the desired lethal temperature is achieved in the neoplasm and safety margin. The spray cannot be applied continuosly because, when the tumour surface is frozen, drops of LN2 would run out and freeze too large an area, without attaining in-depth lethal temperature of the neoplasm. The only inconvenience of the intermitent application of the spray is that it slows down the rate of freezing.

The appearance in the market of a silicone sheet -"Epi-Derm"®- (devised to treat keloids) which inferior aspect adheres to the skin, suggested to the first author that it could be useful, in cryosurgery, as a way to limit the ice front. He verified that when a thin spray of LN2 was applied on its surface, a thermocouple placed under the sheet did not record negative temperatures. The manufacturer (Biodermis Corporation), prepared modified silicone sheets (the so called "Cryosil"®),according to his specifications, so as to be sufficiently adherent to stand the pressure of the thin spray and control the limit of the ice front.

Material and method: Thirty carcinomas and 13 squamous-cell carcinomas, one melanoma and one kerato-acanthoma, located on the face, forehead, neck and limbs, measuring between 6 and 60 mm were treated. The cryosurgical protocol is: part ot the center of the silicone sheet is removed, originating a hole with the shape and size ot the tumour plus the safety margin. The skin around the cancer is cleansed with ether, and the silicone sheet is firmly applied.

Temperature monitoring is done with thermocouples. A continuous thin spray of LN2 is applied through the hole. Cancericidal temperatures (around -50 ºC) are quickly achieved. The peripheral spread of the ice front goes only 1 mm, beyond the limit of the hole. I compared the freezing rate with spray from a Cry-Ac apparatus, (Bryomill Corporation) using either the open intermittent spray method or the spray limited by the silicone sheet. In the latter, the temperature goes down much faster (3 to 4 times) than with the intermitent open spray. The difference is bigger with small cancers, measuring less than 12 mm, which are, precisely those where the intermittent technique is more difficult and where the resulting freezing rate is slower.

Results. All basal-cell carcinomas cured but there were recurrences in two of the first treated cases of squamous-cell carcinomas and one basal-cell carcinoma. The follow-up is between 6 months and 6 years..

Cryosil permits to better comply with one of the golden rules of cryosurgery: freeze quickly and thaw slowly.

A57 Breast Cryosurgery - A New Surgical Procedure for Breast Cancer

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Introduction: Breast cancer is on the increase world-wide. Secondary manifestations such as metastasis and local recurrence by the spread of cancer cells during diagnostic or surgical interventions signify the death sentence for the patient. A new way of thinking about the problem must therefore determine the future of cancer research and treatment. New methods of diagnosis and treatment will increase the cure rate for this disease.

Objective: The authors develop and evaluate the place of cryosurgery as a new surgical procedure for breast cancer

Material and Methods: From 21 patients with malignant breast tumors with various histology treated by cryosurgery in a 4.5-year period, the authors developed the new subcutaneous and repeated step by step directed cryosurgical techniques and evaluated the results of all patients. Breast cryosurgery was used either as a single treatment in all patients. Systemic chemotherapy or local radiotherapy were not used routinely before cryosurgery and after cryosurgery. Breast cryosurgery was performed with „Cryothronic“ apparatus (Cryotechnological Company „Pulse“, Kyiv, Ukraine) designed specifically for different kinds of malignant tumor to deliver liquid nitrogen to the tip of a double lumen probe. The cryosurgical operation was performed in local anesthesia. The following optimal parameters were determined for cryosurgery of breast cancer: freeze temperature at –180°C to –190°C, with rapid freezing of the tumor required, duration of a treatment session: 5-7 minutes, 2-3 freeze-thaw cycles, automatic thawing, which must be carried out very slowly. We used mainly a 30-mm probe and rarely a 40-mm or 50-mm probe according to the size of the tumor.

Results: There was no intraoperative mortality. Postoperative morbidity consisted of one breast fistula (4.8%) which self closed 1 month postoperatively. At a mean follow-up of 37 months, (range, 2-51) local recurrence rate was 0%. After a mean follow-up of 51 months all operated patients are currently disease free.

Conclusion: Modern breast cryosurgery is at present just at the start of its medico-technical development as well as of its international regard and spread. Good results can, however, already be demonstrated. They have also shown that the successful use of this method is really only made possible by high-performance medico-technical devices. The benefit in survival is related to the complete cryosurgical treatment of the breast tumoral disease.

A58 Allogeneic Peripheral Blood Stem Cell versus Bone Marrow Transplantation

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Hematopoietic stem cells from three different sources are being used for the reconstitution of lymphohematopoietic function following myeloablative, or non- myeloablative treatment: bone marrow (BM), peripheral blood (PB) and cord blood. PB-derived stem cell autografts have almost entirely replaced BM as the stem cell source. In the allogeneic transplant setting there is a trend in favor of using PB-derived stem cells based on 1) faster cell recovery, 2) faster immunoreconstitution, 3) improved disease-free and overall survival in high-risk patients. A more pronounced graft-versus-tumor effect when using PB-derived stem cells is offset by a potentially higher incidence of chronic graft-versus-host disease. PB stem cell or BM allografts are either transfused fresh into the recipient or cryopreserved prior to transfusion. The latter approach has the advantage of being performed independently from the transplant procedure although cryopreservation and thawing can reduce the $CD34^+$ cell number in the transfusate as much as 10-20%, mainly because of cell trapping during the thawing process. This is also true for lymphocyte subsets. There is, however, no indication of a specific cell loss of any lymphocyte subset due to the freezing process. PB stem cell allografts are preferred over BM allografts when performing transplants across major HLA barriers such as haploidentical transplants. *In vivo* immunomodulation of stem cell donors prior to stem cell harvest is the latest addition to several clinical advantages of using cytokine mobilized and cryopreserved/thawed PB stem cell allografts.

A59 The Cryosurgical Treatment of Benign and Low-Grade Malignant Bone Tumors

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Cryosurgery is used as adjuvant treatment after intralesional resection (curettage) of active and aggressive benign and low-grade malignant, stage IA skeletal tumors. By spraying liquid nitrogen into the curetted lesion the surgical margin of resection is extended. Tumor cells left behind are destroyed by this thermal injury, which otherwise could be responsible for a recurrence of the tumor. By this method the procedure can be considered to be marginal from the point of view of orthopaedic oncologic principles. The advantage of this kind of treatment, as compared with local (en block) resection, is that as much of the supportive function of bone is preserved and that reconstructive surgery can be limited.

Temperature recordings in and outside the lesion during cryosurgery in orthopaedic oncology are of importance to monitor the freeze/thaw cycles and are helpful in facilitating an effective cryosurgical procedure and in controlling the extent of the freeze, avoiding local complications.

Since the 1992 cryosurgery for orthopaedic oncologic indications has been used in the University Medical Center Nijmegen, The Netherlands. A series of 266 patients were recently evaluated.

Tumor	number	recurrence
enchondroma / chondrosarcoma grade 1	90	0
aneurysmal bone cyst	60	3
giant cell tumor	28	4
fibrous dysplasia	24	1
simple bone cyst	16	3
histiocytosis	6	0
chordoma	5	2
other	29	-

Complications include venous gas embolism, wound infections, fractures, osteoarthritis, damage to nerves and growth plates. According to a learning curve, these complications have declined to an acceptable level.

Animal experiments in goats have shown that cryosurgery significantly diminish the strength of cryosurgical treated femora 4, 7 and 10 weeks after the operation and that a bone graft has no influence on the healing process as measured by torsional strength.

A60 Cryosurgery of the Advanced Cancer of the Extremities

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Squamous cell carcinoma is a common neoplasm in the sun exposed skin of elderly people. When the patients neglect cancer treatment, local progression and invasion occur, making clinical cure more difficult or even impossible. In the more advanced tumours surgical amputation is usually proposed; however it causes considerable morbidity, with a negative impact in the quality of life. Cryosurgery can be a valid alternative to radical surgery in this patients.

From 1984 to 2000, 27 patients (15 female and 12 male, aged 60-94 years), with advanced squamous cell carcinoma of the extremities were treated by cryosurgery in our department. The tumours were located on the dorsum of the hands in 24 patients, in two in the lower arm and in one on the lower leg. All, except one, were primitive tumours.

The squamous cell carcinoma was considered advanced when it was larger then 3 cm, or when it invaded, or was adherent to underlying structures. In seven patients cryosurgery was done because they refused surgical amputation. Palpable lymph nodes were present in two patients.

To confirm the clinical diagnosis, previous incisional biopsy was done in all cases. Cryosurgery with liquid nitrogen was performed under general anesthesia or loco-regional analgesia. Previous debulking was done in three tumours. Thermocouple needles, for temperature monitoring, were strategically inserted in the thickness of the tumour and its margins. Paraffin bandages were firmly applied around the safety margin of the cancer, to avoid the run off of the liquid nitrogen to normal skin. An open spray of pressurized liquid nitrogen was used (CE-4 Frigitronics apparatus). The freezing was performed quadrant by quadrant and sustained until the temperature dropped to –50ºC or less, in the thickness of the tumour. A slow thawing was allowed and a second freezing was done. During the following weeks, necrotic tissue was removed and the ulceration healed by second intention. Persistent tumours needed a second session of freezing and/or chemosurgery with zinc chloride paste.

Local cure was achieved in 24 patients. One tumour recurred 2 years after treatment. The follow-up ranged from 2 months to 10 years (mean: 4). Six patients are still alive and well; four died of the disease, eight died free of the disease and nine were lost to follow-up.

Serious complications were not observed and cryosurgery was well tolerated by all the patients. Post operatory pain and discomfort were easily relieved by oral medication. The main disadvantages of this method include the heavy discharge after the cryosurgery and the long time to heal. Anaplastic conversion of the tumour, as reported by some authors, was never observed.

A61 The Cryovaricectomy (Demonstration of a New Method)

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The operating technique of the primary varicosity has changed recently. The subcutaneous methods have been used nowdays- We give account of making 998 cases by cryovaricectomy, which is a quite new method. Using this technic we can remove the dilated venous branches during a 3 - 4 millimeters wide incision of skin and preserve the sufficient main vein. Summarizing of our advantageous experience: the cryovaricectomy is suitable for principles of minimally invasive surgery, and the operating time is much more briefer, the aesthetic results are best, the attendance far shorter and the postoperative complaints of patients much more fewer.

