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Essentials of Oncothermia

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Abstract

Oncothermia is a method of hyperthermia in oncology, controlling the locally applied deep-heat by selectively targeting the cellular membrane of the malignant cells. The selection of the method is based on various biophysical and biochemical achievements. There are various differences between the malignant and healthy cells, which could be used for their selection by heat targeting. The primary selection factor is a different metabolic activity which creates distinguishable environments of the malignant cells. The other factor is the clear difference of dielectric properties of the membrane and near membrane extracellular electrolytes, marking off the malignancies. There is also a structural factor also, which is clear in the different pathological patterns of the malignancy from their healthy counterparts. This last is described by fractal pattern evaluation technique, which dynamic time-fractal transformation is used for further discernment of the malignancy. My objective is to show a new heating method, which makes oncological hyperthermia controllable and effective.

Keywords: oncology, hyperthermia, heat, nanothermia, oncothermia, selectivity, cell-membrane, Warburg, Szent-Gyorgyi, fractal, radiofrequency, modulation, beta-dispersion

Introduction

Oncological hyperthermia is the overheating of the malignant tissues locally or systemically. The method is deduced from the ancient medical practices, where the heat-therapies had a central role in medicine.

The local hyperthermia by the radiation of red-hot iron was the first known oncological treatment applied by Hypocrites, who described the method [1]. The main idea was originated from sacral considerations formulating the overall force of the "fire". However, physiological consideration was also behind that together with beliefs: the local heat accelerates the metabolic activity without extra supply of this action from the unheated neighboring volumes. This physiological mechanism is accompanied by severe hypoxia and it finally kills the target by acidosis. The working idea has been recently shown, proving the impoverishment of ATP and enrichment of lactate in the locally heated tumor tissue, [2]. Due to the primitive heating techniques the ancient radiative heat is only rarely applied in real cases. The central point of the locally applied oncological hyperthermia is the selective heat-delivery into the deep-seated tumors. The discovery of the electromagnetic heating gave new perspectives for deep heating, and hyperthermia started its first "golden era" in oncology. It was among the first modern curative applications of modern techniques in oncology, [3] and was followed by a controlled clinical study involving 100 patients as early as 1912. It showed remarkable benefit of the combined thermo-radiation therapy [4]. The method was further developed in three various branches: the interstitial hyperthermia, including the galvanic heatstimulation, the ablation techniques and the capacitive coupling. The first capacitive coupled device was launched by Siemens. The skeptical opinion about oncological hyperthermia was also typical: "All of these methods impress the patient very much; they do not impress their cancer at all" [5]. After a small dormant period the phoenix life of hyperthermia in oncology started again. The first start of the new capacitive-coupling technologies was by LeVeen [6] in 1976 and has been widely applied since then [7], [8]. Its efficacy was discussed and proven in the relevant literature in its time, [9], [10], [11], [12], [13].

Treatments with coils (magnetic and inductive) are relatively rarely used due to the negligible magnetic permeability of living systems [14]. In order to improve the magnetic energy absorption within the target tissue, magnetic materials, such as micro-particles [15] and ferrite rods [16] are usually injected into the targeted area [17]. Other inductive heating is typically achieved without inclusion of extra magnetic material into the tumor, it uses only induction of Eddy-currents [18], [19], [20]. The emerging application of magnetic treatments was started by the nano-particle magnetic suspensions [21] and other magnetic liquids.

A method for electromagnetic energy delivery, that has been widely used recently is the antenna-array coupling [22]. Its subsequent developments are the annular phase array [23], the matched phase array [24], the Sigma60 [25], and Sigma-Eye [26], where the applicators use high-frequency RF (60 – 150 MHz). Nevertheless, multiple controlled clinical trials have shown the efficacy of this method [27], [28], [29], [30]. This rapidly emerging period was shadowed by skeptic opponents, they emphasized the increased

dissemination of the malignant cells which supports metastases by hyperthermia, [31], [32], [33]. Direct negative opinion was formulated about the mistakes of hyperthermia investigations [34]: "The mistakes made by the hyperthermia community may serve as lessons, not to be repeated by investigators in other novel fields of cancer treatment." Many researchers had been doubtful and unsettled questioning the future of hyperthermia accepting the impressive biological effects, but blaming the physical realization of the heat-delivery [35]. Annals of Surgical Oncology formulates in the actual clinical experiences of mesothelioma [36]: "The results of adjuvant intrapleural chemotherapy for mesothelioma with or without hyperthermia have been less than hoped for." One of the flagship clinical studies of hyperthermic oncology was published about cervical cancer, with excellent results [37], the method emerged again, [38]. The control study five years later was disappointing [39].

