

## Contact Details

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

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European  
Society of  
Cryosurgery

# CRYOSURGERY

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# Welcome



We are pleased to present to you the seventh issue of CRYOSURGERY. I hope you find this issue interesting and informative.

As you may already know, the next combined meeting of the International and European Societies of Cryosurgery will be held during September 2003 in London, UK. The Board of Directors of both societies (ISC and ESC) hope you will attend the meeting. Please join us and share your clinical experience and discuss further any current issues in the various disciplines of cryosurgery. The rapid advances in cryosurgery have made it important that we meet to refresh and renew our understanding, knowledge and skills, through continued discussion and interaction in meetings such as the ISC ESC 2003.

The International and European Societies of Cryosurgery were pleased with the participation of many cryotechnological companies at the Lisbon 2001 meeting and we welcome and encourage their active participation in London 2003.

The next meeting of the Association of British and Irish Cryosurgery is being held on the 19th October 2002 in Dublin, Ireland. We hope as many of you as possible will attend. The programme includes talks by Dr Gloria Graham, Prof Ablin and Dr John Rewcastle, and also includes practical workshops led by Dr Buckley (see page 4 for further details).

We look forward to making both of these conferences a memorable experience. May I suggest you take the opportunity to attend and discuss further the field of cryosurgery in both an academic and social setting.

There have been a large number of scientific publications in this cryosurgical field, some of which are summarised on pages 21-23.

We welcome articles for inclusion in future issues of CRYOSURGERY, please send them to the address on the back page.

M.O Maiwand

# A Tribute to Dr Esther Stolar

It is with great sadness that the International Society of Cryosurgery announces with regret the death of Dr Esther Stolar. Esther was a very well known, well respected and energetic cryosurgeon. She was a great inspiration to us all in the cryosurgical community. Esther was very enthusiastic in advancing cryosurgery and was a very influential ex President of the International Society of Cryosurgery. On behalf of both societies, we remember her with respect and send our condolences to her husband and family. We are grateful to Dr Gloria Graham from USA, whom has kindly written a special tribute to her.

## Dr Esther Stolar. In Memorium

Esther Stolar was an inspiration to us all. Born in Argentina in 1935, she graduated in the Medical Faculty of Buenos Aires in 1961. She was without a doubt one of the most creative cryosurgeons in all of medicine. When her husband, friend and colleague Dr. Eliezer Turjansky informed me of her death in April, 2002, I was saddened by the loss of this most special person. Esther had been a friend for many years, she and Elie had visited with me in North Carolina and in California. My husband and I had been in the home of Esther and Elie in Buenos Aires, Argentina numerous times. They graciously took us to their beach home in Uruguay and to many points of beauty in that country as well as Argentina. Esther and Eliezer developed many interesting techniques in cryosurgery and combined cryosurgery with electrosurgery for large exophytic tumors. They taught these techniques with enthusiasm and clarity. They wrote a book, made many CDs and lectured around the world. Esther was a gynaecologist by training but became fascinated by the POWER of COLD. She found the skin a great field for study and she and Eliezer tirelessly treated thousands of patients in their hospital and in their private practice. She founded and was President of the Argentinean Society of Cryosurgery between 1990 - 1992 and 2000 - 2002. She was elected President of the International Society of Cryosurgery in 1992. Esther and Eliezer had the meeting for this Society at the Argentine Academy for Cryosurgery in Buenos Aires. In 1992 she was also appointed as Professor of the School of the Argentinean Medical Association and was the first woman to serve on the Board of Directors of the this association. They taught many colleagues in the Department of Cryosurgery in the Hospital Durand. Despite the time Esther gave to cryosurgery and to medicine, she had quality time for her son, daughter and her grandchildren. I watched her swim with them and love them like any good grandmother would do. Esther had many other interests and was a very well-rounded person. She will be missed by her family, her friends, her patients, and her fellow physicians whom she so willingly taught. The international community will miss her as well. There were not many women in cryosurgery when I started. I will miss her.

Dr Gloria Graham, information also supplied by Dr José C d'Almeida Gonçalves

## Section 1 Future Meetings

### Combined International and European Congress of Cryosurgery September 2003



The next combined International and European Society of Cryosurgery meeting will be held during September 2003 in London, England.

We invite you to attend and participate in this meeting and at the same time take the opportunity to explore the city of London with its wealth of history and tradition. There will be well known world-wide experts in cryosurgery and cryobiology giving you the opportunity to discuss issues and broaden your knowledge and share ideas and experiences.

The conference will be held at the National Heart and Lung Institute, part of the Imperial College, University of London.

We look forward to seeing you in London in September 2003. Please contact the society for further details about this meeting (address on back page).

Please check the website for updates on the meeting [www.rbh.nthames.nhs.uk/cryosurgery](http://www.rbh.nthames.nhs.uk/cryosurgery)



## Section 1 Future Meetings



### ASSOCIATION OF BRITISH AND IRISH CRYOSURGERY



The Association of British and Irish Cryosurgery (ABIC) is a society of cryosurgeons, cryobiologists, general practitioners and specialist nurses who came together from primary and secondary care in the UK and Ireland in the year 2000 to share experience and to promote excellence in the field of cryosurgery. The society is holding this year's annual symposium in Dublin on [Saturday 19th October, 2002](#). The programme will include lectures from International speakers, Dr Gloria Graham, Prof Richard Ablin and Dr John Rewcastle. There will also be practical workshops led by Dr David Buckley and Dr Arthur Jackson.

