

Cryo-recanalization - a new method

The characteristics of this probe in comparison to the cryotherapy probe are a greater stability to traction (up to 50 Newtons), greater freezing power due to a larger surface area of the probe tip, a hydrophilic coat and a bend protection at the proximal end of the probe.

Patients, Materials and Methods

After favorable pre-study results with cryo-recanalization we evaluated the feasibility of immediate airway recanalization with the newly developed probe in a prospective study.

Patient inclusion criteria were as follows:

- * High-grade stenosis in the area of the central respiratory tracts with clinical symptoms (dyspnoea or post-obstructive pneumonia)
- * Stenosis or closure of a lobe or segment bronchus with post-obstructive pneumonia
- * No visible tumor attachment to large vessels at the recanalization site on a pre-treatment CT-scan of the thorax and finally
- * A normal thrombocyte count and normal plasma clotting

From January 2002 until January 2003 80 patients who presented at our department were initially evaluated, 48 fulfilled all inclusion criteria, all were offered the experimental protocol, 42 patients (age 23 to 81) were included in the case series. The etiology of airway obstruction was bronchiogenic carcinoma in 34 patients, metastasis of renal cell carcinoma in 1 patient, bronchial lipoma in 1 patient, metastases of carcinoma of the colon in 2 patients, bronchial carcinoid in 2 patients, benign granulations due to tracheal stents in 1 patient and malignant lymphoma in 1 patient. Sites of airway obstruction were trachea in 5 patients, main bronchus in 15 cases, upper lobe bronchus in 8 patients, intermediate bronchus in 6 patients, middle bronchus in 1 patient and lower lobe bronchus in 7 cases. Cryo-recanalisation was performed by flexible bronchoscopy with an Olympus bronchoscope. All patients were intubated with a Bronchoflex® tube (Rüsch GmbH, Germany). Oxygen (6-12 l/min) was continuously insufflated through this tube. The procedure was performed under sedation with Propofol (total dose 200-1200 mg), with spontaneous respiration. Patients were monitored by continuous pulse oximetry, ECG and measurement of blood pressure every 2 minutes. 4 patients required temporarily a Dopamine infusion for arterial hypotension.

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The cryoprobe, guided through the working channel of the bronchoscope, was placed inside the tumor (1-2 cm). The probe tip was then cooled for 5-20 seconds. In most cases, freezing of the tumor tissue was endoscopically visible. Control of the "ice front" allowed good assessment of the local extension of tissue freezing. Before the ice front reached the healthy bronchial wall, frozen tumor tissue was extracted from its surrounding tissue by pulling gently on the probe. Together with the bronchoscope, the tissue stuck to the tip of the cryoprobe was pulled out of the respiratory tract. Frozen tumor tissue was then released from the probe tip by thawing in a water bath. The aim of the intervention was to repeat this procedure until no relevant stenosis from the tumor remained. Mild bleeding around the site of removal of the tumor was treated by topical application of epinephrine. More intense bleeding was treated with argon plasma coagulation.

Results

The procedures lasted for between 4 and 54 minutes (22±19). Treatment success in our patients was independent of the tumor etiology and independent of the localisation of the stenosis. Complete recanalization was achieved in 30 patients. 6 Patients exhibited residual stenosis which were easily passable with a bronchoscope. Their treatment was rated as partially successful. In 6 patients (14%), treatment was not successful. Tumor closures in these patients turned out to be too extensive. None of the patients died during the procedure and during a time interval of at least 30 days after therapy. Rigid bronchoscopy to treat bleeding or other complications was not needed in any of the patients. No patient had to be put on mechanical ventilation after the procedure. 6 patients developed more intense bleeding (total blood loss 100-300ml) at the site of tumor adhesion after removal of tumor tissue. In all of these cases, bleeding could be controlled with suction with the flexible bronchoscope and was stopped by using an argon plasma coagulator in flexible technology.

Comments

Cryo-recanalization with a newly developed probe was immediately effective in 86% of all patients, re-canalization was feasible in flexible technology, afforded no general anesthesia and turned out to be safe. 36 Patients exhibited light bleeding which stopped spontaneously within a couple of minutes. 6 Patients developed medium grade bleeding at the site of tumor adhesion after removal of tumor tissue. In all of these cases, bleeding could be controlled with suction with the flexible bronchoscope and was stopped in all patients by using an argon plasma beamer and flexible technology.

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Cold causes vasoconstriction and capillary microthromboses in the border area between frozen and non-frozen tissue.[5] These effects likely contribute to the low rate of bleeding complications with this method. Visual control of the ice front is possible while the tissue is being frozen and this allows a relatively reliable assessment of the depth of action. The rate of advance of the ice front decreases after longer times of freezing, providing an additional safeguard against accidental freezing of healthy tissue. Accidental freezing of larger rings of cartilage is recognizable, as the probe cannot be removed from the bronchus, even if it is pulled very strongly. At the end of the freezing process, the probe can then readily be released from the bronchial cartilage.

On the basis of our current experience with 48 patients, rigid bronchoscopy is not necessary, but should be kept immediately available for potential complications with this new method. To our knowledge, this is the first feasibility study with cryo-recanalization in patients with respiratory tract stenosis due to exophytic tumors. Still, future studies are still needed to compare this novel technique with other recanalization methods.

In comparison to other recanalisation methods, cryo-recanalisation is the most inexpensive of all recanalization methods, since the total therapeutic system can be purchased for around □7000.

In summary, cryo-recanalization treatment with the newly developed probe is a feasible technique and may offer many advantages in the interventional therapy of stenosing exophytic tumors of the respiratory tract: use of flexible technology, immediate effectiveness, low risk of complications and low costs in comparison to other recanalization methods.

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Cryo-recanalization - A new approach for the immediate management of acute airway obstruction

Martin Hetzel, Alexander Babiak, Christian Schumann, Nikolaus Marx, Juergen Hetzel

Department of Internal Medicine II - Pulmonary Medicine, University Medical Center Ulm, Robert- Koch St. 8 89081 Ulm, Germany.