A62 Cryotherapy in Tonsils

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Twenty years of practicing cryosurgery to treat organ chronic illnesses like tonsillitis support this efficient technique, proving the method to be successful in approximately 1900 cases, thus allowing us to render the results before this scientific meeting, hoping our peers will examine and eventually confirm the conclusions drawn. Among the benefits derived from the implementation of this cryosurgery technique, some definitely stand out: Hospitalization is absolutely avoidable, lack of general anesthetic, decrease in hemorrhage risk, no strong post-op pain, no leave of absence involved, reduced sanitary cost, and no malpractice suits.

Having operated on all kinds of tonsillitis and post- surgical remainders, the results were similar to those obtained by ordinary surgical procedure, except for the undesired typical side effects such as hypertension, age risk, heart problems, aids, diabetes etc.

With the exception of cryoglobulins there are no other counter-indications.

Controls Ranged From 3 to 82 years old. The procedure consists of applying a cryoprobe for a few seconds, at a temperature ranging from –94° F to –130°F (according to patient, condition, number of applications, etc.) following a specific methodology.

In the clinical analysis evaluation we make before cryotherapy, we include the following items: investigation-identification of germs, inmunological infection markers (antibody antistreptolisines, and other exoenzimes), salival secretory inmunoglobulin a (11s) and seric inmunoglobulins; c3 fraction of complement; cryoglobulins to ponderate the risk index of cryotherapy or ENT index, (which is the most important), and some other unspecific parameters of inflammation-infection. (crp, blood counts, etc.). Functioning lymphatic tissue was obtained several months after the procedure, by means of biopsy.This aspect was particularly relevant. So was the fact that no anesthetic or hospitalization is required.This will prevent the patient from losing work.

There is no risk of hemorrhage

No major post-op pain is involved

This cryosurgical procedure provides no risk of mal practice suits.

It also reduces sanitary costs.

A63 Regenerative Cryotherapy

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Classification: Cryotherapy can be classified on the basis of its clinical effect and as a function & temperature parameters which affect the impact of the cold factor on tissue

Cryotherapy 1. Regenerative 2. Destructive, 3. Cryosurgery (exstirpative cryotherapy)

Regenerative Cryotherapy consists of the brief administration of dosed cold treatment to tissues and organs at temperatures close to the cold-resistance threshold of the tissue. The aim of this type of cryotherapy is to bring about regeneration and functional reactivation at the treatment site. Regenerative cryotherapy causes a reaction in the organism which is linked to local tissue irritation and manifests itself in an elimination of the pathogenic factors, regeneration of tissue, and restoration of functional competence. Monitoring of the cooling parameters in the tissues is a very important point during regenerative cryotherapy since the therapeutic effect is directly linked to these parameters.

Treatment of diseases / complaints in my practice with Regenerative Cryotherapy:

- Snoring and Sleep Apnoea
- Chronic Tonsilitis and chronic pharyngitis
- Chronic Rhinitis of Vasomotor and Atrophic Origin

REGENERATIVE CRYOTHERAPY is an effective treatment method via which a stable therapeutic effect can be achieved. Regenerative cryotherapy can be employed to:

1. Stop snoring and stop apnoea
2. Restore nasal breathing
3. Reinstate the protective function of the lyrnphoid tissue in the tonsils and Waldeyer's throat ring
4. Stimulate immune processes
5. Eradicate chronic foci of infection in the tonsils, pharynx and nose, thereby preventing complications or sequelse of these infections. These include systemic and rheumatoid diseases of the heart (i.e. endo-, myo- and pericarditis), the blood vessels (e.g. vasculitis), the joints (e g polyarthritis), the kidneys (e.g. Glomerulonephritis), the internal and external sex organs (e.g. disturbances of potency), the nervous system (e.g. chorea) and the skin (e.g. scleroderma, psoriasis, pustulosis and lupus erythematosus), infectious allergic diseases (e.g. bronchial asthma, atopic and allergic dermatitis, etc) and immuno-deficiency disorders.

If everyone (but especially children) would undergo prophylactic treatment of the lymphoid tissue of the tonsils, pharynx and nasal mucosa using the method of regenerative Cryotherapy, we would observe the following positive effects (especially in Children)

- Improvement of the Protective functions of the organism
- Stimulation of the immune-system

We can assume, moreover, that the general risk of contracting systemic, rheumatoid, infectious allergic and oncological diseases, immune deficiency states, snoring and sleep apnoea syndrome - would be distinctly reduced. With its regenerative effect, cryotherapy opens up vistas for an alternative direction in medicine, namely Regenerative Medicine

A64 Percutaneous MRI-Guided Cryoablation for Renal, Uterine and Bone Tumours

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Renal Tumours

Percutaneous MRI-Guided Cryoablation of Renal Tumors was performed on 48 Tumors in 43 patients. Clinical, Radiological, and Laboratory follow-up was performed with our longest follow-up being two years and two months to date. Results of the treatment and follow up will be presented to include procedure details, images, and complications. Low morbidity and zero mortality are documented to date.

Uterine Tumours

Percutaneous MRI-Guided Cryoablation of Uterine Tumors was performed on uterine tumors in 10 patients. Clinical, Radiological, and Laboratory follow-up was performed. Pre-cryo MRI and 10 week post cryo MRI were used to measure fibroid dimensions and calculate fibroid volume. Clinical follow-up documented the presence, characterisation, and response of the patients clinical symptoms (pain, bleeding, urinary incontinence). Results of the treatment and follow up will be presented to include procedure details, images, and complications. Clinical symptoms significantly or completely resoved at 2 weeks post-cryo. At 10 weeks post Cryo, treated fibroid volume reduction averaged 53%.

Bone Tumors.

Percutaneous MRI-Guided Cryoablation of Benign and Malignant Bone Tumors was performed for palliative reasons. To date, nine tumors in seven patient's have been treated. Tumor locations included vertebral body, posterior vertebral elements, scapula, long bones of the extremeties, and coracoid process. Short term results with specific attention to pain relief as well as long term results regarding osteoblastic stimulation of cryo treated bone was obtained. Results suggest excellent immediate pain relief and aggressive osteoblastic response yielding dense sclerotic bone formation.

A65 Cryosurgery and Radiofrequency in the Treatment of Invasive Feline Nasal Carcinoma.

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The excellent results obtained by using cryosurgery to treat feline nasal carcinoma (FNC) are indeed well known.

This pathology requires the specialist in charge to follow up closely and intelligently the patient so that he may respond energetically and drastically to primary changes in the actinic injuries.

The initial carcinoma often grows deeper and attacks the entire nasal structure. This invasive process is very dynamic and soon becomes impossible to control by means of cryosurgery owing to the extent of the invaded area. In these cases, regrettably enough, euthanasia is the only choice left.

The combined use of radiofrequency and cryosurgery, on selected patients, offers a promising alternative that has proved to be worth trying.

Cryosurgery and Radiofrequency in the Treatment of Feline Facial Squamo-Cellular Carcinoma

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Because of its invasive quality the feline facial squamo-cellular carcinoma (FFC) quickly attacks deep neighbouring anatomic structures from its initially superficial location.

As a single infiltrating injury it invades: a) from the nasal area, the mucous membranes, b) from the eyelids, the tarsus, c) from the ear, the cartilages, and d) from the fronto-temporal skin layer, the underlying muscles.

Multiple location includes two or more of the areas listed above, and various development stages.

- White-coated (hypopigmented) older specimens and those having a coloured coat but a white face are the most affected.
- Conventional treatments have failed.
- The FFC has little metastatic power but its insidiours expansible recurrence causes the death of these patients.

This paper describes the use of cryosurgery or radiofrequency and cryosurgery to treat FFC on ambulatory patients.

A66 Cryosurgery in Proctology, Overview and Update

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Cryosurgery in proctology has always been supported by a number of practitioners who have been using this method to confront several ano-genital pathologies, be they benign or malignant. In more than 30 years of experimentation and application, this method has had varying degrees of fortune in the international scientific literature, but only a proper audit of significant surveys allows a proper analysis of results and complications, followed by precise indications and limits.
From 1984 to 2000 we have treated by this method more than 5000 patients suffering from benign or malignant ano-genital diseases. The Results are illustrated in this Conference, and in many cases they we have already published them in other papers or abstracts. In our Unit of General Surgery we apply by practice all common therapeutic methods (with local anaesthesia, caudal block, medullary or general anaesthesia, or even without it) within the framework of a modern approach of such pathology: our conclusions about cryosurgery are therefore based on our practical and multivaried experience.
Haemorrhoids . We perform surgical technique as Milligan, Morgan or Parks either by radiofrequency (Ligasure) or by Circular Stapler for prolassectomy and we have a significant experience also by rubber band ligation alone, or associated with cryosurgery. We treat outpatiently, using cryosurgery alone, those patients suffering from symptomatic II and III degree haemorrhoids., and those patients with relapses or recurrences arising after varying lapses of time from the surgical operation. Presence of anal hypertonus, abscesses, tromboflebitis contra-indicate cryosurgery, and we do not treat skin tags by this tecnique.
Ano-genital warts After the necessary surgical excision for histological report, we prefer cryosurgery for perianal satellitosis and for anal canal and rectum condilomatosis. This outpatient treatment sometime requires only anaesthetic ointment (EMLA). We believe Cryosurgery is the best method, also because it makes much easier to re-treat the most frequent relapses or recurrences, typical for this disease.
Rectal polyps in familiar adenomatous polyposys after IRA For this disease the correct surgical approach is total proctocolectomy with IleoAnal pouch, but until ten years ago many surgeons used to perfrom total colectomy with IleoRectalAnastomosis. These patients presented recurrent polyposis in the rectal residual tract and we believe that Cryos. is better than laser excision or diatermoexcision or electrocoagulation for treating this disease. Of course it depends on the genetical pattern of the disease and on the dimension of polyps but in many cases we manage to avoid (with young patients) the second surgical procedure of Rectectomy and IleoAnalPouch.
Rectal Polyps or Cryptopapillitis need Histological examination and *Anal Fistulas* need an accurate Evaluation Under Anesthesia: in these cases, therefore, surgical excision is conducted. For *Anal Fissures*, and for *Sinus Pilonidalis* we prefer surgery with local anesthesia
Anal Cancer Only palliative Cryosug. We use this method in case of relapses after RadioChemotherapy or when RadioChemotherapy cannot be applied; in case of relapses and recurrencies after surgery when the histological evaluation and the Miles's procedure are not necessary. We have had some extraordinary results in recurrent Bowen diseases or in cloacogenic cancer. The aim is "to avoid the colostomy" and "to reduce symptoms and local complications". For these patients and for these aims the Cryos. has brought about very few (almost none) complications and has proved to be better than the other techniques (or nothing) as quality of life is concerned.
Rectum cancer Only palliative Cryos. .The same purposes as above. The selected patients cannot operated by surgical rectal-cancer resection. Radio/Chemotherapy can be associated. When the cancer is located within 7 cm from anal verge and it doesn't involve more than 2/3 of the circonference, we have obtained good results, without severe complications, especially when they had an anasthomotic recurrence after anterior resection. The treatment can be performed also in locoregional anesthesia and can be easy repeated. If the cancer is located at more than 7 cm above, we prefer to perform palliative laser-destruction.

