A publication of Oncotherm

November 2010
Volume 1.

ONCOTHERMIA JOURNAL

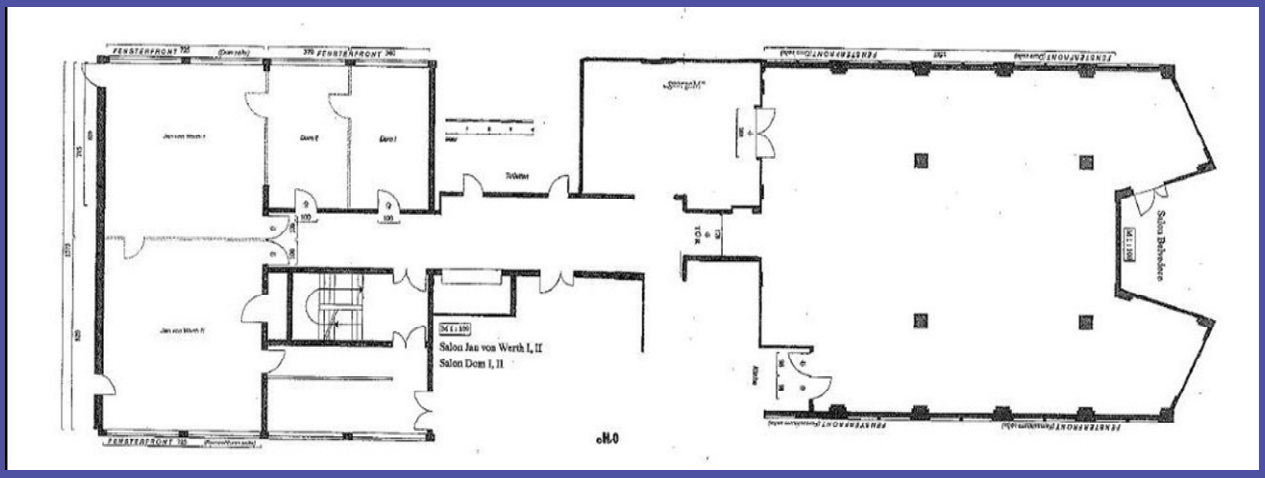
Special: International Oncothermia Symposium, Cologne

Abstracts and information on the First International Oncothermia-Symposium

www.Oncothermia-Journal.com

Information on the First International Oncothermia Symposium

http://www.io-symposium.com



Ms Constanze Feisskohl

Ms Janina Leckler

Ms Anett Gallne-Valyi

Ms Anetta Erdelyi

Mr. Balazs Acs

Mr. Gabor Skrihar

Information on the First International Oncothermia Symposium

http://www.io-symposium.com

PRESIDENT OF THE CONFERENCE

Prof. Dr. med. Harald Sommer, Ludwig-Maximilians-Universität, Munich, Germany

SCIENTIFIC COMMITTEE

Prof. Dr. Harald Sommer (Scientific Leader)
Prof. Dr. Alexander Herzog, Germany
Prof. Dr. Seung-Cheol Kim, Korea
Prof. Dr. Greorgyi Panshin, Russia
Prof. Dr. Helmut Renner, Switzerland
Prof. Dr. Andras Szasz, Hungary

THE CHAIRMEN OF THE SECTIONS

Section I: *Prof. Dr. H. Sommer* (Germany) & Dr. F. Douwes, (Germany)
Section II: *Prof. Dr. A. Herzog* (Germany) & Prof. Dr. M. Al-Masri, (Jordan)
Section III: *Prof. Dr. R. Issels*, (Germany) & Prof. Dr. C. Pang, (China)
Section IV: *Dr. P.Hau*, (Germany) & Prof. Dr. DY Lee, (Korea)
Section V: *Prof. Dr. G. Fiorentini*, (Italy) & Dr. F. Migeod, (Germany)
Section VI: *Dr. R. Moss*, (USA) & Dr. J. Brenner, (Israel)

SPECIAL GUESTS

Dr. Gianhahahel F. Baronzio, Italy
Dr. Haim I. Bicher, USA
Mr. Carl F. Firley, USA
Prof. Dr. Rolf Issels, Germany
Prof. Dr. DY Lee, Korea
Dr. Ralph Moss, USA

SPECIAL PARTICIPANTS

Mr. Stefan Peil, Representative of the Mayor of Cologne
Prof. Dr. R. Issels, President of European Society of Hyperthermic Oncology
Dr. F. Douwes, President of German Society of Oncology
Prof. Dr. DY Lee, President of Korean Oncothermia Study Group
Dr. R. Moss, Leader of forum of "Cancer Decisions"

ONCOTHERM PRIZE 2010:

given to *Prof. Dr. G. Fiorentini*

SPONSORS:

oncotherm hightech medicine

NFÜ Új Magyarország

Editorial

Dear Reader,

The first International Oncothermia-Symposium follows the tradition of the yearly Cologne Symposium organized by Oncotherm. During the last years we recognized that our event is important for our doctors, Oncotherm users and interested parties. They enjoy the input, the gained knowledge and the exchange of thoughts. We are proud of our method and the feedback of our customers as well as the presentations of other events in this year have shown the great importance of Oncothermia. It became more and more obvious that the need of getting together with colleagues is not only valid for the German experts.
Every day the staff of the Oncotherm offices is talking to interested professors and doctors all over the world. We are proud that in this year we are able to include them in our event as well and to offer an international Symposium. On this year's event we will also introduce the just published book "Oncothermia—Principles and Practices", that marks the breakthrough of Oncothermia.
With this booklet we want to start a new tradition of having a regular publication. From now on we will publish the Oncotherm Journal every half year and keep you informed on new developments and experiences.
In this first issue you can find all abstracts of talks and posters presented in the Symposium. We also include the programme and some general information.
If you wish to publish an article in one of the next issues of the Oncotherm Journal, please contact us.
Have a good stay in Cologne and do not hesitate to ask if there are any questions.

Sincerely

Prof. Dr. András Szász

Lieber Leser,

Das Erste Interntionale Oncothermie-Symposium führt die Oncotherm-Tradition des jährlichen Kölner Hyperthermiesymposiums fort. Während der letzten Jahre haben wir immer wieder gesehen, wie wichtig diese Veranstaltung für Ärzte, Anwender und Interessenten ist. Sie schätzen das neu erlangte wissen und den Gedankenaustausch mit Kollegen. Wir sind stolz auf unsere Methode und das positive Feedback der Experten, die unsere Methode im Kampf gegen den Krebs nutzen. Oncothermie wird momentan in 16 Ländern weltweit genutzt und die Nummer der aktiven Geräte hat etwa 200 erreicht. Es ist immer deutlicher geworden, dass der Kontakt zu Kollegen nicht nu rein Bedürfnis deutscher Experten ist und das internationale Interesse hat uns dazu bewogen, unsere Veranstaltung weiterzuentwickeln und ein internationals Oncothermie-Symposium zu organisieren.
Unsere Mitarbeiter sprechen täglich mit interessierten Professoren und Doktoren weltweit. Wir sind stolz, diese Interessenten in diesem Jahr in unsere Veranstaltung integrieren zu können. Auf der diesjährigen Veranstaltung werden wir auch das gerade erschienene Buch „Oncothermia – Principles and Practices", dass den Durchbruch der Methode einläutet, vorstellen. Wir hoffen, dass dieser Durchbruch nicht nur eine Veränderung der biomedizinischen Denkweise über die Anwendung der Hyperthermie im Onkologiebereich hervorruft, sondern auch die Akzeptanz der Oncothermie als Methode des "Gold-Standards" anerkennt.
Mit der Publikation des "Oncotherm Journals" möchten wir eine neue Tradition regelmäßiger Veröffentlichungen beginnen. Von nun an wird das „Oncotherm Journal" halbjährlich erscheinen und Sie über neue Entwicklungen und Erfahrungen informieren. In dieser ersten Ausgabe finden Sie alle Abstracts der Poster und Vorträge, die im Symposium präsentiert werden. Ergänzt werden diese durch das Programm und einige allgemeine Informationen. Falls Sie Interesse haben inder nächsten Ausgabe einen Artikel zu veröffentlichen, können Sie sich gerne an uns wenden. Ich wünsche Ihnen einen guten Aufenthalt in Köln. Bei Fragen und Anmerkungen können Sie uns gerne ansprechen.

Mit den besten Grüßen

Prof. Dr. András Szász

Editor-in-Chief

Prof. Dr. Andras Szasz
Head of the Department of Biotechnics, St. Istvan University, Godollo, Hungary
Chief Scientific Officer (CSO), Oncotherm GmbH, Belgische Allee 9, 53842 Troisdorf, Germany
Tel: +49 2241 31992-0; Fax: +49 2241 31992-11; Email: Szasz@oncotherm.de

Managing Editors

Ms. Janina Leckler
Oncotherm GmbH, Belgische Allee 9, 53842 Troisdorf, Germany
Tel: +49 2241 31992-0; Fax: +49 2241 31992-11; Email: Leckler@oncotherm.de

and

Ms. Anetta Erdelyi
Oncotherm Kft, Ibolya u. 2. 2071, Paty, Hungary

Starting (establishing) Editorial Board

Prof. Dr. Gabriella Hegyi
Department of Complementary Medicine, Medical School, University of Pecs, Hungary

Dr. Gabor Andocs
Department of Pharmacology and Toxicology, Faculty of Veterinary Science, St. Istvan University, Hungary

Prof. Dr. G. Fiorentini
Oncology Unit, San Giuseppe General Hospital, Italy

Dr. Nora Meggyeshazi
1st Department of Pathology and Experimental Cancer Research, Semmelweis University, Hungary

Prof. Dr. A. Herzog
Chief-physician, Fachklinik Dr. Herzog, Germany

Dr. G. Parmar
Director of Integrated Health Clinic, Canada

Dr. Oliver Szasz
CEO of Oncotherm Group, Germany and Hungary

Organizing of the final Editorial Board is in progress.
Our intention is creating representations of all the national areas where Oncothermia is used.

Oncothermia Journal
Submission Information

1. Aims and Scope

Oncothermia Journal is an official journal of Oncotherm Group, devoted to support them, making a collective for using the results and make it common for general use. Oncotherm Journal has an open-minded character, expecting the complete study-papers, case-reports, reviews, hypotheses, opinions, and all the informative materials which could be helpful for the international Oncotherm community. Advertisements connected to the topic are also welcome.

- **Clinical Studies.** Regional or local or multilocal oncothermia or electro cancer therapy (ECT) treatments, case-reports, practical considerations in complex therapies, clinical trials, physiological effects, oncothermia in combination with other modalities, and treatment optimization.
- **Biological Studies.** Mechanisms of oncothermia, thermal- or non-temperature dependent effects, response on electric fields, bioelectromagnetic applications for tumors, oncothermia treatment combination with other modalities, effects on normal and malignant cells and tissues, immunological effects, physiological effects, etc.
- **Techniques of oncothermia.** Technical development, new technical solutions, proposals.
- **Hypotheses, suggestions, opinions** to improve the oncothermia and electro-cancer-therapy methods, intending the development of the treatments.

Further information about the Journal, including links to the online sample copy and contents pages, can be found on the Journal: www.Oncothermia-Journal.com .

2. Submission of Manuscripts

All submissions should be made online at the Oncothermia Journal by email Oncothermia-Journal@oncotherm.org

3. Preparation of Manuscripts

Manuscripts must be written in English, but other languages could be accepted by special reasons, when it has English abstract.

Text should be supplied in a format compatible with Microsoft Word for Windows (PC). Charts and tables are considered textual and should also be supplied in a format compatible with Word. All figures (illustrations, diagrams, photographs) should be supplied in JPG format.

Manuscripts may be any length, but must include:

- **Title Page**. Title of the paper, authors and their affiliations, 1-5 keywords. At least one corresponding author should be identified, whose email address has to be provided with full contact details
- **Abstracts.** Abstracts should include the: Purpose, Materials and Methods, Results, Conclusions.
- **Text.** Unlimited volume
- **Tables and Figures.** Tables and figures should be referred to in text. (numbered figures and tables). Each table and/or figure must have a legend that explains its purpose without reference to the text. Figure files will ideally be supplied as jpg-file (300dpi for photos).
- **References.** Oncothermia Journal uses the Vancouver (Author-Number) system to indicate references in the text, tables and legends, e.g. [1], [1, 3], [1-3]. The full references should be listed numerically in order of appearance, and presented following the text of the manuscript.

4. Copyright

It is a condition of publication that authors assign copyright or licence the publication right sin their articles, including abstracts to the Journal. The transmitted rights are not exclusive, the author(s) can use the submitted material without limitations, but Oncothermia Journal also has right to use it.

5. Electronic Proofs

When proofs are ready, corresponding authors will receive e-mail notification. Hard copies of proofs will not be mailed. To avoid delays in publication, corrections to proofs must be returned within 48 hours, by electronic transmittal or fax.

6. Offprints and Reprints

Author(s) will have the opportunity to download the materials in electric form, and use it for own purposes. Offprints or reprints from Oncothermia Journal are not available.

7. Advertising

Oncothermia Journal accepts advertising in any languages, but prefers English at least partly. The advertising must have connection with the scope of the Oncothermia Journal and must be legally correct, having controlled values and true info.

8. Legal responsibility

Authors of any publications in the Oncothermia journal are fully responsible for the material which is published. Oncothermia Journal has no any responsibility for legal conflict due to any actual publications. The Editorial Board has right to reject any publications if its validity is not enough controlled, or the Board is not convinced by the Authors.

9. Reviewing

Oncothermia Journal has a special peer-review process, representing by the Editorial Board members and specialists, whom they are connected. Avoid personal conflicts the opinion of Reviewer will not be signed, her/his name will be handled confidentially. Papers which are not connected to the scope of the Journal could be rejected without reviewing.

As the editorial team we are committed to a firm and coherent editorial line and the highest possible printing standards. But it is mainly you, the author, who makes sure that the Oncothermia Journal is an interesting and diversified magazine. We want to thank every one of you who supports us in exchanging professional views and experiences. To help you and to make it easier for both of us, we prepared the following rules and guidelines for abstract submission

SYMPOSIUM
November 22nd/23rd, 2010

Dear Colleagues, dear Oncotherm-users,

I am glad that you decided to attend this year's Symposium. It is the first international event we are organizing and we invited experts from all over the world to support us and to benefit from communicating with international colleagues.

There is not only interest in the method of Oncothermia in Germany, but all over the world. Like in most other areas of life international communication is getting more and more important in medicine. Because of this we are very happy about the positive reactions to our Symposium and about registrated participants from 21 countries.

Let us exchange our experiences, get to know new approaches of Oncothermia and discuss new ideas.

I am looking forward to meeting you in Cologne!

Harald Sommer

Prof. Dr. med. Harald Sommer

Ludwig-Maximilians-Universität, Munich, Germany

The event is certified by the Medical Association Nordrhein.

Certificates will of course be given to all participants.

Programme 1st Day

Time	Topic	Speaker	Country
14.45-14.50	Welcome by the scientific leader of the Symposium	Prof. Dr. Harald Sommer	
14.50-14.55	Welcome by the city of Cologne	Mr. Stefan Peil	
14.55-15.00	Welcome by the organizers	Dr. Oliver Szasz, CEO of Oncotherm GmbH	
15.00-15.20	Studies and Guidelines versus daily care	Prof. Dr. Harald Sommer	Germany
15.25-15.45	The adulthood: 21 years of Oncothermia	Prof. Dr. András Szász	Hungary
15.50-16.20	Problems and prospectives of cancer therapies and the possible place of Oncothermia in this development	Dr. Ralph Moss	USA
	Key Note Lecture		
16.20-16.35	COFFEE BREAK		
16.40-17.00	Laudatio Dr. med. Dr. rer. nat. Dipl.-Phys. E. Dieter Hager	Dr. Friedrich Migeod	Germany
17.05-17.25	Relapsed malignant gliomas treated with electro-hyperthermia: report of 24 patients	Prof. Dr. Giammaria Fiorentini	Italy
17.30-17.50	Transurethral thermotherapy in combination with temporally limited androgen blockade in localized prostate carzinoma	Dr. Friedrich Douwes	Germany
17.55-18.15	Treatment of advanced Pancreas Cancer with Chemo-Thermotherapy	Dr. Friedrich Douwes	Germany
18.20-18.40	Why I am doing Prostate Hyperthermia-Data Records	Dr. Marianne Müller	Germany
18.45-19.00	Best possible results of Oncothermia in combination with other treatments without considerable side effects	Dr. Wulf-Peter Brockmann	Germany
19.00-open end	DINNER		

Registered poster presentations by:

- Prof. Dr. Doo Yun Lee, Korea
- Dr. Girolamo Ranieri, Italy
- Prof. Dr. Georgiy Panshin, Russia
- Dr. Balogh Lajos, Hungary
- Dr. Gurdev Parmar, Canada
- Prof. Dr. Gabriella Hegyi, Hungary
- Prof. Dr. Woong Ju, Korea
- Mr. Peter Lorencz, Hungary
- Dr. Mohammad Al Masri, Jordan
- Mr. Gábor Skrihár, Hungary
- Dr. Gábor László Rubovszky, Hungary
- Dr. Henning Saupe, Germany
- Mrs. Anett Gallne Valyi, Hungary
- Prof. Dr. Seong Min Yun, Korea
- Dr. Olivér Sász, Hungary
- Dr. Friedrich Migeod, Germany
- Prof. Dr. Seung Cheol Kim, Korea
- Prof. Dr. Seokijn Haam, Korea

Programme 2nd Day

Time	Topic	Speaker	Country
8.25-8.30	Welcoming		
8.30-8.50	Hyperthermia: Where is the evidence?	Prof. Dr. Alexander Herzog	Germany
8.55-9.15	Cholangiocellular Carcinoma: Survival without symptoms with hyperthermia – A case study	Dr. Ulrich Reimnitz	Germany
9.20-9.40	Locoregional electrohyperthermia as treatment option for primary rectal carcinomas	Dr. A. A. Kovaliev	Ukraine
9.45-10.05	Large field electrodes in the treatment with local-regional hyperthermia	Dr. Joseph Brenner	Israel
10.10-10.30	COFFEE BREAK		
10.35-11.05	Regional hyperthermia in high-risk soft tissue sarcomas	Prof. Dr. Rolf Issels	USA
	Key Note Lecture		
11.10-11.30	Possible activation of neutrophyles by oncothermia	Dr. Henning Saupe	Germany
11.35-11.55	The dolphin-study: 10 years of chemotherapy in combination with whole-body-hyperthermia in ovarian carcinomas	Dr. Julia Jückstock	Germany
12.00-12.30	Oncotherm Prize Lecture: Safety of the proteasome inhibitor disulfiram combined with capacitive hyperthermia in the treatment of advanced solid tumors	Prof. Dr. Giammaria Fiorentini	Italy
12.40-13.40	LUNCH		
13.45-14.15	Clinical Research on Integrative Treatment of Colon Carcinoma with Oncothermia and Clifford TCM Immune Booster	Prof. Dr. Clifford Pang	China
14.15-14.35	Gynecology results by oncothermia	Dr. András Csejtei	Hungary
14.40-15.00	Results of a phase I study of advanced glioma patients	Dr. Peter Hau	Germany
15.05-15.25	Astrocytomas glioblastomas Hyperthermia metabolic inhibitors. Some considerations	Dr. Baronzio	Italy
15.30-15.50	Safety and Complications of Oncothermia in Korean Cancer Patients: A Retrospective Analysis of Single Institutional experience	Prof. Dr. Seong Min Yun	Korea
15.50-16.10	COFFEE BREAK		
16.15-17.05	Effect of Electrochemotherapy in Treating Patients with Intramuscular Vascular Malformations	Prof. Dr. Jing-Hong Li	China
17.10-17.30	Infrared-whole-body-hyperthermia in the relapse-prophylaxis of cancer – Update 2010	Dr. Stephan Wey	Germany
17.35-17.55	Experimental oncothermia in nude mice xenograft tumor models	Dr. Gabor Andocs	Hungary
18.00-18.20	*Honoring of 5-year's customers*		
18.25-18.45	*Discussion, summary and farewell*		

Sponsors:

CONTENTS

Abstracts of oral presentations - Monday, November 22nd. 10

Prof. Dr. Harald Sommer: Studien und Leitlinien versus Versorgungsalltag 11

Prof. Dr. Andras Szasz: The adulthood: 21 years of Oncothermia 12

Dr. Ralph Moss: CAM and Cancer around the world 13

Dr. Friedrich Migeod: Laudatio Dr. med. Dr. rer. nat. Dipl.-Phys. E. Dieter Hager 14

Prof. Dr. Giammaria Fiorentini: Relapsed malignant gliomas treated with electro- hyperthermia: report of 24 patients 15

Dr. Friedrich Douwes: Transurethrale Thermotherapie in Kombination mit zeitlich begrenzter Androgen-Blockade bei lokalisiertem Prostatakarzinom – 10-Jahresverlaufsbeobachtung an 123 Patienten 15

Dr. Friedrich Douwes: Treatment of advanced Pancreas Cancer with Chemo-Thermotherapy 16

Dr. Marianne Müller: Warum ich Prostatahyperthermie mache - Datenlage 16

Dr. Wulf-Peter Brockmann: Elektrohyperthermie in Kombination mit Strahlentherapie und Lowdose – Chemotherapie zu optimalen lokoregionären Krebstherpie bei minimalen Nebenwirkungen 17

Abstracts of oral presentations - Tuesday, November 23rd. 18

Prof. Dr. Alexander Herzog: Hyperthermia: Where is the evidence? 19

Dr. Ulrich Reimnitz: Cholangiocellular Carcinoma: Survival without symptoms with hyperthermia – A case study 20

Dr. A.A. Kovaliev: Locoregional electrohyperthermia as treatment option for primary rectal carcinomas 22

Dr. Joseph Brenner: Large field electrodes in the treatment with local-regional hyperthermia 23

Prof. Dr. Rolf Issels: Regional hyperthermia in high-risk soft tissue sarcomas 23

Dr. Henning Saupe: Possible activation of neutrophiles by oncothermia 24

Dr. Julia Jückstock: Die Dolphin-Studien: 10 Jahre Chemotherapie in Kombination mit Ganzkörperhyperthermie beim Ovarialkarzinom 24

Prof. Dr. Giammaria Fiorentini: Safety of the proteasome inhibitor disulfiram combined with capacitive hyperthermia in the treatment of advanced solid tumors 25

Prof. Dr. Clifford Pang: Clinical Research on Integrative Treatment of Colon Carcinoma with Oncothermia and Clifford TCM Immune Booster 26

Dr. Andras Csejtei: Gynecology results by oncothermia 27

Dr. Peter Hau: Transcranial electro-hyperthermia combined with alkylating chemotherapy in patients with relapsed high-grade gliomas: phase I clinical results 27

Dr. Gian Franco Baronzio: Astrocytomas glioblastomas Hyperthermia metabolic inhibitors. Some considerations 28

Prof. Dr. Seong Min Yoon: Safety and Complications of Oncothermia in Korean Cancer Patients: A Retrospective Analysis of Single Institutional experience 28

*Prof. Dr. Jing-Hong Li:*Effect of Electrochemotherapy in Treating Patients with Intramuscular Vascular Malformations 29

Dr. Stephan Wey: Die Infrarot-Ganzkörperhyperthermie in der Rezidivprophylaxe bei Krebs 29

Dr. Gabor Andocs: Experimental oncothermia in nude mice xenograft tumor models 30

Abstracts of posters **31**

P-01 – Prof. Dr. Seong Min Yoon, et al - A Case of Abscopal effect with Metastatic Non-Small-Cell Lung Cancer 32

P-02 – Dr. Gabor Andocs, et al - Apoptosis induction with modulated radiofrequency (RF) hyperthermia (oncothermia) in immuno-defficient mice xenograft tumors (Review) 32

P-03 – Dr. Nora Szasz, et al - Are we able igniting natural processes to kill cancer cells?....34

P-04 – Dr. Oliver Szasz, et al - Booster for all medication processes 35

P-05 – Prof. Dr. Andras Szasz - Brain glioma results by oncothermia 36

P-06 – Prof. Dr. Clifford Pang - Clifford Hospital – Non-Toxic Integrative Cancer Treatment....37

P-07 – Dr. Nora Meggyeshazi, et al - Clinical studies and evidences of modulated RF conductive heating (oncohtermia) method 37

P-08 – *Dr. Gabor Rubovszky, et al* - Co-administration of electrohyperthermia and bevacizumab in non-small cell cancer: A case presentation 39

P-09 – Mr. Balazs Acs, et al - Development and Designing in Oncotherm Group....39

P-10 – Dr. Eberhard W. Eckert - Die 10 Grundsätze der Elektrophysiologie. Elektrische Ladunge und Elektrowärme in der Onkologie 40

P-11 – Dr. Henning Saupe, et al - Effect of rouleaux formation of erythrocytes in blood of patients treated by oncothermia 41

P-12 – Dr. Oliver Szasz, et al - Effects far from equilibrium in electromagnetic heating of tissues....41

P-13 – Dr. Oliver Szasz, et al - Evaluation of single-arm studies of oncothermia....42

P-14 – Mr. Peter Lorencz, et al - Experience with chronic oncothermia treatments....43

P-15 – Prof. Dr. Seung Cheol Kim, et al - History of hyperthermia and electro-medicine 44

P-16 – Ms. Constanze Feisskohl, et al - History of oncothermia and their devices....45

P-17 – Dr. Frank Breitkreutz – Hyperthermie – Was müssen Krankenkassen und Beihilfe zahlen?....45

P-18 – Ms. Anett Gallne-Valyi - Introduction of the international quality management system: OncoTherm Group 46

P-19 – Dr. Ranieri Girolamo, et al - Liver deep electro-hyperthermia (EHY) following trans-arterial Mitomycin–C chemotherapy as a maintenance treatment in patients with multiple liver colo-rectal metastases 46

P-20 – Dr. Mohammed Al Masri - Middle East Oncotherm Medical Centres for Cancer Treatment....47

P-21 – Dr. Friedrich Migeod, et al - Multicenter, open-label, phase-II-trial to evaluate the efficacy and safety of low-radiofrequency deep hyperthermia with capacitive coupled electrodes (LRF-DHT) in treating patients with recurrent high-grade malignant gliomas 47

P-22 – Dr. Lajos Balogh, et al - Oncological and non-oncological applications of electromagnetic hyperthermia (Oncothermia®) in the veterinary clinics – 2 years of experience....48

P-23 – Prof. Dr. Andras Szasz, et al - Oncothermia combination with traditional Chinese medicine: network approach....48

P-24 – Prof. Dr. Gabriella Hegyi, et al - Oncothermia combination with Traditional Chinese Medicine: Proposal on Chinese Herbal Medicine approach 49

P-25 – Prof. Dr. Andras Szasz - Oncothemia Concensus....50

P-26 – Prof. Dr. Woong Ju, et al - Oncothermia in Gynecologic Oncology (Experience of the EWHA Womans University Hospital, Seoul)....51

P-27 – Prof. Dr. Doo Yun Lee, et al - Oncothermia treatment for small-cell-lung carcinoma....52

P-28 – Prof. Dr. Seokijn Haam - Oncothermia treatment of lung carcinoma....52

P-29 – Prof. Dr. Andras Szasz, et al - Personalization of oncothermia....53

P-30 – Mr. Gabor Skrihar - Research support by LabView-based data-acquisition systems....54

P-31 – Dr. Oliver Szasz - Success of OncoTherm 55

P-32 – Ms. Constanze Feisskohl, et al – The customer is king: The marketing concept of the Oncotherm Group....56

P-33 – Prof. Dr. VA. Solodkii, et al - The first experience of the local electro-hyperthermia (oncothermia) application in Russia....56

Index **57**

Abstracts of oral presentations

Monday, November 22nd

Studien und Leitlinien versus Versorgungsalltag

Prof. Dr. Harald Sommer[1]
(1) Klinik Bad Trissl, LMU Munchen,Germany

In der Onkologie, besonders in der Medikamentösen Tumortherapie wären gegenwärtiger Standard, innovative Therapien und künftige Entwicklungen ohne Studien nicht mehr denkbar. Der empirische Erkenntnisgewinn verliert an Bedeutung, damit auch das individuelle ärztliche Urteil („Erfahrung heißt gar nichts. Man kann eine Sache auch 35 Jahre schlecht machen“ Kurt Tucholsky). Die Überbewertung von Studienergebnissen andererseits birgt die Gefahr, dass ärztliche Erfahrung ignoriert wird, dass ausschließlich nach den möglichst neuesten Studien Therapieentscheidungen getroffen werden und der Arzt zum Erfüllungsgehilfen klinischer (industrieller!) Forschung wird.