Email: martin.hetzel@medizin.uni-ulm.de



Key words: Cryosurgery, cryoprobe, cryo-recanalization, lung cancer

Introduction

Currently, effective methods for the treatment of stenoses and closures of the respiratory tract from exophytic tumors include laser therapy with the Nd-YAG laser, mechanical recanalization (rigid bronchoscopic debulking), photodynamic therapy (PDT) and cryotherapy.[1,2,3] Disadvantages of these methods include the necessity of clean-up bronchoscopy to remove tumor necrosis or fibrin membranes (laser therapy, PDT, cryotherapy) the necessity of a primary procedure with rigid bronchoscopy in total anesthesia (laser therapy, mechanical recanalization), the lack of immediate effectiveness (cryotherapy, PDT), as well as high therapeutic costs (PDT) [1,2,3]. Endobronchial cryotherapy with its application of extreme cold to induce tumor necrosis is an established method in interventional pulmonology. However, previous applications of cryotherapy have not been immediately effective, requiring a second clean-up procedure several days later to finally obtain sufficient recanalisation [4]. For overcoming the lack of immediate efficacy we tried to immediately extract tumor tissue with the flexible probe after tumor freezing. We refer this new application of low temperature as cryo-recanalization. After guidance of the flexible probe through the working channel of the bronchoscope, placement of the probe tip inside the tumor, cooling of the probe for 5-20 seconds, we tried to extract tumor tissue stuck to the tip of the probe together with the bronchocope. Using commercially available flexible cryoprobes we faced a lot of difficulties: low freezing power, lack of stability to traction, dislocation of the central gas channel from the probe tip and difficult guidance of the probe inside the working channel of the bronchoscope. In cooperation with ERBE Germany we developed a new cryoprobe.

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Table 3

Operation	Cause of death			Total deaths
	HCC	Liver failure	Other	
Resection	4 (365 ± 410)	3 (28 ± 21)	2 ^a (119 ± 34)	9 (198 ± 314)
Cryotherapy	6 (781 ± 623)	0	3 ^b (1310 ± 922)	9(956 ± 778)
Resection & cryotherapy	2 (323 ± 72)	4 (357 ± 354)	1 ^c (273)	7 (335 ± 272)

Data are number of cases and mean survival in days ± SD

^a Pneumonia, septicemia. ^b Acute myocardial infarction, acute renal failure, pulmonary complications from radiotherapy. ^c Bowel obstruction

Table 4

Test	Resection (mean ± SD)	Cryotherapy (mean ± SD)	p
Serum albumin (g/L)	35.89 ± 5.11	40.22 ± 4.27	0.0691
Bilirubin (µmol/L)	14.44 ± 8.79	14.89 ± 7.64	0.910
PT (seconds)	12.71 ± 1.976	13 ± 1.87	0.805

Table 5

Test	HCC deaths (mean ± SD)	Liver failure deaths (mean ± SD)	p
Serum albumin (g/L)	39.72 ± 3.26	35.7 ± 5.28	0.1050
Bilirubin (µmol/L)	13.18 ± 6.19	17 ± 9.92	0.386
PT (seconds)	12.71 ± 1.60	14.71 ± 2.69	0.1227

Legend

Figure 1:Kaplan-Meier survival curves of HCC patients treated with resection (n=17) or cryotherapy (n=15).

Table 1:Demography of HCC patients treated by resection or cryotherapy

Table 2:Peri-operative co-morbidity and 30-day mortality rates

Table 3:Cause of death & survival for HCC patients. UNSW Department of Surgery 1990 2001

Table 4:Pre-operative liver function of HCC patients who died following resection or cryotherapy

Table 5:Pre-operative liver function in patients who died from HCC or liver failure

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Figure Legend

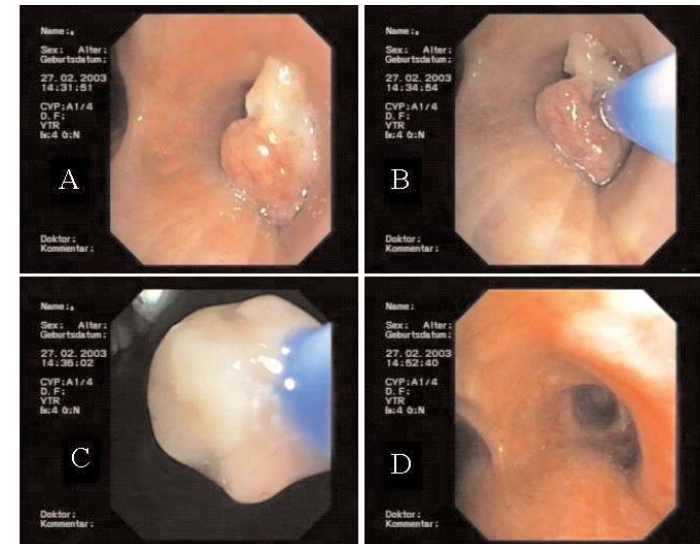
Fig 2A: Exophytic tumor in the right main bronchus

Fig 2B: Freezing the tumor with the cryorecanalization probe

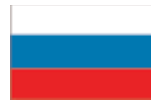
Fig 2C: Extraction of tumor tissue

Fig 2D: Right main bronchus after cryo-recanalization

Figure



Cryosurgical treatment of pelvic tumors



Prokhorov G.G., Zhirnovoy V.M., Prokhorov D.G., Zharinov G.M.
 Clinical Hospital of Russian Academy of Sciences.
 194017, pr. M.Toreza 72.. E-mail: gprokhorov@mail.ru
 Central Research Institute of Roentgenology and
 Radiation Therapy 189646, Leningradskaya str. 70/4. St
 Petersburg, Russia. E-mail: prokhor_off@mail.ru

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Introduction

Treatment of patients with tumor of rectum, cervical or uterus in early phase of the disease includes eradication of the primary tumor. (1-8) Unfortunately, about 75% of patients at initial registration have 3rd and 4th stage of the disease, and the share of radical interventions usually does not exceed 42%. About 30% of primary registered patients with a cancer of the pelvic organs die within the first year of monitoring. For example 40-60% of the patients undergoing operations for cancer of the rectum die from local relapse and the five years' survival rate varies from 40 - 50%.