A67 Cryosurgery of Urethral Caruncle and Prolapse

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Urethral caruncle and prolapse are extrusions of the urethral mucosa. The first is a sessile or pedunculated mucosal pedicle on the lower limit of the urethral meatus: the second is an all-around protrusion of the mucosa with a rose-like shape. They are frequent in post-menopausal women. Sometimes asymptomatic, they can cause mild local discomfort, such as itching, urination disturbances and slight haemorrhaging. They are rarely complicated with thrombosis, but, then, become very painful. The usual treatment for urethral caruncle and prolapse is conventional surgery, but the procedure is delicate, requiring hospitalisation, operating theatre, local or general anaesthesia, and the catheterisation for a few days.

We have treated 63 women, 37 suffering from caruncle and 26 from urethral prolapse with mild symptoms, on an outpatient basis. *The technique* is very simple and takes very little time to perform. Local anaesthesia is not necessary because cryosurgery of these lesions is entirely painless. To treat the caruncle we held it with a small forceps and applied on it a thin cryoprobe cooled by liquid nitrogen. To treat the prolapse the cryoprobe is applied on its centre. In both cases the treatment is discontinued when the whole lesion, including its base, is frozen without safety margin. A single freeze-thaw cycle per session is carried out, with no temperature or impedance monitoring. During the following days, a discreet haematic exudate or slight haemorrhage and oedema will occur, which, however, will not affect urination. In the beginning we were very prudent. Fearing urethral stenosis, we used to partially freeze the caruncle or the prolapse in 2 or more successive procedures. As no urethral stenosis was ever observed we realised that we could be bolder. At present, we always try to treat every case with only one cryosurgical procedure. We carried out two or more procedures, only if the first proved insufficient. Seven patients presented with thrombosis of the caruncle, with lesions measuring between 1 and 2 cm. These were dark, bleeding and very painful. These cases were first treated medically. Four to six weeks later, after complete resolution of the thrombosis, cryosurgery of the remaining lesion was carried out. Previous biopsy was carried out on two patients. Sixty-one patients were cured, the majority of whom with one single treatment. In two other patients the condition improved, but the patients were satisfied with the result and refuse any further treatment: Four lesions recurred: They were again treated by the same method and definitively cured; the fourth, a voluminous recurrence, was treated surgically. Two patients had haemorrhage and one had moderate and transitional difficulty to urinate. The advantages of the method are obvious: it is efficient, comfortable, and painless. It does not require hospitalisation, anaesthesia, operating room, or catheterisation. It is very simple, takes very little time and is quit inexpensive.

A68 Cryosurgical Treatment of Genuine Trigeminal Neuralgia

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A new instrument is described for use in cryotherapy of peripheral nerves, allowing devitalization of the branches of the trigeminal nerve at the infraorbital foramen or the mandibular foramen without exposing the nerve or damaging the surrounding tissue. The probe has an outer diameter of only 2.7 mm, is designed to be inserted transmucosally and is vacuum insulated to protect the adjacent tissue. The technical capacity of the cryoprobe was first examined in-vitro and then the cryoprobe was clinically applied. The results of cryotherapy achieved by using the presented cryoprobe in 19 patients are reported, i.e. of cryoblockades of the infraorbital nerve and/or the inferior alveolar nerve.

Four to eight months following cryotherapy sensitivity returned to the treated nerve branch, while pain continued to be eliminated for a much longer period of time. Unfortunately in 13 out of 19 patients recurrences were observed six to twelve months following therapy. But it is possible to repeat cryotherapy in order to eliminate pain, since it means only little stress to the patient. Thus the range of methods to treat trigeminal neuralgia has been widened by the instrument presented here.

A69 Experimental Study and Clinical Prospective Double-Blind Randomized Trial of Cryoanalgesia

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Objective.- To alleviate and prevent severe post-thoracotomy severe chest pain.

Method:

Animal Study; Freezing of intercostal nerves in dogs to -50°C by different time, observing pathological changes and repair process of the nerves, identifying the best freezing time that could be used clinically.

Clinical Study;Prospective double-blind randomized trial in 200 cases of patients underwent thoracotomy was carried out from Jan. 1996 to 'June, 2000. Cryoanalgesia (Cryo group) and Control group were all 100 cases. Before closing chest 4 routes of costal nerve (incision, above and below incision and one for inserting drainage tube) were frozen for 1.5 minute, separately, Observing postoperative incision pain by VAS(visual analogue scale), recording the dosage of narcotics, measuring pulmonary function after 3, 7,15, 30, 90 days postoperatively.

Results;

Animal Study; Pathological changes of axons; and myelin sheaths progressed along with freezing time from 30 seconds to 2 minutes, but recovered in about one month. As the best freeing time 1. 5 minute freezing provide effective analgesia and quick recovery.

Clinical Study; Clinical application showed a very strong analgesia effect. VAS score of cryo-group was 2.29, control group 7.24 ($p<0.001$). In the cryo-group, No pain(0 degree) 22 (22%), very slight pain (I-2 degree) 44 (44%), slight pain (3-4 degree) 20 (20%), moderate pain(5-6 degree) 8 (8%) cases, with total effective rate (0-6 degree) 94%. Dosage of dolantin in cryo- and control group were 41.3mg and 185mg, respectively ($p<0.001$). The changes of pulmonary function for both of groups showed no difference.

Conclusion-, Freezing intercostal nerves during thoracotomy could effectively prevent postoperative chest pain. It was easy to operate and, moreover, the pathological changes of nerves was reversible.

A 70 Advances of Cryosurgery in Russia

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In June, 2001 in St.-Petersburg during the International Cryo-Congress the Russian Association of Cryosurgery was created. Association included the famous scientists of Russia, scientific cryosurgical societies, medical institutions and organizations, and also founders and producers of cryogenic equipment. The association has united more than 80 members from all regions of Russia, including Far East and Siberia. In Russia the scientific and clinical development projects are carry out in Moscow, St.-Petersburg, Tomsk, Ekaterinburg, Nizhni Novgorod. In the majority of medical centers doctors are used home-produced cryoequipment with liquid nitrogen as a refrigerant. This cryounits differs by technical simplicity of use, high freezing properties and low price. The range of use in clinical practice includes a traditional oncologic direction, treatment of acute inflammatory diseases of a skin, parasitogenic lesions of liver and practically all-surgical specialties. Most frequently cryogenic treatment is applied in Russia to treat neoplasms of a skin and mucosas, the sufficient experience in treatment of tumors and metastases in a liver gained. Most frequently cryogenic treatment is used in Russia in a complex with the traditional schemes of treatment of oncologic diseases, and also in a combination with high-frequency electromagnetic radiation, radial and laser therapy. At the same time cryogenic treatment of tumors of a kidney and prostate is at a stage of a becoming. The analysis of an own clinical material and comparison of results of treatment to the data of experiments testify that the cryogenic treatment for tumors in each concrete case should have the strict indications to application. The excessive expansion of the indications to a cryodestruction, results in unsatisfactory results of treatment, that negatively has an effect for development and establishment of a cryosurgery as reasonable alternative to existing now methods of treatment of tumors.

The accurate application of a cryogenic treatment method in each clinical case will allow achieving results, compared to classical treatment modalities.

The cryosurgery is worthy alternative to existing now methods of treatment of tumors or as addition to them. We suppose that for adequate application of a cryogenic method the development and introduction in clinical practice of the common protocols of cryogenic treatment and monitoring of process of a cryolysis is necessary.

A71 Improved Performance Status and Long Term Survival with Endobronchial Cryosurgery in Stage III and IV Carcinoma Bronchus.