Randomisierte klinische Studien (RCT) sind das zentrale methodische Prinzip um Strukturgleichheit zu erreichen (sonst nur durch aufwändiges paarweises Matching z. B. möglich) und zu objektiven Ergebnisse zu gelangen.
Einschränkungen für RCT stellen folgende Argumente dar: Hohe Kosten, bei seltenen Erkrankungen schwierig durchführbar (z. b. nur international möglich), nicht für alle Fragestellungen geeignet, ethisch nicht vertretbar (?), Ergebnisse aus RCT bilden die Behandlungswirklichkeit nicht ab…(1) da sich selektierte Studienteilnehmer vom Bevölkerungsdurchschnitt unterscheiden.
Die merkantil orientierten Studien wurden von initial 4 % auf 57 % innerhalb der letzten 30 Jahre gesteigert, nachgewiesen an 321 RCT (48 % Mamma-, 24 % Kolon- und 28 % Lungenkarzinom). Ebenso empfahlen die Autoren dieser Studien zunehmend den experimentellen Therapiearm („des kommerziellen Geldgebers….“). Wenn statistisch signifikante Ergebnisse einer RCT logisch mit einer Therapieempfehlung zugunsten der neuen Therapie assoziiert werden (2), so sollte doch in der Praxis trotz RCT und trotz aktueller Leitlinie der Fachgesellschaften jede Entscheidung individuell vom Arzt und im Konsens mit der Patientin getroffen werden dürfen. Aktuell erleben wir immer wieder, dass reflexartig Einzelstudien als Sensation oder „Durchbruch“ vermarktet werden. Ein üblicher Fehler in onkologischen Studien ist, dass die Rangfolge der Zielkriterien mit Gesamtmortalität, Lebensqualität, krebsbedingter Mortalität und Surrugatparametern auf den Kopf gestellt wird. „Ansprechen“ ohne Verlängerung der Überlebenszeit wird für Innovationen als positives Ergebnis gewertet – davon hat die Patientin keinen Nutzen!
Auf dem ASCO-Meeting 2010 zeigte sich Ernüchterung bezüglich der sogenannten zielgerichteten Substanzen (Targeted therapy), die vielfach bereits nach positiven Phase-II-Studien eine Zulassung erhalten hatten, denn in den Phase-III-Studien mit weniger selektionierten Patienten, erreichten die meisten Studien ihren primären Endpunkt nicht. Trotzdem sind die meisten dieser teuren und nebenwirkungsreichen angeblich „maßgeschneiderten“ Präparate bereits Bestandteil von Leitlinien geworden. Bei unkritischem Umsetzen der Leitlinien in den Krebszentren bleiben individuelle Wünsche und Patientenautonomie auf der Strecke.
Kritisch sind Ergebnisse retrospektiver Metaanalysen zu intepretieren: Sie haben zwar den Vorteil höherer statistischer Power, Neutralisierung extremer Ergebnisse und valider statistischer Methoden – aber sie können durch den Publication Bias sogar zu unterschiedlichen Schlussfolgerungen kommen – deshalb: Nicht zu wichtig nehmen (3)!
Die Pharmaindustrie ist verständlicherweise gewinnorientiert tätig, mit dem Ziel Studienergebnisse rasch als Basis Evidenzbasierter Medizin (EbM) in Leitlinien zu fixieren.
Erfolgversprechende Therapien ohne Aussicht auf breite Vermarktung und Höchstgewinn, wie alle Formen der Hyperthermie, sind Verlierer der Forschungsgesellschaft. In diesen scheinbaren Widersprüchlichkeiten gilt es, die Patientinnen vor überflüssigen Studien zu schützen, sie aber in sinnvolle und innovative Trials einzubringen. Wenn Studienärzte meist in der Klinik, die niedergelassen Onkologen und Hausärzte in die Studienarbeit integrieren, dann sind die Voraussetzungen für einen Vorteil für die Patienten durch Studienteilnahme gegeben unabhängig vom wissenschaftlichen Erkenntnisgewinn.

Literatur:

[1] Windeler J, et al (2008) Randomisierte klinische Studien. Z. Evid. Fortbild, Qual Gesundh, Wesen 102:321-325
[2] Booth CM, et al (2008) Evolution of the randomized controlled trials in oncology over three decades. J Clin Oncol 26:DOI 10.1200
[3] Baumann M (2001) Metaanalyse klinischer Studien: Stein der Weisen oder des Anstoßes. Coloproctology 23:60-65
[4] Kienle G, et al (2003) Konkurs der ärztlichen Urteilskraft? Dtsch Arztebl 100:A:2142-2146

The adulthood: 21 years of Oncothermia

Prof. Dr. Andras Szasz[1,2]
(1) Biotechnics Department, St. Istvan University, Hungary (Szasz.Andras@gek.szie.hu)
(2) Oncotherm Group, Germany

Background: Hyperthermia was the very first oncotherapy in human medical history. It was virtually forgotten till the discovery of the electromagnetic radiations. Form that time hyperthermia has a rapid development in the modern oncotherapy, [1], [2]. This relatively simple, physical-physiological method has a phoenix-like history with some bright successes and many deep disappointments. The reason is simple: the technique to deliver the appropriate energy and selectively target the deep-seated tumor, was not available. Oncothermia solved this long time open problem. It is based on the well-known traditional hyperthermia practice but extends it applicability and makes the process controllable and reproducible. Oncothermia works on effective and precisely selective cell-destruction [3]; it mobilizes the natural protecting mechanisms, and kills the malignant cells by apoptosis and immune reactions. To construct the method was a biophysical and technical problem; this is why a non-medical practitioner like myself could have a role in its development.

Discussion: Oncothermia is far not a device alone. It is a method based on the state-of-art of the biomedicine, and the devices are the tools to perform the method optimally [4]. This process is actively exist in all the movement of Oncotherm from its establishment, and decides the 21 year old history. This method was the first which curatively applied the results of the most modern achievements of fractal physiology [5], [6] and reached a cellular selectivity of the method by patented way worldwide. The oncothermia satisfies all the modern requirements of the up-to-date oncological modalities:

- ✓ Oncothermia is personalized, gently, painless treatment-modality, with rare side effects (skin redness);
- ✓ Oncothermia is applicable complementary to all the known conventional oncotherapies;
- ✓ Oncothermia is non-toxic, local and depresses the toxicity of the parallel applied other treatments also;
- ✓ Oncothermia has low risk/benefit ratio,
- ✓ Oncothermia is a definite tool for longer survival;
- ✓ Oncothermia does not suppress the quality of life, even moderates the side-effects of the parallel treatments;
- ✓ Oncothermia is (in comparison to the other treatments) cheap and effective, its cost/benefit ratio is very low.

Oncothermia results are strongly science based. It had long way from laboratory to clinical use [7].

- ✓ Oncothermia is the very first method using the thermally induced electric field effects as curative force in oncology [8], showing the field dependent cell killing of malignancies.
- ✓ The used frequency is 13.56 MHz. This affects the cell-membrane and effectively uses the beta-dispersion to destroy it.
- ✓ This frequency makes higher applicability due to no Faraday cage is necessary by its application.
- ✓ The carrier frequency is modulated in oncothermia method. While the unmodulated methods simple deliver the power (absorbed heat) oncothermia delivers information (making apoptosis and all the other effects which are proven.)
- ✓ The electric field makes the job in condition of moderate temperature increase, and not the absorbed heat makes necrotic processes like in other hyperthermia solutions. The electric field has no physical or physiological contra-reactions (negative feedback) which is the case of temperature (heat) alone.
- ✓ Due to the apoptotic way the applied incident power of Oncothermia is a small fraction of others. This makes the focus of oncothermia precise [no extensive heat-flow is generated from the target to the neighbourhood. The parasite heat-flows at classical heating smear the focus by time.
- ✓ The relatively small incident energy makes the process more controllable, no considerable heat, heat is taken away uncontrolled by the surface cooling. The process is controlled by the impedance of the body in oncothermia, so the target is a part of the electric circuit, it is tightly and real-time controlled.
- ✓ Due to the smaller applied energy the side effects (and generally the safety) in oncothermia is much more optimal, practically no side effects are existing.

- ✓ Due to the power-control, measurement of the temperature is not necessary (even it is not important, due to the temperature makes the "smearing" of the focus), we measure the incident energy (like the "gold-standard radiotherapy does also). This approach makes the oncothermia does physical (the temperature is not a dose), and makes unnecessary to measure the temperature of the target. This avoids many side-complications (possible inflammations, disseminations, ulcerous wounds, etc.).
- ✓ Of curse the electronic solution and the full control and the electrode arrangement are also entirely different to solve the above points to optimize the oncothermia approach.

Conclusions: Oncothermia opened new dimensions in hyperthermic oncology. Summarizing with a simple analogy by a phrase for medicine: "The difference between the medicine and the poison is only the dose". Oncothermia is taking care about the correct dosing. This makes its difference from classical heating processes!
Oncothermia had used its "childhood" for basic developments which are described above. The method had been grown up, and reached the "adulthood". We are proud on these facts and on the versatile devices which we are producing. But the devices are not enough alone! We need their application, we need the cooperation of the smart physicians who are using these equipments. Oncotherm is indebted for the doctors and nurses, whom work realizes the development of the method. We are especially thankful for the German quality-control and quality management which improves the devices day-by-day and raise the reputation of the German medicine and the European innovative habits.

References:

[] DeVita VT. Jr, Hellman S, Rosenberg SA (2001) Cancer Principles and Practice of Oncology 6th edition. Lippincott Williams and Wilkins
[2] Perez CA, Brady LW, Halperin EC, Schmidt-Ullrich RK (2004) Principles and Practice of Radiation Oncology. 4th edition, Lippincott Williams and Wilkins
[3] Szasz A, Vincze Gy, Szasz O, Szasz N (2003) An energy analysis of extracellular hyperthermia. Magneto- and electro-biology 22(2)103-115
[4] Szasz A (2006) Physical background and technical realization of hyperthermia. In: Baronzio GF, Hager ED (eds) Locoregional Radiofrequency-Perfusional- and Wholebody- Hyperthermia in Cancer Treatment: New clinical aspects, Ch. 3., Springer Science, pp 27-59
[5] Szendro P, Vincze G, Szasz A (2001) Bio-response on white-noise excitation. Electromagnetic Biology and Medicine 20(2):215-229
[6] Szendro P, Vincze G, Szasz A (2001) Pink noise behaviour of the bio-systems. Eur Biophys J 30(3):227-231
[7] Andocs G, Szasz O, Szasz A (2009) Oncothermia treatment of cancer: from the laboratory to clinic. Electromagnetic Biology and Medicine 28:148-165
[8] Andocs G, Renner H, Balogh L, Fonyad L, Jakab Cs, Szasz A (2009) Strong synergy of heat and modulated electromagnetic field in tumor cell killing, Study of HT29 xenograft tumors in a nude mice model. Radiology and Oncology (Strahlentherapie und Onkologie) 185:120-126

Monday, November 22nd, 2010
15:50-16:20
(Keynote lecture)

CAM and Cancer around the world

Dr. Ralph Moss[1]
(1) Cancer Communications Inc, USA

The author travels around the world looking for promising cancer treatments for clients of his report and consultation service. He reports here on his site visits to complementary and alternative medicine (CAM) clinics that treat cancer in the United States, Caribbean, Europe, Near East and Asia. What are some of the methods that are commonly found in these clinics? What are the "signature" methods that are unique to each particular venue? Two commonly encountered modalities are those that (a) mobilize the immune system in various ways to fight cancer (immunotherapy) and (b) that use heat and/or fever through various means to combat the disease (hyperthermia). Which clinics and doctors are taking the lead in using these modalities?

He will compare the degree of integration of hyperthermia and immunotherapy in the US and in various other countries. The author will compares cancer treatment in the US with the situation he has encountered in other countries. At a minimum, he will discuss the I.W.I.T. clinic, Austria (Dr. Ralf Kleef); Aeskulap, Switzerland; Humlegaarden, Denmark; and the New Hope Clinic, Israel, all of whom are employing Onctothermia devices and techniques.

Finally, he will assess the state of complementary and alternative medicine on a worldwide basis. What are the main challenges that the CAM movement faces? What is the basis for optimism in its eventual integration into mainstream medicine?

Laudatio Dr. med. Dr. rer. nat. Dipl.-Phys. E. Dieter Hager

Dr. Friedrich Migeod[1]
(1) Biomed Klinik, Bad Bergzabern, Germany

Dr. Dr. Dipl.-Phys. E. D. Hager ist in der Nacht des 13. Dezember 2009 im Alter von nur 62 Jahren, für uns alle dramatisch und erschütternd auf der Höhe seiner geistigen Schaffenskraft und Reife, in der von ihm gegründeten BioMed-Klinik verstorben. Er war uns ein Freund, ein Gefährte, ein Helfer, ein hilfsbereiter Arztkollege, ein Familienmensch für Mitarbeiter und Verwandte und eine Eindrucksvolle, visionäre Persönlichkeit in Einem, mit allen Widersprüchen die einen individuellen Pionier charakterisieren. Der Name von Dr. Hager ist untrennbar verbunden mit der Entwicklung und wissenschaftlichen Erforschung der komplementären Krebsheilkunde seit den 80er Jahren, konsequent und unvoreingenommen, in der Nachfolge von Persönlichkeiten wie Dr. Nieper, Prof. von Ardenne, Prof. Linus Pauly, Dr. Josef Issels und anderen. Dr. Hagers geniale Erkenntnis war, dass die klassische Onkologie trotz Milliarden an Therapiekosten und Forschung im Gesundheitssystem wegen steigender Krebsfälle an ihre menschlichen und finanziellen Grenzen stößt und der Ausweg in der biologisch orientierten komplementären Krebsheilkunde liegen könnte, unter Bewahrung von Integrität und Lebensqualität der Patienten. Konsequent wie Dr. Hager war, bedeutete dies, dass er sich nicht in den Elfenbeinturm der Wissenschaft zurückzog, wie er es unter dem Schutz einer Universitätsinstitution hätte haben können, sondern die BioMed-Klinik vor 20 Jahren gründete, mit den Zielen der Zuwendung zu Patienten, insbesondere des Krebserkrankten. Menschenwürdige Therapien und unablässiger Forschergeist verband Dr. Hager in einer Person und in einem Konzept. Sein ärztlicher Impetus und Ethik zwang ihn über die Grenzen der konservativen Medizin zu schreiten um in der Onkologie heilende klassische Medizin, innovative Methoden wie die Hyperthermie und Naturheilkunde im wörtlichen Sinne zu versöhnen. Die Tragik ist, dass Dr. Hager an derselben Krankheit sterben musste, vor der er so viele andere Menschen gerettet hat.
Persönlich war Dr. Hager bescheiden, hatte wenig materielle Ansprüche, obwohl er es sich hätte bequem machen können. Seine Rastlosigkeit führte ihn auf viele Reisen nach Amerika und Asien auf wissenschaftlichen Kongresse und zu gleichgesinnten Forschern. Selbst als es ihm in den letzten Jahren immer schlechter ging ließ er nicht nach in seiner drängenden Energie, wohl im Bewusstsein, dass seine Zeit begrenzt war. Groß war sein Engagement zugunsten Krebsselbsthilfeorganisationen, weil er dort Menschen fand die ähnlich altruistisch Krebspatienten zur Seite standen. Er schonte sich körperlich und mental nicht trotz Warnungen seiner Freunde.
Es war ihm immer ein tiefes Anliegen, die von ihm vertretenen Thesen in der Onkologie durch wissenschaftliche Studien, Anwendungsbeobachtungen und Hintergrundbetrachtungen zu festigen und zu etablieren. Zusammen mit Mitarbeitern publizierte er Studien über die Effekte des Lithium auf Stammzellen, über die Antitumorbehandlung mit Alkyllysophospholipiden, zur metronomischen Therapie mit Cyclophosphamid und Capecitabine, zu Lebensqualität und Überleben von Patienten mit fortgeschrittenem Pankreaskarzinom, zur lokoregionalen Tiefenhyperthermie von Lebermetastasen nach CRC, zum Thema Fieber, Pyrogene und Krebs, zur intrakavitären hyperthermen Perfusion des Peritoneums bei Aszites und des rezidivierenden Blasenkarzinoms, Prävention, Rezidivprophylaxe und additive Therapie von Krebserkrankungen durch die Kombination von Tiefenhyperthermie, Tamoxifen und Alpha-Interferon bei malignem Melanom und viele andere mehr. Bahnbrechend sind seine Arbeit zur multimodalen Therapie des Glioblastoma multiforme WHO IV und des Astrozytoma WHO III durch die Kombination von regionaler Tiefenhyperthermie, Thalidomid, Boswellia carterii und Selen sowie die intraperitoneale Behandlung des peritoneal metastasierenden rezidivierenden Ovarial-Karzinoms durch eine spezielle intraperitoneale Technik, zu der er auch eine spezielle Apparatur zur hyperthermen Perfusion konstruieren ließ. Darüber hinaus widmete er sich sozial-medizinischen Fragen, wie Kostenexplosion im Gesundheitswesen, speziell in der Onkologie, durch Zulassung innovativer Substanzen mit nur minimalem Überlebensvorteil für den Patienten (z. B. Erlotinib beim Pankreas-Karzinom), der Lebensqualitäts-Messung, dem ethischen Denken in der Onkologie vor dem Hintergrund des Gewinnorientierten medizinisch-industriellen Komplexes. In bestechender Konsequenz vertrat Dr. Hager seine Ideen mit Charisma, Verve und Charme im Ausland, vor allem in den USA und Südkorea, im Inland als Mitglied mehrerer bedeutender wissenschaftlicher Ärzteorganisationen und zeitweise Herausgeber der Deutschen Zeitschrift für Onkologie, gegründet von H. Nieper.
Dr. Hager hinterließ eine Fülle von Wissen, fruchtbare Anstöße in der Onkologie, ein Vorbild in der medizinischen Lebensführung für Mitarbeiter und ein integres, unbeflecktes Weltbild. Sein Verlust ist nicht zu verschmerzen, seine Impulse werden in die Zukunft reichen. Künftige Arztgenerationen werden, unbeeinflusst von kleinteiligen Auseinandersetzungen in der Ärzteschaft, dem Wert seines Wirkens noch mehr erkennen als seine heutigen Mitarbeiter.

Monday, November 22nd, 2010
17:05-17:25

Relapsed malignant gliomas treated with electro- hyperthermia: report of 24 patients

Prof. Dr. Giammaria Fiorentini[1], Dr. Francesco Montagnani[1], Dr. Gina Turrisi[1], Dr. Susanna Rossi[1], Dr. Patrizia Dentico[1], Dr. Sara Licitra[1], Dr. Piergiorgio Giannessi[1]
(1) Oncology Unit, San Giuseppe General Hospital, Empoli, Florence, Italy. oncologiaempoli@usl11.toscana.it

The purpose of this study was to evaluate the activity and toxicity of electro-hyperthermia (ET) on relapsed malignant glioma patients. Twenty four patients with histologically diagnosed malignant glioma entered the study. Sixteen patients had glioblastoma multiforme, four had anaplastic astrocytoma grade III and four had anaplastic oligodendroglioma. All patients were pre-treated with temozolamide-based chemotherapy and radiotherapy. Hyperthermia with short radiofrequency waves of 13.56 MHz was applied using a capacitive coupling technique keeping the skin surface at 20 degrees C. The applied power ranged between 60-150 Watts and the calculated average equivalent temperature in the tumours was above 40 degrees C for more than 90% of the treatment duration. Two complete remission long lasting (13 months and 72 months), 4 partial remissions and 6 stabilizations were achieved, with a disease control of 50%. The median duration of response was 12 months (range 6-72). The median survival of the entire patient population was 11 months, with 30% survival rate at 1 year. ET appears to have effectiveness in adults with relapsed malignant glioma especially in the histological subtype astrocytoma.

Monday, November 22nd, 2010
17:30-17:50

Transurethrale Thermotherapie in Kombination mit zeitlich begrenzter Androgen-Blockade bei lokalisiertem Prostatakarzinom – 10-Jahresverlaufsbeobachtung an 123 Patienten

Dr. Friedrich Douwes[1],
(1) Klinik St. Georg, Bad Aibling, Germany

Die transurethrale Thermotherapie ist eine schonende und nicht invasive Methode, die die Prostata selektiv vom Prostatakarzinomgewebe befreien kann.

Durch eine gleichzeitig eingeleitete komplette Androgenblockade kann dieser Prozess dauerhaft positiv unterstütz werden. In unserer Anwendungsstudie, die vor 10 Jahren begonnen wurde, wurden 123 Patienten mit bioptisch gesichertem und auf die Prostata begrenztem Prostatakarzinom eingeschlossen.
Die Patienten erhielten nach Einleitung einer kompletten Androgenblockade eine zweimalige transurethrale Thermotherapie mit dem PCT der Fa. Oncotherm.

Die Androgenblockade wurde maximal ein Jahr aufrechterhalten und dann beendet.
Das von uns gewählte Therapieschema hat gezeigt, dass 84,5 % aller Fälle nach der initialen Therapie auch 8 Jahre danach noch Rezidiv frei waren, 15,5 % erlitten ein PSA Rezidiv, kein Patient erlitt eine Metastasierung oder verstarb im Beobachtungszeitraum an den Folgen eines Prostatakarzinoms. Diese Ergebnisse sollten in einer randomisierten, klinischen Studien bestätigt werden, was dann zu einem Paradigmawechsel für die Behandlung des klinisch lokalisierten oder lokal fortgeschrittenen Prostatakrebs führen könnte.

Monday, November 22nd, 2010
17:55-18:15

Treatment of advanced Pancreas Cancer with Chemo-Thermotherapy

Dr. Friedrich Douwes[1]
(1) Klinik St. Georg, Bad Aibling, Germany

Background: The results in the therapy of pancreas carcinoma remain disappointing. In nearly all cases the disease progresses, response rates of cytotoxic therapy are low and the 5-year survival rate amounts to 1%. The purpose of our treatment was to enhance the effectiveness of a cytostatic treatment with mitomycin c by combination with regional hyperthermia.

Patients and Methods: In a retrospective analysis 30 patients with advanced pancreatic carcinoma treated with a combined treatment with hyperthermia and chemotherapy were included. 5-fluorouracil (5-FU) (500 mg/m2) and calcium folinat (200 mg/m2) was given on day 1-5, mitomycin c (8 mg/m2) was injected on day 1. Regional capacitive radiofrequency hyperthermia (13.56 MHz) was applied on day 1, 3, 5 and 10, the duration was 60 minutes. The mean
temperature of the tumor tissue was 420C – 440C. Treatment was repeated every 4 weeks until progression.

Results: The 30 patients received a total of 94 cycles (median 3, range 1-9) of combined therapy. According to the standard criteria, 1 patient had a complete remission, 10 patients (33,3%) had a partial remission; 12 (40%) had a stable disease. 7 patients (23,3%) did not respond to the therapy and showed progressive disease. Median survival time was 8 months (range 2-53 months), time to progression was 5.5 months (range 1-40 months). In a follow up study it could be shown that the treatment can be improved with even better results. We will present new data and some successfully treated cases.

Conclusion: The combined treatment shows a remarkable outcome in the therapy of advanced pancreatic carcinoma and is well tolerated. The data suggest further evaluation in randomized trials.

Monday, November 22nd, 2010
18:20-18:40

Warum ich Prostatahyperthermie mache - Datenlage

Dr. Marianne Müller[1]
(1) Institute of Data Analysis and Process Design, School of Engineering, Zurich University of Applied Sciences, Winterthur, Germany

Auf der Basis der Datenlage der ERSPC Studie werden die Hintergründe und Argumentationsgrundlagen beleuchtet. Die Statistiken hinter der Statistik werden mit einbezogen und erläutert. Die Datenlage rückt die Prostatahyperthermie in eine wichtige Position im allgemeinen Therapieschema der gutartigen und bösartigen Erkrankungen. Vor dem Hintergrund der neu erstellten Leitlinien zur activ surveillance findet sich die Prostatahyperthermie in einer Schlüsselposition zur Behandlung der Patienten gerade mit bösartigen Erkrankungen.

Ich biete Prostatahyperthermie an- und das hat gute Gründe.

Elektrohyperthermie in Kombination mit Strahlentherapie und Lowdose – Chemotherapie zu optimalen lokoregionären Krebstherpie bei minimalen Nebenwirkungen

Dr. Wulf-Peter Brockmann[1]
(1) Institut OncoLight, Hamburg, Germany

Gerade in vermeintlich palliativer onkologischer Behandlungssituation ist man gehalten, nur noch Krankheitsrisiken und Symptome zu verhindern oder zu mindern, aber nicht mehr mit minimalen Erfolgsaussichten und maximalen Nebenwirkungsrisiken Heilungen zu erzielen. Das Optimum solch einer Behandlungsstrategie wird anscheinend dann erreicht, wenn man hierfür die Elektrohyper thermie/ Oncothermie in ein relativ anspruchsvolles, teilweise Fachdisziplin-übergrei fen des Gesamtkonzept einbettet.
Gleiches gilt für primär kurative Bemühungen, adjuvante Hochrisikosituationen und für das Ziel, neoadjuvant Tumore oder Metastasen wieder resektabel werden zu lassen.

Das vorzustellende Therapiekonzept wird aus forensischen Gründen nur bei Patienten, die Standard (chemo)-Therapiekonzepte oder verstümmelnde Operationen für sich ausdrücklich ablehnen, angewendet.

Dieses Gesamtkonzept besteht regelmäßig

1. aus einer hyperfraktioniert akzelerierten Strahlentherapie, deren Enddosis eindeutig unter der Verträglichkeitsgrenze der gesunden Gewebe in der Tumorumgebung liegen muss, wobei in der Regel zweimal täglich mit 6- bis 7-stündigem Intervall Einzeldosen in Höhe von 1,1 Gy (Lunge), 1,2 Gy (intrabbdominal, intrapelvin, Leber, pharyngeal/ zervikal) und 1,5 Gy (Ganzhirn/ Myelon) eingestrahlt werden. Ossär können im Einzelfall auch hypofraktionierte Schemata bevorzugt werden.
2. aus einer lowdose-Chemotherapie, die aufgrund ihrer geringen Dosierung immer nur lokal/ lokoregionär im Behandlungszielgebiet sensibilisierend wirken soll und nicht systemisch das (zelluläre) Immunsystem belasten darf. Thrombopenien < 50.000 sollten ebenfalls vermieden werden. Zu den verwendeten Medikamenten gehören in erster Linie Substanzen, deren Behandlungsrisiken sich auch von Nicht-Pharmakoonkologen gut kalkulieren lassen, wie insbesondere Mitomycin C, 5-FU, Carboplatin, Endoxan, Ixoten und Gemcitabine, wobei Mitomycin C und Gemcitabine bei Bestrahlungen im Thoraxbereich wegen ihrer Pneumonitisrisiken kontraindiziert sind. Es werden nur Einzeldosen von 3 bis 4 mg Mitomycin C, 150 bis 200 mg 5-FU, 30 bis 50 mg Carboplatin, und/ oder 200 bis 300 mg Gemcitabine, jeweils pro qm KOF, appliziert, bis zu 2- bis 8mal während einer Strahlentherapieserie, je nach Medikament oder evtl. auch Medikamentenkombination. Hiervon abweichend werden z.B. beim Mammakarzinom bzw. Mammakarzinom-Metastasen Dosen von 50mg Endoxan/ Ixoten täglich als Dauertherapie über ca. 3 Wochen per os verabreicht.
3. aus einer Elektrohyperthermieserie, die schon in der Planungsphase der Radiatio einsetzt, um mindestens bis in die Woche nach Strahlentherapieende hinein anzudauern.
4. Auch die Ganzkörperhyperthermie und Oberflächenhyperthermie werden ggf. ins Konzept integriert, die Oberflächenhyperthermie vornehmlich bei Hautmetastasierungen, die Ganzkörperhyperthermie, um tatsächlich einmal auch in tiefer gelegenen Tumorregionen wie Mediastinum, Leber oder Retroperitoneum während der direkt angeschlossenen Elektrohyperthermie zusätzlich zu den tumoriziden elektromagnetischen Feldern tumorizide Temperaturen von mehr als 40 Grad zu erzeugen.

Zu den teilweise überraschenden qualitativen Ergebnissen, von denen im Poster einige in Labor- und Bilddiagnostik vorgestellt werden:

1. Es gab bislang keine Tumorhistologie, die grundsätzlich von diesen Maßnahmen auszuschließen gewesen wäre - abgesehen von Malignomen aus dem Kreis der primären Lymphome und Leukämien oder Tumoren im Kindesalter, die sämtlich in die Hand der hierfür vorgesehenen Spezialisten gehören – nicht zuletzt auch forensisch bedingt.
2. Es konnte die ganze Leber, aber auch die gesamte Lunge oder das Mediastinum auf diese Weise nebenwirkungsarm behandelt werden.
3. Die Therapiekombination ließ sich durchweg ambulant durchführen.
4. Dabei konnten inoperable Tumore oder Tumorrezidive bis in eine R0-Resektabilität hinein verkleinert werden.
5. Auch recht strahlenresistente Tumore wie das adenoidzystische Karzinom oder das lymphoangioepitheliale Sarkom wurden auf diese Weise angehbar.
6. Unter der synchronen Strahlen- und Elektrohyperthermie konnte man die o.g. Chemotherapeutika zur Wirkungsverstärkung auch dann verwenden, wenn der Primärtumor hiergegen als resistent galt oder im pharmakoonkologischen Therapieverlauf resistent geworden war (z.B. bei Pat. mit Ovarialkarzinomen).
7. Die Logistik für diese Drei- bis Vierfachtherapie war zwar anspruchsvoll und aufwendig, ließ sich aber ausnahmslos bei gutem Willen aller beteiligten Fachdisziplinen meistern – Voraussetzung war hierfür, dass die Konzeptverantwortung in einer Hand blieb.

Abstracts of oral presentations

Tuesday, November 23rd

Hyperthermia: Where is the evidence?

Prof. Dr. Alexander Herzog[1]
(1) Fachklinik Dr. Herzog, Germany

Abstrakt: Seit mehr als 100 Jahren wird auf dem Gebiet der Hyperthermie geforscht. Zahlreiche Wirkungsmechanismen der Hyperthermie auf Krebszellen konnten mittlerweile aufgeklärt werden. Voruntersuchungen auf zellulärem Niveau und in Tierversuchen konnten eine günstige Wirkung der Hyperthermie bei Krebserkrankungen belegen. Auch bei Menschen konnte in Studien mit der Hyperthermiebehandlung eine Wirkungsverstärkung anderer Krebstherapien wie Chemotherapie oder Bestrahlung gezeigt werden.