There are many technical difficulties during operations where the tumor spreads into iliac veins, pelvic muscles or bone structures. Refusal of operation, in turn, makes ineffective the courses of chemotherapy, practically depriving doctors the opportunity to counteract further progression of the disease.

Similar complexity is represented with cases in the occurrence of local relapses of the disease after extirpation of pelvic organs. Implantation metastases, as a rule spread into the whole wound cavity and have a difficult configuration and significant depth, and extended into the pelvic fat and large vessels.

Involvement of ureters results in the development of hydronephrosis and renal insufficiency which can lead the clinical course to a terminal phase. At the same time, at colorectal localization of the cancer tumor, the distant metastases seldomly appear and, thus, are not always factors that determining the outcome of the disease.

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Table 1

Indicator	Resection only (n=17)	Cryotherapy only (n=15)	
	median (upper, lower quartiles)	median (upper, lower quartiles)	p
Age	63, range 25-76	65, range 49-75	0.10
Tumour diameter (cm)	7.5 (9,5.5)	4 (4.5,3.4)	<0.001
Preop AFP (kU/L)	71 (536,6)	18 (339,5)	0.832

Table 2

Indicator	Resection (n=17)	Cryotherapy (n=15)	
	median (upper, lower quartiles)	median (upper, lower quartiles)	p
Admission days	19 (21,16)	11 (13,7)	0.064
Packed cells transfusions (units)	6 (9,3)	0 (0,0)	0.006
Post-operative death ^a	3 ^b	0 (0,0)	0.206

^a There were 2 postoperative deaths in the patients who had both resection & cryotherapy.

^b There were 2 deaths from liver failure and 1 from HCC

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Cryosurgical treatment of pelvic tumors

Patients and methods

Within last 7 years, 14 patients with pelvic tumors, comprising of 8 women and 6 men were treated in our clinics. Amongst these the distribution was - 4 patients with recurrent tumors after anterior intrapelvic resection of the rectum; 3 patients with relapses of a tumor after abdominoperineal extirpation; 3 patients (T4N0-1M0) with initial anal tumors spreading into walls of a pelvis; 2 patients (T3b-T4N0-1M0) with cervical tumors; 2 patients (T4N0-1M0) with hormone resistant prostate cancer. There were no distant metastases in any of the cases. Duration of the disease and previous treatment varied from 8 to 18 months. 11 patients received before cryosurgery adequate treatment, including surgery, sometimes repeated, radiation therapy and regional or systemic chemotherapy.

Our patients were at disease stage where opportunities of treatment at the previous stages were exhausted. After admission to hospital all patients received various surgical interventions with application of the cryoablation of a tumor using cryounit LCS-3000 (firm Candela, USA). Operations were performed in variant only cryoablation of a tumor with use of a shaft or contact cryoprobe of various diameter, and in expanded. Cryodestruction of tumors was carried out by the open or percutaneous approach under visual and (or) ultrasonic control. In all cases the thermometry of a zone of operation was applied. The expanded volume of operation included single-lumen colostomy, ureterolysis and internal stenting of the ureters.

7-10 days after the cryoablation we carried out necrectomy by the line of cryonecrosis. Operations were performed under intravenous anesthesia, with little or no bleeding. 7 days after the necrectomy 11 patients were discharged from the hospital for ambulatory treatment with the control examination at two months. In three cases reconstructive interventions were carried out for closing large intrapelvic cavities formed after cryosurgical removal of the tumor. As a plastic material we used uterus, musculus adductor longus, musculus semimembranosus, semitendinosus and musculus obturatorius internus. Replacement of the femoris muscles always requires the necessity of repeated inspections of the zone of operation and performance of secondary surgical procedures of cavities. Musculus semitendinosus appeared the most vulnerable for secondary necrosis due to the distal arrangement of neurovascular bundle.

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In one case in connection with full destruction of musculus obturatorii and musculus levator ani, we were compelled to perform osteotomy of the anterior surface of the sacrum for fixing muscles to the spongy part of the bone for the maintenance of adequate blood supply and the subsequent fixing of the transplants.

Moving muscle complexes (musculus adductor longus, musculus semimembranosus, semitendinosus, musculus obturatorius internus) did not result in any infringements in function of the lower limbs. Less volumetric transplantations also were not accompanied by infringements of static function and movements of the lower limbs.

It is necessary to note, that the reason for constriction of the distal part of the ureters in one case was due to the direct spreading of the tumor into the wall of the left ureter in place of its transition from parietal to visceral part. Performance of the cryoablation in this case resulted in destruction of the medial wall of the ureter and formation of an incomplete uric fistula opening in a perineal wound. The patient easily adapted for inconveniences accompanying such complication although refused repeated operation within the next two years of life.

Results

Results of treatment have shown, that life expectancy of patients which in similar cases seldom exceeds 6 months, has an average of 18 months. 2 patients are still alive and disease-free to date.

Thus, in the definition of life expectancy in the given group, this included two lethal outcomes within 2 months after the cryoablation of the tumor. In one case the reason for death of the patient with advanced prostate cancer spreading into the rectum was urosepsis owing to formation of the urethrorectal fistula in the zone of operation and occurrence of infection of the ascending urinary prompted by the intensive chemo- and hormonotherapy. In the second case the patient died from wound and cancer exhaustion on a background of the intestine fistula.

