



Personalization of oncothermia

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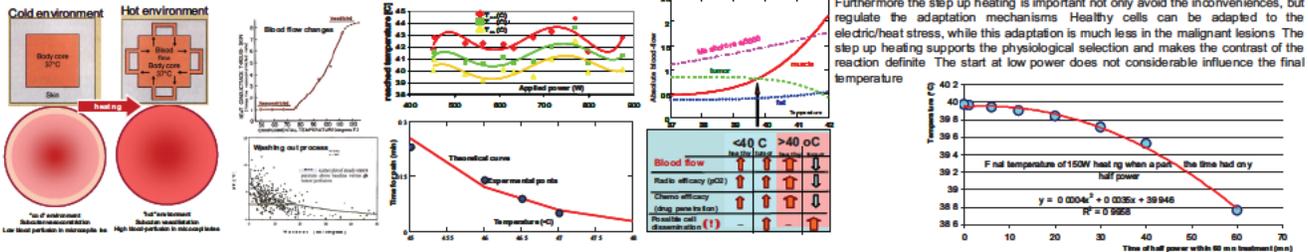
Objective

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

Method

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

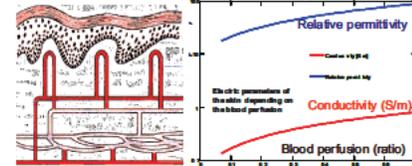
The temperature is physiologically regulated, and regulates the vasodilatation



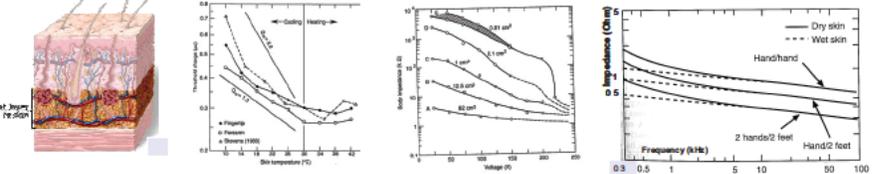
Other factor is connected to the psychological interaction with the treatment process also In any protocols, when the temperature is described as a dose, when the required temperature can not be achieved than of course it is forced by the power, so the incident energy is not limited in this case Oppositely, 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

Bioelectromagnetic considerations

The energy is transmitted through the skin The skin (as described above) is physiologically controlled and changes its blood perfusion and by this the electric parameters are changed as well [4]

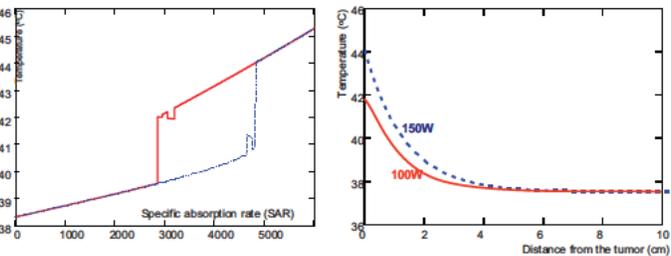
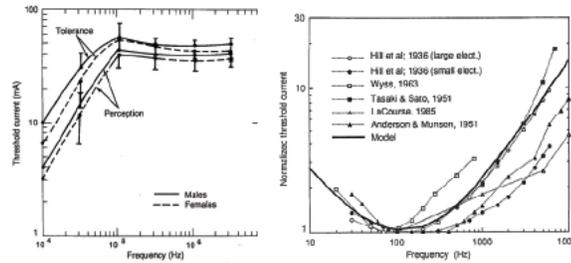


The subcutan adipose tissue is an electric blockade, and its conductivity decides the current transport at a fixed power transmission The applied voltage depends on the contact area and on the applied frequency also



Only the temperature has physiological blood flow response, the current has pain response from the skin This pain tolerance is constant (saturated) at 1356 MHz This allows an objective pain sensing by the current, which depends on the thickness of the adipose layer This creates a **negative feedback signal** when the fat is thick, the temperature grows and make a temperature pain limit which by step up heating increases the blood flow by vasodilatation The current in this way grows, but when the blood conductance became too high, the pain from current will limit the process again, and controls the personal merit, which is pretty objective due to the saturation of the current sensing

The physiological effects (temperature and non temperature dependent bioelectromagnetic interactions) cause a hysteresis of the heating by the provided specific absorption rate, and makes different the step up and step down heating The effect of the side heating is small, no disturbance in healthy tissue is expected



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. **The personalized oncothermia-dose is objective.**

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/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/smoc/content/content_a713628894-0b_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=0973-1462;year=2006;volume=2;issue=4;page=171;page=181;ajust=Szasz>
 [4] Cooper TE and GJ Trezek Correlation of thermal properties of some human tissue with water content Aerospace Med 42, 24 27, 1971