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Objective: Endobronchial cryosurgery is an accepted mode of palliation in tracheobronchial malignancies. We observed that in a group of patients with Stage III and IV Carcinoma bronchus, treated with endobronchial cryosurgery, survived more than 24 months. The aim of this study was to assess the improvement in performance status after cryosurgery and the survival advantage in this group of patients. We also identified significant predictors of prolonged survival beyond 24 months in Stages III and IV Carcinoma bronchus treated with endobronchial cryosurgery.
Methods: This was a retrospective study based at a tertiary level referral hospital. Between 1990 and 1998, 585 patients underwent endobronchial cryosurgery for tracheobronchial malignancies. Fifty patients who survived beyond 24 months, at stages III or IV at the time of diagnosis were included in this study. Survival analysis was performed using the Kaplan-Meier method. The test for significance in improvement of FVC and FEV1 was determined using paired Student's t test. Karnofsky performance status before and after cryosurgery was analysed by Sign Test. Univariate analysis to identify significant prognostic factors for survival beyond 24 months was performed using Mann Whitney U Test, Kendall's Rank Correlation and Kruskall Wallace Test.
Results: Of 585 patients treated by endobronchial cryosurgery, 92.3% (540 patients) had stage III or IV disease. Fifty patients (9.25 %) of this group survived more than 24 months with Stage III and IV disease. The median survival of this subset of patients was 42 months with a mean of 48.6 months (range: 24-164 months). 44 % patients in Stage IIIA, 24% in Stage IIIB and 6.9% patients in Stage IV carcinoma bronchus survived for 10 years after endobronchial cryosurgery with or without other forms of adjuvant therapy. The mean Forced Expiratory volume in the first second (FEV1) improved from 1.35 l to 1.51 l and mean Forced Vital capacity (FVC) from 2.0 l to 2.19 l which are both statistically significant. The mean preoperative Karnofsky score was 70.0 which improved to a mean of 78.4 after cryosurgery. This statistically significant improvement (p value = 0.023) suggesting improved quality of life occurred in 68.2% of the 50 patients. Univariate analysis of the long-term survivors suggested histology, gender, number of cryosurgical sessions, adjuvant chemotherapy and radiotherapy as significant factors improving survival beyond 24 months.
Conclusions: Endobronchial cryosurgery is an effective, simple and safe palliative treatment which should be offered to patients with intrabronchial extension of tumour thereby causing obstructive symptoms of the airways. This study also shows that it improves performance status of patients and survival in Stages III and IV carcinoma bronchus. Adenocarcinoma, male gender, adjuvant palliative radiotherapy and chemotherapy and number of cryosurgical sessions are positive indicators of prolonged survival beyond 24 months after endobronchial cryosurgery in Stage III and IV carcinoma bronchus.

A72 Usefulness of Cryotherapy in a Bronchoscopy Unit of a General Hospital

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Introduction; Bronchoscopic Cryotherapy is an effective treatment in endobronchial lesions and may offer substantial palliation in patients who have failed to respond to other treatments or who cannot have other treatment. Cryotherapy has been shown to be an effective and safe therapy, especially in benign lesions, tumors with endobronchial obstruction and carcinoid tumors.

Materials and Methods; From October of 1997 to June 2001 all the cases of endobronchial Cryotherapy in our institution were reviewed. We performed 32 Cryotherapy sessions in 22 consecutive patients. In this period we performed 3.108 bronchoscopies. The range of age was 22 – 80, and the sex distribution was 16 male and 6 female. Ten patients received a combined multimodal treatment: 6 chemotherapy, 3 laser, and 1 electrosurgery.

We classified the indications in five groups:

1. Benign tracheal stenosis: granulomatous tissues after intubation or tracheostomy.

2. Scar granuloma: granulation tissue at anastomosis sites after surgical resection.

3. Tumoral palliative: 1 small cell carcinoma, 1 squamous cell carcinoma, 2 adenocarcinomas, and 1 benign tumor obstructed right main bronchus.

4. Tumoral curative: 1 breast cancer, 1 carcinoid, 1 hamartoma, 1 carcinoma *in situ*.

5. Miscellaeous: 1 biopsy of vascular tumor, 1 sinequia of vocal cords, and 1 idiopathic bronchial stenosis

Results

We showed the results in the table:

Indication	Patients	Sessions	Flex/Rig	Other treatments	Success
Benign tracheal stenosis	6	14	13 / 1	No	6 / 6
Scar granuloma	4	4	2 / 2	1 Elec*	4 / 4
Tumoral palliative	5	7	5 / 2	1 La, 4Ch*	4 / 5
Tumoral curative	4	4	1 / 3	1 La, 2Ch*,	3 / 4
Miscellaneous	3	3	3 / 0	1 La*,	2 / 3
Total:	22	32	24 / 8	10	19 / 22

* Elec = Electrosurgery, La = Laser, Ch = Chemotherapy

Conclusions; In accordance with literature we can confirm the expectation of successful treatment of Cryotherapy as effective treatment in selected endobronchial lesions (19/22 = 86.36%) but especially in benign granulomas (10/10 = 100%).

A73 Does Cryotherapy Ameliorate the Success of Radiotherapy in Non Small Cell Lung Cancer ?

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In Montreal, we are working with endobronchial cryotherapy since 1997. This technique is effective and very safe.

In 1991(1) and 1992(2) two studies suggested that cryotherapy could ameliorate the success of radiotherapy in NSCLC. Was the observed advantage only due to the de-obstructing effect of cryotherapy?

To distinguish between a de-obstructing effect and other more specific effects, we have planned a study where de-obstruction (if necessary) is obtained by an other tool and cryotherapy is added in half the cases on a random basis.

The study is still going on. Its design will be presented.

Association Cryothérapie/Radiothérapie dans le traitement des cancers bronchiques non à petites cellules et inopérables. A propos de 29 cas. Mémoire présenté et soutenu le 20 septembre 1991 par le docteur Benis Mohamed Yousef, Académie de Paris

Initial combined cryotherapy and irradiation for unresectable non-small cell lung cancer. Preliminary results. Vergnon JM, Schmitt T, Alamartine E, Barthelemy JC, Fournel P, Emonot A, Chest 102(5) :1436-40, 1992

A74 Tracheobronchial Cryotherapy. The Chilean Experience

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Objective: To show our initial experience in the management of tracheobronchial obstruction caused by malignant or benign lesions. This condition could be treated endoscopically in a number of ways: Nd-YAG laser, brachytherapy, photodynamic therapy and cryotherapy with good results. The aim of this article is to analyse our results with this technique.

Methods; Twenty-eight patients were studied between August 1997 and July 2001. There were seventeen male and eleven female patients and the median age was sixty-one. All of the patients had histologically proven malignant or benign conditions prior to cryotherapy. The patients were followed up clinically, radiologically and with lung function tests. Twenty-one patients were eligible after two months post initial treatment, three patients died and four were lost of control.

Results; The main indications for tracheobronchial cryotherapy were lung cancer (59%) followed by tracheobronchial metastasis (32%) and benign conditions (9%). Chemotherapy or radiotherapy were used prior to cryotherapy in (32%) of the cases. The total number of procedures was 58 and (88%) of the patients received two or three applications. Dyspnoea, cough and haemoptysis represent the main symptoms. Radiologically (52%) of the patients presents with lung or lobar atelectasis and (70%) of the cases, resolved after the second session. The right main bronchus (40.7%) and the left inferior lobe (18.5%) were the sites most compromised. Symptomatic improvements in cough ($P< 0.01$), dyspnoea ($P<0.01$) and haemoptysis ($P<0.01$) are found in a cohort of 21 patients selected as having post operative tests for at least two months after initial treatment. The complete results of lung function tests performed on 21 patients show improvement or stasis in values of FEV1 and of FVC in I5 patients (53.5%) for each parameter. The improvement of the pO_2 in blood gases represents (43%). Two patients (7.1%) present a recurrence after three sessions. Mortality represents (3.5%) and morbidity (28.5%). Average survival for lung cancer was 7.5months and 9.3 months for endobronchial metastasis. Patients with benign conditions are well with no recurrence.

Conclusions; Cryotherapy for treatment of tracheobronchial tumours represents a valid option with good results and low mortality. This technique is curative in case of benign tumours, avoiding resective surgery and represents an excellent method of palliation in case of malignant disease.

A75 Endobronchial Cryosurgery

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Lung cancer is the leading cause of cancer death in the world and affects 900,000 people yearly. It is a rapidly disabling disease with a very poor survival rate of only about 10% over 5 years. Surgical resection offers the best chance of cure but unfortunately, most patients (over 80%) are at such an advanced stage that surgical resection is not possible. Around 30% of these patients present with obstruction of the central airway, which leads to significant morbidity and mortality. The standard methods of treatment of lung cancer have been radio or chemotherapy, which have limited effectiveness in reopening the blocked lumen and may have a damaging effect on the surrounding healthy tissue.

We present the results of a study of 370 consecutive patients with histologically proven malignant carcinoma, treated with endobronchial cryosurgery between 1995 and 2000. The mean age was 68 years and the M:F ratio 1.8:1. Patients received an average of 2.5 cryotreatments. There was a high proportion of patients with advanced disease (92% at stage III or IV). Patient histology was, squamous cell carcinoma 67.8%, adenocarcinoma 14.8%, small cell 10.0%, large cell 1.3% and undifferentiated non-small cell 6.1%. Patients were referred for cryosurgery because they were considered inoperable based on the position and stage of their tumour, poor performance status or respiratory function. Results showed improvements in symptom quantification for dyspnoea, cough, haemoptysis and chest pain (65%, 68%, 82% and 59% respectively) and also in Karnofsky and WHO performance status. Respiratory function tests showed improvements from a mean of 1.26 to 1.43 litres for forced expiry volume in one second (FEV1) and from a mean of 1.88 to 2.13 litres for forced vital capacity (FVC). The median survival (Kaplan-Meier) for this elderly, late stage group of patients was 12.9months.

Cryosurgery has also been used for the treatment of a number of benign and low malignancy lesions including carcinoid tumours, granulation tissue following heart/lung transplant, amyloidosis, tracheobronchopathia osteochondroplastica (TBOCP), sarcoid, lipoma, polyps, post-intubation tubal stenosis, leiomyoma and Wegner's granulomatosis.

The use of cryosurgery in the treatment of tracheobronchial disease has been proven to provide a safe, rapid and effective method for the restoration of patency in blocked lumen. It improves symptoms, respiratory function and also quality of life. The technique is easy to perform, economical, has minimal complications and is well tolerated by the patient.

A76 Bronchoscopic Cryotherapy in the Treatment of Airway Obstructions Caused by Tumours.

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A prospective study of bronchoscopic cryotherapy was carried out on 65 consecutive patients with tracheobronchial tumours between January and October, 1992. Of these, 59 had advanced malignant tracheobronchial tumours and were either not fit for, or had already undergone surgery or radiotherapy. The remaining 6 patients had benign tumours for which they under-went cryotherapy as the primary mode of treatment.

Symptoms were graded by a scoring system in order to assess the clinical improvement following cryotherapy. Thirty-eight patients (66.6%) showed an improvement in their dyspnoea; haemoptysis was controlled in 12 (60%) and 6 patients (75%) obtained relief from stridor following cryotherapy. Twenty patients had respiratory function tests measured before and after cryotherapy and of these 10 (50%) showed an improvement. Thirteen patients (24%) showed re - expansion of the lung on chest radiographs following cryotherapy.