Discussion

Cryogenic treatment is widely applied in the treatment of pelvic tumours (9-12). However, at the 4th stage of the disease, the radicalism of undertaken intervention has relative character and cryoablation of tumors in the majority

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(with a 1cm margin on each side) was the treatment of choice for tumours up to 5cm in diameter, but it is avoided in larger HCCs because of technical difficulty in achieving an adequate size cryolesion and poorer results in our colorectal cancer liver metastases with larger lesions [27]. It has also been advocated for unresectable tumours (e.g. proximity to intrahepatic vessels or multiple bilobar lesions) and is used at inadequate or involved resection margins [6].

Although cryotherapy has an operative mortality rate of 1.6% [11], it is associated with a morbidity rate of 50%. The complications are volume-related and include hypothermia with an associated coagulopathy, cardiac arrhythmias, cracking of the liver capsule, pleural effusion, subphrenic or hepatic abscess, biliary fistula, increase in liver transaminases, myoglobinuria, acute renal failure and cryoshock. None of our patients developed cryoshock. In our unit, liver resection has been mostly performed for large tumours that are unsuitable for cryotherapy or alcohol injection. Resection for HCC in cirrhotic liver is well established to be of much greater risk than in normal liver but an operative mortality rate of less than 5% has been described in specialised centres [13]. Operative mortality does not correlate with tumour diameter, but is closely related to pre-operative liver function tests, which are a measure of functional liver reserve and cirrhosis [14,15]. Although survival in our study is apparently better with cryotherapy, this is likely to reflect the effect of tumour diameter on outcomes, as the cryotherapy group had smaller tumours. However the risk of death should not be greatly affected by tumour size, and the reduced peri-operative mortality rate seen with cryotherapy in this series is important.

Until recently, resection and orthotopic liver transplantation (OLT) were the only treatments shown to be curative for HCC [16-19]. The major criteria for OLT are solitary lesions < 5cm in diameter or fewer than three tumours each < 3cm in diameter. Other factors associated with a good outcome after OLT are low serum AFP and the absence of vascular invasion [20-22]. OLT is limited by the shortage of available livers and the cost of the procedure. The operative mortality rate for OLT is about 20% [23,24]. OLT thus has a role in those patients with poor liver function but good prognosis tumours [25,26]. OLT is not available at our Centre. Our results suggest that cryotherapy can be used with good peri-operative safety & long term survival in tumours too large for alcohol injection.

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has the palliative character (13-15). In some cases, the inefficiency or contraindications to application of traditional methods of treatment, such as surgery, chemotherapy and radiation compel physicians to resort to cryosurgery. Thus, cryoablation is actually the last hope of the patient for healing or improvement of quality and life expectancy [16, 17]. As a rule, candidates on the surgical treatment are weakened, in most cases the elderly patients receiving up to it combined methods of therapy [18, 19]. We believe that application of the cryoablation of the tumor for the given heavy category of patients is reasonable. The positive moments of the treatment are removal of a painful syndrome and bleeding, elimination of cancer intoxication, improvement of quality and life expectancy [19-21].

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probes [8-10]. The senior author has experience of liver resections in 560 patients, and cryoablation in 285 patients.

Results for the two groups were compared using the unpaired t-test, Fisher exact probability test, and the Mann-Whitney U test. The Kaplan-Meier method was used to assess survival in the two groups.

Results

There were 43 HCC patients who underwent resection or cryotherapy. Of these, 17 had resections, 15 had cryotherapy, and 11 had both treatments (for synchronous multiple lesions). Seventeen patients remain alive, one patient is lost to follow-up, and 25 have died. Men made up 76 percent of the resection group and 93 percent of therapy cryotherapy group.

Tumour size was much larger in the resection group (mean 14.7cm, median 7.5cm) compared with those treated with cryotherapy (mean 3.99cm, median 4cm). Other differences between the two groups are shown in Table 1. Peri-operative indicators including hospital admission days, blood transfusion units and postoperative mortality are given in Table 2; admission days and blood transfusion units were less in the cryotherapy group ($p=0.064$, $p=0.006$ respectively). There were no post-operative deaths in the cryotherapy group and three post-operative deaths in the resection group.

There was no statistically significant difference in survival between the resection and cryotherapy groups ($p=0.3$), log rank. The causes of death in the two groups are described in Table 3. There were no deaths from liver failure in the cryotherapy group, but three patients died from this cause in the resection group.

Pre-operative liver function tests for the two groups are shown in Table 4. Serum albumin was lower in the resection group, although not significantly so. The serum bilirubin and prothrombin time were almost identical, therefore peri-operative morbidity and mortality might well have been expected to be similar. Regarding liver function in the patients who died of HCC and liver failure, there was no significant difference in serum albumin, bilirubin, and prothrombin time (Table 5).

Discussion

Selection for the different treatment options at our hospital was primarily based on tumour size. Very small tumours (< 2cm in diameter, recently revised to 3cm) were generally treated with percutaneous ethanol injection. Cryotherapy

Original Articles

Comparison of resection and cryotherapy for HCC

Introduction

Hepatocellular carcinoma (HCC) is a common and increasingly important cancer which is responsible for approximately one million deaths per year [1]. For small tumours, treatment with alcohol injection has been associated with good results [2,3], but for larger tumours resection has been the only potentially curative procedure to date. Resection of HCC is much more dangerous because of the risks of liver surgery in cirrhotics [4].

Cryotherapy has been extensively used for the in-situ imaging-controlled destruction of liver tumours, mainly metastases secondary to colorectal cancer [5,6], but there are also reports of its use in the treatment of HCC [7]. The advantage of cryotherapy in HCC is that extensive parenchymal resection is not required.

At present, there have been no studies comparing outcomes from resection and cryotherapy for patients with HCC. This report compares results in HCCs in our liver unit from 1990 to 2001.

Method

The database contained 1962 patients with liver tumours and of these, 186 were diagnosed with HCC and presented for treatment between 1990 and 2001. Forty-three of the 186 primary HCCs were treated by resection or cryotherapy.

