

Chris D'Hont M.D. report of 1st European Congress on Cryosurgery

FIRST EUROPEAN CONGRESS OF CRYOSURGERY March 30 till April 2, 2000 Palacio Miramar Donostia- San Sebastian, Spain

President: Dr. Daniel Luna Sabate M.D.

Meeting report from Dr. Chris D'Hont M.D.

The first European Congress on Cryosurgery - congress under the support from the European Society of Cryosurgery , the International Society of Cryosurgery and the International Institute of Refrigeration - was held in San Sebastian - Spain from march 30 till april 2 , 2000. It turned out to be a very interesting meeting grouping the cryo- experiences from different specialists and in different disciplines.

<u>Day 1</u> was dedicated to <u>basic science</u> in the use of cryogenetic agents both to <u>preserve</u> tissue (transplantation, ...) and to <u>kill</u> tissue (cancer treatment, ...).Dr. Hertzog highlighted the evolution in oral and maxilofacial surgery, dr. Goltsev and dr. Grischenko discussed the use of cryopreservation in clinical transplantology.

On <u>day 2</u> the use of cruyosurgery in <u>endobronchial benign and malignant lesions</u> was discussed.In conclusion, for endobronchial tumors NdYag laser treatment or electrocaugulation is used for debulking and immediate symptom relief, while cryotherapy is used to sucesfully treat the base and the infiltrating tumor.

Cryotherapy for lungtumors is a <u>palliative</u> treatment and is better and safer than other treatment options for infiltrating tumors.Dr. Vergnon also showed good results in <u>curative</u> treatment of carcinoid tumors.1 or 2 cryosessions are needed after debulking with NdYag laser or electrocoagulation.In Benign obstructive lesions, cryotherapy also showed to give the best results on all symptoms (dyspnoe, heamatoptisis, wheezing,). Cryotherapy is performed through a rigid or flexible bronchoscope and a flexible cryoprobe using N2O or Argon gas.

In <u>coloproctology</u> cryotherapy (liquid nitrogen / Argon gas) gives good <u>palliative</u> results in colorectal adenocarcinoma. It is used as a <u>curative</u> treatment in villeous tumors, condylomata, fistula, pylonidal cysts, hemorroids, ... It offers a minimally invasive, very well tollerated, very effective and cost-effective treatment with poor bloodloss.

In <u>livertumors</u> cryotherapy is seen as an excellent <u>palliative</u> (sometimes <u>curative</u> ?) treatment for hepatocellular carcinoma and livermetastasis. More livertissue can be saved and bloodloss is

minimal.Liquid Nitrogen and Argongas based systems are used.

There is a significant gain in survival. In some cases the treatment is curative (2 years).

On $\underline{day\ 3}$ the excellent results of cryotherapy in $\underline{dermatology}$ were discussed. It is successfully used in the treatment of basal cell carcinoma, haemangiomas, melanomas (N0), keloids and cosmetic applications. Preliminary promissing results were shown in the $\underline{gynaecology}$ session. The use of cryotherapy in advanced cancer of the vulva ($\underline{palliative}$), on urethral caruncula and prolaps ($\underline{curative}$) and first trials in breastcancer and cutaneous metastases post mastectomy were discussed.

In another auditoriumn <u>day 3</u> was entirely dedicated to the use of cryosurgery in <u>urology</u> as a <u>curative</u> treatment in prostate cancer. (see programm at the end of this report). After <u>Dr. Chris D'Hont (Belgium</u>) had reviewed the pro's and con's of all possible treatment options for localized prostate cancer (Rad. nerve sparing Prostatectomy, Ext. Beam Radiotherapy, Brachytherapy, High Intensity Focussed Ultrasound, Watchfull waiting, (hormonal therapy), he focussed on the advantages of this new curative, minimally invasive and safe treatment cryoablation can offer our patients.