#### Provisional Programme

- 8.30 Registration
- 9.30 Welcome, Cryobiology, Mr Maiwand
- 10.00 Dermatological Cryosurgery, Dr Graham, Dr Jackson
- 11.30 Coffee Break
- 11.50 Prostate, Liver, Endobronchial Cryosurgery, Dr Rewcastle, Prof. Ablin
- 13.30 Lunch
- 14.30 Workshops on Dermatology & other areas of Cryo. Dr Buckley
- 15.45 Close of Meeting

The Registration Fee 70 Euros before the 31st August 2002 and 85 Euros after the 31st August 2002. Cheques should be made payable to "ABIC"

The meeting will be held at the Radisson SAS St. Helen's 5\* Hotel Stillorgan Rd, Blackrock, 4 Dublin, Ireland  
Tel. +353 1 218 6000  
Fax: +353 1 218 6010

Accommodation should be booked directly with the hotel

For further details please contact the society-  
[address back page](#)



#### 1st Mediterranean Melanoma Meeting

2 - 5 May, 2003



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### Percutaneous Renal Cryosurgery using Argon-Helium Cryoprobe under the Guidance of Horizontal Open MRI System.

Junta Harada, Michiko Dohi, Takuji Mogami, Kunihiko Fukuda, Kenta Miki, Nozomu Furuta, Kouichi Kishimoto, Tadashi Shimizu, Kazuo Miyasaka  
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#### Introduction

Percutaneous renal cryoablation is a minimally invasive nephron-sparing treatment for renal cell carcinomas (1-3). MRI allows accurate depictions of entire extent of the iceball with excellent contrast between ice and surrounding tissue. In this study, we try to demonstrate the efficacy and safety of renal cryoablation using horizontal open MR system (hamburg type).

#### Materials and Methods

Seven men and one woman (46 to 73, mean 61) underwent percutaneous cryosurgery using horizontal open MRI system (Airis 2; Hitachi Med. co.Ltd., Chiba, Japan). In this series, we selected radiographically documented renal cell carcinoma less than 5cm in diameter, and average 2.5cm (range 2.0cm to 4.0cm). Percutaneous cryosurgery was performed using a cryoablation system (CRYO-HIT; Galil Medical Ltd., Yokneam, Israel). It used high-pressure argon and Joule-Thomson effect for freezing, which achieved  $-185^{\circ}\text{C}$  at the needle probe tip. Only about 2 cm of the tip is actually cryo-cooled, while the rest of it remains reasonably close to room temperature (4). A 2 or 3mm probe composed of MR compatible metal was used.

Patients lay on the MR table in supine or prone posture with or without oblique position depending on the location of the tumor. Under MRI guidance, a 2 or 3mm cryoprobe with 1 to 4 cryoprobes was advanced into the renal mass from lateral side under the guidance of MR fluoroscopic monitoring. Introducer sheath of probe (7F sheath for 2mm probe, 10F sheath for 3mm probe) was used for hemostasis after treatment. During freezing of the tumor, 2 and 3 dimensional MR imaging was used for monitoring the growing iceball formation. Cryoablation was performed by 2 freeze/thaw cycles and cryoprobes were withdrawn or advanced between the cycles when necessary. At the end of procedure, the pathway of probe was plugged with the gelatin sponge through the sheath for hemostasis. Follow up dynamic CT and physical examination

were done after 2 and 6 weeks, and in two cases 7-month follow up was carried out.

#### Results

Tumor size averaged 2.5 cm (range 2- 4.0 cm) and the iceball size averaged 3.5 cm (range 3 - 6 cm). Puncture with probe was well controlled under MR fluoroscopy and the growing iceball during cryoablation was well visualized. One patient complained left flank pain, due to perinephric hemorrhage, and was administered analgesia intravenously. The other 7 patients reported no pain during cryoablation. Follow-up CT showed no enhancing area in 8 cases after 2 weeks and in 7 cases after 6 weeks. One case showed a marginal crescent enhanced area on a follow-up CT after 6 weeks. We determined this area was a persistent tumor and re-cryoablation was performed, and no enhancement effect of tumor was observed at 6 weeks follow-up CT image. In 2 cases of 7 months follow-up, ablated area was decreased in one case and disappeared in one case. Two cases of perinephric hemorrhage were observed and were treated conservatively, and completely disappeared after 6 weeks follow-up CT. The hospital-stay was one day for 7 patients and one week for a patient with perinephric hemorrhage.