A retrospective review of patient data was undertaken. All hospital admission and liver unit notes were reviewed for peri-operative and operative data. Pre-operative serum alpha-fetoprotein (AFP) and liver function tests of albumin, bilirubin and prothrombin time were recorded. Tumour diameter was measured from histology reports for resection patients, or from intra-operative ultrasound measurements for cryotherapy patients. Blood transfusions, post-operative admission days and complications, and cause and date of death were recorded.

Patients were followed up by the senior author at three-monthly intervals with serum AFP, and CT scan if appropriate. In the absence of regular follow-up, information was obtained from the patient's general practitioner. One patient who was lost to follow-up when he returned home to Taiwan was excluded from the survival analysis.

Liver resection was performed under inflow occlusion with an ultrasonic disaggregator (Selector, Spembly, UK). Cryotherapy was performed with the LCS 3000 (Cryotech, UK) liquid nitrogen system and 5mm coaxial insulated probes, or the ERBE CRYO 6 (ERBE, Tübingen, Germany) system with 3.5mm

Award Winner's Abstract

Effects of a cryotherapy and a chemotherapy on apoptosis in a non small cell lung cancer xenografted into SCID mice

Valérie Forest, Jean-Michel Vergnon, Lydia Campos, Denis Guyotat.

Laboratoire de Mort Cellulaire et Néoplasies, EA3063. Faculté de Médecine J. Lisfranc, 15 rue Ambroise Paré, 42023 Saint-Etienne, Cedex 02, France.



Preliminary report

Lung cancers represent the first cause of cancer mortality in the world. Surgery is the treatment of choice, but in the case of inoperable tumours chemotherapy can be performed with a response rate of about 30%. Among endoscopic therapies available, cryotherapy can also be proposed in bronchial application. Recent in vitro studies tend to analyse how cell death occurs after cryotherapy. It is now well established that a gene-regulated death, i.e. apoptosis, is implicated. However, few in vivo data are available. We have investigated the implication of apoptosis after cryotherapy or chemotherapy in a model of human non small cell lung cancer xenografted into immunodeficient mice.

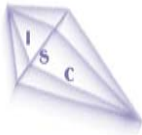
Cells from a human lung adenocarcinoma cell line were injected subcutaneously into SCID mice. Mice were treated either by cryotherapy (3 cycles of freezing/thawing, performed with a nitrous oxide cryoprobe) or by chemotherapy (intravenous injection of Vinorelbine : Navelbine). In a control group, mice received no treatment. Mice were then euthanized after periodic intervals after treatment, tumour nodes were excised and analysed by immunohistochemical stainings. The induction of apoptosis was studied by following the level of cleaved caspase-3 expression. A morphological study was also performed (HES coloration).

A minimal level of cleaved caspase-3 was found in control tumours. This level was increased in tumours treated either by cryotherapy or by chemotherapy. However, the effects were found to vary depending on the treatment : chemotherapy seemed to present a constant efficiency in inducing apoptosis, while cryotherapy showed time-dependent effects. This difference in the ability to induce apoptosis may be due to different modes of action of these methods.

Moreover, tumours treated by cryotherapy and tumours treated by chemotherapy presented a different morphological aspect.

Taken together, these results suggest that cryo and chemotherapy may act at different levels, demonstrating the interest to associate these two modalities to affect the tumour to a greater extent. And this is the topic of our current research : we are currently investigating any additive or synergic effect of the association. Moreover, this study must be completed by techniques of detection based on criteria other than morphological.

Forthcoming Events



13th MEETING INTERNATIONAL SOCIETY OF CRYOSURGERY



Date: 2005, tba
Venue: Beijing, China
Contacts: UK: Omar Maiwand - ISC President
Email: cryotherapy@rbh.nthames.nhs.uk
China: Fengrui Zhao - Chairman
Email: zhaofr2002@yahoo.com.cn
Japan: Junta Harada - Deputy Chair
Email: harada@jikei.ac.jp
Website: <http://www.rbh.nthames.nhs.uk/cryosurgery>



3rd ANNUAL MEETING ASSOCIATION OF BRITISH AND IRISH CRYOSURGERY (ABIC)



Date: Friday 15 October 2004 (tba)
Venue: Crewe, Cheshire, UK
Contact: Arthur Jackson. Email: ArthurJacksonMM@aol.com
Programme: Cryosurgery Workshop on skin lesions
Open Panel Discussion

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 2000 to share their experiences and promote excellence in the field of cryosurgery.



ISC REGIONAL CRYOSURGERY MEETING



Date: September 2004 (tba)
Venue: Montreal, Canada
Contact: Canada: R.Jean-Francois. Email: rjfm@d@hotmail.com
U.S.A.: G Graham. Email: gfgraham@wfubmc.edu

Original Articles

A comparison of morbidity and mortality rates and long term survival following liver resection or cryotherapy for hepatocellular carcinoma

Rohone J. D'Souza, Jason M. Yeo, Julie King, David L. Morris*
UNSW Department of Surgery, The St George Hospital, Sydney,
NSW 2217 Australia. *Email: david.morris@unsw.edu.au



Keywords: hepatocellular carcinoma, hepatectomy, cryotherapy, treatment outcome.

Abstract

Background

Resection has been the treatment of choice for hepatocellular carcinoma (HCC) in patients with good liver function and large tumours. To date, there have been no studies comparing outcomes of patients with HCC treated by resection and cryotherapy. This study compares results in HCCs treated at our unit.

Methods

HCC patients (n=186) who were treated at the UNSW Department of Surgery from 1990 to 2001 were identified by retrospective review of the liver tumour database. Of the 43 patients who had been treated by liver resection or cryotherapy, 17 had resections, 15 had cryotherapy and 11 had both. Data from the resection and cryotherapy groups was examined for differences in preoperative liver function and alpha-fetoprotein level, tumour diameter, peri-operative morbidity and mortality rates, cause of death and overall survival.