What is the problem [40]? Why are conventional hyperthermia with high preciosity of focusing made by modern techniques of radiofrequency and microwave applications not able to serve the proper deep heating requests? The answer is plausible: the temperature spreads into the neighboring volumes independently of how precise the focus of the energy is. The problem is, that because of the misleading aim we get uncontrollable temperature as a dose and we ignore the physiological reactions of the patient. The published temperature patterns of the heating show the problem well: the energy is well focused, but the temperature seeking to be equalized and the focused energy-intake will heat up the tissue outside the focus as well. For example, a tumor is heated in the pelvis, and the elevation of the temperature in the tumor is 4.2 oC after 57 min, with as high power application as 1300 W [41]. The overall heating is obviously show unwanted hot-spots on the MRI pattern. The elapsed time smears the relative focused temperature. The temperature increase in the tumor was in average 4.2 oC, while in the surrounding muscle it was 3.8 °C [41]. (Note, a standard speedy electric tea kettle uses 1300 W to boil a cup of water within a couple of minutes. The increase of the temperature for the ~ 0.3 liter water is ~75 ºC. In these cases we apply the same power reaching a temperature increase of ~7 ºC during 60 minutes for the same volume of tumors as the cup of water in the kettle.) Analyzing the temperature pattern in details shows that the mean tumor-size was less than half a liter (419 ml), the necrosis in the tumor was 36 ml. The volume ratio of the body's cross section and the bolus show, that the bolus has 157% more cross-sectional area than the body. The applied frequency was 100 MHz in average, which loses its 66% of the initial energy (penetration depth definition) within max. 5 cm, so the main energy-absorption was in the water of the cooled bolus. Other publications show the same problem of the heating [42]; [43]; [44]. Comparison of the clinical responses also clearly shows the problem of the bolus heating. The cases of non-responders have higher bolus temperature, the tumor is not heated [45], [46].

The same problems arise by typical capacitive coupling hyperthermia solutions. It pumps enormous energy also (1200 W) into the target and the rise of temperature was 4.8 oC after 45 min. The selection by temperature between the malignant target and the non-targeted healthy tissue was approx. 1 oC [47].

This large volume temperature rise was observed in other capacitive applications too, [48].

All of these problems are caused by the massive heating of the target, which has a physiological reaction to cool it down and to reestablish the homeostatic equilibrium. The complex physiological effects badly modify the desired effects [49]. Even when the focus is proper, the heat is distributed to the full available volume. Furthermore, the same volume heating with the identical absorbed energy will be heated to different temperatures when the blood-flow in the targeted volume is different. This is why the patterns of the specific absorption rate (SAR) of the energy and the temperature are so different in a given fixed heating process, [50]). There are multiple other points that modify the temperature distribution in the body:

- Not only the temperature equalizing process, but the natural, technically non-followable movements of the patients (i.e. due to the breathing) modify the focus.
- The heat flow to the surroundings can damage the healthy neighborhood.
- The enlargement of the sphere having certain temperature gradients increase the area of the injury current, and this supports the cell-proliferation.

Compensating these effects, the acceleration of the heating with high energy has to be applied, when the incident energy might burn the skin. In consequence, certain surface cooling is necessary. The heat-sink of the surface decreases the incident power, but its quantity has no measurable parameters. This way we lose the control of the treatment process by the incident energy, because the missing part by cooling is uncontrolled. It has serious consequences in the vigilance of the process: temperature measurement in situ is necessary to fix the dose of the energy. This measurement is mostly invasive, causing multiple complications, including inflammation, bleeding, infection, dissemination of the cells, etc. The unwanted hotspots are created by the electromagnetic interferences and are uncontrollable with the dynamic changing