#### Discussion

Cryosurgery may provide a method of local destruction of cancerous tissue, preserving most of the surrounding normal tissue. Cooper and Lee in 1961 (5), introduced the first cryosurgical system capable of delivering liquid nitrogen. The design of the probe allowed deep lesion treatment within parenchyma with minimal trauma to remaining organs. During the next 20 years, various locations of organs were treated, however, the lack of method to adequately monitor the freezing process in the depth of an organ did not allow the precise and complete destruction of lesions deep inside the parenchymal organs, leading to incomplete treatment of local recurrence (6). In 1999, Tacke et al (7) reported usefulness of MR imaging of interstitial cryotherapy in comparison with ultrasound, computed tomography, and MRI. The very short T2 relaxation time of ice affords excellent contrast between ice and surrounding tissue allowing accurate depiction of the entire extent of the iceball, and due to better ice/tissue contrast, MR images were superior to CT and ultrasound in monitoring interstitial cryosurgery. Recently, a fast Joule-Thomson cryocycling device for MR-compatible cryosurgery application (4) was developed and clinical trials under MRI-guided monitoring were per-

## Section 2 Original Articles

formed in several sites in the body using vertical open MR system (2,3,8-10). In our series, cryosurgery was performed under the guidance of horizontal open MR system. Using this MR system, an approach to the target was limited from the lateral side of MR gantry, although all of our procedures were safely performed without significant limitations. Punctures with the cryoprobe were clearly visualized with MR fluoroscopy and frozen areas were seen as signal loss enabling easy evaluation of the freezing margin. Campbell et al reported a target temperature less than -20 °C was achieved 3.1mm behind the iceball in all animal tests (11), and less than -20C must be reached to reliably kill malignant and benign renal epithelial cells (12-14). In short term follow-up of our series, hypervascularity of renal tumors had disappeared in 8 cases after 2weeks and 7 cases after 6 weeks follow-up CT. In one patient, persistent tumor was observed as small area of marginal crescent enhancement after 6 weeks follow-up CT, and this patient underwent re-cryosurgery. One renal mass decreased in size and one disappeared after 7 months follow-up. In a series of 20 patients of renal tumor cryoablation revealed no radiographic evidence of disease recurrence or new tumor development, and cryoablated tumor disappeared in six of 20 patients after 6 and 12 months follow-up, including one re-cryoablated persistent tumor (2). In 2000, Gill et al (15) performed renal cryoablations using a laparoscopic approach in 32 patients. Follow-up MRI demonstrated a gradual contraction in the mean diameter of the cryolesion, and cryoablated tumor was no longer visible in five of 20 patients who underwent 1-year follow-up MRI. Results of needle biopsy at the cryoablated area after 3 to 6 months were negative for cancer in 23 of 23 patients (15). One patient with perinephric hemorrhage was conservatively treated, and discharged after one week of cryosurgery, which had completely disappeared after 6 weeks follow-up. Shingleton et al (2) observed 4 perinephric hemorrhage after cryotherapy, which were also resolved conservatively. Campbell et al (11) reported that potential complication could include preoperative hemorrhage, vascular thrombosis, urinary tract stricture and urinary fistula formation.

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The Immunological Role of Cryosurgery in the Treatment of Viral Warts

Weshahy AH, Rateb AA, Shahin ZA, Ismaeil OE, Shams El Din A. Dermatology and Clinical Pathology Depts, Faculty of Medicine, Cairo University, Egypt.



Introduction

Cryosurgery is a well established method for controlled destruction of benign and malignant tissues and it has been reasonably established that in situ freezing constitutes an antigenic stimulus capable of generating a specific immunological response to antigens of the frozen tissue. There have been reports of increased humoral and cell mediated immunity in mice with experimental sarcomas and also of delayed hypersensitivity towards heterologous tumours of the same histotype. Thus cryosurgery is a method which may induce host resistance to the tumour and thus may play an important role in treatment as cryoimmunotherapy. Other authors, however, have not shown any antibody formation or signs of cell mediated immunity. This study assesses the therapeutic and cosmetic outcome of cryosurgery in the treatment of viral warts and the effect of the procedure on the immune system.

Materials and Methods

Forty patients with different types of multiple viral warts, with normal blood analysis and who had not received any treatment for 6 months were included in the study. Ten patients received placebo treatment (saline), 10 cryotherapy spray, 10 cryoprobe and 10 intralesional cryotherapy with Weshahy needles. Blood samples were taken before and 14 days after treatment and analysed by flow cytometry for T helper cells (CD4+), T suppressor cells (CD8+),  $\beta$  lymphocytes (CD19+) and IL-2R expressing cells (CD25+).

Results

Result of the immunological study showed a rise in CD4+ count after cryotherapy regardless of the method used. This rise could be due to enhancement of cell mediated immunity after treatment as cryotherapy triggers vigorous antigenic stimulation through damaging the undesirable host tissues. This would be in accordance with other work (Soanes, Airoldi) which suggested cryosurgery stimulated cell mediated immunity. The changes in CD8+ cells were not as

	CD4+		CD8+		CD19+		CD25+		CD4/CD8+	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
<b>Control</b>										
Mean	40.4	37.4	26.6	26.9	32.6	27.5	17.8	18.2	1.75	1.63
SD	8.5	10.1	9.0	5.7	5.2	10.4	11.7	10.9	0.80	0.81
P	>0.05		>0.05		>0.05		>0.05		>0.05	
<b>Cryotherapy</b>										
Mean	36.0	40.5	23.6	24.0	14.4	15.7	20.7	27.37	1.60	1.81
SD	6.8	6.5	5.4	6.4	5.6	7.2	10.3	11.2	0.48	0.57
P	<0.01		<0.01		>0.05		<0.05		<0.001	