Interessanterweise besteht in Deutschland eine international einmalige Konstellation bzgl. der Kostenerstattung. Während bei den gesetzlichen Krankenkassen die Hyperthermie nach wie vor bei den „Methoden unbewiesener Wirksamkeit“ eingeordnet wird, übernehmen die privaten Krankenversicherungen das Behandlungsverfahren bereits seit Jahren in Verbindung mit Chemotherapie oder Bestrahlung. Wir haben damit in Deutschland eine Situation, wo ganz offiziell Angehörige höherer gesellschaftlicher Schichten eine bessere medizinische Versorgung erhalten, allen Dementi einer Mehrklassenmedizin zum Trotz.

Woran könnte es liegen, dass es durch alle Ebenen einen solchen Widerstand gegen den Einsatz der Hyperthermiebehandlung gibt, während teurere und häufig nicht überzeugende Chemo- oder Antikörpertherapien problemlos akzeptiert werden?

Hier müssen grundsätzliche Erwägungen an erster Stelle genannt werden:

1. Die Hyperthermiebehandlung ist ein unspezifisches Behandlungsverfahren, d. h. theoretisch könnten eine sehr große Zahl von Krebspatienten ergänzend mit Hyperthermie behandelt werden. Wenn nun eine große Zahl von Chemotherapien oder Bestrahlungen mit Hyperthermie kombiniert würde, würde das die Behandlungskosten enorm in die Höhe treiben. So ist verständlich, dass an ein solch umgangreiches Therapieverfahren besondere Maßstäbe bzgl. des Wirksamkeitsnachweises gelegt werden müssen.
2. Die Schwierigkeit Studien durchzuführen: Während in üblichen Studien Kontrollgruppen häufig mit einem Placebo behandelt werden, ist ein solches Vorgehen bei der Hyperthermiebehandlung nicht möglich. Aus subjektiver Sicht des Patienten wird eine möglicherweise wirksame Therapiemaßnahme vorenthalten. Eine Studie mit randomisierter Verteilung von Patienten auf Therapiegruppe mit Hyperthermie bzw. Therapiegruppe ohne Hyperthermie wird vom Patienten nicht akzeptiert.
3. Fehlende finanzielle Voraussetzungen für groß angelegte Studien: Während bei medikamentösen Neuentwicklungen die Herstellerfirmen Zulassungsstudien intensiv fördern, stehen zur Erforschung der Hyperthermiebehandlung kaum Fördergelder zur Verfügung. Die Gerätehersteller können nicht als Sponsor solcher großen Studien auftreten, da mit Hyperthermiegeräten keine solch großen Umsätze wie mit Medikamenten zu erzielen sind. (Schließlich können mit einem Hyperthermiegerät tausende von Patienten behandelt werden, während Medikamente an jeden einzelnen Patienten neu verkauft werden können). Die Erforschung der Hyperthermie beschränkt sich daher im universitären Bereich auf wenige besonders engagierte Forscher, die in der Erforschung der Methode wiederum von den Vorgaben der pharmazeutischen Industrie abhängig sind. Denn diese finanziert die Studienmedikation und bestimmt damit, welche Medikamente für die Studie zum Einsatz kommen.
4. Die Vielzahl verschiedener Anbieter und Techniken mit unterschiedlichen Therapiestandards: Mehrere Firmen stellen Hyperthermiegeräte her, die mit unterschiedlichen Techniken und Applikatoren eine Energieeinstrahlung in Tumorgewebe bewirken. Unterschiede in den technischen Voraussetzungen wie Wellenlänge, Energieeintrag, Feldgröße, Fokusierung auf ein bestimmtes Gebiet sind die einen der Variablen, auf Patientenseite sind die Variablen die Art des Tumors, die Tumorlokalisation, die Abkühlung des Gewebes durch die Blutzirkulation, die Bildung von schmerzhaften Hautspots usw. Darüber hinaus gibt es noch unterschiedliche Hyperthermietechniken wie Oberflächenhyperthermie, regionale Tiefenhyperthermie, Ganzkörperhyperthermie oder hypertherme Perfusion, die z. T. auch miteinander konkurrieren.
5. Anbieter mit ungenügender onkologischer Qualifikation: Durch die in Deutschland bestehende Therapiefreiheit kann sich jeder Arzt oder sogar Heilpraktiker ein Hyperthermiegerät beschaffen und Patienten behandeln. Dies führt dazu, dass Patienten Hyperthermiebehandlungen auch ohne Koordination mit anderen onkologischen Therapieverfahren wie Chemotherapie oder Bestrahlungen erhalten. Dies verbessert nicht die Akzeptanz der Hyperthermiemethode bei den Kostenträgern.

Cholangiocellular Carcinoma: Survival without symptoms with hyperthermia – A case study

Dr. Ulrich Reimnitz[1]
(1) Praxis dr. Reimnitz, Germany

Zusammenfassung: Das intrahepatische cholangiocelluläre Carcinom gehört in Mitteleuropa zu den seltenen malignen Erkrankungen. Die Diagnose wird häufig erst in einem fortgeschrittenen Stadium gestellt. Die Behandlungsansätze sind unterschiedlich, eine Heilung kann nur selten erreicht werden. Beschrieben wird die Behandlung einer 61-jährigen Patientin mit einem intrahepatischen CCC. Es konnte gezeigt werden, dass mit der Kombination von extremer Ganzkörperhyperthermie und Regionaler Tiefenhyperthermie ein dreijähriges symptomfreies Überleben möglich ist.

Schlüsselwörter: Cholangiocelluläres Carcinom (CCC), Regionale Hyperthermie, Ganzkörperhyperthermie, Induzierte Hyperglykämie, Karnofsky-Index

Einleitung: Über den Zeitraum von drei Jahren konnte mit der Kombination aus Regionaler Hyperthermie (RHT) und Ganzkörperhyperthermie (GKH) ein symptomfreies Überleben, Karnovsky-Index 100%, bei einer Patientin mit intrahepatischen Cholangiocellulärem Carcinom erreicht werden. Das Intrahepatische Cholangiocelluläre Carcinom (CCC) ist eine maligne Erkrankung ausgehend von den Zellen des Gallengangepithels. Bei mehr als 90 % der Erkrankungen handelt es sich um Adenokarzinome.(4) Amerikanische Studien geben die Häufigkeit mit 2 bis 6 Neuerkrankungen pro Jahr auf 100000 Personen an. Der Erkrankungsgipfel liegt in der sechsten Lebensdekade.(4) In den letzten Jahrzehnten stieg die Zahl der Neuerkrankungen im Jahr an.(11,27) Cholecystolithiasis, rezidivierende Cholecystitis gelten in Mitteleuropa und im USamerikanischen Raum als wichtige Risikofaktoren für das CCC. Eine familiäre Häufung wird vermutet.(12,13,15) Es erfolgt über abdominelle Sonographie, MRT und Angio-CT die Sicherung der Diagnose. Untersuchungen von Tumormarkern insbesondere Ca 19-9 und histologische Untersuchungen ergänzen die Diagnostik.(4,14,16,19,20) Die Prognose der Erkrankung ist sehr schlecht. Die Dreijahresüberlebensrate bei inoperablen Tumoren beträgt weniger als 10 %. Die Überlebenszeit über alle Stadien beträgt 6 Monate.(4,23) Die einzige kurative Behandlungsmöglichkeit besteht in der frühzeitigen Operation. (7,17,21,22,24) Andere Therapieansätze wie radikale operative Therapie, Strahlentherapie, Chemotherapie oder Photodynamische Therapie können Überlebenszeit und Lebensqualität nicht verbessern.(2,3,1,5,6,7,8,9,10,18) Die Überprüfung anderer Behandlungskonzepte sollte in den Mittelpunkt der onkologischen Forschung gestellt werden.(25,8,)

Falldarstellung: Beschrieben wird der Fall einer 1944 geborenen Patientin. Aus der *Anamnese* bekannt sind ein Colonkarzinom der Mutter und ein Gallenblasenkarzinom der Schwester der Patientin. Bekannt und sonographisch gesichert ist eine Cholecystolithiasis seit 2000. Weitere Erkrankungen in der Vorgeschichte der Patientin ist eine arterielle Hypertonie seit 2002. Die Patientin wurde erstmals 2005 in Zusammenhang mit rezidivierenden Oberbauchbeschwerden zur weiteren *Diagnostik* vorstellig. Sonographisch wurde die Cholecystolithiasis bestätigt, eine operative Therapie jedoch abgelehnt. Ab Januar 2006 massive persistierende auch nahrungsunabhängige Oberbauchbeschwerden führten zunächst über abdominelle Sonographie und 2/2006 durch MRT zur *Verdachtsdiagnose* Intrahepatisches Cholangiocelluläres Carzinom (CCC). Mittels Angio-CT und dem erhöhten Tumormarker Ca19-9 wurde der Verdacht bestätigt. Anhand der vorliegenden Befundkonstellation konnte ein Hepatocelluläres Carcinom (HCC) ausgeschlossen werden. Zusätzlich durchgeführte Untersuchungen (MRT Becken, CT Thorax, Gastroskopie, Coloskopie, Mammographie) konnten andere maligne Prozesse ausschließen. Eine histologische Sicherung der Diagnose lehnte die Patientin ab. *Diagnose:* Intrahepatisches Cholangiocelluläres Carzinom mit bilobulärer Metastasierung. Metastasen im zentralen rechten Leberlappen, den Lebervenenstern infiltrierend und multiple bis 3mm große Metastasen im Lebersegment VIII und im Bereich des Leberhilus. Unter Berücksichtigung aller Befunde konnte eine operative Therapie nicht empfohlen werden. Chemotherapeutische Behandlungsansätze lehnte die Patientin ab. *Therapie:* Wir führten eine Kombination aus Regionaler Tiefenhyperthermie (RHT) und extremer Ganzkörperhyperthermie (GKH) unter Tumorübersäurung und relativer Hyperoxygenierung durch. *Behandlungsprinzip extreme Ganzkörperhyperthermie:* Erhöhung der Körperkerntemperatur auf 42,0°C bis 42,4°C für 90 Minuten mittels wassergefilterter Infrarot-A-Strahlung. Eingesetzt wurden hier die Geräte IRATHERM 2000 und IRATHERM 1000 der Firma "von Ardenne" Dresden. Simultan wurde eine Hyperglykämie induziert. Blutzuckermaximum 25 mmol/l. Ziel der Hyperglykämie ist eine Tumorübersäuerung und damit eine höhere Thermosensibilität der Tumorzellen, Laktatmaximum hier 4,3 mmol/l während des Temperaturplateaus. *(Anlage 1) Behandlungsprinzip Regionale Tiefenhyperthermie:* Elektromagnetische Wellen mit einer Frequenz von 13,56 MHz erzeugen durch kapazitive Kopplung einen

Temperaturgradienten zwischen intrazellulärer und extrazellulärer Flüssigkeit im Tumorgewebe, der über eine Zeit von 60 Minuten zur Zellzerstörung führen kann. Die Fokussierung auf das Tumorgewebe erfolgt durch dessen geringere Impedanz. Eingesetzt wurde hier das Gerät EHY-2000 plus der Firma "Oncotherm Troisdorf". *(Anlage 2) Behandlungsplan:* Es wurden mehrere Behandlungszyklen durchgeführt. Ein Zyklus bestand aus einer Serie von mindestens 7 RHT- Behandlungen und einer extremen Ganzkörperhyperthermie. Der Abstand der Behandlungszyklen wurde nach der Tumorprogression festgelegt. Hier wurde der Tumormarker Ca 19-9 als zuverlässiger Indikator für eine Tumorprogression ausgewählt.

Zusatzbehandlungen und Prinzip: Parallel zu jedem Behandlungszyklus erfolgte eine Sauerstofftherapie nach dem Prinzip der Sauerstoffmehrschritttherapie von Prof. M. v. Ardenne. Über 18 Tage wird nach vorheriger oraler Gabe von 1000 mg Vitamin C und 250 mg Magnesiumorotat jeweils täglich für 2 Stunden reiner Sauerstoff zur Inhalation gegeben, Sauerstoffzufuhr 4l/ min. Eine körperliche Belastung mit einer Belastungsherzfrequenz von in diesem Fall 80 bpm für eine Stunde wird täglich angeschlossen. Medikamentös wurde die Behandlung durch orale Gaben von Zink, Selen und Mutaflor vor dem Behandlungszyklus, durch parenterale Gaben von Vitamin C während des Behandlungszyklus und durch orale Gabe von Artischocke und Ursofalk nach dem Behandlungszyklus unterstützt. Dosierungsplan in *Anlage 3. Behandlungsverlauf und Ergebnis:* In der Zeit von 02/2006 bis 2/2009 wurden insgesamt 16 Behandlungszyklen mit einer Kombination aus GKH und RHT durchgeführt. Zwischen den Behandlungszyklen wurden regelmäßige Kontrollen der Laborparameter Ca19-9, ASAT, ALAT und y-GT durchgeführt. Bei Anstieg des Tumormarkers wurde ein erneuter Behandlungszyklus begonnen. Während der Behandlungszyklen und im behandlungsfreien Intervall wurde der klinische Zustand der Patientin, das subjektive Befinden und die Laborparameter kontrolliert und dokumentiert. Eine regelmäßige bildgebende Diagnostik wurde patientenseitig abgelehnt und war zur Behandlungsplanung und Durchführung auch nicht erforderlich. Während bei Diagnosestellung von der Patientin rezidivierende Oberbauchbeschwerden, Appetitlosigkeit und reduzierte Leistungsfähigkeit beschrieben wurden (Karnofsky-Index 80-90%), konnte in der Zeit von Februar 2006 bis Februar 2009 eine vollkommene Beschwerdefreiheit festgestellt werden (Karnofsky-Index 100%). Dieser Zustand konnte auch in der dokumentierten Labordiagnostik nachvollzogen werden. Die jeweils vor Behandlungszyklus angestiegenen Laborparameter Transaminasen, y-GT und Ca19-9 remittierten nach Hyperthermie. Während des gesamten Behandlungszeitraumes wurde lediglich einmalig eine Verbrennung 2 Grades als Nebenwirkung dokumentiert. Im März 2009 kam es ohne Behandlungseinwirkung zu einem plötzlichen Anstieg der Transaminasen und der y-GT bei gleichzeitigem deutlichen Anstieg des Tumormarkers Ca19-9. In direktem zeitlichen Zusammenhang entwickelte sich eine bisher nicht festgestellte Tumoranämie und ein Ikterus. Hier bestand eine Kontraindikation für einen erneuten Behandlungszyklus. Im Zeitraum von März 2009 bis zum Tode der Patientin im August 2009 wurden keine Hyperthermiebehandlungen durchgeführt.

Diskussion: Im vorliegenden Fall wurden Behandlungsverfahren eingesetzt, deren Wirksamkeit durch medizinische Studien nicht nachgewiesen ist. Da die Behandlung dieser Tumorentität wirksame und erfolgreiche Standards vermissen lässt (4), konnte in diesem Fall, bei einer aufgeklärten und in jedem Punkt complienten Patientin dieser Behandlungsversuch vertreten werden.
Einzig die Arbeiten von Prof. M. von Ardenne in seinem Buch "Systemische Krebs- Mehrschritt-Therapie" dienten als grobe Orientierung.
Vorteile dieses Behandlungskonzeptes liegen hauptsächlich
1. in seiner Verträglichkeit,
2. in der geringen Zahl der Nebenwirkungen
3. in der geringen Hospitalisierungszeit und vor allen Dingen
4. in der nachgewiesenen Wirksamkeit, nämlich dem langen symptomfreien Überleben einer Patientin mit einem Cholangiocellulärem Carcinom (CCC).
Die *Nachteile* sind
1. auch hier die nicht erreichte komplette und dauerhafte Remission und
2. die Notwendigkeit der Wiederholung der Behandlungszyklen.
Wird in Betracht gezogen, dass bei Vorliegen eines intrahepatischen CCC eine mittlere Überlebenszeit von durchschnittlich 6 Monaten angenommen werden kann (4,23), bietet das hier angewendete komplexe Behandlungsschema eine interessante Option für die Behandlung von fortgeschrittenen malignen Erkrankungen ohne bisher wirksame Therapie.
Es kann eindeutig
1. ein Lebenszeitgewinn bei
2. sehr guter Lebensqualität und
3. vertretbarer Patientenbelastung postuliert werden.

Schlussfolgerung: Das vorliegende Behandlungskonzept bietet eine Option für die Therapie des intrahepatischen CCC. Ohne chemotherapeutische Behandlung kann eine Tumorprogression, zumindest zeitlich begrenzt, verhindert werden. Eine Wirkungsverbesserung des Behandlungskonzeptes bei dieser

Tumorentität durch den Einsatz bestimmter chemotherapeutischer Behandlungsansätze oder immunologischer Behandlungsverfahren kann nur vermutet werden. *Ausblick:* Gegebenenfalls steht mit dieser Therapievariante auch eine mögliche Option zur Behandlung anderer maligner Erkrankungen zur Verfügung. Gegenwärtig wird ein vergleichbares Konzept zur Behandlung des Pankreaskarzinoms geprüft.

Literatur:

1. Choi CW, Choi IK, et al.: Effects of 5-fluorouracil and leucovorin in tue treatment af pancreaticbiliary tract adenocarcinomas. Am. J. Clin. Oncol. 2000 Aug; 23(4): 425 -428
2. NAKAgohri T. et al.: Aggressiv surgical resectionfor hilar-invasiv and peripheral intrahepatic cholangiocarcinoma. World J Surg. 2003 Mar; 27(3): 289 -293
3. Bhargava P. et al.:Gemcitabine and irinotecan in locally advanced ob metastatic biliary cancer: preliminary report. Oncology (Williston Park) 2003 Sep; 17(9Suppl 8):23-26
4. Darwin P et al. : Cholangiocarcinoma Web MD newsletter; 2009 Jan.
5. Philip PA, Mahoney MR et al. Phase II study of erlotinib in patients wich advanced biliary cancer. J Clin oncol. 2006 Jul 1; 24(19): 3069-3074
6. Park JS, Oh SY: Single-agent gemcitabine in tue treatment of advanced biliary tract cancers: a Phase II study. Jpn J Clin Oncol. 2005 Feb; 35(2): 68-73
7. Lieser MJ et al. : Surgical managment of intrahepatic cholangiocarcinoma: a 31-year experience. J Hepatobiliary Pancreatic Surg. 1998; 5(1):41-47
8. Ortner ME et al.:Succesful photodynamic therapy for nonresectable cholangiocarcinoma: a randomized prospektive study. Gastroenerology 2003 Nov; 125(5):1355-1363
9. Alden ME: The impact of radiation dose in combined external beam and intraluminal Ir-192 brachytherapie for bile duct cancer. Int J Radiat Oncol Biol Phys. 1994 Mar 1; 28(4):945-951
10. Nakeeb A: Cholangiocarcinoma. A Spektrum of intrahepatic, perihilar, and distal Tumors. Ann Surg. 1996 Oct.;224(4):463-473
11. Patel T. : Increasing incidence and mortality of primary intrahepatic cholangiocarcinoma in tue United States.Hepatology. 2001 Jun; 33(6): 1353-1357
12. Chapmann RW: Risk Faktors for biliary tract carcinogenesis. Ann Oncol. 1999; 10 Suppl 4: 308-311
13. Shaib YH et al: Risk Faktors of intrahepatic cholangiocarcinoma in tue United States: a case-control Study. Gastroenterology 2005 Mar; 128(3): 620-626
14. Lee MG et al. :Preoperative Evaluation of hilar cholangiocarcinoma wich kontrast-enhanced threedimensional fast imaging wich stady-state Prozession Magnetik resonance angiographie: comparison with intraarterial digital Subtraktion angiographie. World j Surg. 2003 Mar; 27(3): 278-283
15. Lee CC et al.: What is the impact of coexistence of hepatolithiasis on cholangiocarcinoma? J Gastroenterol Hepatol. 2002 Sep; 17(9):1015-1020
16. Tillich M et al.: Multiphasic helical CT in diagnosis and staging of hilar cholangiocarcinoma. AJR Am J Roentgenol. 1998 Sep; 171(3): 651-658
17. Farley DR et al.: "Natural history" of unresected cholangiocarcinoma: patient outcome after noncurative Intervention. Mayo Clin Proc. 1995 May; 70(5):425-429
18. Takada T et al. :Is postoperative adjuvante chomotherapie useful for gallbladder Carcinom? A Phase III multicenter prospektive randomized controlled Trial in patients wich resected pancreaticobiliary Carcinoma. Cancer. 2002 Oct 15;95(8):1685-1695
19. Valls C et al.: Intrahepatic peripheral cholangiocarcinoma: CT Evaluation. Abdom Imaging. 2000 Sep-Oct; 25(5): 490-496
20. Zhang Y et al.: Intrahepatic peripheral cholangiocarcinoma: comparison of Dynamik CT and Dynamik MRI. J Comput Assist Tomogr. 1999 Sept-Oct; 23(5): 670-677
21. Burke EC et al.: Hilar Cholangiocarcinoma: patterns of spread, tue importance of hepatic Resektion for curative Operation, and a presurgical clinical staging system. Ann Surg. 1998 Seo; 228(3): 385-394
22. Chamberlain RS, Blumgart LH: Hilar cholangiocarcinoma: a review and commentary. Ann Surg Onc. 2000 Jan-Feb; 7(1): 55-56
23. Henson DE et al.: Carcinoma of tue extrahepatic bilde ducts. Histologic types, stage of desease, grade, and survival rates. Cancer. 1992 Sep 15; 70(6): 1498-1501
24. Nakagohri T et al.: Aggressive surgical Resektion for hilar-invasive and peripheral intrahepatic cholangiocarcinoma. World J Surg. 2003 Mar; 27(3): 289-293
25. Sirica AE: Cholangiocarcinoma: molekular targeting strategies for chemoprevention and therapie. Hepatology. 2005 Jan; 41(1): 5-15
26. Pate T: Worldwide Trends in mortality from biliary tract malignancies. BMC Cancer. 2002 May 3;2:10

Tuesday, November 23rd, 2010
9:20-9:40

Locoregional electrohyperthermia as treatment option for primary rectal carcinomas

Prof. Dr. A.A. Kovaliev[1]
(1) Zaporozhye Mecial Academy, Ukraine

Summary: The article is devoted to the problem of primary operable rectal cancer. The research purpose was to study and to assess the use of local electrohyperthermia in combination with radiaotherapy in primaryoperable rectal cancer and the role of neoangiogenesis in the relapses development. The data of 90 patients with primary operable rectal cancer over a period between December 2005 and September 2006 were analyzed. Depending on the treatment method patients were divided into 2 groups. Patients of the 1 group received complex treatment with use of neoadjuvant radiotherapy and local electrohyperthermia (1 hour after radiotherapy during 60 minutes at 45 °C) and radical surgery the next day. Patients of the 2 group (control) did not receive local electrohyperthermia. Neoangiogenesis was analyzed by expression level of vascular endothelial growth factor receptor and CD34 immunohystochemically. In the first group of patients local relapses occurred in 2 patients (4%). In the control group local relapses occured in 7 cases (17,5%). The expression of VEGFR1 decreased by 34,5% and the expression of CD34 decreased by 35,7% in the 1 group while no significant changes took place in the control group. The use of local electrohyperthermia in complex treatment of primary operable rectal cancer improves treatment results decreasing relapses frequency with the help of neoangiogenesis reduction.

Tuesday, November 23rd, 2010
9:45-10:05

Large field electrodes in the treatment with local-regional hyperthermia

Dr. Joseph Brenner[1]
(1) Dept of Oncology/ Wolfson Hospital/Holon/Israel and "New-Hope" medical center in Tel-Aviv/Israel

Local-regional hyperthermia devices are using round treatment electrodes with different sizes up to 30 cm in diameter. Unfortunately in many patients 30 cm diameter electrodes do not cover all tumors areas in the body. Trying to overcome this problem, many patients are treated with 2 or even 3 fields at any session doubling the treatment time by a factor of 2 or 3. In addition, the round electrodes do not allow a complete cover of the treatment field.
With the new EHY-3000 device by Oncotherm this problem was completely disappeared. The electrodes can be square or rectangular, their size can be variable, they are flat electrodes so they can be fitted to the different body surface shapes and they are light so they do not cause any pressure and discomfort to the patients.
In the 15 months we have treated many patients with electrodes size between 15X15 cm to 30X30 cm. 40X40 cm, 50X40cm, 50X50cm, 60X40cm, 75X50cm and many other treatments sizes electrodes.
Treatment was well tolerated without any major side-effects such as burning sensations, pains, organ damage and more.
Treatment results were excellent and were even superior to these of the older devices such as EHY-2000.
The EHY-3000 allows us to perform a "Whole-body hyperthermia" with local-regional device. In such cases, the hyperthermia electrode will cover disease from the neck to the hips. This will spare the long treatment's hours, the need for general anesthesia sometimes and the life threatening risks of the treatments with "Whole-body hyperthermia"
In addition, the adaptability of the electrodes to the treatment's surface make treatments to areas such as head and neck areas much more feasible and effective.

Tuesday, November 23rd, 2010
10:35-11:05
(Keynote lecture)

Regional hyperthermia in high-risk soft tissue sarcomas

Prof. Dr. Rolf Issels[1]
(1) Medizinische Klinik III, Klinikum der Universität München – Campus Großhadern, München

Purpose: On the basis of the definition of high-risk soft tissue sarcomas and prognostic factors, the most recent developments with spezial emphasis on regional hyperthermia combined chemotherapy are reviewed.

Findings: The most important prognostic factors (e.g. size, grade, depth and resection margins) for localized soft tissue sarcomas have been defined to predict the probability of sarcoma-specific death providing a useful tool for patient stratification and clinical trial eligibility determination that are also relevant in the outcome of paediatric patients with adult type soft tissue sarcomas. Clinical research on innovative preoperative treatment strategies has essentially focused on the combination of preoperative radiochemotherapy or chemotherapy alone. The reported results are based upon retrospective analysis or nonrandomized phase II studies with small sample size. For the use of regional hyperthermia (RHT) therapy, phase II studies have advocated a possible benefit of the use of regional hyperthermia in combination with chemotherapy targeting the heating field to the region of tumour burden. The results of a completed European Organization for Research and Treatment of Cancer–European Society of Hyperthermic Oncology intergroup randomized phase III trial for the most common types of adult high-risk soft tissue sarcomas demonstrate a significant benefit in the clinical outcome of patients receiving regional hyperthermia therapy.

Summary: Regional hyperthermia combined with preoperative and postoperative chemotherapy offers a new appropriate treatment option for high-risk soft tissue sarcomas.

Tuesday, November 23rd, 2010
11:10-11:30

Possible activation of neutrophiles by oncothermia

Dr. Henning Saupe[1], Dr. Christian Buettner[1], Dr. Gabor Andocs[2]
(1) Arkadia Praxis, Kassel, Germany (dr.saupe@arcadia-praxis.de)
(2) Department of Pharmacology and Toxicology, Faculty of Veterinary Science, St Istvan University, Budapest, Hungary

Background: Neutrophil granulocytes are presented in blood stream in greatest strength among white blood cells in mammalians, having crucial role in the immune system. Neutrophils are one of the first responders on inflammations or bacteria infections, and their role is essential in the defense mechanisms of the organism [1]. Various chemical signals activate the migration of neutrophils toward to the site of inflammation [2] and it could effect even in the cancer cases [3].

Methods: Blood samples of nude mice and of voluntary humans were studied before and after oncothermia treatment. Samples were carefully collected from tail's venue of mice and from finger capillaries from humans. The individual blood-collection was made before and after oncothermia treatment, as well as it was regularly and systemically made in cases of all the subsequent treatments. Samples were promptly (freshly) measured by dark-field microscopy and archived by high resolution video-techniques. The systemic effect of neutrophils were studied on double tumorous mice, (femoral inoculation HT29 xenograft), treating one localization and observing effect on the non-treated lesion. High-resolution digital microscopy was applied to evaluate the morphology of hematoxylin-eosin stained samples.

Results: Both in mice and human blood a definite activation (increased migration motility) is observed after oncothermia treatment compared to the situation before. The active motility was characteristic on all the treated donors, irrespective their tumors or their human or mouse origin. The untreated tumor in double-tumorous mice were drastically infiltrated by neutrophils after the oncothermia treatment, indicating the general systemic migration activity of these species. The far away effect form the actual treatment localization gives a hint of the observed abscopal effect [4] by oncothermia treatment.

Conclusions: Observations of the recent study support the hypothesis that oncothermia activates systemic immune reactions by increased motility of neutrophils. The effect is expected in distant lesions from the actually performed local treatment. Further experimental investigations of the phenomenon together with the detailed study of the abscopal effect in humans are in progress.