Introducing cryoprobes transperineally under transrectal ultrasound guidance, the prostate gland is entirely frozen with an Argon/Helium gas based system under excellent safety controll and guidance by the use of temperature aquisition with 5 thermosensors in the perifery of the prostate, to make sure killing temperatures of < - 40 ° C are reached in all periferic (tumor-) areas and no overkill occurs in vital areas as the external sfincter (cave incontinence) and the rectal wall (cave fistulas).

A double freeze / double thaw cycle is necessary to kill all cells, and the urethra is protected with a urethral warming catheter during the entire freezing process. The patient can leave the hospital the same day or 1 day after treatment and can regain his normal working activities and car driving within 2 weeks after treatment.

<u>Dr. Denis Prokhorov (Russia)</u> showed his results on temperature isotherms within the iceball and the killing effect of cryoablation on prostate cancer.

<u>Dr. Duke Bahn (MI - USA)</u> and <u>Dr. Douglas Chinn (CA - USA)</u> highlighted the scientific base and the technique of safe and curative TCPA (Targetted Cryo-Ablation of the Porstate) for prostate cancer. A life video demonstration of TCAP by Douglas Chinn and Wilson Wong at the Alhambra Med. Center in Arcadia CA was shown, and the excellent results from both centers were discussed (see at the end of this report).

Dr. Duke Bahn also compared the results with liquid Nitrogen and Argon gas based systems and showed a significant difference in the results between both systems in favor of the Argon/Helium gas based systems (see at the end for details).

<u>Prof. Uson (Sp.)</u> made some critical remarks on new technology in urology and the importance of carefull patient selection and urologist training. He urged all young urologists to get familiarised with this new technique that he described as being **the best and safest minimal invasive treatment for prostatecancer for at least the first decade of the 21st century.** He also expresed the hope that European governments and insurance companies would quickly see the advantages of TCAP and soon agree to terms of reimbursement for this treatment option in the interest of both the patients and public health.

TCAP is now accepted as a valid treatment for prostate cancer by FDA and Medicare in the USA after a long strugle from patients and urologists. Companies should work on lower prices for their single-use materials (cryoprobes) to make TCAP accessable to all patients with prostate cancer wherever they live.

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<u>In conclusion</u> we can state that **TCAP** is a safe, minimal invasive and curative treatment for localized prostate cancer, with very low morbidity, extremely short hospital stay and quick restore of normal activities. There occurs no bloodloss, no surgical incision and it can be repeated if necessary (unlike R.N.S.P., E.B.R.T., Brachytherapy). In most of cases 1 single oneday treatment session can cure prostate cancer and kill all cancer and BPH cells (unlike HIFU).

In the late afternoon very promissing results in renal cell carcinoma (video from Dr. Franco Lugnani - It.), uterine fibroids and BPH (lecture by Dr. Douglas Chinn) were shown.Dr. Chinn also explained excellent results in his center on hepatocellular carcinoma (work by Dr. Wilson Wong), further exploring new fields of interest for the use of cryosurgery.

We want to thank all speakers and the organisers for this very intersting meeting.

Overview of the results in the treatment of prostate cancer in +/- 1.000 patients all together in both centers (Crittenton Med. Center in Rochester MI and Alhambra Med. Center in Arcadia Ca.) as presented by Dr. Duke Bahn and Dr. Douglas Chinn :

<u>5 years follow-up results - single treatment</u>

neg. biopsies PSA < 0.5 PSA < 1

C: low risk = T1-2b 100 % 76 %

med. risk = T2b-3 74.7 % 66 %

high r. = T4 40.7 % 40 %

B: Virgin: T1 100 %

T2 88.8 %

T1 + T2 89 % 80.1 %

T3 76.8 %

T4 66.7 %

T3 + T4 76 % 66.3 %

T1-4 86.2 % 77.6 %

EBRT-failed:

T1-2 94.7 %

T3-4 50 %

overall: 76 % 52 %

<u>Complications</u>: impotence: 90 - 100 % (freezing of the neuro-vascular bundles =

primary route for tumor spreading!)