Table 1. Results of immunological analyses before and after treatment for control group and all cryotreatments

	CD4+		CD8+		CD19+		CD25+		CD4/CD8+	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
<b>Cryo Spray</b>										
Mean	38.1	40.2	23.2	27.0	12.1	18.4	12.1	22.9	1.71	1.58
SD	5.9	7.2	3.9	7.2	5.9	6.3	0.52	13.2	0.52	0.47
P	<0.05		<0.01		>0.05		<0.05		<0.01	
<b>Cryo Probe</b>										
Mean	36.5	41.6	22.3	21.4	15.7	15.3	22.2	30.5	1.72	2.08
SD	6.8	4.3	6.7	6.3	5.8	8.6	6.0	4.9	0.40	0.53
P	<0.001		<0.001		>0.05		<0.05		<0.001	
<b>Intralesional Needle</b>										
Mean	33.7	40.0	23.8	23.6	15.2	14.2	26	32.8	1.47	1.79
SD	7.9	8.1	4.8	4.6	5.1	5.9	12.3	9.1	0.48	0.64
P	<0.001		<0.001		>0.05		<0.001		<0.001	

Table 2. Results for immunological analyses for each cryo method

great and showed a decrease in the probe and intralesional group. The spray group showed an increase and in agreement with other work by Bagley, Faraci and Ushmed. Ablin has also reported elevation of lymphocyte reactivity after cryosurgery for prostate cancer. Shibata has reported immune suppression in rats bearing fibrosarcoma and suggested this is caused mainly by suppressor cells. The T helper / T suppressor ratio (CD4+/CD8+) showed an increase in the cryotherapy patients as a group although the patients treated by the spray method showed a fall in the ratio when analysed separately. Lakatos reported a reduction in CD4+/CD8+ ratio in female patients with benign HPV, HPV associated with cellular intraepithelial neoplasia and cancer in situ. These findings suggest that cryosurgery has a role in treating viral warts and improving low CD4/CD8 ratio produced by the HPV and also diminishing the

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probability of the infection becoming more disseminated or aggressive and reducing the chance of resisting malignancy.

The B lymphocytes CD19 levels did not show any changes in either the control group or any cryotherapy group. This lack of enhancement of humoral activity is in accordance with the work of Allen who did not find any increase in humoral immunity after hepatic cryosurgery. In an animal study Flocks, Zappi and Ulshmed also failed to demonstrate heightened humoral immunity in patients treated with cryosurgery for pulmonary, epididymal and prostate carcinoma respectively. Ablin, however, reported increased levels of IgG, IgA and IgM in the sera of cryosurgically treated patients with prostate carcinoma and Airoldi and Fazio reported increased serum immunoglobulin levels 7 and 14 days after cryosurgical treatment for oral squamous cell carcinoma. The total cure rate for patients undergoing cryosurgery was 93.8% with 4 patients having a recurrence, generally due to previous contamination of surrounding tissue before cryosurgery, activation of the virus or incomplete killing of the deeper basal cells. After a further treatment, two patients (treated by spray) had a further recurrence and were also found to have decreased immunological parameters after cryotherapy. Two patients, both in the intralesional cryotherapy group, showed spontaneous regression of their other, untreated warts and also a high rise in their immunological parameters which may augment the conviction that the immunological status of the patient plays an important role in control of the human papilloma virus. The incidence of post-operative complications was; transient hypopigmentation 20%, transient alopecia 3.3% and recurrence 13.3%. Results for the control group showed no significant differences before and after treatment but patients treated with cryotherapy did show a statistically significant difference for CD4+, CD8+, CD25+ and CD4/CD8+ before and after treatment. Results analysed by type of cryotherapy (spray, probe and needle) also showed significant changes in CD4+, CD8+, CD25+ and CD4/CD8+.

### Discussion

This study confirms the safety and cosmetic success of cryotherapy. Six patients developed temporary hypopigmentation, which has been reported to be more common amongst people with heavily pigmented skin (Elton). Localised transient alopecia in one patient resolve after 5 months and there were no cases of scarring and neuropathy which are reported to be the most serious complications after cryotherapy (Zacarian).

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The activated lymphocytes CD25+ increased significantly in the cryo group but not the control group and the greatest increase was in the intralesional needle group. This could be due to the vigorous antigenic stimulation of more penetrating cryosurgery. The needle and probe methods both had lower rates of recurrence and the needle method led to spontaneous regression of other warts in the same patient in 2 cases. Coleman reported regression in 22% of patients with genital warts and these patients had the most active cell mediated immune response.

This study demonstrates the benefits of cryotherapy, the low rate of treatment failure, satisfactory cosmetic results and most importantly its possible role in enhancing the immune response against infection and malignancy.