References:

[1] Witko-Sarsat V. Rieu P, Descamps-Latscha B. Lesavre P. Halbwachs-Mecarelli L: (2000) Neutrophyls: Molecules, Functions and Pathophysiological Aspects. Laboratory investigation, 80 (5): 617-653
[2] Waugh, DJ; Wilson (2008). The interleukin-8 pathway in cancer. Clinical Cancer Research 14 (21): 6735–41
[3] De Larco, JE; Wuertz; Furcht (2004). The Potential Role of Neutrophils in Promoting the Metastatic Phenotype of Tumors Releasing Interleukin-8. Clinical Cancer Research 10 (15): 4895–900
[4] Yoon SM, Lee JS. (2010). Tcase of abscopal effect with Metastatic Non-Small-Cell Lung Cancer, Oncothermia Symposium, Cologne, Germany November 22-23

Tuesday, November 23rd, 2010
11:35-11:55

Die Dolphin-Studien: 10 Jahre Chemotherapie in Kombination mit Ganzkörperhyperthermie beim Ovarialkarzinom

Dr. Julia Jückstock[1], Dr. B. Eberhardt[2], Prof. Dr. Harald Sommer[3]
(1-3) Klinik Bad Trissl, LMU Munchen,Germany

Material und Methodik: In den Jahren 1999 bis 2009 wurden 10 Patientinnen im Rahmen der Dolphin-0-Studie (Carboplatin AUC6/ Paclitaxel 175mg/m2 kombiniert mit Ganzkörperhyperthermie (GKHT) bei primärem oder rezidiviertem Ovarialkarzinom) und 29 Patientinnen im Rahmen der Dolphin-1-Studie (Carboplatin AUC5/ Ifosfamid 3g/m2 kombiniert mit GKHT bei rezidiviertem Ovarialkarzinom) behandelt. Nach Abschluss der Dolphin-1-Studie wurden weitere 13 Patientinnen nach dem Studienprotokoll außerhalb der Studie behandelt. Alle Dolphin-0-Patientinnen sowie 18 Dolphin-1-Patientinnen wurden in unserer Klinik therapiert, weitere an Dolphin-1 teilnehmende Zentren waren die Klinik St. Georg/Bad Aibling (6 Pat.), das Universitätsklinikum Eppendorf/Hamburg (2 Pat.), die Medizinische Universität zu

Lübeck (2 Pat.) und das Universitätsklinikum der Charité/Berlin (1 Patientin). Für die GKHT kamen die Geräte WBH 2000® (Oncotherm, Bad Aibling) und IRATHERM®-2000 (von-Ardenne-Institut für Angewandte Medizinische Forschung GmbH, Dresden) zum Einsatz. Es wurde hierbei die radiative Technik mittels Infrarot-A-Strahlung verwandt. Die Behandlung fand i.d.R. unter Analgosedierung mit Midazolam und Fentanyl statt, selten auch in Vollnarkose. Invasive Temperaturmessung mittels Rektal- und Ösophagussonde. Dauer des Temperaturmaximums (41.5 - 41.8 ºC) 1h, hierbei Hyperglykämie von > 300mg/dl.

Ergebnisse: Vorbehandlungen: im Durchschnitt 1,5 Operationen, 1,8 Chemotherapien (0-6). Es erfolgten im Durchschnitt 4,8 Behandlungszyklen pro Patientin, hierbei 58 Zyklen bei Dolphin-0 und 131 bei Dolphin-1. Die mittlere Nachbeobachtungszeit betrug 24,5 Monate (2,4 - 69,6 Monate). Ansprechraten beider Studien nach Abschluss der Therapie: CR 28,2%, PR 15,4%, SD 15,4%, PD 41,0%. Die mediane Überlebenszeit der Patientinnen der Dolphin-0-Studie lag bei 50,9 Monaten. Für die Dolphin-1-Studie lag sie bei 12,4 Monaten. Die 5-Jahres-Überlebensrate lag für Patientinnen der Dolphin-0-Studie bei 50 %. Für die Patientinnen der Dolphin-1-Studie kann nur eine 2-Jahres-Überlebensrate von 25,2 % angeben werden. Toxizität: Leukozytopenie: Dolphin-0: 39,3% Grad 2, 5,3% Grad 3, kein Grad 4, Dolphin-1: 22,5% Grad 2, 33,1% Grad 3, 9% Grad 4. Neutropenie: Dolphin-0: 17,8% Grad 1, 26,7% Grad 2, 3,5% Grad 3, 1,8% Grad 4, Dolphin-1: 20,5 Grad 1, 14,2% Grad 2, 21,4% Grad 3, 20,5% Grad 4. Thrombozytopenie: Dolphin-0: 17,9% Grad 2, 3,6% Grad 3, 1,8% Grad 4, Dolphin-1: 9% Grad 2, 24,1% Grad 3, 10,5% Grad 4. Anämie: Dolphin-0: 41,5% Grad 1, 16% Grad 2, 2% grad 4, Dolphin-1: 46,5% Grad 1, 30% Grad 2, 3 % Grad 3, 3% Grad 4. Infektionen: Dolphin-0: 22,4% Grad 1-2, kein Grad 3, Dolphin-1: 17,6% Grad 1-3, hiervon 2 x Pneumonie, 3 x schwere erosive Mucositis Emesis: Dolphin-0: Grad 1 17,9%, Grad 2 4,5%, Dolphin-1: Grad 1 19,5%, Grad 2 18%, Grad 3 und 4 jeweils 2%. Verbrennung: Dolphin-0: 6,8% Grad 1, Dolphin-1: 3,7% Grad 1, 1,5% Grad 2, 2,3% Grad 3. Pulmonale Komplikationen: Dolphin-0: 13,8% Dyspnoe Grad 1-2, Dolphin-1: 2 Pat. Pneumonie, 2 Pat. Dyspnoe Grad 2-3 in mehreren Zyklen Dosisreduktion: Dolphin-0: 2 Zyklen (Myelotox.), 1 Zyklus (Emesis), Dolphin-1: 24 Zyklen (Myelotox.), 2 Zyklen (Nephrotox.). Intervallverlängerung: Dolphin-0: 6.9%, Dolphin-1: 18,3%. Gabe von G-CSF: Dolphin-0: 89,7%, Dolphin-1: 39,7%, Gabe von Erythropoetin: Dolphin-0: 79,3%, Dolphin-1: 24,4%. Die Ergebnisse der GKHT-Behandlungen nach Abschluss der Dolphin-1-Studie werden momentan ausgewertet.

Fazit: Die Ganzkörperhyperthermie kombiniert mit Chemotherapie beim Ovarialkarzinom zeigte eine akzeptable Ansprechrate und tolerable Toxizität. Sie sollte jedoch weiterhin im Rahmen klinischer Studien überprüft werden.

Tuesday, November 23rd, 2010
12:00-12:30

Safety of the proteasome inhibitor disulfiram combined with capacitive hyperthermia in the treatment of advanced solid tumors

Prof. Dr. Giammaria Fiorentini[1], Dr. Francesco Montagnani[1], Dr. Gina Turrisi[1], Dr. Susanna Rossi[1], Dr. Patrizia Dentico[1], Dr. Sara Licitra[1], Dr. Piergiorgio Giannessi[1]
(1) Oncology Unit, San Giuseppe General Hospital, Empoli, Florence, Italy. oncologiaempoli@usl11.toscana.it

Background: Disulfiram is an old drug used to treat alcholism. Recently some authors has demonstrated antineoplastic activity in preclinical settings on various cancer types. The mechanisms of action is not fully understood but seems to rely mainly on the inhibition of proteasome, comparable to that of other specific drugs like bortezomib. Previous complexation of disulfiram with heavy metal ions, mainly Cu and Zn, is mandatory for disulfiram activity.
Hyperthermia on the other hand proved to be sinergistic with proteasome inhibition in cancer cell lines. On these basis we started a phase I trial to test the safety of concurrent combination of disulfiram with zinc supplementation and hyperthermia in the presence or absence of chemotherapy.

Materials and methods: Disulfiram 400 mg and zinc sulphate 200 mg daily were both given orally without interruption. External capacitive hyperthermia (40-43℃ range) was performed on target lesions twice a week for 1 hour with an EHY2000 equipment. Concomitant chemotherapy was allowed. Re-evaluations were done every 2 months. Treatment was protracted until disease progression.

Results: 15 patients with different pretreated solid malignancies entered the study, 7 of them were also given concurrent chemotherapy with various drugs. Absence of important co-morbidities at the time of enrolment was mandatory.

In the absence of chemotherapy the main toxicity was diarrhea G1-2 which occurred in 4 out of 8 patients. Occasional mild fatigue and nausea were also observed. One patient discontinued treatment because of reappearance of symptoms of a pre-existing cardiac failure (NYHA 2).
One patient died of unknown causes after one month and was not evaluable for response.
Treatment was well tolerated also when chemotherapy was added although toxicity was increased. However only two patients, experienced G3 toxicities, fatigue and neutropenia respectively. No toxicities related to hyperthermia were observed.
Overall we observed 1 CR (7 %), 2 PR (14 %), 7 SD (50 %) and 4 PD (29 %) with a disease control rate of 71 %. On the target lesion we recorded Interestingly partial responses were observed in a sarcoma and glioblastoma in the absence of chemotherapy.

Conclusions: Disulfiram with zinc supplementation and hyperthermia is feasible and safe alone or in combination with chemotherapy. However attention has to be used when treated patients with a history of cardiac failure. Although this study was not designed to assess efficacy, a moderate activity seems to be present as responses were recorded both with and without chemotherapy, together with an high disease control rate.

Tuesday, November 23rd, 2010
13:45-14:15

Clinical Research on Integrative Treatment of Colon Carcinoma with Oncothermia and Clifford TCM Immune Booster

Prof. Dr. Clifford Pang[1]
(1) Clifford Hospital, Guangzhou, Guangdong, P.R. China (adm@clifford-hospital.com)

Objective: Study and research of the therapeutic efficacy and adverse reactions of integrative treatment of colon carcinoma with Oncothermia and Clifford TCM (Traditional Chinese Medicine) Immune Booster.

Methods: 157 hospitalized cancer patients with colon carcinoma in Clifford Oncology Center were randomly divided into three groups: Group A (Treatment) treated by Oncothermia combined with Clifford Immune Booster (Group A consisting of 53 patients), Group B (Control) treated by Oncothermia only (Group B consisting of 50 patients), and Group C (Control) treated by Clifford Immune Booster only (Group C consisting of 54 patients). The patients were followed up for 2 years, during which survival data were collected, analyzed and survival curves drawn. At the same time, we observed the clinical therapeutic efficacy, Karnofsky Performance Status (KPS), Visual Analogue Scale of pain (VAS) and survival time. Adverse reactions were recorded. The above data, observations and records of the three groups were subsequently compared.

Results: At the conclusion of the clinical research, 3 cases were lost: 2 in Group A, 1 in Group C and none in Group B. On therapeutic efficacy comparison, there were 30 patients of CR+PR and 42 patients of CR+PR+NC in Group A. Both were better than those of Groups B & C. There was significant difference between the Group A and Group B, and between Group A and Group C ($P<0.05$), but no significant difference between Groups B & C ($P>0.05$). On the comparison of improving performance status and controlling pain, both in Group A were better than those in the Groups B & C. There were significant difference between the Group A and Group B, and between Group A and Group C ($P<0.05$), but no significant difference between the two Groups B & C ($P>0.05$). Survival curves were drawn according to the survival results. The survival time of Group A was longer than those of Groups B & C. There was significant difference between Group A and Groups B & C ($P<0.05$). 3 cases with Oncothermia had small solitary fat nodules under the skin and slight stabbing pain, 2 cases had skin flushes over the surgery scars, but all disappeared in a short period of time without treatment. There was no adverse reaction for those treated with Clifford Immune Booster. There was no other adverse reaction in Oncothermia integrated with Clifford Immune Booster.

Conclusions: Integrative treatment of colon carcinoma with Oncothermia and Clifford TCM Immune Booster was found to be safe and proved to have good therapeutic efficacy. It can prolong the survival time and improve the quality of life of the patients. Only minor adverse reactions appeared in this treatment and disappeared shortly without further attention.

Tuesday, November 23rd, 2010
14:15-14:35

Gynecology results by oncothermia

Dr. Andras Csejtei[1], Mr. Peter Lorencz[1]
(1) Markusovszky Hospital, Department of Oncoradiology, Szombathely, Hungary

Background: Learning from the widely published literature we started to treat our gynecology patients who were eligible for oncothermia to treat in harmony with brachy- chemo- and external radio-therapies. Our aim was in this article to report our observations and results.

Method: We had offered for the eligible patients receiving complementary oncothermia to their standard treatment protocols. In the actual circumstances and financial conditions, we were able to recruit 80 patients for this study. Most of the patients were treated by standard after-loading brachy-therapy or in some cases additionally by external radiotherapy as well. Patients had pathologically proven diseases, and evaluated as eligible for these treatments despite of their inoperable stage. The inoperable category contained the patients predicted unsuccessful resection or having contradicting morbidities or contraindicated by anesthesiology reasons. Oncothermia was applied after the brachy-therapy or 20 minutes before the external radiotherapy. Patients receiving curative (non-palliative) care received their treatments two times a week before the external radiation, or in some cases promptly after the chemotherapy.

Results: Oncothermia had accelerated the historically expected curative processes, as well as the side effects of the standard therapies were suppressed in most of the cases.

Conclusion: Compared to the gold-standard radiotherapies, the result could be obtained queicker in gynecological cases by complementary application of oncothermia. The results were accompanied with better quality of life.

Tuesday, November 23rd, 2010
14:40-15:00

Transcranial electro-hyperthermia combined with alkylating chemotherapy in patients with relapsed high-grade gliomas: phase I clinical results

Dr. Cacilia Wismeth[1], Dr. Christine Dudel[1], Dr. Christina Pascher[1], Dr. P. Ramm[1], Dr. T. Pietsch[1], Dr. Birgit Hirschmann[1], Dr. C. Reinert[1], Dr. M. Proescholdt[1], Dr. P. Rümmele[1], Dr. G. Schuierer[1], Dr. Ulrich Bogdahn[1], Dr. Peter Hau[1]
(1) Department of Neurology, University of Regensburg Medical School (UKR), Regensburg, Germany

Non-invasive loco-regional electro-hyperthermia (EHT) plus alkylating chemotherapy is occasionally used as salvage treatment in the relapse of patients with high-grade gliomas. Experimental data and retrospective studies suggest potential effects. However, no prospective clinical results are available. We performed a single-center prospective non-controlled single-arm Phase I trial.
Main inclusion criteria were recurrent high-grade glioma WHO Grade III or IV, age 18-70, and Karnofsky performance score > or = 70. Primary endpoints were dose-limiting toxicities (DLT) and maximum tolerated dose (MTD) with the combined regimen. Groups of 3 or 4 patients were treated 2-5 times a week in a dose-escalation scheme with EHT. Alkylating chemotherapy (ACNU, nimustin) was administered at a dose of 90 mg/m(2) on day 1 of 42 days for up to six cycles or until tumor progression (PD) or DLT occurred. Fifteen patients with high-grade gliomas were included. Relevant toxicities were local pain and increased focal neurological signs or intracranial pressure. No DLT occurred. In some patients, the administration of mannitol during EHT or long-term use of corticosteroids was necessary to resolve symptoms. Although some patients showed responses in their primarily treated sites, the pattern of response was not well defined. EHT plus alkylating chemotherapy is tolerable in patients with relapse of high-grade gliomas. Episodes of intracranial pressure were, at least, possibly attributed to EHT but did not cause DLTs. A Phase II trial targeting treatment effects is warranted on the basis of the results raised in this trial.

Tuesday, November 23rd, 2010
15:05-15:25

Astrocytomas glioblastomas Hyperthermia metabolic inhibitors. Some considerations

Dr. Gian Franco Baronzio[1], Dr. C. Mainini[1], Prof. Dr. Giammaria Fiorentini[1], Dr. A. Guais[2], Dr. L. Schwartz[3]
(1) Oncology Unit, San Giuseppe General Hospital, Empoli, Florence, Italy. oncologiaempoli@usl11.toscana.it
(2) Service de Radiothérapie Hôpital Pitié-Salpétrière, bd. de l'Hôpital, 75013 Paris, France.

Astrocytomas and glioblastomas are a class of aggressive neoplasms that are resistant to convectional therapies. Recent studies have demonstrated that Temozolomide (TMZ) is a well tolerated chemotherapy for brain tumors and is active as single agent or in combination with radiotherapy. Several studies in vitro have demonstrated that hyperthermia plus chemotherapy has a higher cytotoxic effect than chemotherapy alone. We have studied 29 patients with aggressive brain tumors [11 glioblastomas (GBM), 6 Astrocytomas IV , 8 Astro II, 1 Oligoastrocytomas) 2 ependymomas and 1 medulloblastomas]. 25 of these patients have been treated with Conformal radiotherapy (CFRT) + TMZ+ capacitive HT and compared with a group treated with CFRT + TMZ. Patients treated with HT have demostrated an increase in life survival compared to the group treated with CFRT + TMZ alone. Recently after Schwartz L studies we have introduced a combination of glycolysis inhibitors hydroxycitrate + α lipoic acid (Metabloc) + TMZ at low dosage 20 mg day. Glioblastoma develop resistance to chemo and radiotherapy, in part as a result of a switch from mitochondrial oxidative phosphorylation to cytoplasmic glycolysis. A first patient with Astrocytoma IV operated and treated with chemotherapy, has reached disease stabilization and treated with metabloc for rejection of classic therapy. She is maintaining after six months the disease stabilization. The reasons for associating capacitive hyperthermia with glycolysis inhibitors is discussed as the differences between the patients treated with Oncothermia (Fiorentini Group) and ours.

Tuesday, November 23rd, 2010
15:30-15:50

Safety and Complications of Oncothermia in Korean Cancer Patients: A Retrospective Analysis of Single Institutional experience

Prof. Dr. Seong Min Yoon[1], Dr. Kyung Tae Park[1]
(1) Division of Hematology-Oncology, Department of Internal Medicine, Samsung Changwon Hospital, Sungkyunkwan University, Changwon, South Korea

Purpose: Oncothermia has been started in South Korea since 2007 and its treatment is getting gradually expanded in Korean cancer patients. Though this device is widely accepted that it is safe and beneficial, Korean experience of oncothermia was not known until now. Thus this study was underwent retrospectively to determine the safety and complications of oncothermia

Methods: From June to November in 2009, 127 cancer patients were received oncothermia alone or combined with other cancer treatment at SAM general hospital. Totally 1332 sessions (range: 1~61 sessions) were performed during the period.

Results: The median age of the patients was 55.5 years (range: 20~85). Sixty-three patients were male and 64 were female. The kinds of cancer were stomach (35, 27.5%), colon and rectum (21, 16.5%), lung (15, 11.8%), pancreas (10, 7.8%), ovary (9, 7%), liver (8, 6.3%), breast (6, 4.7%), biliary tract (4, 3.1%), , cervix (4), brain tumor (3, 2.4%), pleural mesothelioma (3), bladder (2, 1.6%), malignant lymphoma (2), sarcoma (2), esophagus (1), nasopharyngeal cancer (1) and malignant thymoma (1). Erythema (2 cases, 1.5%) and fat burn (2 cases, 1.5%) were major complications and transient fever (25 cases, 19.6%) was observed. In case of erythema and fat burn, we stopped 1-3 sessions and then retried carefully. All patients continued oncothermia with no problem. Transient increase (> 0.5℃) in body temperature were also observed in 59 sessions of 25 cases. Average temperature change was 1.3℃ and maximum was 2.5℃ which all were restored in 1 hour. Ten patients (7.9%) complained mild to severe fatigue and 2 patients (1.6%) of them refused oncothermia because of condition deterioration. It happened within first 3 sessions and it seemed to be related with their disease state. Fifty-four patients discontinued due to death (17), disease progression (22) and cost burden (15).

Conclusion: Our data suggests that oncothermia is extremely safe and a feasible cancer treatment option in Korean cancer patients. However, the benefit is not defined yet. So, further prospective clinical investigation and study are required by the first Korean oncothermia study group have been formed recently.

Acknowledgement: I would like to thank Hospi company for providing EHY-2000 device.

References:
[1] Andocs G, Szasz O, Szasz A (2009) Oncothermia treatment of cancer: from the laboratory to clinic. Electromagn Biol Med. 28: 148-165

Tuesday, November 23rd, 2010
16:15-17:05

Effect of Electrochemotherapy in Treating Patients with Intramuscular Vascular Malformations

Prof. Dr. Jing-Hong Li[1]
(1) Dept. Electrochemical Treatment, China-Japan Friendship Hospital, Beijing, P.R. of China

Background: Treatment of intramuscular vascular malformations (IVMs) poses a major clinical challenge for the contemporary medicine. Surgical resection is difficult and frequently unsuccessful, radiological intervention with embolization has an ill-defined role, and conventional sclerotherapy has little to offer for a large scale disease.

Objective: To evaluate the efficacy and safety of electrochemotherapy (EChT) in treating intramuscular vascular malformations.

Methods: EChT was applied on 665 patients with IVMs of limbs and trunk and 505 cases were followed up for half to 6 years. There were 228 males and 277 females, aged 2-59 years and 17.5 years on average. Diagnosis was made by clinical manifestations, ultrasonic examination and/or magnetic resonance imaging (MRI).Inserting the platinum electrodes into tumor through a trocar with plastic insulating cannula percutaneously and connecting the electrodes with the electrochemical therapeutic apparatus in anodes and cathodes separately. Then electricity was given. The treating voltage is 8-12V and volume 100-180mA, the total electricity used is in general 80-100 coulombs per 1.0 square centimeter of tumors' area.

Results: The primary efficacy end point was defined as an improvement of patients' symptoms and a reduction in size of tumor 6 months after completion of the treatment. Clinical results were graded as follows: Grade 1, clinical obliteration, functional impairment of the diseased limbs recover to normal and the tumor decreases over 75%; Grade 2, most clinical symptoms disappear and functional impairment of the diseased limbs improve significantly, the tumor decreases 50-70%; Grade 3, clinical symptoms and functional impairment of the diseased limbs improve, the tumor decreases 25-50%; Grade 4, poor, little or no improvement of symptoms and functional impairment of the diseased limbs, the tumor decreases less 25%. The efficacy in 152 (30.1%) patients was classified as grade 1, 234 (46.3%) as grade 2, 96 (19.0%) as grade 3 and 23 (4.6%) as grade 4. The total efficacy was 95.4%.

Conclusion: EChT shows special superiorities in treating IVMs ,it is proved to bring a confirmed clinical efficacy、less injury、quick recovery、being simple in operation and less complications.

Tuesday, November 23rd, 2010
17:10-17:30

Die Infrarot-Ganzkörperhyperthermie in der Rezidivprophylaxe bei Krebs

Dr. med. Stephan Wey[1]
(1) Gemeinschaftspraxis Wey und Partner, Lauf, Germany

Im Konzept der biologischen Krebstherapie spielt die Ganzkörperhyperthermie eine wichtige Rolle, meist jedoch in palliativer Situation. In der adjuvanten Situation gibt es bisher nur kasuistische Daten.

Im Vortrag wird die Immunologie bei/nach Chemotherapie beleuchtet und ein Überblick zur immunologischen Bedeutung von Fieber gegeben, welches Krebspatienten meist langjährig vor der Erkrankung nicht mehr erlebt haben. Seit Praxisniederlassung Anfang 2002 wird ein Kollektiv von

zwischenzeitlich 47 Patienten (überwiegend Mamma-Ca.) beobachtet, dass adjuvant mit mind. zwei Ganzkörperhyperthermien behandelt wurde. Das Follow-up zeigt bisher eine hohe Zahl von Patienten mit tumorfreiem Überleben auch bei hoher Risikokonstellation. In der Tumornachsorge sollte dieses Konzept mehr beachtet und evaluiert werden.

Tuesday, November 23rd, 2010
17:35-17:55

Experimental oncothermia in nude mice xenograft tumor models

Dr. Gabor Andocs[1], Dr. Nora Meggyeshazi[2], Dr. Peter Galfi[1] P. Dr. Lajos Balogh[3], Dr. Laszlo Fonyad[2], Dr. Linda Muller[4], Dr. Oliver Szasz[6], Prof. Dr. Andras Szasz[5,6]
(1) Department of Pharmacology and Toxicology, Faculty of Veterinary Science, St Istvan University, Budapest, Hungary,
(2) 1st Department of Pathology and Experimental Cancer Research, Semmelweis University, Budapest, Hungary,
(3) National Research Institute for Radiobiology and Radiohygiene, Budapest, Hungary,
(4) Department and Clinic of Reproduction, Faculty of Veterinary Science, St Istvan University, Budapest, Hungary,
(5) Biotechnics Department, St. Istvan University, Hungary (Szasz.Andras@gek.szie.hu)
(6) Oncotherm Group, Germany

Background: Oncothermia method (OTM) uses well controlled modulated radiofrequency (RF) current-flow through the target tumor. It is an emerging technique for oncology [1]. OTM is based on solid scientific roots [2], and its experimental support connects the in-silico, in-vitro and in-vivo experiments in a synergic harmony with the permanent development of its clinical success [3]. Oncothermia has not simple a benefit from the rising temperature, but due to its non-equilibrium conditions it has a strong non-temperature dependent cell killing behavior, which is at least three times higher than the temperature induced conventional hyperthermia (HT) actions, [4]. Our present article summarizes the in-vivo experimental proofs of OTM mechanisms, pointing the direction of further development.

Method: The in vivo studies were performed using a BalbC/nu/nu mice xenografted with HT29 human colorectal carcinoma cell line. Numerous experiments were performed with highly specialized experimental setup (EHY110, Oncotherm, Germany) studying the various effects of OTM alone and compared to HT. Control better the anyway huge biovariability of the mice, the tumor was inoculated into the animals to two distant localizations (left and right femoral region) using this pair for treatment-control comparison. Regularly the right side tumor was treated with single shot OTM by 30min, and the effects were studied histomorphologically (HM) and immunhistochemically (IHCH) by various antibodies with digital microscopy system (MiraxWiev, 3D Histech).

Results: Both HM and IHCH experiments showed drastic and selective tumor-destruction by single shot OTM treatments. Compare to HT the quantity of destroyed area was larger. Definite dynamic (time-delay) processes were observed in OTM samples, suggesting to study the apoptotic initialization of the method. According to the IHCH analysis of OTM treated samples immediate activation of p53 and special relocalization of β-catenin from the cell-membrane to the nuclei was detected after 24 h. Indications of reestablished gap-junction connections (connexin) was also measured in this time period.

Conclusion: Tumor-distortion effect of OTM is mainly time-delayed, the treatment probable activates mechanisms to disintegrate the tumor and destroy the malignant cells. Further experimental support and repeating controls are desired.

References:
[1] Szasz A. (2007) Hyperthermia, a modality in the wings. J Cancer Res Ther. 3:56-66.
[2] Andocs G, Szasz O, Szasz A. (2009); Oncothermia treatment of cancer: from the laboratory to clinic. Electromagn Biol Med. 28(2):148-165.
[3] Szasz A. Szasz N. Szasz O. (2010) Oncothermia. Principles and Practices. Springer Verlag, (http://www.springer.com/biomed/cancer/book/978-90-481-9497-1?changeHeader) Heidelberg, Dordrecht
[4] Andocs G, Renner H, Balogh L, Fonyad L, Jakab C, Szasz A. (2009) Strong synergy of heat and modulated electromagnetic field in tumor cell killing. Strahlenther. Onkol. Feb; 185(2):120-126.

Abstracts of posters

P-01

A Case of Abscopal effect with Metastatic Non-Small-Cell Lung Cancer

Prof. Dr. Seong Min Yoon[1], Dr. Kyung Sik Choi[2], Dr. Jung Suk Lee[2]
(1) Division of Hematology-Oncology, Department of Internal Medicine, Samsung Changwon hospital, Sungkyunkwan University, Changwon, South Korea
(2) Department of Radiation Oncology, Anyang SAM General Hospital, Anyang, Gyeonggi-do, South Korea

Introduction: During the last decade, there has been an amazing progress in cancer research and treatment in the world and also in Korea. Nevertheless, the overall 5-year survival rate of lung cancer patients in 2001 - 2005 period was still 15.6% in South Korea. This type of cancer is usually diagnosed in advanced stage, consequently the overall survival did not show noticeable improvement.
Poor performance status and/or multiple co-morbidities limit the treatment options for elderly patients. Their poor prognosis is commonly accompanied with a common refusal of cytotoxic chemotherapies even though adequate chemotherapy would be available with acceptable expected tolerance. In such cases radiotherapy can be considered as curative or palliative treatment option. The abscopal effect proposed by R.H. Mole in 1953, is originally defined as the observational effect of radiation therapy at site distant to the treated field. Recently systemic effects of local radiotherapy including hyperthermia and immunotherapy have received attention as a new therapeutic modality. We report a case of abscopal effect observed in a patient with multiple metastatic non-small-cell lung cancer. Patient was treated with fractional radiotherapy, modulated electro-hyperthermia (oncothermia) and granulocyte-macrophage colony stimulating factor (GM-CSF).

Case report: A 72-year-old male patient was diagnosed with unclassifiable NSCLC by lung biopsy at other hospital in July 2009. The classification of the tumor at first diagnosis was cT2N2M0, stage IIIB. Despite of the advanced case the patient refused any treatment. Five months later (December 2009), he visited outpatient department of complementary and alternative medicine with complaints of hemoptysis and dyspnea on exertion gradually worsened 4 weeks before. He was referred to medical oncology department and admitted for re-evaluation. Staging work-up including chest CT and PET scans showed 9.5cm sized cavitary mass at right middle lobe with multiple regional and metastatic lymph nodes. He had no co-morbidities and no medical history. However, he still refused chemotherapy and together with his family members requested other possible treatment options. In these circumstances we made radiotherapy in combination with oncothermia and GM-CSF expecting to induce abscopal effect. Local field radiation therapy to lung mass was delivered at a dose of 1.7 Gy in 28 daily fractions for 5-6 treatments in a week. It was followed by oncothermia after radiation 3 times a week. After 2 weeks of treatment, GM-CSF (250 microgram, Leukine®, USA) was administered subcutaneously once a day for 10days. Treatments were provided without any complications. Patient presented no severe adverse effects except grade 1 fatigue at the end of treatment period. By follow-up process, just after finishing radiation treatment series PET scan showed nearly complete remission in multiple metastatic lymph nodes, which were distantly away from radiotherapy field. Patient was satisfied and discharged with successful response. The follow-up of the patient is continuing.