Therefore, we can conclude that cryotherapy offers good palliation and improved quality of life, particularly in patients with proximal intraluminal malignant tumours. Cryotherapy is also very effective in the treatment of benign tumours and, in many cases, may result in a cure

A77 Cryosurgical Technology: Concept of Modern Development

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Background New scientific research on freezing-application indicates the effective mechanisms of low temperatures on the tissue as well as impairment and local destruction of cells under the cryoinfluence using liquid nitrogen. One of the crucial factors influencing the development of cryosurgery is the level and technical properties of the cryosurgical devices, i.e. the efficiency of the cryosurgical method in curative practice firstly depends on technical facilities of the cryosurgical devices used in performing cryooperations.

Objective: The: aims of this study was to develop new high-efficiency universal cryo technology for the application of modern cryosurgery in treating primary and secondary cancer patients.

Study Design: On the basis of our own theoretical, experimental and practical experience, and after examining the work of cryosurgery schools the world over, but also on the basis of our own knowhow (21 national patents, including 5 world-wide patents), we have elaborated a concept of modern cryosurgical technology which can be used universally. It is produced by an automated system known as ‘Universal Cryosurgical Complex’ (UCC). It will make it possible to apply the advantages of cryosurgery to all fields of medicine. Experimental studies show that if the cryosurgical device provides temperatures of -170 to -190°C on the working surface in contact with the bulk of the tissue to be frozen, then most of the cells die. If the temperature is not lowered quickly enough during the cryosurgical procedure, there is an increasing probability that cells will be preserved in the bulk of the tissue being frozen, and recurrences of malignant malformations become possible. Thus, during cryoactivity the temperature of the working surface of the cryodevice in contact with the tissue, should not be higher than -170°C. Our new cryosurgical technology is able to create sub-zero temperatures of up to –196°C where required, ie, where the cryosurgical instrument makes contact with the tissue, and this accurate freezing procedure can be repeated again and again. Although essential for cryosurgery to be effective, repeated lowering of the temperature to such a degree has up to now not been possible.

Conclusion: Long years of practical experience and numerous internationally published papers have provided evidence of the good results obtained with modern cryosurgery. It has become clear that the best use of this method is only possible through the development of efficient high-tech medico-technical devices. One of the crucial factors, which has influenced the development of cryosurgery, is the standard and technical competency of cryosurgical devices; ie efficiency of cryosurgery in curative practice firstly depends on the technical proficiency of the devices used to perform cryooperations. Among these state-of-the-art devices are the new generation of cryoinstruments produced by the industrial company ‘Pulse’ (Kyiv, Ukraine). Simplicity, reliability, efficiency and safety are, of course, also essential qualities of this new technology.

A78 Cryosurgical Method of Ulceration Venous Treatment

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Ulceration venous is a prevailing symptom of most advanced stage of protracted insufficiency of lower limb venous .

Casual treatment of venous ulcerations relies on elimination of venous hypertension. To do that it is necessary to destroy all junctive veins (perforators) in the ulceration neighbourhood to stop pathological blood flow from deep vein system to superficial. At coexisting varices a saphenous vein must be removed and also small sphaenous vein should be removed if possible.

Cryosurgical method of ulceration venous treatment depends on suprafascial extraction (cryostripping) of junctive veins and removal of lower limb varices.
Method of junctive veins extraction in ulcerations neighbourhood by insertion of cryoprobe through small hole in healthy skin area was described. Fifty two patients have been operated using that treatment. Observations have been provided by 18 months and longer after intervention. Very good and good results have been obtained in 80% of all cases. An analysis of advantages of cryosurgical method in comparison with other methods has been performed.

A79 Cryolaser Destruction of Larynx Tumors Through Laryngofissure

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While the majority of laryngooncologists insist on the deep frost or $C0_2$ laser destruction of larynx tumors through direct laryngoscope, surgical access through thyroid cartilage dissection followed by tracheostomy through cryodestmction or laser radiation of larynx tumors is more commonplace in Russia.

We have combined surgical cryogenics with laser methods in the radical T2-T3 larynx tumor treatment in the absence of complete arytenoids cartilage fixation in 96 patients using fixed cryogenic and (Icelet) portable units along with special cryoapplicators of our own design and (Daisy) $C0_2$ laser unit. The surgery included cryogenic cutting of larynx tumor with prior cryodestruction of tumor in the anterior commeasure in direct laryngoscopy and dissection of pathological tissue within the frozen organ focused by laser radiation always directed along the median line. Thus the ablation method allowed the most comfortable access to tumor, which was cut in two separate parts then independently destroyed by cryolaser.

Under cryolaser destruction we mean the following sequence: freezing of neoplasm, stratified laser evaporation of the frozen tumor within the primary tumor-affected node, visualization of its borders and depth followed by cryodestruction of tumor infiltrate and temperature lowering. Temperature lowering of thyroid cartilage inner surface in each freezing-thawing cycle as limited to -20° y drop at mean application temperatures of-170°C. In case with temperatures lower than - 30°C, the outer surface of the thyroid cartilage was dissected. In case with epiglottal cancer, tissues in the vestibule of the larynx and epiglottal space proper were further laser evaporated and cryogenically destroyed. To arrest hypothermia and prevent the development of post-operative edema and dysphasia, temperatures in laryngopharyngeal and esophageal mucous membranes were kept near +20° C with a special device concurrently with the deep local freezing of the tumor-affected tissue in the posterior segments of the organ.

All patients underwent operation well. Tracheostomy was performed within 2-7 days. Cryonectrotic rejection and epithelialisation lasted 1 to 3 months with the patients feeling no discomfort. Post-operative screening revealed 92% and 76% of the patients with T2 and T3 phases respectively had no recurrences for the last five years following cryolaser destruction of larynx tumor through laryngofissure. Method of cryolaser destruction of larynx tumor allowed:

1. To locally ablate immediately tumor-affected tissues without damaging the healthy ones thus directing the course of operation from pathological to normal tissues;
2. To bring total tumor destruction a step closer individualizing the bulk and depth of physical detection through better visualization of tumor node borders;
3. To maximize advantages of laser and cryogenic methods minimizing their adverse effects;
4. To provide for a most comfortable and least traumatic access to tumor disintegration beyond the reach of other methods;
5. To improve efficiency of laser attack on tumors evaporating frozen tissues in the absence of burns, hemorrhages or coagulational crusts;
6. To provide for a reliable and easier cryodestruction of tumor infiltrate left in the larynx following target node evaporation;
7. To reduce Cryonectrotic mass volume in larynx, speed up decannulation, prevent dysphasia, to considerably reduce accompanying deem in the esophagus, larynx and epiglottis;
8. To employ advantages of tumor cryodestruction healing plasticity in the absence of tissue defects and specific antitumoral(antineoplastic) immune stimulation.

Cryolaser detection was not accompanied by any negative influence on reactivity of an organism. Cryolaser detection of larynx tumors through laryngofissure appeared to be a sparing, organ-saving method (whereas traditional methods would imply extensive resection or laryngectomy in most cases), yet it is reasonably radical and can be used independently in the absence of radiotherapy.

Cryolaser destruction can be used in the treatment of cancer of any location.

U.S.S.R. Regd. Patent Nos. 170919, 1732947, 1710075, 1650106, 1438035, 1316113, 1281257, 1231654,1153409,1117877,1958821,1105192. Russian Patents Nos. 2018273, 2018274.

A80 Benefits and Safety of Cryosurgery for Locally Advanced Pancreatic Cancer.

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Cancer of the exocrine pancreas remains a therapeutic challenge and continues to have a poor prognosis. At the time of the diagnosis most patients present with locally advanced inoperable disease, where surgical options are limited to palliative bypass. The aim of the study was to evaluate results of cryotherapy in patients with unresectable pancreatic cancer.

Fifty-six patients with histologically proven locally advanced adenocarcinoma of the exocrine pancreas with mean age 61.5 (range 26-74) underwent operation. In 11 cases tumor was located in the head of the pancreas, in the body or tail in 28, seventeen patients had total pancreatic cancer. Cryosurgery alone was performed in 35 patients, other 21 underwent combined operative procedure consisted of cryosurgery and bypasses. Cryotherapy of primary lesion in the pancreas and synchronous liver metastases was performed in 7 cases. The temperature of the cryoprobe was decreased to -185-196 degrees, duration of freezing was 3-20 minutes, thawing 3-4 minutes. In several cases we used cryoresection of the pancreas to prevent tumor spread. The accurate extent of tumor and the depth of cryodestruction was monitored by intraoperative ultrasonography.

Patient follow-up ranged from 8 to 40 months. Three patients (5,3%) died within 30 days after operation. Causes of death were disease progression in 2 cases and hepatorenal syndrome in one. Postoperative complications occurred in 14 cases (25%). The 1-, 2-, 3-year survivals were 64%, 28%, and 12.5%, respectively. Two patients lived 40 months.

Thus, cryosurgery proved to be safe and effective treatment option for patients with unresectable pancreatic cancer with promising results regarding survival.

A81 Application of Cryodestruction for Treatment for Internal Hemorrhoids and Neck of the Uterus Dysplasia under Ambulatory Conditions

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Hemorrhoids is one of the most frequent diseases of rectum. The ratio of proctologic hospitals patients with this pathology makes from 13 % to 28 %. More than 10% of the country's adult population suffer from hemorrhoids. High degree of hemorrhoids spreading determines the necessity of search and introduction into practice of such methods of treatment, which could be used under ambulatory conditions. The cryosurgical method is one of these.

In spite of the fact that cold has been used in medicine for a long time, only during the last decades application of low temperatures (up to -196 °C) began. This has become possible owing to creation of modern cryosurgical equipment, which allows not only to cool the tissues to such a temperature but also to regulate the exposure of cryoinfluence and also to secure the necessary zone of cryodestruction. The cryosurgical plant with automatic control "Krioelektronika-4" developed by the scientific and production firm "Puls", city of Kyiv, corresponds to all this terms.

The cryodestruction method for rectum diseases has been used at the Republican Proctologic Centre (Kyiv) from 1980. The cryodestruction of hemorrhoids has been used, under ambulatory conditions to 625 patients (440 men, 185 women). Hemorrhoids of the I degree has been observed in 23.5% of patients, 2 degree in 26%, 3 degree in 47% and 4 degree in 3% of patients.