Success of Oncotherm

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Objective

Oncotherm company became this year 21 years old. It 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 from the Eotvos University Budapest in 1998. The first contacts with Germany were established almost immediately. Dr. Dörries (St.Georg KH/Hit, Bad Aroling), asked the human medical applications of the till that time only theoretically formulated ideas. The actual requests of the clinical use formulated by Dr. Dörries were successfully performed, starting with palliative therapies, and continuing to the basis of the presently well known oncothermia method. The company is certified in all aspects by the agencies German TÜV services having the CE and the ISO approvals for the products and production processes, respectively. The German approval is combined with the high-quality manufacturing in Hungary, following that traditional line which other typical German products (like Audi, Bosch, Mercedes, etc.) does. Our objective is show the market success of the company.

Method

Our marketing aim to keep the full developing and manufacturing process in the EU. Oncotherm does not follow the large multinational companies making their productions outside of the Community. We are committed to show the high-level of the famous German medical knowledge, ("MED in Germany") together with the well-known traditions of the German products: we are engaged for the best quality, for the immediate application of the newest research results, and for the highest reliability of the method. Oncotherm sells not simple devices. We are selling a method of ONCO-THERMIA, we are selling our high level expertise, which is supported by scientists and medical practitioners, smart and engaged doctors, diligent and precise nurses. Oncotherm in its own is a company which would like to give the best instruments to the hand of professionals supporting them in their responsible and important everyday work. Oncotherm developed all the parts and details according to the optimal harmony technically together and with the users. We have chosen the way when did not bought ready parts and units, mounting them together, but step-by-step developed own units to offer the best for the actual tasks.

APPROVALS, CERTIFICATES ("Production of Germany, manufactured in EU")
 Product CE certificate, TÜV Product Service, Munich, Germany (in past notified body in EU);
 TÜV - Technischer Überwachungsverein Technical Monitoring Office
 Marketing, sales: ISO 9001, approved by TÜV Management Service, Munich, Germany
 Manufacturing: ISO 13485, approved by TÜV Product Service, Munich, Germany
 EMC: German Approval Office (Deutscher Administrations Rat, DADR)
 Additional approvals: China, Russia, Ukraine, S.Korea, Canada (TÜV America).



The strong commitment and philosophy of Oncotherm opened new dimensions of hyperthermia treatments, and it is based on 3E+3S concept:

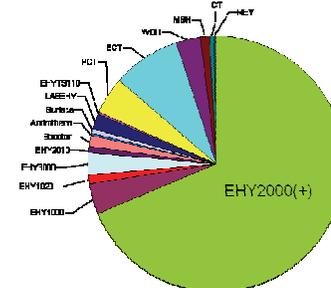
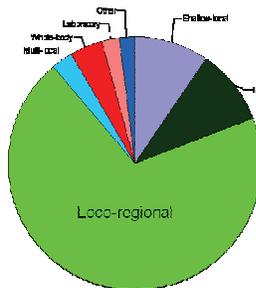
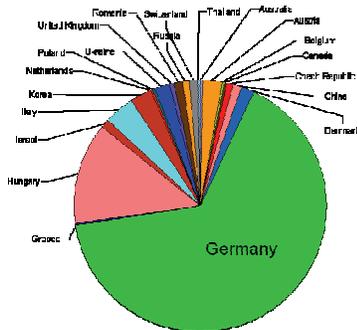
Efficacy principles

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

Safety principles

- 3S**
1. safety for the patient with optimally personalized energy-absorption, based on the inducing 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.

Results



252 oncotherm in 21 countries
 (some are sold in a center, others only on the local - 200 devices in 17 countries)

17 types of devices in 7 categories were developed during the history of oncothermia.

Multi-focused	EHY 2000(+)
Inter-focal	TCT, EHY1000, EHY100
Local-regional	EHY2000, EHY1000, EHY100
Multi-focused	EHY2000
Whole-body	WBY, EHY
Lab-oncology	LABONC, EHY1000
Other	Jonckhe, Jandrićević

Conclusion

New paradigm is necessary for hyperthermia in oncology Necessity of oncothermia

- Hyperthermia contradiction (1): "The biology is with us while the physics is against us" (J.Overgård, [1])
 Oncothermia changes the paradigm (1): "The biophysics is with us"
 Hyperthermia contradiction (2): "The biology and the physics is with us while the physiology is against us" (S.Osinsky, [2])
 Oncothermia changes the paradigm (2): "The fractal physiology is with us"
 Hyperthermia contradiction (3): "Reference point is needed" (J.van der Zee, [3])
 Oncothermia changes the paradigm (3): "Back to the gold standards, use the energy instead of temperature"

Oncothermia is a personalized, non-toxic treatment which supports the natural processes (apoptosis, immune reactions, conditional effects, etc.) to be a helper of electro-hyperthermia actions. Oncothermia is a new paradigm of the modern oncotherapies.