incontinence: 4.3 % overall (85 % only occ. drops < 1 pad/d)

but: 2 % in virgin group; 53 % in EBRT-failed group

obstruction needing TURP: 9 % (25 % in EBRT-failed group)

fistula: virgin: 0 % - EBRT-failed: 6 %

Comparison Liquid Nitrogen ◆ Argon/Helium gas :

L.Nitrogen Argon

- neg. Biopsie rate at 2 years follow-up:

T1-2 87 % 99 %

T3-4 65 % **93** % = stat. sign.

All 83 % **98** %

- PSA < 1 77 % 82 %

Home in less than 24 hrs; shopping after 1 week; driving and working after 2 weeks

Conclusion TCAP: - safe

- curative T1-3
- excellent tumor controll
- EBRT-failed patiënts can still be treated
- minimal invasive
- no bloodloss
- no surgical incision
- Argon is better than Liquid Nitrogen.
- more probes and good temperature aquisition

- = better results
- low morbidity
- high patient satisfaction
- single day treatment
- can be repeated

Urology Speakers:

Dr. Chris D'Hont M.D.

Chief of the dept. of Urology at the Military Hospital Queen Astrid in Brussels

Urologist at the A.Z. Middelheim in Antwerp

Belgium

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Dr. Douglas Chinn M.D.

Urologist at the Chinn Urology group

Urologist at the Alhambra Medical Center in Arcadia California

USA

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Dr. Duke Bahn M.D.

Chief of the dept. of Radiology / Prostate center at the Crittenton Medical Center in Rochester - Michigan

USA

Dr. Denis Prokhorov M.D.

Urologist at the Russian Academy of science and the Central Research Institute for radiology in St.

Petersburg

Russia

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Prof. Dr. Aurelio Uson M.D.

Urology prof. at the University of Madrid

Spain

Dr. Franco Lugnani M.D.

Urologist at the hosp. of Trieste

Italy

fmlugnani interware.it

Last minute programm adaptations:

Due to last minute cancellations by some of the American speakers, the programm had to be reviewed.

1st. European Congress on Cryosurgery - Donostia-San Sebastian Spain

Urology meeting april 1, 2000.

Chairman: Dr. Chris D'Hont (Belgium)

Morningsession:

- Introduction : C. D'Hont : Options in the treatment of localized prostate cancer /

What is cryosurgery?

- Session 1 : Overview asn Standard Protocol

Moderator: C. D'Hont

- D. Chinn: Targetted Ablation of the Prostate

- D. Chinn: Evolution of TCAP

- D. Bahn: Importance of T.R.U.S.-guided staging biopsies for successfull TCAP

- D. Bahn: Technique of Cryosurgery

- Q&A

- Session 2 : Clinical Experience and protocol adaptations

Moderator: Douglas Chinn

- Videotape of life demonstration TCAP by D. Chinn and W. Wong
- D. Chinn: 5-years experience at the Alhambra Medical Center Arcadia Cal.
- D. Bahn: 5-years experience at the Crittenton Medical Center Rochester MI
- D. Bahn: Salvage TCAP after EBRT-failure
- D. Bahn: QuOL after cryosurgery patients questionnairs
- Q&A

Afternoonsession

- Session 3 : Exp. and new frontiers for cryosurgery

Moderator: Duke Bahn

- D. Prokhorov : Themperature measuring and evaluation of tumor cells viability

in different zones of an iceball; practical application of in vitro results.

- D. Chinn: Cryosurgery for Uterine fibroids
- D. Chinn: Cryosurgery for BPH
- D. Chinn: Cryosurgery for hepatocellular carcinoma
- C. D'Hont : video on renal cryosurgery (Franco Lugnani)
- C. D'Hont : Video on Seed-net TCAP
- Q&A
- Closing remarks take home message : C. D'Hont

Abstract

TEMPERATURE MEASURING AND EVALUATION OF TUMOR CELLS VIABILITY IN DIFFERENT ZONES OF AN ICE-BALL. PRACTICAL APPLICATION OF IN - VITRO EXPERIMENTS RESULTS.