Conclusion: Our case describes a successful abscopal effect with local radiotherapy in combination with oncothermia and GM-CSF immune stimulation. This combination attempt seemed to be more effective in immune response than radiotherapy alone. Further studies on the abscopal effect are necessary to evaluate action mechanism and the significance of cancer treatment option.

P-02

Apoptosis induction with modulated radiofrequency (RF) hyperthermia (oncothermia) in immuno-defficient mice xenograft tumors (Review)

Dr. Gabor Andocs G[1,2], Dr. Lajos Balogh[1], Dr. Nora Meggyeshazi[3], Dr. Csaba Jakab[4], Dr. Tibor Krenacs[3], Prof. Dr. Andras Szasz[5]
(1) National Research Institute for Radiobiology and Radiohygiene, Budapest, Hungary
(2) Department of Pharmacology and Toxicology, Faculty of Veterinary Science, St Istvan University, Budapest, Hungary
(3) 1st Department of Pathology and Experimental Cancer Research, Semmelweis University, Budapest, Hungary
(4) Pathological Department, Faculty of Veterinary Medicine, St. Istvan University, Budapest, Hungary
(5) Department of Biotechnics, Faculty of Engineering, St. Istvan University, Budapest, Hungary

Introduction: Oncothermia method is more than twenty years serves the cancer treatments demands. It is successfully applied both in monotherapy and as complementary therapy with other oncotherapeutic modalities, irrespective their specialties. The experimental preclinical research started five years ago to

investigate the theoretically predicted mechanisms by rigorous basic science approvals. The complexity and interdisciplinary of the in vivo experimental series requested a wide cooperative scheme of various respected and honored research institutes and university laboratories. Our objective is to summarize the results of this intensive work and show the conclusions at the recent phase of the investigations.

Method: Immuno-defficient nude mice (BalbC/nu/nu) were used for xenograft and allograft models with HepG2, PC3, HT29, A431, GL261 cell-lines. The definite amount of cell-line suspension was injected to the femoral region of the 6-8 weeks old female mice and after started the oncothermia treatment after 18-20 days, when the tumors were developed symmetrically in both sides on diameter 1-1.5 cm. The single shoot treatment was identically performed for all the mice on their right lesion, while the left lesion was kept as untreated individual control to reduce the inaccuracies due to the individual variability of the animals. Slides of the paraffin-fixed samples were studied by standard HE and by special immuno-hystochemical as well as fragmented (apoptotic) DNA-marking staining. Their structure images were examined by special digital microscopy (PanoramicView, 3DHISTECH, Budapest). Special software made possible various qualitative and quantitative studies of the tissue-morphology facilitating the precise, molecular-based comparison of the efficacy of different therapies.

Treatments were performed by highly specialized laboratory equipment (Lab-EHY, Oncotherm), optimized on mice dimensions, taking into account the physiology of the small animals, collecting all the important technical and biological parameters [1]. The impedance selection and automatic focusing which is well known in human clinical practices were applied in these experiments too [2].

A few sequences were steadily investigated in our program:

1. Qualitatively studied the effect on various animal models.
2. Qualitatively and quantitatively compared oncothermia effect on tumor tissue with the classical heating (hyperthermia) in identical temperature taking attention on the dynamic stress effects also.
3. Studied the development of the tumor by molecular morphological and immuno-histochemical methods in the elapsed time from the single shoot treatment.

Results: Investigations of the time-development of the tumors shown:

1. Oncothermia had induced a certain and significant distortion of malignant-cells in all the allograft and xenograft models compared to their own control tumors. The healthy tissues around the tumors had no effect, their remained intact in both sides (treated and control) of the animals.
2. The high promotion (~70-100 %) of the efficacy of the studied chemotherapies (e.g. MMC) was observed.
3. The constricted RF-current rearranged the ionic structure of the extracellular electrolyte, rearranging the adherent connections (E-cadhetin, beta-catenin, p120 catenin). These reconnected connections probable promote or ignite some signal-transductive pathways to destroy the malignant cells, [3].
4. Both the classical heating (hyperthermia) and the modulated electro-heating (oncothermia) have significant tumor-destructive capability in the studied model, however the oncothermia is approx. three-times more efficient [4].
5. On the basic of the well documented tumor-destruction (measured by immuno-histochemical and TUNEL experiments) is dominantly apoptotic and accompanied by considerable leukocyte infiltration. The observed phenomenon allows the possibility of the role of p53 tumor-suppressor gene in these processes.

Conclusion: The applied mice models were suitable to study the effect of oncothermia on molecular level. The dominant role of apoptosis in the oncothermia cell-destruction is highly probable. Further investigations are in progress to study the mechanism of apoptotic induction and its connection with the leukocyte infiltration as well as the role of the adherens and other cellular connections.

References:

[1] Szasz A, Szasz N, Szasz O. (2010) Oncothermia Principles and Practices, Springer Scientific, Heidelberg

[2] Szasz A. (2006). Physical background and technical realization of hyperthermia, in: *Hyperthermia in cancer treatment: a primer*, (Eds: Baronzio GF, Hager ED), Springer Science pp. 27-59, 2006;

[3] Andocs G, Szasz O, Szasz A (2009 e) Oncothermia treatment of cancer: from the laboratory to clinic. Electromagnetic Biology and Medicine 28:148-165

[4] Andocs G, Renner H, Balogh L, Fonyad L, Jakab Cs, Szasz A (2009 d) Strong synergy of heat and modulated electromagnetic field in tumor cell killing, Study of HT29 xenograft tumors in a nude mice model. Radiology and Oncology (Strahlentherapie und Onkologie) 185:120-126

Are we able igniting natural processes to kill cancer cells?

Dr. Nora Szasz[1], Dr. Gabor Andocs[2,3], Dr. Oliver Szasz[1,4], Dr. Lajos Balogh[3], Dr. Linda Muller[5], Dr. Nora Meggyeshazi[5], Prof. Dr. Andras Szasz[1,4] ✉

(1) Department of Biotechnics, Faculty of Engineering, St. Istvan University, Budapest, Hungary
(2) Department of Pharmacology and Toxicology, Faculty of Veterinary Science, St Istvan University, Budapest, Hungary
(3) National Research Institute for Radiobiology and Radiohygiene, Budapest, Hungary
(4) Oncotherm Group, Germany
(5) 1st Department of Pathology and Experimental Cancer Research, Semmelweis University, Budapest, Hungary
(6) Department and Clinic of Reproduction, Faculty of Veterinary Science, St Istvan University, Budapest, Hungary

Background: Long-time living ancient paradigm is eliminating the tumor cells by drastic, artificial effects (resection and necrosis) in the actual lesions. Original idea of the very first interventions in oncology had favored the necrosis by elevated temperatures in the local area. The original hyperthermia (HT) concept used the consequences of the definite high temperature in the tissue and in the physiology reactions. Oncothermia method (OTM) is a modern heir of this ancient thinking. However it changed the paradigm, emphasized more the natural physiological and biophysical-chemical processes instead of the temperature which anyway has many complications in local applications. OTM uses well-controlled modulated radiofrequency (RF) current-flow through the target tumor [1]. Temperature dosing has problems on the control and the selection of the malignancy [2], so OTM definitely uses special non-temperature dependent effects [3] avoid the normal temperature spreading promoting undesired blood-flow by the time, as well as selectively and effectively acting to eliminate the tumor [4]. OTM applies electric field to modify the natural processes, which is a well-established research area, [5]. Our present article summarizes the possible explanations of the natural OTM mechanisms, focusing on the way to proof the actual hypotheses.

Method: We performed various experiments studying the natural factors of the cell-destortion effects by OTM. A highly specialized experimental setup (EHY110, Oncotherm, Germany) was used for in-vitro and in-vivo experiments, having single shot treatments in every cases. Effects were studied histomorphologically (HM) and immunhistochemically (IHCH) by various antibodies with digital microscopy system (MiraxView, 3D Histech).

Results: Experiments show a definite time delay of tumor-destruction. The effect of OTM immediately after single shot is weak by both the HM and IHCH experiments. However, the elapsed time shows accelerated development of the cell-killing. This not immediate effect suggests the action of natural processes, which we measured. Reestablishing the adherent connections (E-cadherin) and its signal pathways (beta-catenin, p120 catenin) can be measured by IHCH, and cells start to shrink (instead of swelling expected by necrosis). Appear a definitely enhanced expression of p53 protein. After longer time in vivo (4-24 h) observable the expression of connexins (gap-junctions), and nuclear relocaliztion of beta-catenin starts, which is finished after 72 hours of the treatment. During this development apoptotic bodies could be observed.

Conclusion: OTM probable ignites natural apoptotic processes selectively in the tumor. Further in vivo and in silico experiments are in progress.

References:

✉ Szasz.Andras@gek.szie.hu

[1] Szasz A (2006) Physical background and technical realization of hyperthermia, in: Locoregional Radiofrequency-Perfusional- and Wholebody-Hyperthermia in Cancer Treatment: New clinical aspects, (Eds: Baronzio GF, Hager ED), Springer Science Eurekah.com, Ch.3. pp. 27-59
[2] Szasz A, Vincze Gy (2007) Dose concept of oncological hyperthermia: heat-equation considering the cell destruction. Journal of Cancer Research and Therapeutics, 2:171-181
[3] Andocs G, Renner H, Balogh L, Fonyad L, Jakab C, Szasz A (2009) Strong synergy of heat and modulated electromagnetic field in tumor cell killing.. Strahlenther. Onkol. Feb; 185(2):120-6.
[4] Szasz A. Szasz N. Szasz O. (2010) Oncothermia. Principles and Practices, Springer Verlag, (http://www.springer.com/biomed/cancer/book/978-90-481-9497-1?changeHeader) Heidelberg, Dordrecht
[5] Szasz N (2003) Electric field regulation of chondrocyte proliferation, biosynthesis and cellular signalling, PhD theses, MIT, Cambridge, USA, http://tim.bookmaps.org/e/l/ele_9.html

Booster for all medication processes

Dr. Oliver Szasz[1], Dr. Gabor Andocs[2], Mr. Bela Gnädig[1], Mr. Balazs Acs[1], Prof. Dr. Andras Szasz[1,3]
(1) Oncotherm Group, Germany
(2) National Research Institute for Radiobiology and Radiohygiene, Budapest, Hungary
(3) Department of Biotechnics, St. Istvan Universtiy, Budapest, Hungary

Objective: One of the problematic point of the medication its targeting. The systemically administered drugs are distributed in the whole body by the blood, irrespective its origin by i.v. infusion, orally taken or getting by muscular injection, rectal suppository, skin-addicted, inhalations etc. However the delivery and the in-situ effect of the given drug to the target is a crucial point of the treatment. This is also the main pont of the personalization of the drug-administration in every medial actions and especially important in the oncology, where the toxicity is an effective danger. Objective of our presentation is to introduce the device, which is devoted to help in this line of the problems: the chemo-booster.

Method: The drug in all systemically administered cases delivered and distributed by the blood-stream. The task to increase the drug-concentration in a given volume is increasing the blood-flow in the targeted area. The higher temperature could activate the microcirculation of the capillaries (capillary filtration capillary pressure, etc), increasing the micro vascular perfusion, local tissue oxygen, nutrients, and phagocytes to the area being targeted. It could also regulate the cell cycle by changing calcium ion binding. Following actions also could be generated:

1. increased fibroblastic activity and capillary growth
2. increases the nutrition concentration in the volume
3. increases the metabolic activity in the volume (higher quantity of nutrition, oxygen and higher local temperature)
4. synergically increases the field-dependent effects, (optimizes the membrane excitation and helps activating the signal pathways, etc.)
5. increases the effects on the blood-structure in the volume,
6. increases venous and lymphatic flow
7. changes in physical properties of tissues
8. increases tissue extensibility
9. possible changes in enzyme reactions
10. increases the heat- and field-stress reactions (mainly the developments of heat-shock-proteins, HSP)

Further actions are:

- Muscular relaxation
- Edema reduction
- Lymphedema reduction
- Treatment of venous stasis ulcers
- Assists in removal of cellular debris and toxins
- Alters diffusion rate across the cell membrane
- Increases intramuscular metabolism
- Superficial wound healing
- Analgesia – pain relief, pain-killing device
- Could help the analgesic drugs to be activated

Results: A small device had been developed to heat up the full volume under the electrode in full depth. It has no treating effect like oncothermia had (it has no cellular selection or focusing), it is a simple local heater in depth. The heating is generated by the Joule-loss in the body, and makes vasodilatation there. The vasodilatated volume has higher blood perfusion which delivers more drug (and more oxygen) to the target, and relatively deprives it form the other areas of the body. This is a drug-boosting in a requested volume, but it does not make any more selection. The temperature range is 37-39°C, which is optimal for boosting function. The booster works not only by the vasodilation but also could be combined by the pharmacokinetic parameters of the given drugs, activating the chemo-reactions and the reaction rates by the higher temperature in the targeted volume. Its application covers a wide range of diseases. For example it could be used for rheumy, goat, pain-management, arthritis, dermatology, muscle spasms, sport supports, gynecology, allergy, rhinitis, common cold, pediatric ear diseases, nerve healing, bone Healing (unsure of any published clinical studies that are proven), cosmetics (like adipose problems, cellulites, acnes, blisters, etc.), support of the general rehabilitation process. It has a little curative effect on wound healing as well.

Conclusion: The newest device from Oncotherm Company is not for oncology alone. This universal small device could be indispensable support for the actual treatments by various medications, and could be essential for the personalization processes.

P-05

Brain glioma results by oncothermia

Prof. Dr. Andras Szasz[1,2]
(1) Department of Biotechnics, St. Istvan University, Budapest, Hungary (Szasz.Andras@gek.szie.hu)
(2) Oncotherm Group, Germany

Objective: None of the established state-of-the-art treatments in malignant primary brain tumors, especially in glioblastoma multiform (GBM), could show effective or commonly accepted curative potential until today. The editorial question of JAMA [1] in 2005 is actual even now: "Where to go from here?" Our objective to show a feasible way to go, summarizing the results obtained till now made by modulated electro-hyperthermia (oncothermia) in various clinics in EU.

Method: Data are collected from GBM and anaplastic astrocytoma (AA) published observational studies. The method is transcranially applied modulated RF-current capacitive coupled at 13.56 MHz carrier frequency, (Oncotherm, EHY2000+) described in details elsewhere [2]. The applied protocol was unified step-up heating, 40-150 W RF-power with water-bolus cooling. Treatment is applied in combination with chemo- and/or radio-therapy or used as monotherapy if the conventional therapies fall.

Results: On brain-gliomas, the Groenemeyer Institute (Bochum Germany) was active [3], [4], [5], [6], [7], [8], [9], together with the BioMed Clinic (Bad Bergzabern, Germany), [10], [11], [12], [13], [14]; as well as the Empoli University had publication, [15]. Presently two German Universities (Regensburg [Prof. Bogdahn] and Heidelberg [Prof. Wick] are working on prospective clinical study on brain gliomas with hyperthermia. A dose escalating Phase I clinical study was made on Neurology Clinic, University of Regensburg, showing the safe process in the brain as well, [16]. The safe treatment could be shown by spectacularly documented near-eye cases, when the tumor disappeared by the oncothermia treatment, while the eye remained unhurt, intact from the treatment [17]. A well designed Phase I study is shown in other paper [18]. To see more evidences we show the retrospective data of independent clinics [19], having the same oncothermia protocol. The data are well correspond to each other and significantly higher than the data of the large international databases.

Conclusion: The results are strongly indicating the feasibility and the benefit of the oncothermia showing a valid treatment potential and safe application. Oncothermia is a potential way to escape from the present impasse situation and treat brain gliomas successfully. Performing prospective, randomized clinical trials in the future is mandatory.

References:

[1] Fisher PG, Buffler PA: Malignant gliomas in 2005: where to GO from here?JAMA 293:615-617, 2005
[2] Szasz A (2006) Physical background and technical realization of hyperthermia. In: Baronzio GF, Hager ED (eds) Locoregional Radiofrequency-Perfusional- and Wholebody- Hyperthermia in Cancer Treatment: New clinical aspects, Ch 3, Springer Science Eurekah.com, pp. 27-59. http://www.springer.com/west/home/biomed/cancer?SGWID=4-125-22-150459762-0&detailsPage=ppmmedia%7CotherBooks&seqNo=0&CIPageCounter=CI_MORE_BOOKS_BY_AUTHOR0
[3] Sahinbas H, Baier Je, Groenemeyer DHW, Boecher E, Szasz A (2006) Retrospective clinical study for advanced brain-gliomas by adjuvant oncothermia (electro-hyperthermia) treatment. www.gimt-online.de/uploads/media/Therapieergebnisse_Giloma_Studie_01.pdf
[4] Sahinbas H, Groenemeyer DHW, Boecher E, Szasz A (2006) Retrospective clinical study of adjuvant electro-hyperthermia treatment for advanced brain-gliomas. Deutche Zeitschrifts fuer Onkologie 39:154-160. http://www.thieme-connect.com/ejournals/abstract/dzo/doi/10.1055/s-2007-986020
[5] Szasz A, Sahinbas H, Dani A (2004) Electro- hyperthermia for anaplastic astrocytoma and gliobastoma multiforme. ICACT, Paris, 9-12 February 2004
[6] Sahinbas H (2004) EHT bei Kindern mit Hirntumoren und nicht-invasive Messverfahren am beispiel von Hirntumoren. Symposium Hyperthermie, Cologne, 15-16 October 2004
[7] Sahinbas H, Grönemeyer D (2005) Oncothermia: An effective treatment for advanced gliomas. Deutsche Kongress im Komplementare Medizine, Jun.2005, Schortens
[8] Sahinbas H (2004) Deep RF hyperthermia treatment of advanced gliomas. Oncology Conference, Basel
[9] Sahinbas H, Grönemeyer D, Boecher E, Szasz A (2004) Hyperthermia treatment of advanced relapsed gliomas and astrocytoma. The 9th International Congress on hyperthermic oncology, ICHO, St. Louis, Missuri, 24-27 April 2004
[10] Hager ED, Dziambor H, App EM, Popa C, Popa O, Hertlein M (2003) The treatment of patients with high-grade malignant gliomas with RF-hyperthermia. Proc ASCO 22:118, #47;Proc Am Soc Clin Oncol 22: 2003 http://www.asco.org/portal/site/ASCO/menuitem.34d60f5624ba07fd506fe310ee37a01d/?vgnextoid=76f8201eb61a7010VgnVCM100000ed730ad1RCRD&vmview=abst_detail_view&confID=23&abstractID=102803
[11] Hager ED, Sahinbas H, Groenemeyer DH, Migeod F (2008) Prospective phase II trial for recurrent high-grade malignant gliomas with capacitive coupled low radiofrequency (LRF) deep hyperthermia. ASCO, Journal of Clinical Oncology, Annual Meeting Proceedings (Post-Meeting Edition) 26:2047. http://meeting.ascopubs.org/cgi/content/abstract/26/15_suppl/2047?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&fulltext=Hager&searchid=1&FIRSTINDEX=0&volume=26&issue=15_suppl&resourcetype=HWCIT
[12] Hager ED (2004) Response and survival of patients with gliomas grade III/IV treated with RF capacitive-coupled hyperthermia. ICHO Congress, St. Louis, USA
[13] Hager ED (2004) Clinical Response and Overall Survival of Patients with Recurrent Gliomas Grade III/IV Treated with RF Deep Hyperthermia – An Update. ICHS Conference, Shenzhen, China
[14] Fiorentini G, Giovanis P, Rossi S, Dentico P, Paola R, Turrisi G, Bernardeschi P (2006) A phase II clinical study on relapsed malignant gliomas treated with electro-hyperthermia, In Vivo. 20:721-724

http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=PubMed&list_uids=17203754&dopt=Citation
[15] Fiorentini G, Giovanis P, Rossi S, Dentico P, Paola R, Turrisi G, Bernardeschi P: A phase II clinical study on relapsed malignant gliomas treated with electro-hyperthermia, In Vivo. 20:721-724, 2006
[16] Wismeth C, Hirschmann B, Pascher C, Dudel C, Szasz A, Ogdahn U, Hau P (2009) Transcranial electro-hyperthermia combined with alkylating chemotherapy in patients with relapsing high-grade gliomas – Phase I clinical results. Expanding the Frontiers of Thermal Biology, Medicine and Physics Annual Meeting of Society of Thermal Medicine, Tucson, USA, 3-7 April 2009
[17] Cases from Prof. Dr. H. Renner (Nuernberg, Germany) and Prof. Dr. A. Herzog (Nidda, Germany). It could be sent by request for medical doctors.
[18] Wismeth C. Dudel C. Pascher C. Ramm P. Pietsch T. Hirschmann B. Reinert C. Proescholdt M. Rümmele P. Schuierer G. Bogdahn U. HauP. (2010) Transcranial electro-hyperthermia combined with alkylating chemotherapy in patients with relapsed high-grade gliomas - Phase I clinical results, Journal of Neuro-Oncology 98:395-405. http://www.ncbi.nlm.nih.gov/sites/entrez
[19] Szasz A (2009) Brain glioma results by oncothermia, a review. Expanding the Frontiers of Thermal Biology, Medicine and Physics Annual Meeting of Society of Thermal Medicine, Tucson, USA, 3-7 April 2009

P-06

Clifford Hospital – Non-Toxic Integrative Cancer Treatment

Prof. Dr. Clifford Pang[1]
(1) Clifford Hospital, Guangzhou, Guangdong, P.R. China (adm@clifford-hospital.com)

Clifford Hospital is the first JCI (Joint Comission International) accredited Chinese hospital, a National Grade ”Triple-A” Hospital and a ”Famous Traditional Chinese Medicine Hospital” of China. It is a large modern general hospital, has been accredited by JCI three times. (The JCI accreditation surveys are carried out once every 3 years.)

Bestowed the titles of National Education Base for Preventive and Curative Cancer Treatments, and reputable TCM Oncology Center of Guangdong Province, Clifford Hospital Oncology Center achieved breakthroughs in medical treatment, utilizing modern techniques such as hyperthermia, chelating, medical ozone therapy and traditional therapies including Chinese Medicine, acupuncture, herbal cuisine, psychotherapy, medical Qigong, music, argon-helium cryoablation, gamma knife, photodynamic therapy, bio-targeted therapy, stem cell immunotherapy, genetic therapy and others combined with the latest advanced medical procedures which are surgery, radiotherapy and chemotherapy of international standard. The whole body hyperthermia and the loco-regional hyperthermia (oncothermia) is an integrated treatment modality in the curative concept of the hospital. For different needs at different periods of cancer prevention, treatment, recovery and remission, individualized protocols are made by medical experts in Joint Case Conference according to the patient’s specific conditions so as to strengthen the patient’s immune system, prolong the patient’s life and improve the patient’s quality of life. The quality of the care is impressive: over 30 international oncologists participate in Joint Case Conference, providing individualized protocols; over 20 advanced procedures are available for cancer prevention, treatment, recovery and remission; over 1,000 cancer patients were cured without cancer metastasis and recurrence for many years.

We propose non-toxic integrated cancer therapies to help the overall recovery of body and mind. It breaks the limitation of mono anti-cancer treatment and maximally improves the therapeutic effect, so as to prevent metastasis and relapse of cancer, improves patient’s quality of life and prolongs their life span. In this scheme the oncothermia has a definitive role, successfully integrated in the line of the integrative processes.

P-07

Clinical studies and evidences of modulated RF conductive heating (oncohtermia) method

Dr. Nora Meggyeshazi[1], Dr. Tibor Krenacs[1], Prof. Dr. Andras Szasz[2,3]
(1) 1. sz. Patológiai és Kísérleti Rákkutató Intézet, Semmelweis University, Budapest, Hungary
(2) Department of Biotechnics, St. Istvan University, Budapest, Hungary
(3) Oncotherm Group, Germany

Background: Hyperthermia is an ancient treatment modality, but more than two millennia were not enough for its wide acceptance. Modulated RF-conductive heating (oncothermia [1]) introduces a new controllable, successful paradigm. It has twenty years experience in the clinical practices. During this long time, a huge number of patients were treated with the method in their advanced states, in combination with conventional therapies, or sometimes, when those were fall, applied as monotherapy. Object of our present paper is to show the clinical evidences collected by application of Oncothermia.

Methods: Oncothermia method is well described in the relevant literature [2]. In our present paper we had collected results of some retrospective and a prospective studies performed by oncothermia for higher (usually third and subsequent) treatment-lines, boosting or resensitizing the effect of the conventional therapies. We show some results when oncothermia was applied as monotherapy when the conventional therapies fall. These high-lines of treatments are mostly determined by the individual decisions of the physicians, usually without having help from any evidence based statistical approvals. The results have to be concluded from observational studies and their historical and data-base comparisons. Make the result as objective as could be, we compared the collected results of the same localizations and same protocols from various clinics. They common significant difference from the databases could be accepted as a kind of evidence.

Results: The 1st year survival and its improvement compared to the largest US database (SEER) is shown in the table. This presentation is an invitation to share the challenge of the new method, share the excitement to apply a new effective treatment, and share the enjoyment of the results. We concentrate on the results of anyway complicated diseases, like brain gliomas, pancreas carcinoma, metastatic liver from colorectal carcinoma. In glioma cases a prospective study (Regensburg University, [3]) had shown the safety of oncothermia even in dose escalation. The efficacy results are everywhere significantly better than any of the data in public databases (SEER, Eurocare):

Tumor	1st year survival (%)	Gain to SEER (%)
Bone	100	42
Brain glioma (1)	79.3	90.63
Brain glioma (2)	86.2	107.21
Breast	97.1	7.5
Cervix Uteri	86.8	5.2
Colo-rectal	84.9	20.5
Corpus uteri	100	15
Esophagus	41.7	34
Head&Neck	92.2	29.5
Kidney	84.6	22.2
Liver	72	250.9
Lung	64.7	96.7
Ovary	100	51.1

- ASCO (2003) [3] the median survival time (MST) for anaplastic astrocytoma (AA) 106m (n=9) and 20m (n=27) for glioblastoma multiforme (GBM) patients,
- ASCO (2008) [4] 38.2m (n=53) and 20.3m (n=126) for AA and GBM respectively,
- Witten-Herdecke University published [5] 70.2m (n=17) and 25.2m (n=19) as well as [6] 26.1m (n=40) and 16m (n=92) data for AA and GBM MST, respectively.
- ACNU combination was used in Phase II trial recurrent glioblastoma (n=19) [7]. MST was 21.8m; while MST from first oncothermia was 8.8m.
- HTT-Med MST results [10] were 36m (n=8) and 14m (n=10) for AA and GBM, respectively.
- Empoli Hospital shown in very advanced relapsed cases [8] 9m MST (n=12) for GBM.

In pancreas carcinoma mEHT results

- ASCO (2002), [9]; first year survival 41.7%, while the subsequent years are: 20.6%, 13.5%, 9.4%, 4%, with MST 10.8m.
- ESHO (2003), DEGRO (2004) [10], [11], the 1yS in HTT-Med (n=73) 52.1% (MST=12.7m), and in Peterfy Hospital (n=26) 46.2% (MST=12.0m). In the subsequent years were 31.5% &15.4%, 16.4&11.5%, 9.6&3.8% and 2.7&3.8%, which data are higher than expected from the large databases
- Results were repeated in six different clinics in two countries significantly improving the achievements of the conventional treatments shown in summary [12]. In addition to the above two more clinic showed its 1yS: Veramed (n=42) 52.4% and Nurnberg Nord (n=13) 46.2%

In metastatic liver cases mEHT has also distinguished results:

- The colorectal liver metastasis was the topic of four different studies on liver [13],
- ASCO (2007) [14], MST was 20.5w, 50% presented evidence for increase well being.
- ICACT [15], had shown definite benefit for 25 patients (n=30) by mEHT
- ESHO (2005) [16], had shown in second line treatment 80% response rate.

Conclusions: Summary of our results conclude the feasibility of the oncothermia and despite of the high-line treatments shows evidences by the parallel studies in the various clinics.