Oncotherm understood the update demands of the modern oncology:

- Personalized treatments
- Demand and conditions is important
- Preventive and follow-up procedures
- Oncothermia is a convenient treatment for all the demands
- Non-toxic treatments
- Minimal toxicity with maximal benefit
- High selectivity, local actions
- Oncothermia is non-toxic, local and depresses the toxicity of others also
- Increase of the quality of life
- Low QoL with long survival is not satisfactory
- QoL has a great economic importance also
- Oncothermia is an ideal method to increase the QoL.
- Increase of the survival time:
- It is the most important factor, it is ranked before the clinical results
- It is not enough if a method offers only clinical success-rates
- Oncothermia together with the clinical success-rates is definitely a tool for longer survival
- Economic points:
- The cost/benefit ratio is frequently counted
- Financial background of the medical treatment is an important issue
- Oncothermia is a cheap and easy to use method, low contraindications and complications

Acknowledgement

Oncotherm workers feel themselves like a value-maker doing: trying to produce the best v. clin. ever, making innovation as such as possible, and dreaming about a 'top concept' BUT we never make concept. The concept is given by the oncothermia users.

Oncotherm is deeply indebted for the capable and clever physicians using oncothermia, we are thankful for talented supporters and users, and gratitude for researchers and scientists who are all helping oncothermia on the way of further developing and reaching new heights to help the suffering patients and win the war against cancer.

References

[1] Overgård, J., Nilsen, O.E., Einbu, A., & Dr. Biological basis for the rational design of clinical treatment with localized hyperthermia and radiation. In: Field, R.B., Proctor, C. (eds) Physics and Technology of Hyperthermia. No. 89. NATO ASI Series, II, Applied Sciences, Boston: Kluwer, 1994, pp. 36-59 (1994)

[2] Osinsky, S., Gaid, Y., Zhigalov, V. et al. (2016) Local and global hyperthermia in combined treatment of malignant cancer: 20 years experience in Ukraine. The 18th World International Forum, Aard, Japan, 11-16 June 2016

[3] Van der Zee, J. (1990) Temperature dose analysis for 25 patients with advanced cervical carcinoma treated in Rotterdam using radiotherapy, hyperthermia and chemotherapy: a reference point is needed. Int J Hyperthermia 2:243-262

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



Ms Constanze Feißkohl¹, Ms Janina Leckler¹

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CONCEPT AND MARKETING TOOLS

The focus of our work is informing doctors from all over the world about the method and possibilities of Oncothermia. We are dealing with oncothermia as a complex method and not simply market and sale of devices.

Our driving force is 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. Physicians who are applying oncothermia are not only passive users, they are active helpers to build up the next development step for their better services and for wider possibilities of the oncothermia method. We are building up the future together with all the oncothermia users. 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 include for example publications, website, newsletters, events, brochures, patient information and so on present our successful synergy of professional technique and the science.

The Menu of our new Website: www.oncotherm.org



Our newsletter is sent out monthly and informs the customers about news in science, the company and on events and new developments

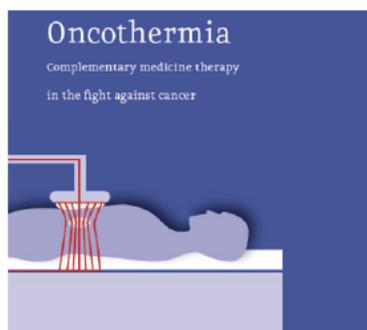


NEWSLETTER

OCT 21st 2010

The yearly organized Symposium is also a tool to inform about the method and support the customers with new studies and scientific results

New brochure design



INTERNATIONAL ONCOTHERMIA SYMPOSIUM



CONCLUSION

Oncotherm works with a professional marketing concept based on the needs of our customers and their own „customers“, the suffering patients. Our aim is to make the method more prominent to help patients and to support the doctors using the oncothermia method. Oncotherm knows very well: we are united community with our customers, regarding them our partners in recognising the demands and introducing it in the permanent development of the oncothermia method. Oncothermia devices can not fulfill their intended prospective without our smart and active partners who are the complete medical personal applying everyday the method and using the oncothermia skills to win the war against cancer.



Institute for Hyperthermia and Immunotherapy IWIT, Vienna 14 Years Experience in locoregional and whole body hyperthermia



Kleef R, Kekić S, Hadžić D, Rigler W, Pecher O.