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## Section 2 Original Articles

### Regenerative Cryotherapy

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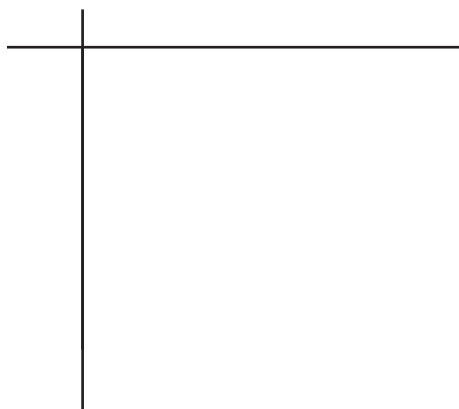
Regenerative cryotherapy consists of the brief administration of calculated doses of cold treatment to tissues and organs at temperatures close to the cold-resistance threshold of the tissue. The aim of this type of cryotherapy is to bring about regeneration and functional reactivation at the treatment site. It 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. During the administration of regenerative cryotherapy, the same pathophysiological changes take place in the tissues that were described by I. V. Davydovskij (1969) in connection with inflammatory processes:

Stage 1: Reactions caused by the activity of vasoactive mediators,  
Stage 2: Hyperaemia,  
Stage 3: Exudation and odema,  
Stage 4: Leukocytic infiltration,  
Stage 5: Regeneration.

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.

Regenerative Cryotherapy is used for the treatment of chronic tonsillitis and chronic pharyngitis. Both of these conditions are chronic inflammatory oedematous processes affecting the lymphoid tissues of the tonsils and lymphoid follicles (Waldeyer's throat ring). Cryotherapy application to this lymphoid tissue simultaneously activates the regenerative process and a cyclic reaction lasting for 4 to 6 weeks. Following R.cryotherapy, the following therapeutic mechanisms of action can be observed:

1. Heightened non-specific reactivity of the organism
2. Attenuation and subsequent eradication of infectious processes
3. Distinct hyposensitization of the organism to bacterial & histoid antigens
4. Germination of young neurites without the degenerative changes usually



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observed in chronic inflammatory processes, restoration of the normal trophism of the lymphoid tissue, and enhancement of cell repair and regeneration

5. Restoration of the protective function of lymphoid tissue within the framework of local and systemic immune reactions. In chronic rhinitis of vasomotor or atrophic origin the administration of cryotherapy to the nasal mucosa activates the regenerative processes and like previously triggers a cyclic reaction lasting for 4 to 6 weeks.

In this situation the following therapeutic mechanisms of action can be observed:

1. Restoration of normal trophism via germination of new nerve fibers and the corresponding receptors in the nasal mucosa, one of the important receptor areas in the body
2. A noticeable hyposensitization effect
3. A stimulating effect on the organism
4. Restoration of nasal breathing
5. The improvement of afferent innervation in the nasal mucosa stimulates the trigeminal nerve, thus restoring the normal function of the higher vegetative nervous centers.

Regenerative Cryotherapy is also used for the treatment of snoring and sleep apnoea. Snoring is caused by vibration in the lower part of the throat. It occurs when the soft palate and uvula have lost their muscle tone and become inelastic. The sleep apnoea syndrome manifests itself as a brief respiratory standstill caused by the irritation of reflexogenic areas; this irritation is attributable to a loss of muscle tone in the soft palate and uvula allowing these structures to slip down into the lower part of the throat.

The reflexogenic areas of the throat constitute a nerve plexus, the plexus pharyngeus consisting of the sensory and motor fibers of the glossopharyngeal nerve, the vagus nerve and the sympathetic nerve. The glossopharyngeal and vagus nerves play an important role in the pathogenetic mechanism responsible for the sleep apnoea syndrome since they innervate the middle and lower part of the pharyngeal space. The vagus nerve is also responsible for the innervation of the larynx and its muscular apparatus. When the soft palate and the uvula slip down into the pharyngeal space, they are recognized as foreign bodies and thus cause an irritation of the reflexogenic areas in this space. Protective reflexes are activated, the glottis seizes up and

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respiration stops. Owing to the resulting oxygen deficit, however, the vocal cords open again and respiration resumes.

Possible causes of the loss of muscle tone in the soft palate and uvula include special anatomic features in certain individuals. However, it is more commonly caused by inflammatory dermopathic processes in the tonsils, pharynx and nasal cavity. As the name suggests, the application of regenerative cryotherapy to the muscles of the soft palate and uvula activates regenerative processes and improves the contractibility of the muscle fibers. The normal muscle tone of the soft palate and uvula is restored: these anatomic structures are again held in place from above and vibration stops. The most important result, however, is that the patient stops snoring and the reflexogenic areas of the pharynx are no longer irritated. In short, the patient has been cured of the sleep apnoea syndrome.

Regenerative cryotherapy can be employed to:

1. stop snoring and sleep apnoea
2. restore nasal breathing
3. reinstate the protective function of the lymphoid tissue in the tonsils and lymphoid follicles (Waldeyer's throat ring)
4. stimulate immune processes
5. eradicate chronic foci of infection in the tonsils, pharynx and nose, there by preventing complications or sequelae 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 immunodeficiency disorders.

Prophylactic treatment of the lymphoid tissue of the tonsils, pharynx and nasal mucosa using the method of regenerative cryotherapy would lead to improvement of the protective functions of the organism and stimulation of the immune system particularly in children. We can assume, moreover, that the general risk of contracting systemic, rheumatoid, infectious allergic and oncological diseases, immune deficiency states, snoring and sleep apnoea would be distinctly reduced. Monitoring of the cooling parameters is an important point to be observed during regenerative cryotherapy since achievement of the desired therapeutic effect depends directly on

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these parameters.