References:

[1] Szasz A, Szasz N, Szasz O. (2010) Oncothermia Principles and Practices, Springer Scientific, Heidelberg
[2] Szasz A: in: Locoregional Radiofrequency- (Eds: Baronzio GF, Hager ED), Springer, pp. 27-59, 2006
[3] Wismeth C. Dudel C. Pascher C. Ramm P. Pietsch T. Hirschmann B. Reinert C. Proescholdt M. Rümmele P. Schuierer G. Bogdahn U. HauP. (2010) Transcranial electro-hyperthermia combined with alkylating chemotherapy in patients with relapsed high-grade gliomas - Phase I clinical results, accepted Journal of Neuro-Oncology
[4] Hager ED, Sahinbas H, Groenemeyer DH, Migeod F (2008) Prospective phase II trial for recurrent high-grade malignant gliomas with capacitive coupled low radiofrequency (LRF) deep hyperthermia. ASCO, Journal of Clinical Oncology, Annual Meeting Proceedings (Post-Meeting Edition) 26:2047
[5] Sahinbas H, Grönemeyer DHW, Böcher E, Lange S (2004) Hyperthermia treatment of advanced relapsed gliomas and astrocytoma, The 9th International Congress on hyperthermic oncology, St. Louis, Missuri, ICHO, 24-27 April
[6] Sahinbas H, Greoenemeyer DHW, Boecher E, Szasz A (2006) Retrospective clinical study of adjuvant electro-hyperthermia treatment for advanced brain-gliomas. Deutche Zeitschrifts fuer Onkologie 39:154-160

[7] Douwes F, Douwes O, Migeod F, Grote C, Bogovic J (2006) Hyperthermia in combination with ACNU chemotherapy in the treatment of recurrent glioblastoma.
[8] Fiorentini G, Giovanis P, Rossi S, Dentico P, Paola R, Turrisi G, Bernardeschi P (2006) A phase II clinical study on relapsed malignant gliomas treated with electro-hyperthermia. In Vivo 20:721-724
[9] Hager ED, Dziambor H, Hoehmann D (2002) Survival and quality of life patients with advanced pancreatic cancer. Proc. Am. Soc. Clin. Oncol 21
[10] Dani A, Várkonyi A, Nyiro I, Osváth M (2003) Clinical experience of electro-hyperthermia for advanced pancreatic tumors. ESHO Conference, Munich, June 04-07
[11] Dani A (2004) Electro-hyperthermia for advanced pancreas tumors. Deutscher Kongress für Radioonkologie, Strahlenbiologie und Medizinische Physik, Erfurt, 10-13 June
[12] Dani A, Varkonyi A, Magyar T, Szasz A (2008) Clinical study for advanced pancreas cancer treated by oncothermia. Forum Hyperthermie, 1:13-20
[13] Hager ED, Dziambor H, Hohmann D, Gallenbeck D, Stephan M, Popa C (1999) Deep hyperthermia with radiofrequencies in patients with liver metastases from colorectal cancer. Anticancer Research 19(4C):3403-3408
[14] Ferrari VD, De Ponti S, Valcamonico F, Amoroso V, Grisanti S, Rangoni G, Marpicati P, Vassalli L, Simoncini E, Marini G (2007) Deep electro-hyperthermia (EHY) with or without thermo-active agents in patients with advanced hepatic cell carcinoma: phase II study. Journal of Clinical Oncology 25:18S, 15168
[15] Fiorentini G, deGiorgi U, Turrisi G, Rossi S, Dentice P, Bernardeschi P (2006) Deep electro-hyperthermia with radiofrequencies combined with thermoactive drugs in patients with liver metastases from colorectal cancer (CRC): a Phase II clinical study. ICACT 17th, Paris, 30 January – 2 February
[16] Panagiotou P, Sosada M, Schering S, Kirchner H. (2005) Irinotecan plus Capecitabine with regional electrohyperthermia of the liver as second line therapy in patients with metastatic colorectal cancer; ESHO, Jun.8-11, Graz, Austria

P-08

Co-administration of electrohyperthermia and bevacizumab in non-small cell cancer: A case presentation

Dr. Gabor Rubovszky[1], Dr. Tünde Nagy[1], Prof. Dr. Andras Szasz[2,3], Prof. Dr. Istvan Lang[1]
(1) National Institute of Oncology, Budapest, Hungary
(2) Department of Biotechnics, Faculty of Engineering, St. Istvan University, Budapest, Hungary
(3) Oncotherm Group, Germany

The backbone of therapy in non-operable non-small cell lung cancer (NSCLC) is systemic treatment. The principle goal is to prolong survival with the least toxicity keeping in mind the importance of patients' quality of life. Bevacizumab (bev) has been accepted as first line and maintenance therapy in NSCLC. Bev can be added safely to several chemotherapeutic agent and radiation therapy, however there is no data on co-administration with thermotherapy. Only scarce data exist about loco-regional thermotherapy in regard of prolongation of survival, but it can be used successfully in symptom palliation. Electrohyperthermia is a form of thermotherapy using electromagnetic field.

A male patient was operated for stage III NSCLC in February 2008. He rejected adjuvant chemotherapy. After one mono-localized (hip bone) osseal metastasis appeared in June 2009. In July 2009 a combination therapy of paclitaxel/carboplatin (to November 2009, six cycles all) and bevacizumab plus zoledronic acid was introduced, which stabilized the disease. Hyperthermia (HT) has been added in November 2009 by the request of patient. He was given HT three times a week with the maximal tolerated dose of 70W (EHY 2000®, Oncotherm Ltd, Pagy, Hungary, 20 cm electrode). Since that time no new adverse event emerged, the patient's pain diminished. The patient insisted to continue HT, although it was voluntary and without a proposal of his physician.

In this case HT did not compromise bevacizumab efficacy, and it makes probable that they can be co-administered safely.

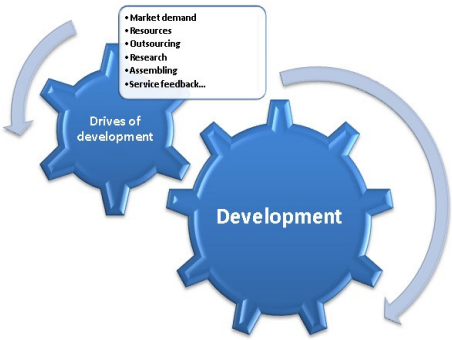
P-09

Development and Designing in Oncotherm Group

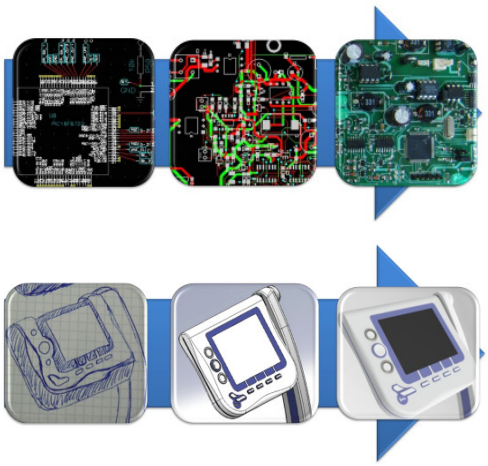
Mr. Balazs Acs[1], Dr. Gabor Andocs[2], Mr. Bela Gnädig[1], Dr. Oliver Szasz[1]
(1) Oncotherm Group, Germany
(2) National Research Institute for Radiobiology and Radiohygiene, Budapest, Hungary

Objective: The modern development and design is based on the harmony of the integrated parts, and also their updates with the state-of art of the science and other professional knowledge. Oncotherm is devoted to the highest available efficacy and safety, which requests a real interdisciplinary thinking and wide range knowledge in both the scientific and technical fields. Our objective is to show how Oncotherm follows this interdisciplinary trend and develops its devices.

Method: To satisfy the highest market demands Oncotherm had chosen a hard way of the development. It does not buys commercially ready units for parts of the device, but had developed every units completely fitting to the global visions of the device. The most important and necessary during the planning and the assembling is: the highly qualified and experienced employees and a network of professionals connected to the activity. The policy of Oncotherm is the flexibility, which makes possible the adaptability to the new challenges and to the latest scientific achievements. For flexibility the company limits the number of employees, and the high performance manufacturing is mostly based on smart subcontracted companies. In case of Oncotherm the relation of the employees and the number of subcontracted outsourcing places is 1/7. This small number of employees understands the main demand: the high-quality. The research is in one side the market info (including the service experience) on other stimulates the development processes and allows its dynamism to follow the state of art. This is supported by modern software and hardware facilities in the company. These factors all moving the "development wheel" ahead.



Results: This approach has a double-sword effect: requests intensive development of the employees themselves with demand of interdisciplinary approach and follow up the latest results in the area of the personal expertise, and on the other hand this dynamism must be accompanied with the stability of the devices, the strict quality requests and the high-standard of administration skills. The company employees understand that they are all important "screws" in the "machinery of the company" irrespectively their own actual status there, and also they are convinced that the development of the devices is parallel with the development of the company and their personal knowledge and professional skills as well. The rough planning, the production-document leads to the realization of the finished product in every units irrespective its mechanical or electrical character. These developments are interacting organically making the product at the end a stable unified integrity optimized on the intended function.



Conclusion: Everybody knows in the company and in the large network of R&D and manufacturing that our devices are such instruments, which in the hand of health professionals effectively helps for the suffering patients.

P-10

Die 10 Grundsätze der Elektrophysiologie. Elektrische Ladunge und Elektrowärme in der Onkologie

Dr. Eberhard W Eckert

Die Elektrophysiologie ist noch weitgehend von Denkweisen und Ansichten aus der Elektrophysik und Elektrotechnik geprägt. Da international eingeführte Meßgrößen, Normen und Meßverfahren sowie Bezeichnungen übernommen werden mußten, ist das verständlich. Der elektrische Leitfähigkeitsmechanismus im Körper weicht aber von demjenigen in der üblichen Elektrotechnik gravierend ab. So erwächst das Problem, die physikalisch-technischen Meßwerte humanbiologisch richtig zu interpretieren.

Eine Zusammenstellung der wichtigsten Fakten findet sich in "Die 10 Grundsätze der Elektrophysiologie". Daraus leiten sich für die Hyperthermie bezüglich Wirkung und Überwachung wesentliche Dinge ab. Zur Abschätzung der Wirkung von Hyperthermie auf das Vegetativum eines Patienten gibt es ein relativ einfaches Verfahren, die Biotonometrie nach Rilling, oder eine etwas komplexere Weiterentwicklung; beide auf der Basis Bioimpedanzmessung.

P-11

Effect of rouleaux formation of erythrocytes in blood of patients treated by oncothermia

Dr. Henning Saupe[1], Dr. Christian Buettner[1], Dr. Gabor Andocs[2]
(1) Arkadia Praxis, Kassel, Germany (dr.saupe@arcadia-praxis.de)
(2) Department of Pharmacology and Toxicology, Faculty of Veterinary Science, St Istvan University, Budapest, Hungary

Background: Observation and explanation of rouleaux phenomenon induce permanent debate started from its discovery. The aggregation of erythrocytes is a prominent feature in humans and other species "athletic" species [1]. In vitro studies have shown that aggregation of blood increases as shear rate decreases. Aggregation also depends on hematocrit and the concentration of macromolecules in the plasma or suspending medium [2], and in the presence of high molecular weight polymers, such as plasma proteins or dextrans, aggregate to form rouleaux and rouleaux networks [3]. However, the circumstances in which aggregation occurs is not well understood. Correlations of aggregation parameters with C-reactive protein and fibrinogen was proven in unstable angina, acute myocardial infarction, and bacterial infection [4] as well.
Our aim in this paper is to describe the systemic observations of blood samples before and after oncothermia, trying to clarify the oncothermia effect on blood.

Methods: Blood samples nude mice and voluntary humans were studied before and after oncothermia treatment. Samples were carefully collected from tail's venue of mice and from finger capillaries of humans. Samples of venous blood from humans were also collected for comparison. The individual blood-collection was made before and after oncothermia treatment, as well as systemically performed in subsequent treatments. Samples were promptly (freshly) measured by dark-field microscopy and archived by high resolution photo- or video-techniques.

Results: The rouleaux formation of blood samples characteristically was obtained from the individuals before the treatment, but this phenomena was not observable in every cases in mice. However, in the cases, when the rouleaux formation was shown, oncothermia treatment has changed the aggregation, and the samples were mostly free of erythrocyte aggregates. These phenomena were independent of the treatment localization and also from the venous or arterial origin of the blood sample, and were observed both in humans and mice. In blood specimens where the rouleaux formation of the erytrocytes were observed, oncothermia dissolved the aggregates.

Conclusions: Measurement of the oncothermia effect on rouleoux phenomena could lead us a simple control of the treatment efficacy, but our present data are not eligible for definite conclusions. Establishing a theoretical model and further experimental investigations of the phenomenon is in progress.

References:

[1] Popel AS, Johnson PC, Kameneva MV, Wild MA (1994) Capacity for red blood cell aggregation is higher in athletic mammalian species than sedentary species. J Appl Physiol 77: 1790–1794
[2] Baskurt OK, Meilselman HJ, Kayar E (1998) Measurement of red blood cell aggregation in a "plate-plate" shearing system by analysis of light transmission. Clin Hemorheol Microcirc 19: 307–314
[3] Chien S, Jan K-M (1973) Ultrastructural basis of the mechanism of rouleaux formation. Microvascular Res 5:155–166
[4] Ben Ami, R., G. Barshtein, D. Zeltser, Y. Goldberg, I. Shapira, A. Roth, G. Keren, H. Miller, V. Prochorov, A. Eldor, S. Berliner, and S. Yedgar (2001) Parameters of red blood cell aggregation as correlates of the inflammatory state. Am J Physiol Heart Circ Physiol 280: H1982–H1988

P-12

Effects far from equilibrium in electromagnetic heating of tissues

Dr. Oliver Szasz[2], Dr. Gabor Andocs[3], Prof. Dr. Andras Szasz[1,2]*
(1) Department of Biotechnics, Faculty of Engineering, St. Istvan University, Budapest, Hungary,
(2) Oncotherm Group, Germany
(3) Department of Pharmacology and Toxicology, Faculty of Veterinary Science, St Istvan University, Budapest, Hungary,
*Corresponding author e-mail: Szasz.Andras@gek.szie.hu

Introduction: One of the very first treatment "technologies" for oncology is the regional heating of the tissues and body-parts, (hyperthermia, HT). This long history was not enough to be accepted as conventional treatment, facing mostly skeptic opinions among the oncology experts. The main reason is its controversial results and poor control, the missing of appropriate selective, controllable safe deep heat-delivery. Constrained balance of physiological feedback and the sophisticated transport network with very heterogenic tissue structures block applying the simple heating practices. This situation requests definite bioengineering tasks as well as new paradigm for the medical applications. The modern

heating technologies based on electromagnetic interactions made a huge step ahead in this complex field, but not enough yet to solve some crucial problems in deep heating [1]. The commonly applied microwave and high radio-frequency (RF) radiation is challenged by the magnetic and capacitive heating techniques, applied lower frequencies. Oncothermia method, (OTM) heats by the dielectric loss in the various body electrolytes and makes possible to select between the tissues and concentrate on the malignant cells. Due to the constrained RF-current conduction of OTM, the complex impedance determines the actual flow-direction of the current. This could distinguish by the microscopic heterogeneity in the treated tissue [2].

Materials and methods: The relatively low frequency RF-current dominantly flows in the extracellular electrolyte. The energy absorption creates a temperature gradient through the cellular membrane, which drives non-equilibrium processes by constrained heat-flow through the membrane, [3]. The ion- and mass-flows could be well approached by Onsager's theory in the frame of non-equilibrium thermodynamic description. The polarization conditions are effectively approached in frame of β-dispersion of the aqueous electrolytes. The dose is measurable on the ignited chemical effects [4] instead of the temperature. The actual realization of OTM is capacitive coupled heating, using the constrained conduction of 13.56 MHz RF [5], amplitude modulated by time-fractal pattern [6], which is not limited by the thermal-energy [7]. In vitro and in vivo experiments were accomplished on identical 42 °C reference temperature by conventional HT and OTM methods, respectively. The experimental systems are in vitro cell-lines (HT29, B16, HepG2, A431) and their in vivo xenografts in nude mice. The changes of the adherent connections the cell membrane-associated effects (activation of the apoptotic signal transduction pathways, heat shock protein mediated stress-responses) were studied in vitro, while the cell-destruction mechanisms were investigated in vivo.

Results: Conductance differences between the cell-culture/tissue-parts automatically control the focus at cellular/tissue level. Due to the change of metabolic activity OTM acts selectively, which was proven in co-culture experiments. The emergent thermal- and electric-gradients force higher membrane permeability, larger intracellular pressure, imbalance of the ion-exchange, and finally challenges the membrane stability. An over-expression of HSP70 (heat-shock protein by 70 thousand Dalton weight) on the outer membrane was detected by immunohistology. Longer recovery after OTM was also measured. HSP production of OTM was compared to HT, measured by PCR and luciferase indicated gene measurements were also performed. Significant reconstruction of adherent connections of the cells could be detected in a time-delay after OTM, casued by the polarization conditions of the field gradients. This was not observed by HT. Experiments staining the double strains of DNA (DAPI) and enzymatic labeling of the strand-break of DNA (TUNEL-FICT) had shown the high rate of apoptotic cell deaths caused by OTM compared to the dominantly necrotic HT. This observation was supported with the follow-up the β-catenin development during 24h. Significant difference between HT and OTM was measured in vivo as well. Effective characteristic cell-destructions of tumor lesions was observed in such low temperature where HT was ineffective. Experiments by combination of the heating methods with various drugs (mitomycine, liposomal-doxorubicine, Tc-radiopharmacon labeled liposomes, etc.) also emphasize the definite advantages OTM versus HT.

Conclusions: The non-equilibrium thermodynamics makes OTM feasible to go over the difficulties of the problem of the selective deep-heating. With this new paradigm OTM could be a candidate in the branch of modern therapies in medical practice. OTM could be applied in various biomedical fields where the selection and the drug-targeting as well as the personalized treatment are important requests.

Acknowledgments: Authors acknowledge financial support of the Hungarian National Office for Research and Technology, application KMOP-1.1.4-07/1-2008-0083 and the Oncotherm Kft.

References:

[] Szasz A (2006) Physical background and technical realization of hyperthermia, in: Locoregional Radiofrequency-Perfusional- and Wholebody-Hyperthermia in Cancer Treatment: New clinical aspects, (Eds: Baronzio GF, Hager ED), Springer Science Eurekah.com, Ch.3. pp. 27-59
[2] Szász A (2007) Hyperthermia a Modality in the Wings. Journal Cancer Research and Therapeutics, 3:56-66
[3] Szasz A, Vincze Gy, Szasz O, Szasz N (2003) An energy analysis of extracellular hyperthermia. Magneto- and electro-biology, 22:103-115
[4] Szasz A, Vincze Gy (2007) Dose concept of oncological hyperthermia: heat-equation considering the cell destruction. Journal of Cancer Research and Therapeutics, 2:171-181
[5] Szasz A, Szasz O, Szasz N (2001) Electrohyperthermia: a new paradigm in cancer therapy. Wissenschaft & Forschung, Deutsche Zeitschrift für Onkologie, 33:91-99
[6] Szendrő P, Vincze G, Szász A (2001) Pink-noise behaviour of biosystems. Eur.Biophysics J. 30:227-231
[7] Vincze Gy, Szász A, Szasz N (2005) On the thermal noise limit of cellular membranes. Bioelectromagnetics, 26:28-35

P-13

Evaluation of single-arm studies of oncothermia

Dr. Oliver Szasz[1], Dr. Nora Szasz[1], Prof. Dr. Andras Szasz[1,2]
(1) Oncotherm Group, Germany
(3) Department of Biotechnics, St. Istvan University, Budapest, Hungary

Background: Oncothermia survival studies are problematic due to the missing control arm. This is a problem is general, when the treatment targets advanced, mostly refractory, relapsed malignancies in high treatment lines, when the only way is the sequential treatment. The sequential trial [1], [2], [3], is well known, and applied frequently in the case of small trials [4]. The sequential trial (like the oncothermia) is applied for the same patient in sequences, In this approach the development of the patient is measured and documented. Our objective to show how the evaluation of the single-arm study could be realistic enough to be evidence based.

Methods: The basic of the idea of the data-separation is the appropriate parameterization of the non-parametric Kaplan-Meier survival pattern by poly-Weibull fit. However we have some qualitative assumptions:

- Patient starts the new sequence when the previous had not (or had not satisfactory) result.
- The new sequence gives positive addition (no worsening of the patient's stage due to the applied therapy in the actual sequence).
- The new sequence does not block the possibility of subsequent sequences, the patients will not be excluded from the possible other therapies by the actual one.
- The effect of the new sequence affects the survival curve, so the studied Kaplan-Meier plot includes the information.
- The sequence is medically controlled at least on the same way, as were done in pervious therapies. No uncontrolled "side therapies" are in use.

Studying the median of a survival curve alone disregards the real success measurable at the end of the study. Correcting this "mistake" the average (mean) of the distribution is considered.
The mean is more affected by the "tail" of the distribution, so it gives more accurate idea on the cure-rate. The median is more responsible for the information how quick the loss of the patients, while the mean has more part on the information how long the effect of the high-success patients. Both are important for characterization, the time-scale and the shape of the distribution are independent parameters. The distribution curve must be characterized at least by two parameters. These two parameters are the mean and the median, supposing to characterize the non-parametric distribution, and so in fact this is a hidden parameterization of the Kaplan-Meier plot. Application the parametric Weibull distribution function approaching the survival curve for clinical applications is established theoretically and practically, [5], [6], [7], [8]. It is used for a long time for survival description in gerontology [9], [10] and in oncology [11] as well.

Results: The evaluation of the Kaplan-Meier plot by parametric distribution works well in the practice. Patients responding to the treatment are well distinguishable from the responders, and on this basic the overall survival benefit can be evaluated. The significance level depends on the number of patients, but over 25 patients it usually fits better than 95% confidence. We evaluated numerous single-arm clinical trials, showing the efficacy of the study. The evaluation was well correlated with the independently measured other parameters as well as the criteria of start of oncothermia also shows stable reference distribution.

Conclusions: Parametric evaluation of Kaplan-Meier non-parametric distribution works well for single arm studies. The single parameter reference of the Kaplan-Meier (median survival) is unsatisfactory; the two parametric Weibull distributions describe the situation much more exactly.

References:

[1] Bellissant, E., J. Benichou, and C. Chastang. 1996. The group sequential triangular testfor phase II cancer clinical trials. American Journal of Clinical Oncology 19:422–430
[2] Williams, PL. (1996) Sequential monitoring of clinical trials with multiple survival, endpoints. Statistics in Medicine 15:2341–2357
[3] Whitehead, J. Donaldson AN, Stephens R. Machin D. (1993) A simulated sequential analysis based on data from two MRC trials. British Journal of Cancer 68:1171–1178
[4] Evans, CHJr. Ildstad ST (2001) (eds) Committee on Strategies for Small-Number-Participant, Clinical Research Trials, Small Clinical Trials: Issues and Challenges, National Academy Press, Washington DC, http://www.nap.edu/catalog/10078.html
[5] Hajian-Tilaki KO, Hanley JA, Joseph L, Collet J-P (1997) A Comparison of Parametric and Nonparametric Approaches to ROC Analysis of Quantitative Diagnostic Tests. Medical Decision Making 17:94-102
[6] Jones G. Rocke DM (2002) Multivariate survival analysis with doubly-censored data: application to the assessment of Accutane treatment for fibrodysplasia ossificans progressive. Statistics in Medicine 21:2547-2562
[7] Avrami MA (1939) Kinetics of phase change I-III. J. Chem. Phys. 7:1103
[8] Wilson DL (1994) The analysis of survival (mortality), data: fitting Gompertz. Weibull and logistic functions, Mech. Aging Dev. 74:15-33
[9] Piantanelli L (1986) A mathematical model of survival kinetics. I. Theoretical basis, Arc. Gerontol. Geriatr. 5:107-118
[10] Economos AC (1982) Rate of aging, rate of dying and the mechanism of mortality, Arc. Gerontol. Geriatr. 1:3-27
[11] Weston CL, Douglas C, Craft AW, Lewis IJ, Machin D; (on behalf of UKCCSG), (2004) British Journal of Cancer, 91:225-232

P-14

Experience with chronic oncothermia treatments

Mr. Peter Lorencz[1], Dr. Andras Csejtei[1]
(1) Markusovszky Hospital, Department of Oncoradiology, Szombathely, Hungary

Background: We provide oncothermia treatment to our patienst from 2001. Approximately 700 patients received oncothermia in this time, with more than 3500 sessions. Our aim in this article is to show what causality condition could be established between the curative rate and the time of care.

Method: Patients receiving at least 50 oncothermia treatments were selected retrospectively into this study. This selection resulted 13 patients, 1.8% of the full patients population receiving oncothermia. All the included patients had primary of metastatic liver cancer. The other localizations (like the gynecology cases or head&neck tumors) were not reaching such eligibility to select them in this group. Due to the partially private financing of the treatments not all the patients whom medically was recommended this therapy could receive oncothermia. Despite of the financing bias (which mainly limited the number of applied sessions) the benefit of chronic treatment approach was clearly observable. From the 13 patients (all having large number [>50] of treatments) in the case of 5 the chronic regular oncothermia made such

definite improvement of the patient, that it was not rational to continue the treatment, and two was interrupted due to private reasons. The staging was regularly controlled by combination of three different methods to avoid any misstaging. The methods were: (1) imaging diagnostics (US, CT or MRI), (2) blood analysis (tumor markers and other labor parameters) and (3) personal investigation. Patients receiving chemotherapy were treated immediately after or concomitantly with oncothermia, while patients receiving radiotherapy the oncothermia was started within 20 minutes after. 12 patients received weekly two, while one received partly 2 and 1 oncot5hermia sessions pro week.

Results: Our results definitely show a chronic treatment possibility by oncothermia application. Interruption of the oncothermia series caused immediate worsening of patients stage, increased the progression of the disease. Continuing the treatments afterwards the efficacy of the therapy was lower than before.

Conclusion: In cases of liver malignancies (primary or metastatic) oncothermia is able to handle this disease as chronic morbidity without mortal event, like dialysis does. Our experience suggests continuing oncothermia in liver malignancies at least 12-16 times after finishing the conventional oncotherapy protocols. These observations make feasible work out the protocol of oncothermia treatment as chronic procedure.

P-15

History of hyperthermia and electro-medicine

Prof. Dr. Seung Cheol Kim[1], Prof. Dr. Woong Ju[1], Prof. Dr. Andras Szasz[2,3]
(1) Department of Obstetrics & Gynecology, College of Medicine Ewha Womans University, Mok-Dong Hospital, Seoul Korea (South)
(2) Department of Biotechnics, Faculty of Engineering, St. Istvan University, Budapest, Hungary
(3) Oncotherm Group, Germany

Introduction: Hyperthermia was one of the very first treatments in human medicine, having 5 thousand years history. Of course it had a sacral meaning at the beginning, and Hippocrates was convinced about its overall efficacy, telling when hyperthermia (fire) does not help, than the disease has to be declared as incurable. Our objective is to follow the development of the heat-therapies by selection important moment from its history.

Discussion: Heat was applied to locally affected parts of the body and to its entirety by means of hot water, steam, sand, and mud baths. Natural hot air caverns connected with volcanic sources. The first known oncotherapy by heat was made by an Egyptian priest/physician Imhotep in the 5th century BC. He had infected tumors before surgically removing them, which was in fact the very first immune approach as well. By the development of the medical knowledge, more and more heat applications were applied in practice. Hippocrates told later: Give me the power to produce fever and I will cure all diseases". His followers in the line were Aurelius Cornelius Clesus and Rufus of Ephesus, who believed on the curative effect of fever. The priogress was continuing in the middle ages, when the ablation techniques (burn out the tumor) and hot-bathes were in practice, while step-by step the temperature measurement was worked out. The first clinical thermometer was introduced only late: Sir Clifford Allbutt did it in 1868. This was the start of the modern history of heat-therapies, which was characterized with such famous names like Virchow, Busch, Warren, Coley and the Nobel-laureate Wagner-Jauregg. The technical revolution of the heat therapies was when the modern microwave heating was developed, and applied in medicine. This temperature based focused deep heating became one of the line (focused loco-regional heating), while the other was the whole body heating with various methods. In local heating the paradigm is to reach the appropriate temperature locally. The main representatives of this techniques are the Brucker (French) BSD-Medical (USA), Thermotron (Japan), Alba (Italian).
Other line of the development was parallel: the electromagnetic treatments in cure of cancer. The first famous name was D'Arsonval. His method had fantastic popularity at the turn of the 19th-20th centuries. Numerous devices were developed and applied widely, but the expected breakthrough result was missing. Entirely new line was started with Professors Rudolf Pekar, Bjorn Nordenstrom and Xin You Ling. They used the galvanic electric current to treat cancer. Their method had delivered remarkable results.
Based on the best knowledge of the heat- and electro-therapies, combine them with the most modern fractal physiology Oncotherm was established in 1988. This had opened a new paradigm in the field. Instead of the necrosis, the immuno-specific answers were forced supporting the natural protective and defending mechanisms of the human body. A large number of various devices were developed, and presently working worldwide.

Conclusion: Oncothermia is a direct follower of the ancient heat-therapies combined with the modern bioelectromagnetic and fractal physiologic knowledge. This new paradigm is feasible to reach new heights in the historic war against cancer.

P-16

History of oncothermia and their devices

Ms. Constanze Feisskohl[1], Ms. Janina Leckler[1], Mr. Balazs Acs[1], Dr. Oliver Szasz[1]
(1) Oncotherm Group, Germany

Objective: Oncothermia concept was found when the company was established, however the way of realization is a long process, having various steps forward and sometimes dead-ends. Our objective to show the history of oncothermia through its devices, giving a picture how stable development was achieved by the years, and conclude with a lesson how to go further.

Description: The university spin-off in 1988 was based on a biophysical idea. The medical value was added with the first device in use. This was the "Ducat" device, (started to work in 1989 at Clinic St. Georg, in Bad Aibling, Germany). This was a galvano-device, which was on exhibit in the first Congress of ECT knowledge in Beijing, China in 1991. The next step was a non-invasive device the very first EHY (1992) and parallel was further developed the galvano technique. (ECT) which reached the German GS-approval in 1994. The first EHY2000 was produced in 1994 and reached the CE sign (first ever in the category of hyperthermic oncology according to European medical device Directive) from TUV Munich, Germany in 1998. In the meantime the first intraluminar device (PCT) was developed on the same theoretical basis like the previous devices, and was in clinical probe in 1995, and the first whole body hyperthermia (WBH) was also parallel developed and tried in 1997. (Its moderate version (MSH) was launched in 1999.) In 2001 a venture capital was invested to the company, and Oncotherm GmbH was established in Troisdorf in 2002. The first device for this company was developed and launched in 2004 (EHY2000plus). The first multi-local device (EHY3000 series) was shown in 2008, and soon, less than a year later, the first very modern intraluminar devices (EHY1000 series) were placed on the market.