Results

At the time of data review, 17 patients were alive, 25 had died and one was lost to follow-up. Tumour diameters were much larger in the resection group than the cryotherapy group (15 ± 14 cm versus 4.0 ± 0.8 : mean \pm SD : $P < 0.001$). The mean hospital stay for the resection/cryotherapy patient groups was 19 ± 8 days versus 14.7 ± 13 , ($p = 0.06$), and blood transfusion requirements were higher at 6.1 ± 3.4 units versus 1.2 ± 2.4 ($p = 0.006$). For those patients who died from their HCC, the mean survival time was 365 ± 410 days for the resection group and 781 ± 623 days for the cryotherapy group. The postoperative mortality rate was higher in the resection group, but there was no significant difference in overall survival between groups ($p = 0.3$).

Discussion

Our results suggest that cryotherapy can be used with good peri-operative safety and long-term survival as an alternative treatment to resection in patients with tumours that are too large for alcohol injection.

BoD Meeting Minutes & Accounts

- 6 Proposal for Registration fees at the forthcoming Congress in 2005:
 Early Registration: (Up to 3 months to the meeting)
 Members = \$200 + \$100 (\$50 membership p.a.)
 Non members = \$350.
 Late Registration (From 3 months prior to the meeting and on site).
 Members: \$ 250 + \$100 (\$50 membership p.a.)
 Non members = \$400.
- 7 Tribute was given to the Society's biannual publication CRYOSURGERY and it was agreed that this journal should continue to be published at the Society HQ, at Harefield Hospital, UK. Original papers are required from members for future publications.
- 8 Library - The importance of retaining a Library with up-to-date clinical and original publications was highlighted. This could be achieved by the collection of old and new papers. The library would be based at the ISC HQ at Harefield Hospital and organised by O.Maiwand, with support from N.Korpan and C.Zouboulis
- 9 Suggestion was made to look into developing internet facilities, particularly for those who could not attend meetings.

ACCOUNTS - 2001 to 2003

INCOME		EXPENSE	
Carried forward			
from previous meeting:	\$ 5,767		
Delegate Registration:	\$16,599	Welcome Reception	\$ 4,350 (£2,538)
		Conference Catering	\$ 7,787 (£4,544)
Exhibitors	\$ 8,969	Conference Dinner	\$15,064 (£8,790)
		Audio Visual	\$ 4,202 (£2,452)
Sponsorships	\$ 2,206	Venue Hire & Set-up	\$ 2,108 (£1,230)
		Printing costs (Journal (& Meeting Literature)	\$ 3,139 (£1,832)
TOTAL:	\$33,541	TOTAL	\$36,651 (£21,080)
BALANCE (deficit):		(\$3,110)	

Please note that the Secretary's salary (2001 - 2003) @ \$30,846 (£18,000) per annum has not been included in the Society's expenditure.

Forthcoming Events



British Thoracic Oncology Group

Annual National Meeting 2004

Including Breakfast Satellite Meetings by Merck Pharmaceuticals and Ortho Biotech

Date: Thursday 22 & Friday 23 January 2004
 Venue: The Burlington Hotel, Upper Leeson Street, Dublin 4, Ireland.
 Tel: 00 353 1 6605222
 Fax: 00 353 1 6603172
 Contact: British Thoracic Oncology Group
 Hospital Management Offices, Glenfield Hospital, Leicester LE3 9PQ.
 Email: dawn.mckinley@uhl-tr.nhs.uk
 Phone 0116 2587602. Fax 0116 2587599



Cryogenics 2004 - IIR Conference



Date: April 27-April 30, 2004
 Venue: Prague, Czech Republic.-
 Contact: Vaclav Chrz.
 Tel: +420 412 507 628.
 Fax: +420 412 510 209.
 Email: vaclav.chrz@chart-ferox.com
 Web site: <http://www.isibrno.cz/cryogenics2004/>

Forthcoming Events



12th Annual Theoretical and Practical Course of Cryosurgery and Radiofrequency

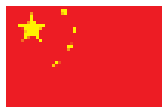
Organized by The Argentine Society of Cryosurgery and the Post Graduate School of the Argentine Medical Association

Date: 13 April - 9 November, 2004
Venue: Buenos Aires
Objective: Appropriate use of Radiofrequency and Cryosurgery in Dermatology and Gynecology
Programme: 70 Practical sessions. 12 Theory classes.
Contact: Eliezer Turjansky
Email: rjan@intramed.net.ar



2nd Asian Conference on Refrigeration and Air Conditioning (ACRA2004)

Co-sponsored



Date: 12 - 13 May, 2004
Venue: Beijing, China
Contact: Pan Qiusheng
Fax: +86 10 6843 4679
Tel: +86 10 6842 0686
E.mail: car@car.org.cn
Web site: <http://ACRA2004.car.org.cn>

BoD Meeting Minutes & Accounts

12 September 2003, London

Present:

D.Buckley -Ireland, A.Delbello - Italy, A.Gad - Egypt, JCA Goncalves - Portugal, G.Graham - USA, R.Jean-Francois - Canada, N.N.Korpan - Austria, F.Lugnani - Italy, D.Luna Sabate - Spain, O.Maiwand - UK, M.Peralta - Chile, S.Sumida - Japan, E.Turjansky - Argentina, U.Zoras - Greece, A.Weshahy-Hany - Egypt, F.Zhao - China, C.Zouboulis - Germany, J.Harada - Japan, J-M.Vergnon - France