The preoperative preparation included purgation on the eve of the operation. The anesthesia was not carried out. The cryodestruction was fulfilled by the methods of local phased cryoinfluence on individual internal hemorrhoids by the working part of the cryoprobe. For this into the rectum they introduced an anal dilator having a side "notch-trap" through which they probed the internal hemorrhoids. The cryoinfluence was carried out at the applicator temperature of -180°C. Freezing of the hemorrhoid to its base acts as a criterion for stoppage of the cryoinfluence. The time of the cryoinfluence varied from 1.5 to 5 minutes. After its thawing out the hemorrhoid was exposed to repeated cryoinfluence. A two-cycle cryoinfluence allows to reach a reliable necrosis of the hemorrhoids. The hemorrhoids cryodestruction was carried out for 3, 7, and 11 hours. After finishing the operation an ointment tampon was introduced into the rectum. For the postoperative period posterisan and methyluracil tapers. metronidazole, aperient diet were prescribed. Subfebrile fever, serosanguinolent discharge from the rectum were observed at the patients during several days. When observing the course of the wound process the following regularities were determined. At once after the hemorrhoid cryodestruction there develops an edema of tissues reaching its maximum by 3-4 days after the operation. The hemorrhoids acquire a dark-purple colouring with non-uniform intensity. On the third-fourth day a line of demarcation can be distinguished. The necrotic tissues rejection takes place on the 7th -14th day. The epithelization becomes completed in 3-6 weeks. The disablement terms varied from 4-7 to 15- 18 days.

The cryodestruction method has been also applied with the neck of the uterus dysplasias for 150 patients. The cryodestruction was carried out by ambulatory method, without anesthesia. The time of cryoinfluence took from I up to 2 minutes. Regeneration begins immediately after rejection of the necrotic sites of pseudoerosion: by the 7th day there comes reepithelization of the open wound larger part. A complete healing of the wound and recovery of multi-layer squamous epithelium is noted in 4-6 weeks. On the next day after the cryodestruction of the neck of the uterus dysplasias the patients recover their working capacity.

It is necessary to attribute to the undoubted merits of cryodestruction of internal hemorrhoids and the neck of the uterus dysplasias the following: carrying out it under ambulatory conditions, that the patients endure it well, its painlessness and bloodlessness, the possibility to carry out the operation without anesthesia, decrease of complications, shortening of terms of disablement.

A82 Treatment of Epithelial Formations of Blepharons by a Method of a Cryolysis.

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The epithelial tumors of blepharons are seen in 68,6 % of cases of all formations of an organ of vision. The tumors are capable to give in downstroke of vision and blindness, not speaking about cosmetic flaw. The number of the patients step by step is enlarged with age. Traditionally at treatment of good-quality epithelial tumors of blepharons will be utilized: a surgical oncotomy, diathermocoagulation, radial therapy, laser and cryolysis. Important for each patient to spot an individual method of treatment in view of age both blanket state of the patient and attendant diseases. Taking into account, that the epithelial formation of blepharons more often meets for faces of elderly and senile age it is desirable erosion of neoplasms to conduct by the most sparing fashion which is not requiring a padding blanket premedication. Most sparing for this category of the patients on our view is the cryolysis.

By the purpose of our operation was to study efficiency of cryosurgical action for faces of elderly and senile age with troubleshot good-quality epithelial formations of blepharons with usage of a general purpose computerized cryosurgical complex a Cryotronics.

Materials and methods: Under our observation there were 96 patients with epithelial neoplasms of blepharons. The papilloma is troubleshot for 40 patients (41,7 %) senile papiloma for 36 (37,5 %), keratoacanthorna for 12 (12,5 %) tichoepithelioma for 4 (4,14 %), adenoma for 4 (4,15 %). Age of the patients from 60 till 93 years. More often tumors were localized on the inferior blepharon - 46 patients (48,0 %) then for an interior angle of an eye - 32 (33,3 %), for an outside angle of an eye - 10 (10,4 %), on the upper blepharon - 8 (8,3 %) patients.

After treatment the good effect is marked in 95,8 % of cases. For 4 (4,2 %) in 0,5 years the cryolysis was iterated.

The obtained results of treatment of epithelial tumors of blepharons allow making the following deductions: the method of a cryolysis is bloodiness, painless, not demanding special medicamental preparation before the operation and postoperative treatment. Is easily transferred, saving the patient from a stress; the method allows to conduct erasion of neoplasms of a forward segment is outpatient. Duration of interference till 10-15 of minutes; provides stable function and cosmetic effect. To recommend a cryolysis as a self- maintained method of treatment especially for the patients of high age group.

A84 Malignant Melanoma Eight years after Treatment by Cryosurgery-A Case Report.

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Case Report: A-5-year-old girl had a Melanoma "CLARK 111". Located between the 3rd an 4th toes of her left foot; both sole and the top of the foot were affected.Accompanied by enlarged nodules on the same side. She underwent Cryosurgery April 14, 1993.

Conclusion-. This case of Malignant Melanoma treated by Cryosurgery, were cured an show no sign of metastases, and no side effects.

A85 Cryosurgery of malignant tumors of mouth cavity and skin

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Malignant tumors of mouth cavity's mucous membrane, as a rule, undergo of combined treatment with wide using of post-operative chemotherapy's and radiotherapy's course of treatment and subsequent operation.

Operation brings about abnormality of important anatomical structures of the mouth cavity: tongue, cheeks, jaw, with beginnings of consistent malfunctions, and, quite often, about mental disorder. At the moment of primary patient's visit to oncologist the decomposing bleeding tumor of mouth cavity is often observed. The bleeding from tumor is the contra-indication of radiotherapy.

We suggest the method of simultaneous treatment of the primer tumor of the mouth cavity's mucous membrane with radio- or chemotherapy. Since radiotherapy, cryodestruction of decomposing tumor part of mouth cavity's mucous membrane takes place once a week. During first three days after cryoprocedure the edema of the nearest soft tissues evolves, painful syndrome intensifies tumor bleeding stops. Patient must irrigate mouth cavity with tan decoction and grease it with anesthesin, dissolved in oil.

In a week the emeda vanishes, a tumor regresses, tumor's sizes can be palpated neatly. And a tumor (all or its part) undergoes with cryodestruction again. Thus, the patient receives from 2 to 4 cryoprocedures during (against the background of) radiotherapy or chemotherapy course of treatment. Tumors of upper jaw's toothless area, of fore two thirds of tongue, of fore-part mouth cavity's bottom submit to the lysis very well, but tumors of cheek and lower jaw mucous membrane submit to the lysis worse. In some cases we observed recovery of primer tumor point. **(Fig.1)** The low lip vermilion border makes a complete recovery from nodulous cancer, if deep tumor's growing to lip muscle is absent. The treatment of primary small basal and squamous cell carcinoma tumors by cryodestruction is always successful, recurrences are rarely observed.

We'd like to show some of the most difficult and interest cases of our 11-year clinical experience.

(Fig.2 A, B) The squamous cell carcinoma of face skin (low eyelid, interior corner of eye, lateral surface of nose, under-eye area), which arised in 30-year-old scar after radiotherapy of basal cell carcinoma. The patient was healed by simultaneous cryodestruction and gamma therapy.
(Fig.3 A, B, C, D) The total squamous cell carcinoma's, failed of skin of upper lid on the right, is healed by simultaneous cryodestruction (ones a week) and medicinal course of radiotherapy.
(Fig.4 A, B) The skin basal cell carcinoma's recurrence of cartilaginous part of the nose after X-ray therapy was healed by 3-time cryotherapy during 3 months.
(Fig.5 A, B) The squamous cell carcinoma of face skin (low eyelid, under-eye area, lateral surface of nose) of 86-year-old woman was remedied by 3-time cryodestruction for one month.
(Fig.6 A, B) The cryo-treatment of primary-multiple face skin basal cell carcinomas of 72-year-old patient was the tradeoff method (unique solution).
(Fig.7 A, B, C, D) The sanitational cryodestruction of the 32-year-old patient, suffering the decomposing tumor of right face half.

Cryodestruction is the method, which has no contra-indications for treatment of external localization malignant tumors, and sometimes is the tradeoff method, for example, for somatically aggravated patients, with aged decrepitude and with late stages of disease.

A86 PSA Elevation During Cryosurgical Ablation of the Prostate and Decline Curve Following the Procedure

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Objectives: To determine the acute influence of cryosurgery of the prostate on serum PSA level, and its subsequent decline curve.

Methods: 15 consecutive patients with prostate cancer underwent cryosurgery. Blood was taken for PSA during anesthesia, after cryoprobe placement, following termination of freezing, and 24 hours, 1 week, 2 weeks, 4 weeks, 6 weeks and 3 months postoperatively. A confidence interval for the difference between preoperative and maximal PSA levels was calculated. The observed rate of PSA decline following cryosurgery was compared with calculated values based on a serum half-life of 2.5 days. The actual PSA half-life was then calculated in each patient. The correlation between prostate size and maximal PSA level and between preoperative and maximal PSA levels were determined. Student t-test and Pearson`s correlation statistics were applied.

Results: PSA serum level increased from an average of 8.22 ng/ml preoperatively to a maximum average of 168.3 ng/ml (ranges: 0.1 preoperatively to 490.5 ng/ml maximal level; 95% CI 126.07 to 210.52 for the increment). Serum PSA declined slower than expected: at 1 week postoperatively the average PSA level was 31.8 ng/ml versus the calculated value of 22.0 ng/ml p=0.04; at 2 weeks the observed average PSA was 11.2 ng/ml versus 3.67 ng/ml, p=0.012; at 4 weeks the observed average PSA was 1.45ng/ml versus 0.064 ng/ml, p=0.037; and at 6 weeks postoperatively the average PSA was 1.196 versus a calculated expected level of 0.000055 ng/ml, p=0.029.

The average serum half-life of PSA was 4.65 days (ranges 0.58 to 8.37 days). No correlation was found between prostate size and maximal PSA level or between preoperative and maximal PSA levels ($r2 = 0.04$; $p = 0.47$ and $r2 = 0.0$; $p = 0.99$, respectively).