Parallel with the oncological hyperthermia Oncotherm had developed very unique devices for special use. For a special request a device for asthma treatment (REY) was developed in 2000, and for laboratory use (in vivo and in vitro applications) a high preciosity device series (LabEHY series) was launched in 2006. This was extended with a special temperature measuring device (EHYTS). A non-treating (non-curative only complementary) small device was developed in 2009 (ChemoBooster), which is for boosting any chemotherapy efficacy. Our new field the andrology, and the first probe device had been appeared in 2010 (AndroTherm).

Conclusion: The Oncotherm company and its method is based on stable scientific, medical and technical knowledge with specially developed details for the actual tasks in every devices. Oncothermia has been maturated for wide acceptance.

P-17

Hyperthermie – Was müssen Krankenkassen und Beihilfe zahlen?

Dr. Frank Breitkreutz[1]
(1) Breitkreutz und Kollegen, Kanzlei für Lebens- und Arzneimittelrecht, Berlin

Trotz beeindruckender Therapieerfolge ist die Hyperthermie noch keine allgemein anerkannte Behandlungsmethode. Hyperthermische Behandlungen werden deshalb bislang nur eingeschränkt erstattet.
In einem grundlegenden Urteil des Bundesverfassungsgerichtes aus dem Jahre 2007 wurde die therapeutische Bedeutung der Hyperthermie erstmals höchstrichterlich anerkannt. Seither ist es aussichtsreich, mit einer individuellen Begründung bei der Krankenkasse oder Beihilfestelle die Übernahme der Kosten zu beantragen.

P-18

Introduction of the international quality management system: OncoTherm Group

Ms. Anett Gallne-Valyi[1]
(1) Oncotherm Group, Germany

Introduction: The most important aspect for the Oncotherm Group is that our medical devices are prepared according to the concerning international standards and fulfill the inquiries of our customers.
These standards are the followings:

- ISO 9001:2008 Quality Management Systems. Requirements
- ISO 13485: 2003 Medical Devices. Quality Management Systems. Requirements for regulatory purposes
- 93/42/EEC MDD (Medical Device Directive)

Method: I would like to introduce the organizational structure and processes of Oncotherm Group and the requirements which should be adapted (see above).
The Oncotherm Group consists of two parts: the Oncotherm Kft, which is in Hungary and the Oncotherm GmbH, which is in Germany, but these two firms are one unity.
They are working together and they have got common quality management systems.
The research, design and development, and the manufacturing are in Hungary, but the marketing, sales, costumer service and service activities are in Germany, so these two parts create one well operative company.
The Company-Group is a marketing method (Oncothermia Method, OTM) which is in synergy with the devices (Oncothermia Device, OTD) and integratively presented on the market as Oncothermia System (OTS). This unification of the German medical and constructive knowledge with the general European manufacturing culture based on European Medical Device Directive and ISO standards. Oncotherm does not follow the practice of the large globalized German companies who are transferring the manufacturing outside Europe. We do everything in Europe and proud on that high level production culture which is represented by our 21 years old company.

Summary: Our devices are prepared by team-working of Hungarian and German highly qualified specialists.. This is the basic of our recent approval by TUV Product Service (TUV SUD, Munich) that our devices are: "Product of Germany, Made in EU".

P-19

Liver deep electro-hyperthermia (EHY) following trans-arterial Mitomycin–C chemotherapy as a maintenance treatment in patients with multiple liver colo-rectal metastases

Dr. Ranieri Girolamo[1], Dr. Vinciarelli Gianluca[1], Dr. Fazio Vito[1], Dr. Goffredo Veronica[1], Dr. Gadaleta Cosmo Damiano[1]
(1) Interventional Radiology Unit, with Integrated Section of Medical Oncology, National Cancer Institute Giovanni Paolo II, Bari, Italy

Background: New treatments are being investigated in patients with multiple or unresectable liver metastases, usually characterized by poor prognosis. Based on the predominant arterial blood supply of hepatic neoplasms, liver trans-arterial chemotherapy administers Mitomycin-C is characterized by a high liver extraction rate. Low-frequency 13.56 MHz deep hyperthermia (Oncotherm-EHY 2000) treatment of liver cancer is another possible treatment for liver metastases.
We evaluated the feasibility, the effectiveness and toxicity of capacitatively coupled low-frequency 13.56 MHz deep hyperthermia as a maintenance therapy following hepatic trans-arterial chemotherapy with Mitomycin-C in patients affected by liver metastases from colo-rectal cancer.

Patients and methods: From February 2009 to June 2010, we enrolled 15 patients with liver metastases from colo-rectal cancer. Median age was 66,5 years (range 48-78), male/female 9/6. ECOG PS was 1 or O. All patients enrolled were heavily pre-treated with systemic chemotherapy with final hepatic progression of disease and were not eligible for surgery. Patients enrolled had not extra-hepatic disease. Patients received several course of liver trans-arterial 35 mg of Mitomycin-C chemotherapy (mean 3 course; range 1 to 5). Treatment was performed under angiography guide and general anesthesia. Deep electro-

hyperthermia (DE-Y) (Oncotherm-EHY 2000) was achieved by arrangements of capacitative electrodes with a radiofrequency field of 13.56 Mhz (RF-DHT) at 80- 100 W equivalent to 41 °- 44° C for 60 minutes, 3 times/week for 3 weeks. Patients received several course of this schedules until progression disease. Median number of EHY cycles was 4 (range 2–9), total DE-Y applications were 527.

Results: DE-Y treatment following hepatic trans-arterial chemotherapy with Mitomycin-C of liver metastases is beneficial on clinical conditions of treated patients with an excellent compliance on out-patients. 3 patients had skin reaction after application of DE-Y. In 2 pts we observed cutaneous hyperemia on the area of treatment and mild burn on the skin; all symptoms disappeared after local steroid therapy, treatment was interrupted until resolution. According to modified RECIST criteria we observed 1 complete response, 11 partial response and 3 progression disease. With special references to DE-Y median maintenance time until disease progression it was 5 months range 3-14 months).

Conclusions: The feasibility, the good tolerability and the preliminary data of efficacy of this procedure make it an interesting option in the therapeutical strategy for heavily pre-treated patients with advanced metastatic liver disease. Further randomized studies comparing the combination between DE-Y treatment following liver trans-arterial Mitomycin-C chemotherapy versus trans-arterial Mitomycin-C alone in these heavily pre-treated patients with metastatic liver disease are required to further confirm our preliminary data.

P-20

Middle East Oncotherm Medical Centres for Cancer Treatment

Dr. Mohammad Al Masri[1]
(1) Audiology and Speech Pathology Department, Amman University, Amman, Jordan

Hyperthermia is a leading edge, proven treatment option for cancer patients which can be integrated approach. Oncothermia, was founded in Germany twenty years ago. Since that time, oncothermia has been accepted by many oncological practitioners and institutions as a viable and successful treatment option. Presently oncothermia is used in many countries around the world, and by more than 180 institutions. More than 100,000 oncothermia treatments are conducted yearly and have delivered remarkable survival elongation with good quality of life.

Tamer Corporation for Medical supplies is proudly to introduce Ocothermia treatment approach for patients in the Middle East and North Africa. The first clinic will be opened in Jordan before the end of this year and more than 4 clinics will be opened in 2011 in KSA, Lebanon, AUE, and Kuwait. Oncothermai treatment will become available for patients who are suffering from different types of cancer which will help more than 5000 patients per year. TCMS was also signed an agreement with Amman University, faculty of pharmacology and medical sciences to investigate the effectiveness of oncothermia treatment for cancerous patients.

P-21

Multicenter, open-label, phase-II-trial to evaluate the efficacy and safety of low-radiofrequency deep hyperthermia with capacitive coupled electrodes (LRF-DHT) in treating patients with recurrent high-grade malignant gliomas

Dr. Dr. E. Dieter Hager[1], Dr. Friedrich Migeod[1], Dr. Hüseyin Sahinbas[2], Porf. Dr. Dietrich Grönemeyer[2], Dr. E. Böcher[3]
(1) BioMed-Klinik, Bad Bergzabern, Germany
(2) Witten/Herdecke University, Germany
(3) Klinik Kloster Paradiese, Soest, Germany

LRF-DHT is feasible in treating patients with brain tumours without any severe side effects. LRF-DHT may induce complete impartial remissions. Overall median survival time (MST) could be increased by 13 and 7 months from onset of LRF-DHT after progression or recurrence in grade III and grade IV gliomas (astrocytoma WHO III, Glioblastoma muliforme WHO IV). Quality of life and overall survival could be improved by this method compared to historical control groups. Further trials are urgently warranted.

P-22

Oncological and non-oncological applications of electromagnetic hyperthermia (Oncothermia®) in the veterinary clinics – 2 years of experience

Dr. Lajos Balogh[4], Dr. Gabor Andocs[3], Dr. Julianna Thuroczy[3], Dr. Andras Polyak[4], Dr. Oliver Szasz[1], Prof. Dr. Andras Szasz[1,2]
(1) Department of Biotechnics, Faculty of Engineering, St. Istvan University, Budapest, Hungary,
(2) Oncotherm Group, Germany
(3) Department of Pharmacology and Toxicology, Faculty of Veterinary Science, St Istvan University, Budapest, Hungary,
(4) National Research Institute for Radiobiology and Radiohygiene, Budapest, Hungary,

Objective: Advantageous thermal and induced non-thermal effects of electromagnetic hypertermia (EHT, Oncothermia®) in human medicine is in use for decades. Surprisingly there are much less references about the veterinary utilities.

Material and Methods: We applied EHT with capacitive coupled modulated 13.56MHz radiofrequency method (oncothermia OT). OT was provided for different canine and feline oncological patients (altogether more than 64 cases) as a single treatment (6/64), and in a combination with fractionated Cobalt irradiation (51/64) or with medical treatments (7/64). Dog patients suffering in other chronic diseases (4 osteoarthroses, 2 heart insufficiencies, 2 epileptic, 2 non-healing skin abscesses) were also co-treated with local (or regional) OT so that the original, non-eligible medical treatments were not changed.

Results: Single OT in oncological diseases resulted significant tumor size decrease 2 out of 6 cases, 3 stable disease and 1 progression of disease. Cobalt irradiation followed by OT resulted 5/51 tumor-free status, 42/51 partial remissions, 3/18 stable disease, and progression of disese in 1 case. Chemotherapy boostered with OT resulted 2/7, 3/18 stable disease, and 2/7 progression of disese in late stage, metastatic cases. Side effects eg.: erythema (2 cases), necroses (2 cases) occurred at the learning phase of technique, later on we could prevent this side effects with the constant superficial and deep temperature control in or patients. OT proved to be useful in all the non-oncological diseases and no side effects, contraindications were remarked.

Conclusion: We concluded that local and regional OT could be a useful tool as a single antitumoral modality but even more clinical utilities could be reached in a combination with radiotherapy and with chemotherapy. OT could be advantageous in the treatment of a variety other chronic diseases too. Further pro- and retrospective clinical studies needed to implement this novel technique into veterinary medicine.

P-23

Oncothermia combination with traditional Chinese medicine: network approach

Prof. Dr. Andras Szasz[1,4] ✉, Prof. Dr. Gabriella Hegyi[2], Dr. Gabor Andocs[3], Dr. Oliver Szasz[4]
(1) Department of Biotechnics, Faculty of Engineering, St. Istvan University, Budapest, Hungary,
(2) Department of Complementary Medicine, Institute of Forensic Medicine, Medical School, University of Pecs, Pecs, Hungary;
(3) Department of Pharmacology and Toxicology, Faculty of Veterinary Science, St Istvan University, Budapest, Hungary;
(4) OncoTherm Group, Germany

Background: Acupuncture and their connective pathways the meridians are ancient Chinese knowledge but it is not understood yet in details [1]. Request of the stable homeostasis of the complex organisms is demanding interdisciplinary approach and new paradigm for the topic. The detecting and reconstructing the deviation from the normal balance of the homeostasis is the basic principle of TCM. The Chinese herbs, the physical (mechanical or electromagnetic acupuncture, acupressure) and mixed forms of heating and diffusion-therapies (moxa therapies) approaches are pointing these problems, and solving it with ancient methods. Oncothermia method (OTM) uses also the deviations from the normal homeostasis for selecting the tumor cells and on this basis ignite natural processes to eliminate them from the system, reestablishing the communication harmony between the cells [2]. This technique [3] is well proven from the laboratory level to the clinical applications [4]. Our aim is to synergize the TCM with OTM on the common basis of equilibrium demand; and use the recognition of the deviations from the complex harmony of the organism or its part for selection to act properly.

Method: An extended network approach was presented in the topic [5], and we would like to continue our research on this basis. The in silico studies will have their roots from the network analysis together with the

modern fluctuation theory for complex living organisms (fractal-physiology) was developed in the last decades to study this complexity: like self-organization ([6], [7], [8], [9]), fractal physiology ([10], [11], [12], [13]), and the bioscaling ([14], [15], [16]). Oncothermia widely using these new scientific results [17], [18]; as well as the resonance phenomenon is studied and used in the light of a new theory [19], and special vector-potential theory [20], [21], [22] helps to complete the method. The problems of the thermal limit in the deep-seated tissues is theoretically [23] and experimentally [24] solved, so it has no any barrier for the wide investigations in synergy experiments. TCM involves electro-acupuncture and laser acupuncture, which are similar in their electromagnetic (conductive) approach to oncothermia effects. The in vivo studies will be performed using a BalbC/nu/nu mice xenografts; using specialized experimental setup (EHY110, Oncotherm, Germany). The effects will be studied histomorphologically (HM) and immunhistochemically (IHCH) by various antibodies with state-of-art high tech digital microscopy system (MiraxWiev, 3D Histech).

Conclusion: Recognition of the distortions in the healthy tissue have some common principles and possibilities in TCM and OTM. The synergy of the ancient knowledge and the high-tech state-of-art of the medical knowledge could be established with this research.

References

✉ Szasz.Andras@gek.szie.hu

[1] Ernst E, Pittler MH, Wider B, Boddy K. (2007). "Acupuncture: its evidence-base is changing". Am J Chin Med. 35 (1): 21–5
[2] Szasz A. Szasz N. Szasz O. (2010) Oncothermia. Principles and Practices, Springer Verlag, (http://www.springer.com/biomed/cancer/book/978-90-481-9497-1?changeHeader) Heidelberg, Dordrecht
[3] Szasz A (2006) Physical background and technical realization of hyperthermia, in: Locoregional Radiofrequency-Perfusional- and Wholebody- Hyperthermia in Cancer Treatment: New clinical aspects, (Eds: Baronzio GF, Hager ED), Springer Science Eurekah.com, Ch.3. pp. 27-59
[4] Andocs G, Szasz O, Szasz A. (2009); Oncothermia treatment of cancer: from the laboratory to clinic, Electromagn Biol Med. 28(2):148-65
[5] Szasz A. (2008) Electromagnetic considerations of meridian network (A network approach), International Council of Medical Acupuncture and Related Techniques, (ICMART), XIII World Congress, Oct.10-12, Budapest
[6] Haken H (1987) Self-Organization and Information. Phys. Script. 35(3), 247-254
[7] Sornette D (2000) Chaos, Fractals, Self-Organization and Disorder: Concepts and Tools. Springer Verlag, Berlin-Los Angeles
[8] Walleczek J (ed) (2000) Self-organized biological dynamics & nonlinear control. Cambridge Univ. Press, Cambridge
[9] Mar'Yan MI. Szasz A. (2000) Self-organizing processes in non-crystalline materials: from lifeless to living objects, Oncotherm GmbH, Neubeuern, Germany
[10] Deering W, West BJ (1992) Fractal physiology. IEEE Engineering in Medicine and Biology 11(2):40-46
[11] West BJ (1990) Fractal Physiology and Chaos in Medicine. World Scientific, Singapore, London
[12] Bassingthwaighte, J.B., Leibovitch, L.S., West, B.J. (1994): Fractal Physiology, Oxford Univ. Press, New York, Oxford
[13] Musha, T., Sawada, Y. (eds.) (1994): Physics of the living state. IOS Press, Amsterdam
[14] Brown JH, West GB (eds) (2000) Scaling in Biology. Oxford University Press, Oxford
[15] Brown JH, West GB, Enquis BJ (2005) Yes, West, Brown and Enquist's model of allometric scaling is both mathematically correct and biologically relevant. Functional Ecology 19(4):735 –738
[16] West GB, Brown JH (2005) The origin of allometric scaling laws in biology from genomes to ecosystems: towards a quantitative unifying theory of biological structure and organization. Journal of Experimental Biology 208:1575-1592
[17] Szendrő P, Vincze G, Szász A (2001) Pink-noise behaviour of biosystems. Eur.Biophysics J. 30:227-231
[18] Vincze G, Szasz A, Liboff A (2008) New theoretical treatment of inon resonance phenomena. Bioelectromagnetics, 29:380-386
[19] P. Szendrő, G. Vincze, A. Szász (2001) Bio-response to White Noise Excitation. Electro- and Magnetobiology 20:215-229
[20] Szász A, Vincze Gy, Andocs G, Szasz O (2009) Do Field-Free Electromagnetic Potentials Play a Role in Biology? Electromagnetic Biology and Medicine, 28:135-147
[21] Szász A, Vincze Gy, Andocs G, Szasz O (2009) Effect of Curl-Free Potentials on Water. Electromagnetic Biology and Medicine, 28:166-181
[22] Hegyi G, Vincze G, Szasz A (2007) Axial-vector interaction with bio-systems. Electromagnetic Biology and Medicine, 26:107-118
[23] Vincze Gy, Szász A, Szasz N (2005) On the thermal noise limit of cellular membranes. Bioelectromagnetics, 26:28-35
[24] Andocs G, Renner H, Balogh L, Fonyad L, Jakab C, Szasz A. (2009) Strong synergy of heat and modulated electromagnetic field in tumor cell killing. Strahlenther. Onkol. Feb; 185(2):120-6.

P-24

Oncothermia combination with Traditional Chinese Medicine: Proposal on Chinese Herbal Medicine approach

Prof. Dr. Gabriella Hegyi[1], Prof. Dr. Li Ji'an[2] , Prof. Dr. Han Bingsheng[3], Dr. Gabor Andocs[4], Dr. Oliver Szasz[5], Prof. Dr. Andras Szasz[6,5] ✉
(1) Department of Complementary Medicine, Medical School, University of Pecs, Pecs, Hungary;
(2) North China Coal Medical University, Tangshan City, China;
(3) Shenzhen TCM Hospital, Shenzhen, China;
(4) Department of Pharmacology and Toxicology, Faculty of Veterinary Science, St Istvan University, Budapest, Hungary;
(5) OncoTherm Group, Germany;
(6) Department of Biotechnics, Faculty of Engineering, St. Istvan University, Budapest, Hungary

Background: Hyperthermia is an ancient oncology method. It is the very first treatment modality for this type of disease, having 5000 year history [1], based on the Sun as the overall curative force in ancient Egypt. Later Hippocratic paradigm described it using physiological process (acidosis) to eliminate the malignant tissue. This natural approach is in well correlation with the far-away developed medical concept in the same ancient time: the Traditional Chinese Medicine (TCM) [2]. This medical philosophy was also based on natural harmony inside and outside the human organism. In progress of historical time TCM had been more sophisticated and developed, but the hyperthermia could not keep abreast with the development of the medicine, and was hindered by other western medical methods (WMM). However in late 80th of last century a new paradigm of hyperthermia was developed, the oncothermia method (OTM) [3]. OTM applies the ancient hyperthermia on different way, replacing the static thermal driving force to dynamical equilibrium concept, promoting the natural processes in curative direction [4]. It is a matter-of-course to make synergy between the two approaches, uniting the best line of TCM and OTM. Our present

article underlines the main connections with the herbal medicine of TCM (Chinese Herbal Medicine CHM) and oncothermia.

Method: There are various CHM substances acing palliative or curative on tumorous diseases. For example of pain reduction the "Senecio palmatus". For curative treatments special moxibustion techniques with various complex mixture of herbs could be applied [5]. Synergetic effects of the OTM and CHM is expected due to the well targeted tumor-tissue by OTM in combination with the effective CHM like Tongyou-sum plant. The effect of synergy will be investigated by in silico, in vitro and in vivo experiments, using special OTM device for laboratory use (EHY110, Oncotherm). The latest histomorphological and immunohistochemical methods will be used for evaluation,; mainly concentrating on p53 tumor-suppressor protein and the apoptotic pathways, including beta-catenin. Protocols of clinical studies will be worked out on the basis of the experimental results.

Conclusion: Potential of the synergy of high-tech OTM and TCM is extremely huge. We are ready to work out the European alternative of the "East meets West in cancer care collaboration" [6] on the basis of the widely applied TCM evidences [7].

References:

✉ Szasz.Andras@gek.szie.hu

[1] Seegenschmiedt MH, Vernon CC (1995) A Historical Perspective on Hyperthermia in Oncology. In: Seegenschmiedt MH, Fessenden P, Vernon CC (eds) (1995) Thermoradiotherapy and thermochemotherapy, Vol 1. Springer Verlag, Berlin, Heidelberg.
[2] Unschuld, Paul Ulrich (1985). Medicine in China: A History of Ideas. University of California Press
[3] Andocs G, Szasz O, Szasz A. (2009) Oncothermia treatment of cancer: from the laboratory to clinic, Electromagn Biol Med. 28(2):148-65.
[4] Szasz A. Szasz N. Szasz O. (2010) Oncothermia. Principles and Practices, Springer Verlag, (http://www.springer.com/biomed/cancer/book/978-90-481-9497-1?changeHeader) Heidelberg, Dordrecht
[5] Longo F. (2007) "Traditional Chinese Medicine in Oncology", in "Proceedings of the 56th S.C.I.V.A.C. National Congress"; June 1/3, 2007 (pp. 230 - 232) Rimini.
[6] McMaster university Explores Evidence-based Chinese medicine, http://www.integrativeonc.org/mcmaster-university-explores-evidence-based-chinese-medicine
[7] Jin-Ling Tang, Bao-Yan Liu, Kan-Wen Ma (2008) Traditional Chinese Medicine. The Lancet, 373:1938-1940

P-25

Oncothemia Concensus

Prof. Dr. Andras Szasz[1,2]
(1) Department of Biotechnics, Faculty of Engineering, St. Istvan University, Budapest, Hungary
(2) Oncotherm Group, Germany

Background: Oncothermia became a widely used and popular method in over 15 countries of the world. It is not a "gold standard" yet, but it is on the way to reach its stable and important position as a "fourth column" among the main oncotherapy modalities. It has wide-range applicability for every solid tumor in all possible localization, irrespective its primary or metastatic form. It could be applied together with all the known oncotherapy methods, and it is applicable in higher lines of the therapy protocols, even in the refractory and multirelapsed cases as well. Its applicability contains the curative and palliative approaches as well as it is well personalized to provide the optimal available treatment for the given case. Our objective is to propose a convention for various treatment conditions, to make a frame of the protocols which has to be filled up by the actual and well personalized details.

Methods: A comprehensive book [1], and numerous scientific and technical papers were published on oncothermia, [2], so the technical basis is stable. Oncothermia has collected during its 21 year existence a massive expertise and large data-collection, which are the basic of any convention for treatment protocols. The main factors to fix a personalized protocol are (1) kind of the complementary treatment, [decisional basic is the protocol of the "gold standard" therapy], (2) kind of the tumor entity, (3) kind of the personal status (4) physiological factors of the patient. The most frequently applied bimodal treatments are the oncothermia combined with chemotherapy or radiotherapy. While in trimodality it is combined with the radio-chemo-therapy.

Results: Protocols for combination with radiotherapy (RT) has to consider the blood perfusion of the tumor. When the tumor has adequate blood-perfusion than due to its high oxygen content it is sensitive for RT. In this case RT has to be applied first, immediately following by oncothermia with the highest tolerable power. This combination process is repeated every second day, (while the fractionated radiation could be on its own protocol every day). Oncothermia follows RT immediately (in 30 min range). In case of low blood-perfusion oncothermia has double role: increases the blood-flow to sensitize the RT and supports the cell-killing mechanisms. Fractionated RT follows oncothermia in this case in everyday application. In case of chemotherapy oncothermia has to be started when the highest chemo-perfusion is expected in the tumor-

lesion to support the chemo-infiltration and the chemo-metabolism in the tumor. All the protocols have to be fitted to the request of the tumor-localization, and its duration has to be actualized by the stage and the progress of the cancer.

Conclusions: Oncothermia is a versatile treatment for various solid tumors, its applicability is not limited to specialties, its universal applications could be easily fitted to all the "gold-standards" as well as it could be a good complementary support for other oncotherapies too.

References:

[1] Szasz A, Szasz N, Szasz O (2010) Oncothermia – Principles and Practices, Springer Verlag, Heidelberg http://www.amazon.com/Oncothermia-Principles-Practices-Andras-Szasz/dp/9048194970

[2] Szasz A (2006) Physical background and technical realization of hyperthermia. In: Baronzio GF, Hager ED (eds) Locoregional Radiofrequency-Perfusional- and Wholebody- Hyperthermia in Cancer Treatment: New clinical aspects, Ch 3, Springer Science Eurekah.com, pp. 27-59. http://www.springer.com/west/home/biomed/cancer?SGWID=4-125-22-150459762-0&detailsPage=ppmmedia%7CotherBooks&seqNo=0&CIPageCounter=CI_MORE_BOOKS_BY_AUTHOR0

P-26

Oncothermia in Gynecologic Oncology (Experience of the EWHA Womans University Hospital, Seoul)

Prof. Dr. Woong Ju[1], Prof. Dr. Seung Cheol Kim[1]

(1) Dept of Ob/Gyn, College of Medicine Ewha Womans University Mok-Dong Hospita, Seoul Korea (South)

Introduction: Our hospital intensively uses oncothermia for gynecological malignancies. The time for the application of the new technology is not enough to present statistically evaluable number of patients in cohorts, so our objective is reporting a few interesting cases from our practice.

Method: We apply for the treatment the EHY-2000 oncothermia device with variable electrode sizes. A treatment cycle contains 10 sessions in average, made 2-3 times a week, having at least a day between the treatments. Every session was performed in duration of 60 min. Patients of advanced uterine, cervix and ovary tumors are treated. Oncothermia was applied complementary to various chemotherapies.
The case which we show is advanced patient (32 y), diagnosed in April of this year. Past history was three years ago a cesarean section, with medical history: DM/HTN/Tb/Hepatitis (-/-/-/-). No family history was registered. The uterine cervix punch biopsy was positive: adenocarcinoma, as well as the cytology of the ascetic fluid was also positive for adenocarcinoma. The images (CT, MRI, PET) show large ovarian mass, suspected double primary cancer (uterine cervix and ovary). The peritoneum had serious ascites, (probable carcinomatosis peritonei with unilateral Krukenberg disease). From April to June was treated with oncothermia and three times with neoadjuvant chemotherapy (Genexol+ Carboplatin). Patient was operated in August.

Results: Diagnosis in June shows curative improvement:

- Decreased extent of mass in uterine cervix and in right ovary.
- Improvement of hepatic metastasis in both lobes of the liver with residual lesion.
- Improvement of peritoneal carcinomatosis with residual lesion.
- PET shows impressive improvement of cure.

The operative results in August showed the pelvic cavity with a vengeance 4*3*3 cm^3 a nodular mass with a thick wall of the right ovary was observed in peritoneum, omentum, rectal serosa findings necrotic nodular mass. Abnormalities are not visible on the left ovary. The CA-125 and CA-19-9 tumor-markers had been normalized.

Conclusion: Oncothermia treatment is looks feasible to treat advanced gynecologic malignancies. For evidences perspective, randomized studies, and measuring the overall survival as end-point is desired.

P-27

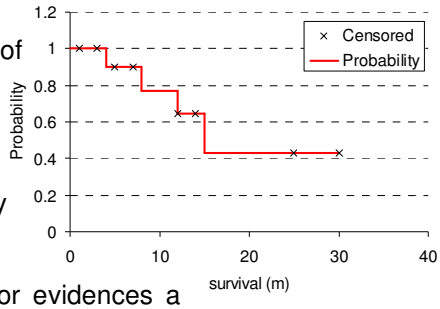
Oncothermia treatment for small-cell-lung carcinoma

Prof. Dr. Doo Yun Lee[1], Dr. Hyo Chai Paik[1], Dr. Ji Won Kim[1], Dr. Se Eun Jeon[1], Dr. Dong Uk Kim[1]
(1) Dept of Thoracic & Cardiovascular Surgery, Gangnam Severance Hospital,Yonsei University, College of Medicine, Seoul, Korea

Introduction: Small cell lung carcinomas (SCLC) were studied combined with various chemotherapies. This is a running study, we present only interim results. Our objective was to obtain reliable data of SCLC treatment with oncothermia.

Method: The treatments were provided with device EHY-2000, 60 min in all sessions, using the electrode of 30 cm diameter. Data of the patients (n=14) are registered and evaluated retrospectively. The average age of patients is 64.4 y (50-77, St.Err.: 1.94), having 12/2 male/female ratio. Ten patients had only one oncotherapy cycle, while four got two cycles. Seven patients had distant metastases two of them multiple, involving their brain. Some cases are discussed in details for further considerations.