On the basis of my extensive experience with cryotherapy, I have designed and patented (German Patent Office in Munich 1993) a mobile cryotherapy unit suitable for use in medical practices. With the aid of this unit, it is possible to keep tissue cooling under control, especially in the ears, nose and throat regions.

It is evident from the above discussion that cryotherapy offers a viable alternative to radical surgery and the removal of tissues and organs it usually involves. For this reason, we should publicize the benefits of cryotherapy and add it to the arsenal of methods we use in our medical practices daily. With its regenerative effects, cryotherapy opens up vistas for an alternative direction in medicine, namely regenerative medicine.

## Section 2 Original Articles

### Cryosurgery in a Specialised Gerontological clinic



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Some patients may require radical treatment but if they are elderly they may have some contraindications such as, multiple pathology, cardiovascular disease, diabetes mellitus or complicated with angiopathia. Also wound healing and poor post operative reparation are slower for elderly people. These factors can decrease the quality and length of patients life. Alternatives to radical surgery are needed and cryosurgery is a mild form of tissue destruction, which avoids pain and bleeding. It produces a locally necrotised centre followed by regeneration (8-12). The surrounding healthy tissues are not altered and cryosurgery can be considered as "physical extirpation" (4) The development of cryosurgery techniques has followed to the availability of cryogens. The first cryosurgery was carried out with ice, salt or Co2 and snow (1), but liquid nitrogen (B.P -195.6 C) is more commonly used today. The first automatic cryogenic system was developed by the American surgeon I. Cooper in 1961 for use in neurosurgery (13) In Russia, the application of cryosurgery to neurology where initiated by Kandel in 1962. Cryosurgery has been sucessfully used in paediatrics, paediatric surgery, otorhinolaryngolgy, ophthalmology, urology, oncology, dermatology and cosmetology. (1-12) The application of cold has two main effects a destructive one, used on pathological tissues and a stimulation effect providing protection of surrounding tissue. Repair to necrotised regions is rapid and rough scars tend not to develop. Rapid repair is an important factor in the treatment of elderly patients. Cryosurgery also has a beneficial effect on pathogenic microflora. The treatment can be carried out in an outpatient department, there are very few side effects and anaesthesia is not required. These factors have led to the setting up of a cryosurgery department with the geriatric department of a multispeciality hospital. Patients are referred from surgical, dermatological, gastroenterological, gynaecological, pulmonological, ophthalmological and otolaryngology departments with pathological neoplasms. Cryosurgery is also carried out during some surgical operations. Cryosurgery has been used in the hospital since 1976

### Materials and methods

We have examined the records of 19,941 patients (60-90 years) treated between 1976 and 2000. Patients were treated with a cryodestructor KR-02, an applicator designed by Shalnikov and a MAK-1 developed by Repnikov and Shafranov. We also used a range of applicators and tips designed by Mezhov-Deglin (6). All the devices used liquid nitrogen. The tumours were frozen for 3-10 minutes, depending on their size, with 1-3 freeze-thaw cycles. Patients received 1-5 treatments and biopsy was carried out in all cases. After cryosurgery the surface was treated with 71% spirit and potassium permanganate solution.

### Results and discussion

The group of patients with malignant skin lesions, mainly basal cell and plane cell cancer, showed complete destruction of the neoplasm and formation of tender scar tissue.

1) Malignant skin tumours. Patients with basal cell cancer of the face showed localised destructive growth affecting the nose, jaws, eyelids and ears. Cryosurgical treatment showed complete destruction of the neoplasm and formation of scar tissue. No post-operative complications were found and patients were followed up for 3-5 years. Patients with plane cell cancer localised to the face, ears and skin of lower extremities showed complete destruction of the neoplasm with a thin atrophic scar. Patients were followed up for 5 years. Patients with melanomas also showed complete destruction of the tumour and regenerated skin or soft atrophic scar.

2) Benign skin tumours. Patients underwent 2-3 sessions of cryosurgery and in all cases good surgical and cosmetic results were obtained with either no scar or atrophic scar

3) Patient with purulent disease and trophic ulcers. Patients carbuncles, abscesses, furunculosis and hidradenoma showed necrosis and separation of the capsula, replacement with granulate tissue and formation of atrophic scar. Cryosurgery was also used for patients with non-healing wounds prior to plastic surgery.

4) Ear, Nose and Throat Organ. Complete regeneration of mucous membrane was found after cryotreatment. Patients with Randu-Ossler disease showed

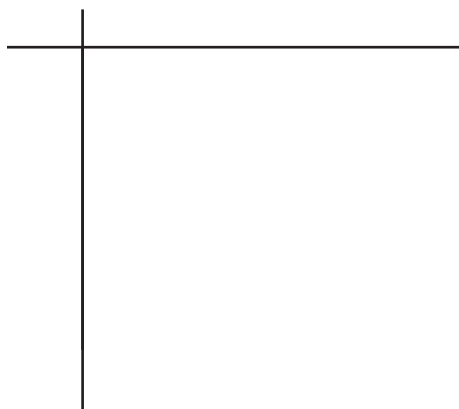
absence of nose bleeding during 3-5 year follow up.