Conclusion: cryosurgery of the prostate is associated with a steep rise in serum PSA followed by a slow decline. Therefore, high postoperative PSA serum levels should be regarded as part of the decline curve rather than a sign of biochemical failure. Consequently, prostate biopsies should be withheld in the 6-12 postoperative weeks while following the PSA decline.

A87 Laproscopic Cryoablation of Liver Tumours

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During the years 1998 to 2001, 18 patients (9 males, 9 female age range 62-81, mean 72 years) with unresectable liver tumours underwent laproscopic cryoablation (LC) treatment. Ten patients had colorectal liver metastatic disease and 8 patients hepatocellular carcinoma. Patient evaluation included CT and US scans and serum tumour markers. Eight patients had bilobar liver involvement while 10 had unilateral disease.

Materials and Methods; Laparoscopic treatment was performed under general anesthesia commencing with laparoscopy and laparascopic ultrasound (LAPUS) for accurate disease staging. Patients having extrahepatic liver spread were excluded. Patients with unresectable liver tumour with no evidence of extrahepatic disease were then treated with laparoscopic cryoablation.

The laparoscopic cryoablation system consisted of two integrated parts. The cryoablation system (Cryo-hit, Galil Medical, Israel; employing Argon Helium gases using 5mm needles) combined with Laparascopic ultrasound system using a 10mm US probe (Sharplan U-sight system Israel). Cryoablation treatment (two cycles of 10min each) starting with insertion of the cryoneedle under US guidance. Two or more needles are inserted according to tumour configuration. Treatment is continuously monitored by LAPUS.

Resullts; Morbidity consisted mostly of fever (4/18, 22%) due to athelectasis. Two patients bled and were treated conservatively. One patient died of following the development of a myocardial infarction 3 days after treatment.
Follow up 4-29 months, mean 16. Eight patients are alive (17, 18 and 29 months, hepatocellular carcinoma 4-21 months, metastatic disease). Importantly, 2 patients have had repeat LC and one patient had 3 LC treatments for recurrent metastatic disease.

Conclusions; LC of irresectable liver tumours is feasible, well tolerated and carries relatively low morbidity with no procedure related mortality. Repeat treatment is possible. Long term survival may be achievied.

A88 Cryosurgery for the Treatment of Tracheobronchial Benign Polyps

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Background: Benign polyps of the tracheobronchial tree, are rare in occurrence and may cause airway obstruction. The standard methods of treatment include bronchoscopic removal, laser ablation or occasionally radiotherapy. Endobronchial cryosurgery is widely accepted as a palliative modality for malignant and benign endobronchial tumours. We describe six cases of benign polyps of the tracheobronchial tree, which were treated using endobronchial cryosurgery.

Methods : Between January 1995 and May 2001, six patients were diagnosed with airway obstruction caused by benign tracheobronchial polyps. Histologically, 5 patients had benign squamous papillomas (BSP) while 1 patient had from recurrent respiratory papillomatosis (RRP). All patients were treated with endobronchial cryosurgery and followed up prospectively for a period ranging from 1 to 6 years.

Results : The 5 patients with benign squamous papilloma had good clinical response following endobronchial cryosurgery. The patient with recurrent respiratory polyposis had multiple episodes of recurrence, though he enjoyed good quality of life and had symptomatic relief in between recurrences. Clinical response was judged by the resolution of the polyps by bronchoscopic assessment and monitoring improvement of symptoms. None of the patients developed any major complications after endobronchial cryosurgery and the procedure was well tolerated in all cases. One patient developed aspiration pneumonia which was managed by medical measures with a good outcome.

Conclusions: Endobronchial cryosurgery is an effective, safe and simple alternative treatment modality for benign tracheobronchial polyps. Apart from being curative in benign tracheobronchial squamous polyps it also offers symptomatic relief in the resistant varieties as in recurrent respiratory polyposis. Patient tolerance and compliance to this form of treatment has been excellent in our experience.

A89 Lymph Node Cryosurgery (LNC)- A New Surgical Approach For Lymph Node Metastases

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Introduction: Surgical excision of metastatic nodes is the only effective treatment for cure or local disease control. Some surgeons prefer to excise only clinically demonstrable metastatic nodes. This type of excision has been termed a therapeutic or delayed lymph node dissection. But there is some controversy concerning the benefit of lymph node dissection.

Objective: To develop cryosurgical technique and to evaluate the place of cryosurgery as a new surgical procedure for lymph node metastases.

Material and Methods: 23 patients with lymph node metastases were treated by own developed cryosurgical technique in our clinic. This new surgical operation has been termed a lymph node cryosurgery (LNC). There were 9 patients with inguinal nodal metastases from primary breast cancer and melanomas, 11 patients with cervical nodal metastases from primary breast cancer, melanomas and squamous cell carcinoma and 3 patients with parotid lymph node metastases from melanomas and hypernephroma. LNC was performed with „Cryothronic“ apparatus (Cryotechnological Company „Pulse“, Kyiv, Ukraine) designed specifically for different kinds of malignant tumor to deliver liquid nitrogen to the tip of a double lumen probe. The cryosurgical operation was performed in local anesthesia. The following optimal parameters were determined for cryosurgery of lymph node metastases: freeze temperature at –180°C to –190°C, with rapid freezing of the tumor required, duration of a treatment session: 5-7 minutes, 2-3 freeze-thaw cycles, automaticly thawing, which must be carried out very slowly. We used mainly a 20-mm probe and rarely a 30-mm probe according to the size of the tumor. The operation was normally carried out with local anesthesia (18 patients). When an affected metastatic lymph node lies deep in soft tissue, the surgery should be carried out under general anesthesia (5 patients), in order to be able to expose and dissect all the lymph nodes. The operation is usually ended without a drain and wound is closed by intracutaneous suture.

Results: There was no intraoperative mortality. In an analysis of 23 patients who underwent inquinal, cervical and parotid lymp node cryosurgery, the short-term complications were infrequent and of short duration. Edema was a frequent long-term complication (in 34.7% of patients). Seroma occured in 34% of patients. Pain (17% of patients) and skin slough (8.7% of patients) were uncommon. A wound complication was not observed. The age was not the risk factor for the development of any complications.

Conclusion: For the first time, new cryosurgical operations have been developed and used with clinical success in patients with lymph node metastases after breast cancer surgery, melanoma, squamous cell carcinoma hypernephroma extirpation performed with conventional methods.

P11 Cryosurgical Treatment on Perfused Organs by means of Contact Freezing

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In cooperation between the Department of Oral and Maxillofacial Surgery, Universitätsklinikum Dresden and the Institut fuer Luft- und Kältetechnik GmbH Dresden a cryoapplicator was for the contact freezing with optimized heat transfer developed (contactapplikator FSV 5 p3 with sinter-metal-contact-surface). This probe was tested and its capacity acsessed via phantom model (by Raschke, A., Med. Diss. TU Dresden ,in preparation). Before using the probe on the patient animal-experiments are required. To reduce animal testing and for ethical reasons we used the possibilities, offered by Mediport Biotechnik Berlin to carry out the examination in artificial perfused animal organs (pig-paw).

16 pig paws were normotherm perfused. Before the 1th cryoapplication we took a reference-biopsy. The cryoapplication took place with the contactapplikator FSV 5 p3 at variable pressure and a mass-stream of the nitrogen of 3 - 4 g/sec. Hereby the temperature reached was held over a time of 5 minutes steadily. The thawing time amounted to 7-10 min without any influence. The temperature front in different tissue-depths was registered by means of thermo-elements. The entire duration of each single-examination up to the end of the perfusion amounted to 7 hours. A reference-biopsy was taken before we started. After 3h, 5h and 7h, tissue was taken from different situation to the cold-center in each case. All tissue-types were defined locally and were examined histologically.

The cooling rate in a tissue-depth of 4 mm amounted to 100 K/min with physiological perfusion for the 0°C until –20°C isotherms. In depth of 6mm -40°C was reached. The perfusion is biologically possible for about 7h. The necrobiosis is verifiable light-microscopically in a distance of 6 mm to the cryoapplicator.

Despite relatively high transferable cold-performance of the new cryo applicator FSV 5 p3s the depth of freezing front (devitalized cold) is restricted to 6 mm.The necrobiosis is notable after 6h. A verification of the necrosis is not possible because of the artificial perfusion is restricted to a time maximal 7 h. Examinations with apoptose-markers should substantiate the result.

P12 Cryosurgery in Older Patients

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Introduction: since 1985, the Division of Surgical Oncology at our Institution has been working in an outpatient setting for cryosurgical treatment of patients addressed by plastic surgery, gynaecology, ENT, infective disease and dermatology services. Cryosurgery was the treatment of choice for some patients while for others the treatment was proposed due to advanced age and/or co-morbidity factors as an option to standard surgical treatment. Patients with serious cardio-respiratory impairment, undergoing anticoagulant pharmacological treatment, or undernourished patients could be treated by means of cryosurgery due to the low invasiveness and post-operative morbidity of the procedure.

Materials and Methods: between 1995 and 2000, 90 patients (47 female; 43 males) over 65 years of age (mean 74.5, median 76 years) underwent cryosurgery, and had a follow-up of at least six months. Overall, 174 operations were performed (126 in outpatient setting, and 48 in the operative room); nitrous oxide was used in 139 cases, and liquid nitrogen in the remaining 35 cases. As regards the site and type of lesions, there were 45 cases of the head and neck (23 preneoplastic lesions of the oral cavity, 10 squamous cell carcinoma of the oral cavity, 2 nasopharingeal carcinoma, 3 basocellular carcinoma of the lip, 2 peritracheostomal granulomatosis, 1 lingual metastasis secondary to clear cell renal carcinoma, 1 oral cavity metastasis secondary to cutaneous melanoma, 1 angioma of the nasal cavity, 2 nasal polyposis, and 1 hypertrophic tonsil), 39 cases with skin invasion (23 basocellular carcinoma, 9 squamous cell carcinoma, 3 Kaposi's sarcoma, 4 angiomas), 5 lesions of the genito-urinary tract and/or perineum (1 penile condilomatosis, 1 penile Kaposi's sarcoma, 1 penile squamous cell carcinoma, 2 perineal recurrences of transitional cell carcinoma and rectal adenocarcinoma), and 1 breast cancer recurrence.