Results: The local clinical response is impressive, shows shrinking of tumor in ten cases while tumor growth was observed in two and no change in two cases as well. The interim results for survival shows median survival 7.5 m, (1-30) with mean survival of 10 m (St.Err.:2.35). The Kaplan-Meier plot is shown. Case reports well demonstrate the efficacy of the oncothermia as complementary treatment for SCLC.



Conclusion: Oncothermia treatment has feasibility to treat SCLC. For evidences a perspective, randomized study, and the overall survival end-point is desired. The further work is in progress.

P-28

Oncothermia treatment of lung carcinoma

Prof. Dr. Seok Jin Haam[1]
(1) Dept of Thoracic & Cardiovascular Surgery Gangnam Severance Hospital,Yonsei University, College of Medicine, Seoul, Korea, Hamsj@yumc.yonsei.ac.kr

Introduction: Advanced lung carcinomas were studied combined with various chemotherapies. Our objective was to obtain reliable data of lung-cancer treatment with oncothermia.

Method: The study was started in August 2008, and was sequentially evaluated in December 2009 (n=66) and September 2010 (n=118), retrospectively. In first period 54.5% in the second one 64.4% was in advanced stages, and additionally 21.2% and 33 % had recurrence or metastases, respectively. The other stages were only 24.2% and 9% in the investigation sequences respectively. We studied only the cases with eligible number of sessions, excluding those who had not such number (less than 12 sessions) of the treatments. Consequently the numbers of included patients are n_i=38 and n_i=79, respectively. The treatments were provided with device EHY-2000, 60 min in all sessions, using the electrode of 30 cm diameter.

Results: We had measured the local clinical response only, the survival analysis could be done later. The local data shows improvement (CR+PR) 47.4% and 46.8%, NC 31.6% & 35.4%; PD 15.8% & 15.2 %; n.d. 5.2% & 2.5% in first and second sequences of the study, respectively. Regarding the advanced and relapsed cases, the overall local response-rate (CR+PR+NC) is 79% and 82.2%.

Conclusion: Oncothermia treatment has feasibility to treat advanced and relapsed cases of lung-cancer. For evidences a perspective, randomized study, and the overall survival end-point is desired. The further work is in progress.

Personalization of oncothermia

Prof. Dr. Andras Szasz[1], Dr. Gyula Vincze[2], Dr. Oliver Szasz[3]
(1) Department of Biotechnics, St. Istvan University, Budapest, Hungary
(2) St. Istvan University, Budapest, Hungary
(3) Oncotherm Group, Germany

Objective: Dosing of oncothermia is based on the energy delivery to the targeted tumor [1]. This energy is well focused on cellular level [2], and makes the dose of energy optimal for cell destruction [3]. The personal feedback of the patient is the important control of the process; the patient became the primary sensor of the treatment protocol. This gives good safety records and low toxicity and side effects for the patients, however the objective dose is not equal for them. We know it well, that the dose is an important factor, the too low is ineffective, the too high is toxic. Our objective is investigating the personalized feedback in point of view of the objectivity of the dose.

Discussion: The objectivity of the treatment is definitely depends on the radiofrequency current and its gained voltage on the given impedance on the tumor. This current is well regulated by the skin-conductance and by the connected physiological changes. The inconvenient feeling of RF-heating defines a pain-limit, which depends on many objective and individual factors. A good approach is regarding the nerve-cell sensitivity objective (the cellular processes are well unified), and regarding the personal differences as influence of physiological factors. The main factor for heat-sensitivity is the blood-perfusion and blood-flow in the subcutaneous layers where the heat-sensing nerves are located. The high blood-flow is an effective heat-exchanger, cools the given volume, and the nerves tolerate higher energy-flow through the layer. The high blood cooling is not only the facility to have higher energy-flow, but also getting more current through the volume. The higher current density excites the nerve-sensing, and the feeling again an overheating, requests down-regulation. In the case of low blood-perfusion the current is small, so the nerves can tolerate more intensities than anyway. The crucial point is the surface heat-regulation, which has to be carefully done by the electrode systems. When the surface temperature kept constant, the nerves mainly regulate the current density, which is the clue of the objective regulation. A detailed mathematical model is worked out for this regulation mechanism, and applied in oncothermia treatment.
Furthermore the step-up heating is important not only avoid the inconveniences, but regulate the adaptation mechanisms. Healthy cells can be adapted to the electric/heat-stress, while this adaptation is much less in the malignant lesions. The step-up heating supports the physiological selection and makes the contrast of the reaction definite.
Other factor is connected to the psychological interaction with the treatment process also. In any protocols, when the temperature is described as a dose, when the required temperature can not be achieved than of course it is forced by the power, so the incident energy is not limited in this case. Oppositely, if the patients can not tolerate the prescribed power (and required temperature), than a lower one is applied in their cases. The pain in the body depth is independent from the temperature sensing nerves, the pain there has other mechanisms, which are not part of the prevention of damage (like the temperature sensing), but sensing the actual damage itself. Consequently blocking the surface heat sensors is a high risk factor, which is never made in oncothermia therapies.

Conclusion: Oncothermia with its surface stabilized sensing (patented action) uses the personal sensing in objectivity of the actual energy-dose. The synergy of the technical and psychological regulations makes objective dose control for oncothermia processes, keeping the energy dose in the curative range.

References:

[1] Szasz A, Szasz O, Szasz N (2001) Electrohyperthermia A new paradigm in cancer therapy. Wissenschaft & Forschung, Deutsche Zeitschrift für Onkologie 33:91-99. http://www.thieme-connect.com/ejournals/abstract/dzo/doi/10.1055/s-2001-19447
[2] Szasz A, Vincze Gy, Szasz O, Szasz N (2003) An energy analysis of extracellular hyperthermia. Magneto- and electro-biology 22:103-115. http://www.informaworld.com/smpp/content~content=a713628984~db=all
[3] Szasz A, Vincze Gy (2007) Dose concept of oncological hyperthermia: heat-equation considering the cell destruction. Journal of Cancer Research and Therapeutics 2:171-181. http://www.cancerjournal.net/article.asp?issn=0973-1482;year=2006;volume=2;issue=4;spage=171;epage=181;aulast=Szasz

Research support by LabView-based data-acquisition systems

Mr. Gabor Skrihar[1]
(1) Oncotherm Group, Germany

The aim of all scientific experiment and measurement is to collect information about the measured object or incident. On the field of research it's especially important to acquire all of measurable information during the experiments, because often we don't know exactly, which of the parameters will give us new and useful information. But in a lot of cases the data acquisition could be quite difficult, because:

- If during the measurement more instruments are used, the simultaneous and continuous observation all of them is not possible.
- A lot of instruments don't provide built-in data acquisition and storing
- Although some instruments have this function, it could be difficult to synchronize the data acquired by various instruments.

The solution of this problems is such a data collection system, that in real-time collects and synchronizes all of the information, that the used instruments provide during the measurement and than stores them into a common database, allowing the common processing of them. By this way the efficiency of the scientific research could be greatly increased. For us at Oncotherm is a priority to make more efficient our R&D activity, so we started to develop integrated data-acquisition systems to support our research projects.
The main element of this system is the LabView program suite, which is developed especially for data-acquisition and instrument control and is provided by National Instruments. The main task of LabView is to control the NI's own DA units, but the products of the most important instrument manufactures are controllable by the suite too. During our projects we use both NI instruments and the instruments of other manufacturers (Tektronix, Rhode & Schwartz) too.

One of our main ambitions is the monitoring of the LabEHY oncothermia device, which is especially designed for medical experiments. The device sends some information about its state by RS232 serial port and the inner signal lines of the device are monitored by NI data-acquisition devices.
A typical data acquisition system consists of the following instruments and provides us the following information:

- LabEHY:
  - By serial port: time after the start of the treatment, output power, tuner positions and the S11 scattering parameter, which represents the efficiency of the tuner built into the LabEHY
  - By direct monitoring of signal lines: voltages proportional with the forwarded and reflected power
- Luxtron thermometer: this four-channel device gives us information about the temperature changes of different parts of the tumor during the treatment.
- Oscilloscope: by a two-channel oscilloscope we measure the voltage on the experimental animal and the current flowing through it. From this two data we can calculate the power emitted by the tumor.

By using the data provided by the reviewed instrumentation we can get a clear picture about the energetical efficiency and heat effects of the treatment, which are important questions on the field of oncothremia.

Of course, the data-collecting systems always follow the demands of the current research projects, capitalizing the flexibility of the LabView-based DA systems. On the grounds of our experiences until now we have more ways of improvement on this field. The most important of them are:

- LabView-LabEHY: the direct control of the LabEHY by a LabView-based surface, by an NI device built into the instrument. This solution will give us the opportunity to monitor all of the inner activities of the instrument.
- Production support: automated testing of our products by LabView-based instrumentations.

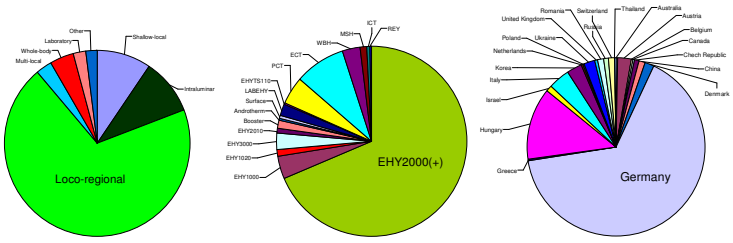
By realizing these conceptions we can improve both the effectivity and the speed of our R&D projects and improve the quality of our products, so we are committed towards these ways.

Success of OncoTherm

Dr. Oliver Szasz[1]
(1) Oncotherm Group, Germany (Dr.Szasz@oncotherm.de)

Background: Oncotherm has started its life in the Universities. The ideas were formulated as a part of the surface science in Glasgow (Scottish Surface Centre, Strathclyde University), followed by a spin-off form the Eotvos University Budapest in 1988. The first contacts with Germany were established almost immediately. Dr. Douwes (St.Georg Klinik, Bad Aibling), asked the human medical applications of the till that time only theoretically formulated ideas. The actual requests of the clinical use formulated by Dr. Douwes were successfully performed, starting with galvano-therapies, and continuing to the basic of the presently well known oncothermia method. The company is certified in all aspects by the rigorous German TUV services having the CE and the ISO approvals for the products and production processes, respectively.

Results: Oncothermia became a known therapy worldwide. Its results are beneficial and popular in every places where it is applied. Presently oncothermia is present in 21 countries, and our production was 262 devices in the time of existence. From this we have active contacts with 200 devices in 17 countries, During our existence we had developed different devices in seven categories: shallow local (ECT, ICT, Surface), intraluminar (PCT, EHY1000, EHY1020), loco-regional (EHY2000, EHY2000+, EHY2010, REY), multi-local (EHY3000 series), whole body (WBH, MSH), laboratory devices (LabEHY, EHYS110) and other devices (Booster and Androtherm). having … devices in work and developed transurethral (EHY1000 series), local and regional (EHY2000 series) and multi-local (EHY3000 series) treatments and their devices.



(a) *(b)* *(c)*

Oncothermia production during its entire history: distribution of the developed devices by their categories (a), distribution of the devices sold on the market (b), and distribution of the countries where the devices were sold (c).

Presently our Oncotherm Company works now on entire brand new concepts (OTD devices) and developing huge number of new scientific projects and ideas. The actually working devices perform more than 100.000 treatments yearly in the market, and no any safety problem was arisen till now. Our philosophy is based on 3E+3S concept:

3E:
1. efficacy by large energy-absorption with electric field assistance,
2. efficacy by cellular self-selective focus realized by modulated RF-current,
3. efficacy by distinct improvement of the survival rate and by unambiguous increase of the quality of life

3S:
1. safety for the patient with optimally personalized energy-absorption, based on the enduring control of the RF current through the patient.
2. safety for the treating medical personnel with high electromagnetic standards, making possible to use oncothermia even in dwelling-houses,
3. safety for your quiet daily work by the solid scientific, biomedical and clinical proofs.

Conclusions: Oncothermia opened new dimensions in hyperthermic oncology. We are proud, that the modern technical solutions and the “Med-in-Germany” medical practice had such a synergy which has changed the 2000 years old paradigm and made the hyperthermia ready to be accepted widely by the medical communities.

P-32

The customer is king: The marketing concept of the Oncotherm Group

Ms. Constanze Feisskohl[1], Ms. Janina Leckler[1]
(1) Oncotherm Group, Germany

Introduction: Advertising, distribution and selling are words often identified with marketing. But this is not all. Of course they are part of every marketing concept. Oncotherm however sees something else in the centre of the work: the customer. Oncotherm sells for them not devices only, but a complete method and permanent help to use it.

Method: Marketing of Oncotherm is the process of identifying, anticipating and satisfying the customers' needs. While in the past our marketing was seen as a creative progress with its focus on selling and advertising, it is today judged as an academic study. Marketing in our philosophy is not only a science of itself, but also benefits and lives from other fields like psychology, sociology, mathematics, economics and neuroscience. It is a combination of objective analyzing and creative works and cultural studies, it is completely interdisciplinary like the oncothermia method itself.
We would like to introduce the marketing strategy and the aims of the Oncotherm Group. The focus of our work is informing doctors from all over the world about the method and possibilities of Oncothermia. We want to help the suffering patients. Only when the doctors see and accept the complementary treatment option of Oncothermia, the patient can be helped by us. Through different actions we are trying to offer the best possible service and support for our customers, mainly by keeping them informed on scientific results and backgrounds.
Our different tools, publications, website, newsletters, events, brochures, patient information and so on present our successful synergy of professional technique and the science and shall be introduced here.

Conclusion: Oncotherm works with a professional marketing concept based on the needs of our customers. Our aim is to make the method more prominent to help patients and to support the doctors using our devices. Oncotherm knows very well: we are united community with our customers, our devices can not fulfill they intended prospective without our smart and active customers.

P-33

The first experience of the local electro-hyperthermia (oncothermia) application in Russia

Prof. Dr. V.A. Solodkii[1], Prof. Dr. GA. Panshin[1], Dr. MA. Ilyin[1]
(1) Russian Scientific Centre of Roentgenology and Radiology, Moscow, Russia

Russian Scientific Centre of Roetgenology and Radiology carries out hyperthermia of oncologic patients, predominantly with gynecologic cancer, for a relatively long time. In particular, we used combination of radiotherapy with modern laser-induced hyperthermia.
At the same time, about a half-year ago we started clinical research of application of local electro-hyperthermia (oncothermia) in combination with radiotherapy and chemotherapy using still the only in Russia oncothermia unit "EHY2000" (Oncotherm, Hungary). During this period, we performed a special treatment of 18 patients with various malignant neoplasms, mainly with gastrointestinal tumors and disseminated breast cancer, with this device.
Hyperthermia combined with radiation therapy was applied for 10 patients, combined with chemotherapy for 2 patients, and hyperthermia alone for 4 patients.
Despite of it's too early to make final conclusions, the first results obtained clearly indicate that combination of oncothermia with radiation and/or chemotherapy causes a very noticeable improvement of immediate and near outcomes of the treatment, and that application of oncothermia alone favours obvious improvement of life quality of the patients, mainly due to relief of pain syndrome.
With all this going on, any negative impact on the condition of the patients treated with this unit was not observed.
In general, these preliminary results have enabled us to extend the area of application of local electro-hyperthermia at our Center for now, and to turn to the targeted research on its use, particularly as adjuvant treatment of malignant tumors of the lungs and brain, as well as pre-surgery neoadjuvant therapy of locally advanced breast cancer.

Index

A

Acs B. 35, 39, 45
Al-Masri M. 47
Andocs G. 24, 30, 32, 34, 35, 39, 41, 48, 49

B

Balogh L. 30, 32, 34, 48
Baronzio F. 28
Bingsheng H. 49
Böcher E. 47
Bogdahn U. 27
Breitkreutzl F. 45
Brenner J. 23
Brockmann WP. 17
Buettner C. 24, 41

C

Choi KS. 32
Csejtei A. 27, 43

D

Damiano GC. 46
Dentico P. 15, 25
Douwes F. 15, 16
Dudel C. 27

E

Eberhardt B. 24
Eckert EW. 40

F

Feisskohl C. 45, 56
Fiorentini G. 15, 25, 28
Fonyad L. 30

G

Galfi P. 30
Galne-Valyi A. 46
Gianluca V. 46
Giannessi P. 15, 25
Girolamo R. 46
Gnadig B. 35, 39
Grönemeyer D. 47
Guais A. 28

H

Haam SJ. 52
Hager ED. 47
Hau P. 27
Hegyi G. 48, 49
Herzog A. 19
Hirschmann B. 27

I

Ilyin MA. 56
Issels R. 23

J

Jakab Cs. 32
Jeon SE. 52
Ji'an L. 49
Ju W. 44, 51
Jückstock J. 24

K

Kim DU. 52
Kim JW. 52
Kim SC. 44, 51
Kirchner H. 57
Kovaliev AA. 22
Krenacs T. 32, 37

L

Lang I. 39
Leckler J. 45, 56
Lee DY. 52
Lee JS. 32
Li JH. 29
Licitra S. 15, 25
Lorencz P. 27, 43

M

Mainini C. 28
Meggyeshazi N. 30, 32, 34, 37
Migeod F. 14, 47
Montagnani F. 15, 25
Moss R. 13
Muller L. 30, 34
Müller M. 16

N

Nagy T. 39

P

Paik HC. 52
Pang C. 26, 37
Panshin GA. 56
Park KT. 28
Pascher C. 27
Pietsch T. 27
Polyak A. 48
Proescholdt M. 27

R

Ramm P. 27
Reimnitz U. 20
Reinert C. 27
Rossi S. 15, 25
Rubovszky G. 39
Rümmele P. 27

S

Sahinbas H. 47
Saupe H. 24, 41
Schuierer G. 27
Schwartz L. 28
Skrihar G. 54
Solodkii VA. 56
Sommer H. 11, 24
Szasz A. 12, 30, 32, 34, 35, 36, 37, 39, 41, 42, 44, 48, 49, 50, 53
Szasz N. 34, 42
Szasz O. 30, 34, 35, 39, 41, 42, 45, 48, 49, 53, 55

T

Thuroczy J. 48
Turrisi G. 15, 25

V

Veronica G. 46
Vincze Gy. 53
Vito F. 46

W

Wey S. 29
Wismeth C. 27

Y

Yoon SM. 28, 32

NOTES

NOTES

THE POCKWOOD CORPORATION

We trust in - oncothermia!
We are proud to be a partner of ONCOTHERM!
Go ahead with - oncothermia!

THE POCKWOOD CORPORATION is thinking ahead on realizing its job and projects and ensures high quality solutions.

THE POCKWOOD CORPORATION is proud about its success, mainly in the segment of consulting sales (USA, Europe), product consultancy (Northern Europe), capital goods (Northern Europe), difficult transfer solutions (USA) and research (USA).

Due to a on-going expansion (currently Middle East), improvement and extension of the networking as well as due to co-workers concentrating on customer service, solution of demands and sustainability the future of **THE POCKWOOD CORPORATION** is secured.

Ask for hyperthermia, cryothermia and more specialities, also the new products "Hemagel", "Icefeel" and "Thermoskin".

oncotherm

The Pockwood Corporation

391 N.W. 179 th Avenue
Beaverton, Oregon 97006

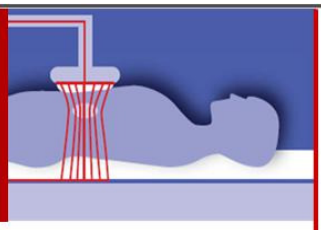
1005 West Fourth Street
Carson City, Nevada 89703

European Representative – The Pockwood Corporation

Neuer Wall 80
D-20354 Hamburg
contact@pockwood-corp.com

Oncothermie - Elektro-Hyperthermie

Mehr als 100.000 Behandlungen jährlich!



oncotherm hightech medicine

TreaTherm

© Powered by Oncotherm

Produktportfolio:

EHY-1000 Serie
zur Behandlung von Prostataerkrankungen

EHY-2000 Serie
zur regionalen Anwendung

EHY-3000 Serie
zur multilokalen Anwendung

EHY-100 Serie
zur Anwendung im Labor (in-vivo, in-vitro)

Booster
Zur Anwendung bei Onkologie, Rheumatologie, Sportmedizin, Neurologie etc.

Oncothermie wird als spezielle Form der Hyperthermie komplementär zu den schulmedizinischen Behandlungsmethoden der Krebstherapie angewendet.

Unsere Oncothermie-Methode wird bereits seit über 20 Jahren erfolgreich praktiziert.

Oncotherm Group

Deutschland / Germany:

Oncotherm GmbH
Belgische Allee 9
53842 Troisdorf
Deutschland
Telefon +49 (0) 2241 31992-0
Telefax +49 (0) 2241 31992-11
info@oncotherm.de
www.oncotherm.de

Ungarn / Hungary:

Oncotherm Kft.
Ibolya u. 2.
2071 Páty
Ungarn
Telefon +36 (06) 23 555-510
Telefax +36 (06) 23 555-515
info@oncotherm.org
www.oncotherm.org

TÜV SÜD

phytoVital • shop

Wir helfen Ihnen,
ein gesundes Leben zu leben.

· Gesundheitsprodukte für die ganze Familie
· Höchste Produktqualität
· Stetiger Dialog mit Forschungsinstituten

Warum Produkte von PhytoVital?

Die Produkte in unserem PhytoVital-Shop zeichnen sich durch qualitativ besondere und einzigartige Merkmale aus.

Oecopharm: Höchste Wirksamkeit – keine Zusätze

Oecopharm Produkte werden in einem aufwändigen Verfahren in manueller Produktion produziert – ohne sonst übliche Zusätze wie Gleitmittel, Talkum, Farbstoffe, Wachse oder Konservierungsstoffe.

Dadurch wird eine biodynamische Verfügbarkeit bis zu 100% erzielt.

Setzen Sie sich mit uns in Verbindung!

www.phytoVital.com

Bestellungen über LuxXPharma s.a.
13, Wuelesser Wee, L- 9838 Eisenbach, Luxembourg
Telefon 0 03 52 – 26 90 39 21 · Fax 0 03 52 - 24 61 11 62
E-Mail info@phytovital.com
Für Händler und Therapeuten gelten gesonderte Einkaufsbedingungen.

Die Kraft der Natur!

DR. BREITKREUTZ & KOLLEGEN
KANZLEI FÜR LEBENS- & ARZNEIMITTELRECHT

Ihre Rechte als Patient

In der Praxis ist seit der Entscheidung des Bundesverfassungsgerichtes eine zunehmende Tendenz zur Erstattung zu beobachten.

Dies gilt vor allem für hyperthermische Behandlungen von Krebserkrankungen.

Angesichts der aussichtsreichen Studienlage von hyperthermisch-onkologischen Therapien einerseits und der lebensbedrohenden Krankheit andererseits, für welche zwar etablierte, allerdings nur bedingt wirksame Therapien existieren, verurteilen in jüngster Zeit mehr und mehr Gerichte die Krankenkassen bzw. Beihilfestellen zur Übernahme der Kosten.

Um die Erstattungsansprüche erfolgreich durchzusetzen, ist ein auf den individuellen Therapieverlauf zugeschnittener Antrag entscheidend. Für diesen empfiehlt es sich, qualifizierte rechtliche Beratung in Anspruch zu nehmen.

Die Kosten für die Durchsetzung der Erstattungsansprüche werden von allen Rechtsschutzversicherern übernommen. Im Erfolgsfall müssen sie von den Krankenkassen oder Beihilfestellen getragen werden.

Ansprechpartner:

Rechtsanwalt
Dr. Frank Breitkreutz

- Spezialisierung auf komplementär-medizinische Therapien
- Umfangreiche Prozesserfahrung
- Bundesweite Vertretung
- Abrechnung mit sämtlichen Rechtsschutz-versicherungen

Kontakt:
Rechtsanwälte
Dr. Breitkreutz & Koll.

Potsdamer Platz 11
10785 Berlin

030-2589-40-85
dr-breitkreutz.de

Weitere Informationen:
www.dr-breitkreutz.de/hyperthermie

Booster

Verstärkt die Wirkung von Arzneimitteln im Bereich der Onkologie, Rheumatologie, Andrologie u.v.m.

Erreicht wird die Wirkung des Boosters durch Steigerung des Blutflusses im Bereich des Tumors mit einer Tiefenerwärmung von 37 bis 39°C.

oncotherm
high tech medicine

Oncotherm GmbH
Belgische Allee 9
53842 Troisdorf
+49-2241-319920
+49-2241-31992-11
info@oncotherm.de
www.oncotherm.de

Schulmedizin und Naturheilkunde aus einer Hand

Praxisklinik Dr. Schuppert

Krebs? Wir helfen Ihnen!

Ihre Spezialisten für moderne tumorbiologische Behandlungsformen:

- reduzierte Chemotherapie
- innovative Tiefenhyperthermie
- individuelle Misteltherapie
- aktuelle Antikörpertherapien
- Immuntherapie-Verfahren
- biophysikalische Diagnostik
- ursachenorientierte Psychotherapie
- Traditionelle Chinesische Medizin

Wir nehmen uns Zeit für Sie!

Dr. med. Achim Schuppert
Facharzt für Allgemeinmedizin
Naturheilverfahren
Ganzheitliche Krebstherapie*

Dr. med. Irmgard Schuppert
Ärztin, Naturheilverfahren
Traditionelle Chinesische Medizin*
Biologische Medizin*

Dr. med Dietrich Schmitz
Facharzt für Allgemeinmedizin
Ganzheitliche Krebstherapie*
Naturheilverfahren,
Palliativmedizin, Schmerztherapie

… und weitere Fachärzte

* Schwerpunkte nach eigenen Angaben

25 Jahre Kompetenz in ganzheitlicher Onkologie

Praxisklinik Dr. Schuppert ▪ Friedrich-Ebert-Allee 63 (B9)
53113 Bonn ▪ Tel.: 02 28 / 96 95 73 ▪ alle Kassen ▪ eigene Tiefgarage
Sie finden uns unter www.praxisklinikbonn.de

EHY-3010 ML

Die EHY-3000 Serie dient der simultanen und multilokalen Behandlung fortgeschrittener, metastasierender, maligner und fester Tumore.

Sie ist eine neue Entwicklung im Bereich der multilokalen Anwendung von Oncothermie-Systemen.

oncotherm
hightech medicine

Oncotherm GmbH
Belgische Allee 9
53842 Troisdorf
+49-2241-319920
+49-2241-31992-11
info@oncotherm.de
www.oncotherm.de

Integrative Onkologie

Europäisches Zentrum für Elektro- & Thermotherapie

Von den gesetzlichen und privaten Krankenversicherungen anerkanntes Akutkrankenhaus für Onkologie (nach § 108/109 SGB 5)

Die BioMed-Klinik ist ein onkologisches Fachkrankenhaus. Wir ergänzen die konventionelle Schulmedizin mit komplementären Methoden der Krebstherapie.

Konventionelle Behandlungen

- Chemotherapie
  (in Kombination mit Hyperthermie)
- Hormontherapie
- Schmerzbehandlung
- Molekularbiologische Therapie (Biologika)

Komplementäre biologische und physikalische Behandlungen

- Hyperthermie
  - Tiefenhyperthermie
  - Ganzkörperhyperthermie
  - Perfusionshyperthermie
  - Oberflächenhyperthermie
- Immuntherapie
- Psychoonkologie
- Kunst- und Musiktherapie
- Naturheilverfahren u. Physiotherapie

Interventionelle Onkologie

- direkte Überwärmung des Tumors (HITT/RFA)

BioMed
Fachklinik für Onkologie, Immunologie und Hyperthermie
Bad Bergzabern

BioMed-Klinik Betriebs-GmbH
Tischberger Str. 5+8
D-76887 Bad Bergzabern
Tel.: +49 (0)6343 - 705-0
Fax: +49 (0)6343 - 705-928
info@biomed-klinik.de
www.biomed-klinik.de

DR. BREITKREUTZ & KOLLEGEN
KANZLEI FÜR LEBENS- & ARZNEIMITTELRECHT

Hyperthermie

Was müssen Krankenkassen und Beihilfe zahlen?

Abbildung mit freundlicher Genehmigung der Oncotherm GmbH

Bundesverfassungsgericht bestätigt die therapeutische Bedeutung

Trotz beindruckender Therapieerfolge ist die Hyperthermie noch keine allgemein anerkannte Behandlungsmethode. Hyperthermische Behandlungen werden deshalb bislang nur eingeschränkt erstattet.

In einem grundlegenden Urteil des Bundesverfassungsgerichtes aus dem Jahre 2007 wurde die therapeutische Bedeutung der Hyperthermie erstmals höchstrichterlich anerkannt.

Seither ist es aussichtsreich, mit einer individuellen Begründung bei der Krankenkasse oder Beihilfestelle die Übernahme der Kosten zu beantragen.

www.dr-breitkreutz.de/hyperthermie

Klinik für Integrative Onkologie

Konventionelle Verfahren

Chemotherapie

Hormontherapie

Schmerztherapie

Spezielle neue Verfahren

Biologische Krebstherapie

Stärkung des Immunsystems

Naturheilverfahren

Psychologie

Physiotherapie

Entgiftung

Hyperthermie

Lokale Hyperthermie

Moderate Ganzkörper-hyperthermie zur Immunmodulation

Extreme Ganzkörper-hyperthermie

Jeder mit Freude gelebte Tag ist unendlich wertvoll !