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St.-Petersburg, Russia.

The goal of radical cryosurgical interventions for malignant tumors is the complete destruction of tumor cells. But normal tissue surrounding a tumor, should be minimally damaged to avoid postoperative complications.

Performing radical cryosurgical operations on a prostate, the trans rectal ultrasound image of an iceball does not predict the entire killingzone of complete cell destruction.

It is obviously necessary to have the distinct visualization of the location of the so-called "zone of the critical isotherm" inside an ice-ball to be able to predict the succes of the treatment..

The PURPOSES:

- 1. Study of the temperature parameters inside an ice-ball.
- 2. Rating of viability of cells after cooling / freezing in various zones of an ice-ball.
- 3. Development of practical references on the basis of experimental results.

MATERIALS and METHODS:

1.Temperature in an ice-ball around a cryoprobe of 3.8 mm diameter (cryoequipment - <u>Candela Cryotech LCS 3000 with liquid nitrogen</u> as a cooling agent) was measured by ten thermocouples of 150 microns diameter.

- 2.Determination of amount of affected cells (line A 131 epidermoid carcinoma) at temperature regimens corresponding to various zones of an ice-ball.
- 3. Study of viability of the unaffected frozen tumor cells.
- 4.Use of the obtained results at cryosurgical operations on a prostate

for a cancer.

RESULTS:

In experiments temperature in a gelatinous medium or normal saline solution around the cryoprobe of 3,8 mm diameter was measured by ten thermocouples of 150 microns in diameter placed from the center of the cooled zone of a cryoprobe towards the perifery of the iceball.

During the experiments the essential differences between parameters of ice-balls after the first and second freezing without change of a position of a cryoprobe were revealed. So, the diameter of an ice-ball at the first freezing was 35 mm, at second freeze 42 mm; the temperature was decreasing inside and at the periphery of an ice-ball.

Temperature at the center of an ice-ball reached -186 °C within two minutes from

the moment of switching on the cryoequipment to the maximal capacity. At the periphery of the iceball temperature lowered to only -6°C after 10 min. of freezing.

In experiments on cell cultures the temperature regimens in various zones of an ice-ball were simulated. The viability of cells after freezing was estimated by adhesive properties and ability to divide.

The centrifuged cell culture (line A - 431 epidermoid carcinoma) in the cryocamera "ICE-CUBIE 1810" was cooled at temperature regimens corresponding to various zones of an ice-ball.

Cells frozen to < - 40 °C, underwent direct destruction, or died completely during hours after thawing, forming a " zone of direct cell destruction ", irrespective of the time of exposure at final temperature.

Changes in temperature in the range of > -40 °C to -6 °C, corresponding to the peripheral part of an ice-ball, exerted damaging action on the cell culture. However after thawing, more than 75 % of tumor cells kept their ability to divide, forming a "zone of partial cell damage" but no real cell destruction.

CONCLUSION

The presence of the "zone of partial damage", somewhat limits the indications for a radical cryosurgical operation on a prostate in case of tumor localization in the posterior part of the capsula, close to the rectal wall, and requires development of protective measures of adjacent normal tissue.

COMMENT from C. D'Hont: the experiments of dr. Prokhorov show once again the importance of temperature measurement at the perifery of the prostate. On one hand they give us vital information on sufficiant tumor kill (reaching killing temperatures of < - 40 °C) in these zones, on the other hand they guide us to keeping vital areas safe from complete destruction (safe temp. even inside the edge of the iceball visable on TRUS). They add both safety and efficacy to the treatment and are most important to help stear the freezing process to a safe but complete kill of all tumor cells with respect of the vital areas as are the rectal wall and the external sfincter.

C. D'Hont M.D.