Results and Conclusions: cryosurgery proved to be effective in most of cases, and was well tolerated with no post-operative complication. As regards head and neck lesions, a complete healing of all precancerous lesions and squamous cell carcinoma without cervical lymph-node metastases was observed; patients with advanced disease experienced an improved quality of life, due to the cyto-reductive effect, foul smelling secretions, bleeding and pain control. Skin epithelioma could be successfully treated in 90% of patients. Vascular lesions of Kaposi's sarcoma in the lower limbs were particularly cryophilic and amenable to treatment. Good results were obtained in genital lesions such as penile condilomatosis, in 2 cases of penile squamous cell carcinoma, and one case of penile Kaposi's sarcoma; in these last cases, cryosurgery could avoid surgical amputation. Thus, cryosurgery may represent in selected cases a valid option to standard surgery due to the ease of the procedure, rather low risk of intra- and post-operative bleeding, satisfactory pain control, and reduced number of post-operative visits that may represent a serious impairment in older patients.

P13 Development of a Device for Intralesional Cryosurgery and its Application in the Treatment of Old Recalcitrant Keloids

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Cryosurgery, as monotherapy or in combination with other therapeutic regimens, is a successful modality for the treatment of keloids and hypertrophic scars. The disability of skin surface cryosurgery to freeze beyond 20 mm makes techniques for applying cryosurgery in depth attractive for old fibrotic and large keloids. We modified the method introduced by Weshahy (1993) and developed a device constituted of a small liquid nitrogen dewar engaging a sterile disposable, 20-G needle connected by a flexible, long metallic cryoprobe stem. The cryoprobe stem is luer-locked to the needle and its shape is variable so that the dewar can stay upright during freezing. The shape of the needle can also be changed in order to form an angle, curve or hook. The needle is introduced into the skin after topical anesthesia, runs through the deeper tissues of the lesion and appears at the surface on the opposite border. Liquid nitrogen is then sprayed through the needle exiting to the atmosphere. An ice cylinder is formed around the embedded part of the needle within the deeper tissue. The distance of extension of freezing can be clinically estimated by the degree of extension of the whitish ice balls formed around the contact points of the needle to the skin surface. Compression of the lesions is accomplished by pooling up the visible parts of the needle. We evaluated the efficacy of intralesional cryosurgery on recalcitrant keloids older than 1 year (1-10 years, median 4 years) with a vertical diameter of ≥3 mm by conducting a pilot open study with 10 patients (5 male, 5 female) aged 22 to 62 years (median 31 years) treated The lesions were photographically documented and plaster imprints were made before and after each session of treatment. Scar volume was objectively evaluated by measuring the imprints volume using peripheral quantitative computed tomography. A marked flattening of the lesions (50-100%) was achieved in 2 patients, a moderate improvement (<50%) in 5 patients, while 1 showed no change and 2 patients experienced a progression. No significant difference in the duration of the complete lesional freezing and the lesional volume was assessed for the whole patients group when the data of the first three subsequent treatments were evaluated. Topical necrosis and hypopigmentation, in 4 patients each, were the sole adverse events. In conclusion, intralesional cryosurgery is effective and safe on old recalcitrant keloids, however, it exhibits, like surface cryosurgery, moderate effects in this type of lesions. It is, therefore, advisable, as we have shown before, to apply cryosurgery in young keloids to obtain satisfactory therapeutic results.

P 14 Cryosurgery in Dermatology - State of the Art

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Successful cutaneous cryosurgery requires rapid freezing and slow thawing speeds, minimum tissue temperature of -25°C to -60°C and, in malignant lesions, repetition of freeze-thaw cycle. Cryosurgery induces physical and vascular skin reactions, while a postulated immunological effect has not been sufficiently studied. Modern cutaneous cryosurgery is performed by the contact or spray techniques as well as intralesionally. Nitrous oxide (-86°C) and liquid nitrogen (-196°C) are the refrigerants mostly used. In cryosurgery of skin tumours, tissue temperature has to be monitored either by measurement of the lateral spread of freeze, or by application of thermocouples to estimate temperature or electrical impedance in frozen tissue, or by ultrasound. Frozen tissue reacts with peripheral erythema immediately following thawing, and consequently with oedema, bulla formation, exudation, mumification and healing with a fine atrophic scar during a 4-week period. Cryosurgery is considered treatment of choice in keloids and hypertrophic scars, granuloma annulare and capillary haemangioma of the newborn. It also consists a valuable alternative therapy for various skin diseases, including common warts, solar lentigo, actinic keratoses, superficial basal cell carcinoma and Kaposi's sarcoma. Cryosurgery is a safe regimen with only a few adverse effects and contraindications. Pain during and/or shortly after treatment, bulla formation and local oedema are the major temporary adverse effects; lesional hypopigmentation and/or peripheral hyperpigmentation is the most common long-term complication occurring.

P15 Cryotherapy of Uterine Fibroids under Interventional Magnetic Resonance Imaging Guidance.

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Objective: Uterine fibroids affect approximately 65% of all women by age 45. They are a large source of morbidity in the United States and throughout the remainder of the world. The predominant treatment is hysterectomy. This results in approximately 300 hysterectomies performed annually in the United States. Recent advances in diagnostic imaging suggests that minimally invasive image guided tissue ablation procedures can be developed as an alternative to traditional surgical resection for many disease processes. Our goal is to define and develop a minimally invasive guided procedure to treat large symptomatic uterine fibroids.

Study Design: After establishing an IRB protocol, women were selected on the basis of symptoms related to large uterine fibroids (bleeding, uterine pain, bladder compression and stress incontinence, and pelvic congestion). All women denied any desire of future child bearing. Physical examination was performed followed by diagnostic MRI to determine the anatomy of the uterus and the amount of fibroid burden. After selecting the patients, each patient was treated in the interventional MRI unit with percutaneous cryoablation. MRI was used to monitor probe position and to monitor the development of the ice ball formation. Following the procedure, follow-up MRI was obtained at eight to ten weeks to determine the size reduction of the lesion. Clinical evaluation was utilized to access reduction of clinical symptoms and to access for any subacute and chronic complications.

Results: Clinical evaluation revealed a mild syndrome of pain, which required non-steroidal anti-inflammatory drugs but no narcotics. The pain typically began between five and fourteen days after the procedure. On imaging studies, reduction in size ranged from 33% volume to 88% volume. The mean was approximately 55%.

Conclusions: Preliminary results suggest that this procedure is highly affective at accomplishing a rapid reduction and the bulk of large symptomatic uterine fibroids. Clinical symptoms resolved rapidly on the order of two weeks and diagnostic imaging studies at ten weeks demonstrated a significant reduction in uterine volume ranging between 33% and 88%.

P16 **Interventional MRI Guided Percutaneous Cryoablation of Renal Tumors.**

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Objective: In an on-going study, two and a half year data is demonstrated to define the success and complications with regard to this on-going study.

Study Design: Patients with renal tumors as identified on diagnostic imaging studies were selected for minimally invasive treatment titled "Percutaneous MRI Guided Cryoablation of Renal Tumors". Candidates included those patients with solitary kidneys, bilateral tumors, and those patients with co-morbidity preventing traditional surgical resection. Additionally, any patient who could benefit from nephron sparing surgery was offered this procedure. The study design is outlined in previous reports published in the Journal of Urology. The protocol has not been altered.

Results: A total of fifty patients have been treated to date. Five patients required re-treatment as their post-cryo imaging studies demonstrated tissue suspicious for residual tumor. Four patients have died of non-renal tumor disease. These patients had significant co-morbidity such as extensive pulmonary disease or second malignancies unrelated to their renal tumors. 92% overall survival is noted to date with a median 15- month follow-up. There is a 100% cause specific disease for survival at a median 15- month follow-up.

Conclusion: 2.5-year results are consistent with the 1-year results. Low morbidity and mortality of this provide along with successful target tumor destruction suggests this is a successful nephron sparring treatment for direct tumors. Disease specific mortality is zero to date. Disease specific morbidity is low with 6 patients demonstrating gross hematuria in the acute post-operative period with spontaneous resolution. Complications include one post-operative wound abscess, which was treated successfully with conservative therapy. Follow-up imaging studies demonstrate excellent results with no evidence of residual tumor after complete treatment although five patients did require re-treatment. Those patients had tumor adjacent to a large heat sink such as the renal vein or the renal artery, which prevented complete cryoablation at the initial time of treatment.

P17 Percutaneous MRI Guided Cryoablation of Bone Tumors.

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Objectives: To develop a minimally invasive image guided treatment for primary and secondary benign and malignant bones tumors as a substitute or a replacement for current therapies.

Study Design: Patients with primary bone tumors who were poor surgical candidates due to the high incidence of potential complications secondary to anatomy, or patients with secondary bone tumors resulting in pain were enrolled in the IRB approved study. Diagnostic imaging pre-operatively consisted of a CT or a MRI along with plain film x-rays. Treatment goal was relief of pain.

Each patient underwent IMRI guided percutaneous cryoablation. General anesthesia was utilized. Ten tumors in eight patients were treated. Tumor locations included vertebral body, posterior vertebral elements, scapula, long bones of the extremities, and the coracoid process.

Results: Short term results demonstrated excellent and near immediate relief of pain. Long term results obtained in three of the patients demonstrate continued pain relief, with no immediate or long-term complications identified in any patient. Imaging findings demonstrated aggressive osteoblastic response in the cryo treated tissue resulting in sclerotic bone formation. In the cases of the vertebral body cryotherapy, bone replaced the soft tissue malignant tumor resulting in increased stability of that vertebral body post-cryo.

Conclusions: Early results suggest excellent pain relief for cryo treated primary and secondary bone malignancies. And unforeseen yet welcome side affect of cryotherapy appears to be osteoblastic stimulation resulting in formation of new bone. This suggests the possibility of cryo treatment of bone with the goal of skeletal strengthening might be possible.

AUTHOR INDEX