BACKGROUND

The IWIT is the leading Institute for Hyperthermia in Austria

- > 17.000 h of whole body hyperthermia
- > 5.000 Treatments with locoregional Hyperthermia
- Largest center to successfully combine oncological and non-oncological treatments

Conditions treated

- Autoimmune diseases, Allergies
- Chronic Infections
- Chronic Fatigue Syndrome, Burn Out, SAD
- Pain Syndromes
- Cancer

PURPOSE AND HYPOTHESIS

Whole Body Hyperthermia

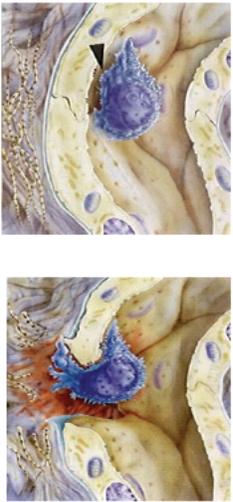
Whole Body Hyperthermia – the carefully monitored creation of artificial fever – is one of the most promising therapeutic strategies in physical medicine in use today. The central mechanisms of hyperthermia are the regulation of the matrix reaching deeply into the body's core and the modulation of the immune system. Healthy individuals benefit from increased stress resistance levels and deep regeneration effects.

Locoregional Hyperthermia in cancer therapy is combined with cytostatics, radiation or immunotherapy. Cytostatics whose effect will be amplified by the produced heat are especially apt for treatment. Amongst others Cis-Platin, Mitomycin, Bleomycin and Epirubicin are known to have this effect. Also a combination with radiation seems to be reasonable. The radiation therapy affects all cells that are well-supplied with oxygen, while hyperthermia increases oxygen partial pressure in tumor cells.



MATERIALS AND METHODS

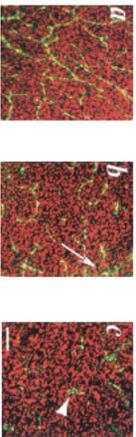
Pleiotropic & Complex Effects of Hyperthermia
- Immunological Effects - at fever-range Temperature



- Emigration & Migration (Expression: ICAM-1, L-Selectin ↑; ELAM-1 ↓)
- Chemotaxis ↑
- Cytokine-Induction (IL-1,-2,-6,-12, TNFα, NO, CSF)
- Activation of Effector Cells (NK, MO, DC, CTL)
- HSP-Expression (clapponosis, HSP-1AA-complex)

Anti-angiogenic effect of heat

- Large control tumor
- Hyperthermia (44°C, 60 min) disrupted 25-50% of the blood vessels in the small tumor
- The anti-vascular activity was more potent (is more distinct) in larger tumors



Eikelsdal, HP et al Int J Hyperthermia 2002; 18 141-152

RESULTS

Locoregional Hyperthermia

In locoregional hyperthermia the application of hyperthermia with external plate electrodes is employed with radio short waves 13-56 MHz which invade about 12cm into biological tissue. There is a distinction between direct and indirect effect. The direct effect relates to the tumor cell itself. It has an influence on protein metabolism, energy metabolism as well as on the character of the cell membrane. The indirect effect relates to the attached tumor cells as a whole, i.e. disturbances of the micro circulation.



CONCLUSIONS

Summary of Basic Research in HT

- Increased blood perfusion at mild and moderate T
- Immunological effects at fever-range T
- Synergism with radiation, antineoplastic agents, antihormones, and immunomodulators
- Induction of apoptosis at T > 40°C
- Antiangiogenic, molecular and genetic effects
- Reduction of drug-resistance
- Induction of necrosis at T > 45°C

BIBLIOGRAPHY

- Kleef R: Die mild und moderate Ganzkörperhyperthermie. Karger Academic, Springer, Langhans, Spiez
- Niederwieser A, Rugeleberg J 2006
- Kleef R, Kekić S, Hadžić D, Rigler W, Pecher O: Hyperthermia in der Onkologie. Gustav Fischer, Stuttgart, New York, Thieme, Stuttgart, Mosby, Wien 2003
- Kleef R, Jovan V, R, Kekić S, W, Storzinger T, Pecher O: Cancer induced endotoxinemia mimicking Neisseria meningitidis 2001; 9:215-44
- Kleef R: Molecular characterization of hyperthermia in the Onkologie. Biologischer Medizin 2002; 7: 124-131
- Kleef R: Hyperthermia in Cancer Therapy. In: Locoregional Hyperthermia: Principles and Whole Body Hyperthermia. In: Cancer Treatment and Control. Boca Raton, FL: CRC Press, 2005
- Kleef R: Hyperthermia and Dose-Response. In: Steven - Hagen - Schwabach. Market, Robert, Handbuch (ed). Springer, Wien, New York, 2006