of physiologic parameters. These could be controlled only by a large volume temperature pattern, which requires costly and complicated MRI measurements parallel with the hyperthermia
treatments for control.
The physiological feedback of the large volume temperature equalizing is the increased blood-flow. The high blood-flow promotes the glucose influx (delivery), and supports the malignant proliferation by this supply. The increased temperature anyway gains the metabolic rate and the proliferation even by the cells in dormant (G0) phase. The higher blood-flow creates other malignant danger too: the risk of the forced disseminations and metastases, decrease the prognostic factors of survival of the patient.
The well-focused local hyperthermia treatment creates a competitive pair of effects: killing the tumor-cells by heat and support them by nutrients together with the risk of dissemination. The result of this competition is unpredictable and depends on the patient and on the applied techniques as well. The explanation of the controversial results of local hyperthermia in oncology may be simple: a reference point was missing, [51]; the temperature is not a correct reference.
The present main-stream thinking of oncological hyperthermia is a typical loss of aims by illusions, believing the overall control of temperature. The temperature however is only a condition for the treatment and not its aim. The question "Tool or goal?" has become relevant to study the temperature alone. Take a simple example of mixing the tool and the goal in our everyday life: the graduation is a tool for our professional life, however when somebody regards the certificate of studies as a goal, its application, the aim of the study is lost. Mixing the tool with the action creates false goal in hyperthermia application: increase the temperature alone. This "auto-suggestion" creates such a situation in which magnetic resonant imaging (MRI) is applied to control the temperature during the treatment instead of using this capable imaginary method to see what is happening in the tumor indeed.
Our tasks are finding the correct heating and control the hyperthermia process. For this we have to precisely select the malignant cells and we must not heat up all the materials in the targeted tumor, only the membrane of the cancerous cells. This selected nanoscope energy-absorption liberates not as much heat energy which heats up all the mass equally, so its efficacy could be significantly higher. The main advantage however is its independent action from? the physiologic feedbacks, no contra-action starts to compensate its effect.
Furthermore, the membrane excitation could excite special cellular signal-transduction pathways, which are connected with the natural apoptotic cell-death, and so the negative feedback loop of the complex living system is supported. (The conventional hyperthermia by its overall heating excites negative feedback mechanisms act against the temperature growth, so the system starts "fighting" against the healing process.)
The temperature as the average of kinetic energy in the system has a double role in the control of the heatabsorption.
It characterizes the heat-absorption, when the heating is homogeneous (see before), and its gradients (non-homogeneities) are the driving forces of the dynamic processes in case of microscopic (non-homogeneous) heating. The average temperature does not inform us about the distribution of the real energy-absorption (see Figure 1.).

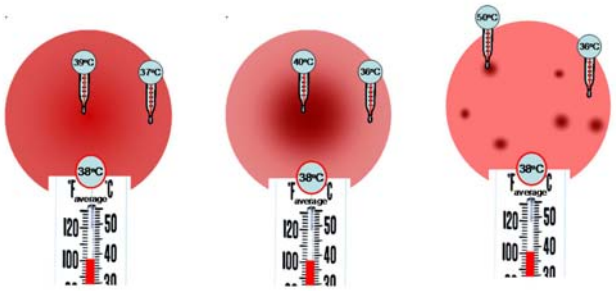

Figure 1. The average temperature is not able to characterize the thermodynamic situation. The internal temperature differences could serve as driving forces of various processes on the same average temperature of the system

Method

The efficacy of the energy depletion intended to be pumped into the tumor is limited by the energy loss outside the malignant target. The main factors of the useless energy absorptions are:

- The absorbed energy by the tissues transfers the effect to the deep-seated tumor.
- The heat-exchange by the blood-flow.
- The heat exchange by the heat-conduction from the tumor to the surroundings.

These heat-sinks modify the overall performance of the treatment and make the full heating process for the malignancy uncontrolled. The real effect, which is used for the intended treatment is less than the losses, and the efficacy is usually less than 25%, which is very low. The problem of this is not only that the large part of energy is wasted, but also the useless energy part could be dangerous by overheating the healthy tissues as well as increasing the metabolic rate and also having physiology reaction to this effect which tries to break the homeostasis. The massively heated tumor volume intensifies the control of physiology, and weakens the expected effect.

The adequate corrective actions for these challenges would be the more precise targeting, decreasing the losses in the surrounding and avoiding the physiological corrections to suppress the desired effect. To construct the solution some new effects have been used to increas the efficacy:

- Apply the electric field as carrier of the energy, and that field cannot be compensated by homeostatic control.
- Apply a correct microscopic targeting, using the cell-by-cell energy-absorption efficiently.
- Apply such mechanisms, which initialize natural effects to kill the malignant cells.
- Apply a mechanism, which carries info that disseminated cells have to be blocked.

Oncothermia changes the paradigm of local hyperthermia in oncology to solve the above problems [52].

This hyperthermia technology heats non-equally; concentrating the absorbed energy to the extracellularelectrolytes [53]. This method creates inhomogeneous heating, microscopic temperature differences are far liquids changes the membrane processes, ignites signal pathways for natural programmed cell-death, avoiding the toxic effects of the simple necrosis. The synergy of electric field with the thermal effects effectively and selectively does the job [54]. Oncothermia uses nano-heating technology to select and heats effectively the membrane of the malignant cells. The heating is concentrated mostly on the cellmembranes, so the nano-range energy-liberation could be precisely controlled without considerable wasted energy and without having disadvantages by the heating of the tumor-environment in average.

The general idea of microscopic heating is simple: the heating energy is not liberated in a sudden single step, but regulated and multiple small energy liberation does the same job, Figure 2. In our case, the forwarded energy selectively targets the most influential areas. Instead of the high, general energy pumping into the lesion, the energy is liberated at the membranes of the malignant cells.