### Conclusion

Cryosurgery provides an effective, painless easily performed method for treatment of ontological disease in the elderly without bleeding cryosurgery destroys neoplasms and results in skin regeneration that is indistinguishable from surrounding skin or atrophic scar. This is an important factor in the treatment of elderly where skin healing can be very slow. Cryosurgery is also beneficial in treating patients with diabetes mellitus and inflammatory wounds. Cryosurgery is very important treatment of patients for whom traditional surgery is contra-indicated and provides minimal operative risk and post-operative complications. The authors are grateful to Prof. V.V. Shafranov for many valuable discussions and to Dr. E.N. Borkhounova for her help with preparation the paper.

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## Section 2 Original Articles

### Cryosurgery and Radiofrequency in the treatment of the Invasive Feline Nasal Carcinoma

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The conventional treatment of this condition has yielded poor results. Invasive growth develops actively from ulcerated lesions and expands through mucosa onto nasal cavity, affecting cartilage, facial muscle and the membranous septum. Active multiplication, leads to tissue loss due to onconecrosis and it is difficult, if not impossible to distinguish the boundaries of the tumour and define the transition zone between normal and affected tissue.

Acting fast is essential, some tumours are so aggressive that it takes only 15 days to turn an initially limited surface structure into a larger and more extended one.

The nasal mucosa is known to be highly susceptible to invasion. The range of application of radiofrequency and cryosurgery is upto 2mm from the visible edge of the nose.

#### Procedure

After Anaesthetising the patient, its skin has to be very well moistened prior to the radiofrequency treatment. In ulcerated lesions, a Vari tip electrode and cutting current intensity, are used to defined the volume and shape of the tumour.

A triangular or oval loop, and the same current intensity are used to obtain material for biopsy. Then the tumour is removed by means of **Laminar dieresis** with circular movements. Dorsal and secondary nasal cartilage are dried out, and th inner folds of the nasal conducts are exposed. Hemorrhage is controlled using clamps and haemostasia is acheieved by means of a ball electrode and partially screened clotting current.

In exophytic lesions, the tumour is removed using circular loop as well as cutting the clotting and current intensities.

Cryosurgery, is applied in 3 freeze-thaw cycles using the spray cone technique with a 3mm safety margin.

If tumour resection is funnel shaped, first the deep central region is forzen using a conical contact point, carefully keeping the cold halo (ice ball) under

## Section 2 Original Articles

control. Leaving the point cryo adhered to the lesion, the remaining part is frozen using the spray cone.

Haemorrhage in thawing time is controlled by compression or using the radiofrequency ball electrode. After recovering from the effects of anaesthesia the patient returns home, but most come back for examination one and two weeks after the operation; tissue healing is controlled in 30 and 40 days the patient is finally discharged 6months later.

Owners are warned that this condition is frequently recurrent and that they should consult as soon as they notice any changes in colour aspect or shape of the treated area.

This treatment should not be used on cats suffering from invasive carcinoma affecting the ventral area of the phyltrum and/or the skin at the bottom edge of the upper lip.

The best results are obtained in unilateral lesions. The combination of radiofrequency and cryosurgery allows the treatment of patients that would otherwise face euthanasia. This method is simple and can be carried out in any surgery.

## Section 3 Recent Publications

**Initial experience of percutaneous renal cryosurgery under the guidance of a horizontal open MRI system.** Harada J, Dohi M, Mogami T, Fukuda K, Miki K, Furuta N, Kishimoto K, Simizu T, Miyasaka K. Radiat Med 2001 19(6):291-6

Study demonstrates preliminary results of cryoablation of renal tumors using a percutaneous approach, guided by a horizontal open MRI system, and assessment of the safety and efficacy of this procedure. Four patients with renal tumors underwent percutaneous cryosurgery with local anaesthesia. Growth of the iceball during cryoablation was monitored by two-dimensional MR images. The size of the mass was 4 cm or less in diameter and a 2- or 3-mm cryoprobe was advanced into the renal mass under real-time MR monitoring. Iceball growth was monitored by two-dimensional MR images. Dynamic CT and physical examination follow-ups were done after two weeks and six weeks. MR imaging demonstrated the iceballs as sharply marginated regions of signal loss that expanded and engulfed the renal mass. There were no serious complications and no clinically significant changes during the procedures and follow-up study. In conclusion this limited intraprocedural MR-guided cryosurgery can be used as a safe modality, although further studies are essential to determine the long-term efficacy.

**Bone grafting of cryosurgically treated bone defects: experiments in goats.**

Keijser LC, Schreuder HW, Boons HW, Keulers BJ, Buma P, Huiskes R, Veth RP. Clin Orthop 2002 Mar;(396):215-22

It is hypothesized that cryosurgically treated bone defects are inappropriate host sites for cancellous bone grafting. Gap defects of long bones was investigated in goats. Bone strength and graft incorporation in the goat was studied by conducting in-vivo experiments. Liquid nitrogen cryoprobe was applied to 62 goats, to the cylindrical defect lining of the femoral diaphysis. Two groups of goats. Thirty one goats received an impacted, morselized, cancellous bone graft harvested from the sternum. The remaining 31 goats served as controls. At 0, 4, 7, 10, 13, 16, and 26 weeks animals were euthanized and the femurs were evaluated for torsional strength, computed tomography, and histologic assessment.