Apologies: R.Ablin - USA, R.Herzog - Germany, G.Onik - USA

- 1 The BoD unanimously decided to support the decision of members of the general assembly that the ISC and ESC should merge to one society. The merged society would be called the International Society of Cryosurgery.
- 2 O Maiwand was nominated as President with the responsibility of successfully bringing the two societies together over the next two years
3. It was agreed to nominate 2 Vice Presidents - the 1st Vice President would be in charge of organising the next meeting in 2005 (elected from the country hosting the meeting). Both V.P.'s would be based in different parts of the world.
4. It was agreed that the new BoD should have no more than 10-12 members (excluding society officers and honorary members).
5. Venue for next meeting - Proposals were received from Luxor (Egypt), New York (USA), North Carolina (USA), Crete (Greece), Trieste (Italy), Beijing (China) Montreal (Canada). USA was later requested to be withdrawn. Results in order of preference, via a secret ballot, were:
1.Beijing (China) 2.Luxor (Egypt), 3.Crete (Greece), 4.Montreal (Canada), 5.Trieste (Italy).
Venue of 2005 Congress - Beijing, China in 2005. Fengrui Zhao was elected Vice President, to chair this forthcoming congress. Junta Harada (Japan), was given the responsibility to assist F.Zhao in organisation of the congress, and to play a key role in attracting more support from Japan. G. Graham was retained as 2nd Vice President with special responsibility to the Americas.
R Jean-Francois was nominated Treasurer/Secretary and as a support to G. Graham in her role of promoting Cryosurgery in the American continent.
6. Finance: A summary of accounts has been given at the end of these minutes

London 2003



ISC & ESC Board of Directors Meeting



Left
Dinner Cruise on the River
Thames



Right
Gloria Graham (ISC Vice
President) and Omar Maiwand
giving a Vote of Thanks at the
close of the meeting.

Forthcoming Events



31st Annual Meeting of the Japanese Society for Low Temperature Medicine

*In collaboration with the International Institute of Refrigeration (IIR) and
International Society of Cryosurgery (ISC)*

Date: 19 - 20 November, 2004
Venue: Tokyo Conference Centre
Shinagawa, Tokyo, Japan
Contact: Junta Harada
Email: cry@jikei.ac.jp
Main topics: Cryobiology, Cryopreservation and
Cryosurgery.
Web site: <http://homepage2.nifty.com/cryomedicine>



Society of Cryosurgery of Russia 3rd International Meeting of Cryomedicine

Date: 2005 - tba
Venue: Chernogolovka, Moscow
President: Dr Shafranov
Contact: Email: gprokhorov@mail.ru
Main topics: Workshops
Cryosurgery of angiomas in pediatrics
Other themes of cryomedicine are welcome

Cryotechnology

The International Society of Cryosurgery is grateful for the continuing support and sponsorship of the following companies, particularly at the 2nd Congress of the International & European Societies of Cryosurgery, London 2003.

ONCURA
an Amersham Business


Cariad
TECHNOLOGIES LTD.


Brymill
CRYOGENIC SYSTEMS

ERBE


KOOLAND

Beijing Kooland Medical Devices Co., Ltd.

CORTEX TECHNOLOGY - DENMARK

CRYOMED LTD - U.K.

HITACHI CORPORATION LTD - JAPAN

UNITED MEDICAL PARTNERS - SWITZERLAND

London 2003

I particularly enjoyed some of the very concise, but clear presentations given by a few of our younger cryosurgeons, some of who had travelled all the way from Australia to be at the conference. One such paper on "Cryoablation of Non-Resectable Colorectal Liver Metastases", was given by Tom Mala of Norway.

In all this apparent academia, the most memorable aspect of this International Cryosurgery Conference was of friendships renewed and made with our international colleagues. This was best illustrated during the wonderful evening meal and Thames Boat Trip which was part of the social programme the organising committee, and in particular Ann Dudhia with the help of the Cryoresearch team Julia Beeson, Joy Daffon and Jo Evans had organised as part of the fellowship of this cryosurgery meeting.

Finally, in summarising the two-day conference, our President announced that the Board of Directors had decided that from now on, the International and European Societies of Cryosurgery would be called the "International Society of Cryosurgery". The next ISC meeting is to be held in Beijing, China in 2005. Preliminary talks with Fengrui Zhao (China) are shortly to take place and the Society will be kept informed.

New Investigator's Award

 **VALERIE FOREST**

Presented a preliminary report on

Effects of a cryotherapy and a chemotherapy on apoptosis in a non small cell lung cancer xenografted into SCID mice

Valerie Forest, Jean-Michel Vergnon, Lydia Campos & Denis Guyotat

Valerie was presented with a gift by the Society President for her excellent presentation of the above report.

See Page 25 for the above abstract

London 2003

Dr Arthur Jackson

Associate Specialist in Dermatology, Mid & East Cheshire Trust, UK

What a pleasure it was to be part of this International Cryosurgery Congress in this London venue. As our President pointed out, the delegates present represented 26 countries from the increasing membership of the Society.

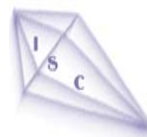
Follow the opening address by the Society President, Mr Omar Maiwand (UK) on behalf of the Board of Directors and the Scientific Organising Committee, Professor Gloria Graham (USA) paid a very meaningful tribute to the late Dr Esther Stolar, an outstanding International Cutaneous Cryosurgeon whose skills, enthusiasm and kindness had influenced many individuals in the Cryosurgery field. The eight scientific sessions and poster presentations which followed over the next two days, were of an excellent standard and represented the expanding use in recent years of low temperature surgery.

Following a clear and well-illustrated introduction to the basis and principles of cryosurgery by Mr Maiwand, papers were presented covering cellular biology and immunology. China presented a historical perspective of cryosurgery. Cryosurgical treatment of fibroids, cardiovascular disease, various benign skin conditions, the management of malignant lesions in kidney and prostate, endobronchial and lung, advanced skin lesions, secondary liver disease, primary and secondary bone disease as an alternative to destructive surgery and troublesome lesions in the dog, cat and even the pet gold fish were presented. Excellent comparisons between cryosurgery and other treatments were made and we were brought right up to date with the sophisticated cryosurgery equipment now being used under image guidance for the more serious and otherwise inaccessible cancers.