No significant increases were seen in torsional strength in specimens with a bone graft compared to the controls (inc. time). Bone grafting does not accelerate healing of cryosurgically treated, stable, diaphyseal defects in the goat.

## Section 3 Recent Publications

**Percutaneous renal cryoablation of renal tumors in patients with von Hippel-Lindau disease.** Shingleton WB, Sewell PE Jr. J Urol 2002 Mar;167(3):1268-70

This clinical work provided excellent result, and determines the feasibility and safety of performing percutaneous cryoablation of renal tumors in patients with von Hippel-Lindau disease. Results were rather interesting in this initial trial. 2 men and 2 women with von Hippel-Lindau disease and radiographic determined solid renal tumors were selected to undergo percutaneous cryoablation.

The procedure was performed with a 2 or 3 mm. cryoprobe using a pressurized argon gas system for ice ball formation. Over night hospitalization required for observation. A follow up at 1 week, 1, 3, 6 and 12 months and every 6 months thereafter, along with a physical examination. A total of 5 tumors were treated ranging from 2.8 to 5.0 cm. in diameter. 2 patients required re-treatment due to residual tumor for a total of 7 treatments. There has been no radiographic evidence of recurrence at the cryoablated areas in a followup from 2 to 23 months. Percutaneous cryoablation of renal tumors in patients with von Hippel-Lindau disease proved to be successful.

**Phase I study of percutaneous cryotherapy for colorectal liver metastasis.** Huang A, McCall JM, Weston MD, Mathur P, Quinn H, Henderson DC, Allen-Mersh TG. Br J Surg 2002 Mar;89(3):303-10

This study was conducted to determine the safety and feasibility of percutaneous cryotherapy for treating irresectable colorectal liver metastases. Fifteen patients received 25 single-probe treatments and seven patients received 14 dual-probe treatments. Results showed very interesting findings. Treatment related mortality rate was zero. Dual-probe delayed liver metastasis growth for 2 months but nothing was observed for single probe treatment. It was evident after looking at serum CEA levels that dualprobe treatment had upregulated immunity. In Conclusion, Percutaneous cryotherapy for treatment of colorectal liver metastases is feasible and may produce excellent results in combination with chemotherapy.

**Cryosurgical treatment of genuine trigeminal neuralgia.**

Pradel W, Hlawitschka M, Eckelt U, Herzog R, Koch K. Br J Oral Maxillofac Surg 2002 Jun;40(3):244-7

## Section 3 Recent Publications

This article discusses a newly developed cryoprobe for peripheral nerves allowing surgeons to freeze branches of the trigeminal nerve at the infraorbital or the mandibular foramen without nerve exposure or damaging surrounding tissue. This cryoprobe was used in 19 patients inserted transmucosally to freeze the infraorbital nerve or the inferior alveolar nerve. Sensitivity returned in the treated nerve at four - eight months following cryotherapy . Pain was absent for at least 6 months followed by recurrence of pain in 13 of the patients within 6-12months. repeat procedures were not an issue due to the simplicity of the procedure.

### Focal "nerve-sparing" cryosurgery for treatment of primary prostate cancer: a new approach to preserving potency.

Onik G, Narayan P, Vaughan D, Dineen M, Brunelle R. Urology 2002 Jul;60(1):109-14

A Clinical study with 9 patients treated with focal, unilateral nerve-sparing cryosurgery with a 6 year follow up. Cryosurgery, in which the whole gland is frozen, has a high rate of impotence, similar to non-nerve-sparing radical prostatectomy. Prior to focal nerve-sparing cryosurgery, all patients underwent repeated biopsy on the side opposite the previous positive biopsy. A 22-gauge spinal needle was placed into Denonvilliers fascia using a transperineal route with saline was injection to separate the rectum from the prostate. In all patients postoperatively, combined hormone therapy was stopped . The prostate-specific antigen (PSA) level was obtained every 3 months for the first 2 years and then every 6 months thereafter. Between June 1995 and November 2000, 9 patients underwent focal, nerve-sparing cryosurgery.follo up of 6 to 72 months (mean 36). Stable PSA levels where seen in the last follow up. Six patients routinely biopsied had negative biopsies. Potency was maintained in 7 of 9 patients. Focal nerve-sparing cryosurgery, appears to preserve potency in most patients without compromising cancer control. These preliminary results allow for further studies to be conducted.

### Cryoneuroablation for pain in a 12-year-old girl.

Weber BA, Farran P, Donnelly BJ, Saliken JC. J Pain Symptom Manage 2002 Mar;23(3):180-1

**Current developments and uses of cryosurgery in the treatment of keloids and hypertrophic scars.** Zouboulis CC, Zouridaki E, Rosenberger A, Dalkowski A., Wound Repair Regen 2002 Mar-Apr;10(2):98-102

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