We take the use of English at such an international conference rather for granted. Yet amongst all these international speakers, only one presenter had to make use of an interpreter and his colourful illustrations were so good, it did not detract from the message of his talk. Even with the occasional hiccup in lecture room technology, the content and illustration of the papers was excellent and very instructive. I think there was a genuine consensus that both these attributes were highlighted in the paper on:

"Effects of Cryotherapy and Chemotherapy on Apoptosis in a Non Small Cell Lung Cancer Xenografted into SCID Mice", superbly presented by Valerie Forest of France.

Membership Form



APPLICATION TO JOIN

Please complete and return with your payment to: Ann Dudhia, International Society of Cryosurgery, Harefield Hospital, Harefield, Middlesex UB9 6JH, U.K.
Email: A.Dudhia@rbh.nthames.nhs.uk or cryotherapy@rbh.nthames.nhs.uk

Membership charges: \$50 per annum
Cheques should be in US dollars, made payable to "Society of Cryosurgery".

SURNAME & TITLE:Mr/Ms/Dr/Prof

FIRST NAME:

POSITION:

EMAIL:

TELEPHONE:

FAX:

AFFILIATION:

ADDRESS:

..... Postcode:.....

SPECIALITY/ACTIVITIES:.....

MEMBERSHIP OF OTHER SOCIETIES:.....

Applicants Signature: Date:

Board of Directors

President

Omar Maiwand



Vice Presidents

FenGrui Zhao & Gloria Graham

Treasurer/Secretary

Rita Jean-Francois

ISC & ESC BOARD OF DIRECTORS 2001 - 2003

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JC d' Almeida Goncalves <i>Portugal</i>		Sajio Sumida, <i>Japan</i>
Gloria Graham, <i>U.S.A</i>		Eliezer Turjansky, <i>Argentina</i>
Ralf Herzog, <i>Germany</i>		Jean-Michel Vergnon, <i>France</i>
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		Ulysses Zoras, <i>Greece</i>
		Christos Zouboulis, <i>Germany</i>

W e l c o m e

It is my great pleasure to bring to you the latest publication of cryosurgery. I hope that you find the contents useful.

We have just hosted the 2nd Combined Meeting of the European & International Societies of Cryosurgery in London on 11th & 12th September. I am very pleased that members from 26 countries participated this year. The Meeting was one of the largest gatherings of cryo-practitioners.

Based on correspondence received from the participants, we are very pleased that this gathering was a success, both scientifically and socially. The overall scientific programme was reported to be of a very high standard, with excellent clinical and research papers. We welcomed, for the first time, the contribution of delegates from Australia (who presented some outstanding papers) and also from Jordan.

In my view, the most important achievement of this meeting was that members recognised the advantages of having one strong, effective society, as the reasoning behind the initial partitioning has been resolved. As a result, on 11th September 2003, members of the General Assembly in London unanimously agreed that we revert to one united society. This was agreed and supported by both the European and International Board of Directors and a decision was made that we retain the name of "International Society of Cryosurgery", which was first established in Vienna in 1971. I do not think that this undermines the position of all the good meetings that have been held under the names of the European Society of Cryosurgery and the Central European Society of Cryosurgery, but really indicates that we should concentrate on one solid, well-organised and democratic Society. However, this can only be achieved if you, as a member, accepts this as your own Society, by your active participation and contribution towards maintaining and improving the standard of the Society and it's events further.

The Board of Directors decided that the next meeting of the ISC would be held in Beijing, China in 2005. We aim to have another large and successful gathering under the chairmanship of Fengrui Zhao (China), supported by Junta Harada (Japan). I realise that we all require time to enable us to arrange our busy schedules and I hope that you will do this in advance for the Beijing meeting. We are planning to organise the forthcoming conference in a way that it is not only a scientific success, but also a good social gathering for yourself and perhaps your partners and families.

In this edition, along with our normal features, we include news and reviews of the London meeting, a summary of the Board of Directors' meeting minutes, Income and Expenditure account, photographs and as usual, some original papers.

I hope you enjoy reading this publication and thank you all for your valuable comments and support.

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Contact Details

If you would like to contribute to the next issue, your articles, views and comments would be most welcome

Please send your correspondence to:

Ann Dudhia
International Society of Cryosurgery
Cryosurgery Research Department
Harefield Hospital
Harefield
Middlesex
UB9 6JH
U.K.

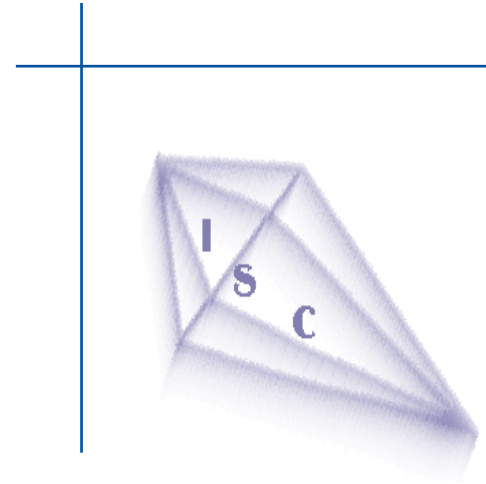
Tel: 00 44 1895 828 528
Fax: 00 44 1895 828 528
Email: cryotherapy@rbh.nthames.nhs.uk

Website: <http://www.rbh.nthames.nhs.uk/cryosurgery>

Contact details for the Cryosurgery Research Department

Julia Beeson Tel/Fax: 00 44 1895 828 528
Email: cryotherapy@rbh.nthames.nhs.uk

Joy Daffon: Tel/Fax: 00 44 1895 828 528
Email: cryotherapy@rbh.nthames.nhs.uk



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Harefield Hospital
Hill End Road, Harefield
Middlesex UB9 6JH
United Kingdom
Tel/Fax: 00 44 1895 828 528
Email: cryotherapy@rbh.nthames.nhs.uk
Website: <http://www.rbh.nthames.nhs.uk/cryotherapy>

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