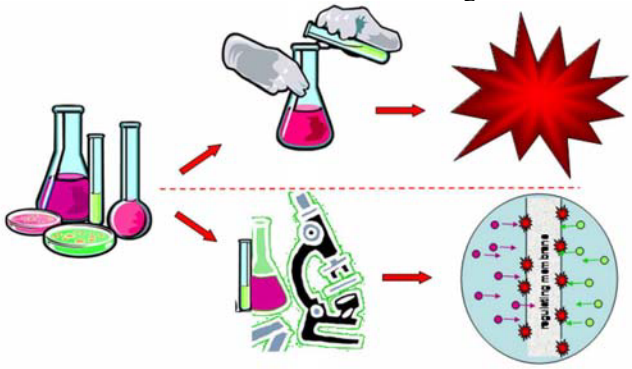

Figure 2. The difference of macro- and micro-liberation of energy. The efficacy of the last one is much better

The precisely targeted power and its efficacy are usually not connected. The microscopic effects, instead of the large energy liberation, is one of the most update thinking in energy source developments. The relatively low efficacy combusting engines are intended to be replaced by the fuel-cell energy-sources and electric motors, which are based on the membrane regulated microscopic reactions of gases. (Mostly hydrogen and oxygen gases are in use.)

Good examples are the standard incandescent bulb and the energy saving fluorescent ones, using a fraction of the power for the same light. The incandescent bulb creates light by high-temperature filament, which heats up the environment, having only 10% efficacy, while the fluorescent has more than 40%. It could be developed further by the higher nanoscopic energy-liberation, when not the molecules but the electrons are directly involved in the light-production. These are the LED bulbs, having more than 90% efficacy in producing light.

Oncothermia [55] is a kind of hyperthermia with nanoscopic heating processes. Instead of the undistinguished cells by the classical overall heating of hyperthermia, oncothermia nanoscopically selects and attacks the malignant cells. It has a simple setup. The modulated radiofrequency current (RF) flows through the targeted lesion, see Figure 3.

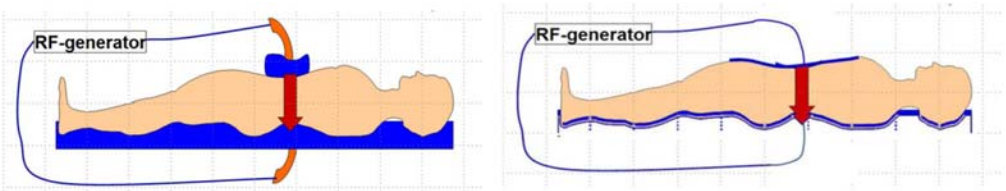

Figure 3. Oncothermia setup. The cell-culture/animal/human is a part of the electric circuit. Energy is carried by 13.56 MHz RF-current, (fractal-modulated) (a) EHY2000 local/regional treatment, (b) EHY3000 multilocal treatment

The radiofrequency current (RF-current) flows through the body and delivers energy to the malignant cells. The frequency is low (13.56 MHz) chosen to satisfy multiple requests:

- It is a free-frequency for medical applications in hospitals and clinics, as well as in general use of for example RF-identification.
- It is in the range of the beta-dispersion which is one of the selection factor of oncothermia.
- It is low enough to have long wavelength for near-field use with high penetration into the body when the impedance matching [56] is fixed.
- It is high enough to be modulated by time-fractal fluctuations.

The discussion of all these behaviors is seen below.
The current which flows through the chosen part of the body starts from one electrode and ends on the other one, periodically changing its direction according to the carrier frequency. The current is directed by the impedances inside the targeted volume, the current automatically flows to the "easiest" direction, where the conductance and dielectric conditions are optimal. Oncothermia uses three factors to direct the current to select malignant cells, i.e. those current paths which include malignant cells are favored. Certainly, the biophysical behaviors have to be studied to fix the optimum. The first selection factor is the well-known metabolic differences between the malignant and healthy cells. Due to the high energy demand of the malignant proliferation, the malignant cells metabolize more to supply their needs. Furthermore, the process to produce ATP differs in malignant cells from the normal ones. While the dominance of the mitochondrial ATP production characterizes the healthy tissue, when 36 ATP is produced from one glucose molecule during the complete cycle, the fermentative ATP production dominates the metabolism of malignant cells, only two ATPs are produced from one glucose molecule [57]. Consequences of this huge difference are enormous: the requested glucose influx of malignant cells is considerably higher, which is standardly measured by Positron Emission Tomography (PET). The considerable glucose consumption certainly produces high concentration of adducts, the extracellular electrolytes enriched by metabolites and lactates in the vicinity of the malignant cells, robustly enhances the ionic concentration in the connected electrolytes. The applied RF-current naturally flows with higher density in the areas where dense ionic conditions allow the easy flow, Figure 4. This could be measured by current density images with MRI [58], by simple impedance measurements in vitro [59] and in vivo too [60].

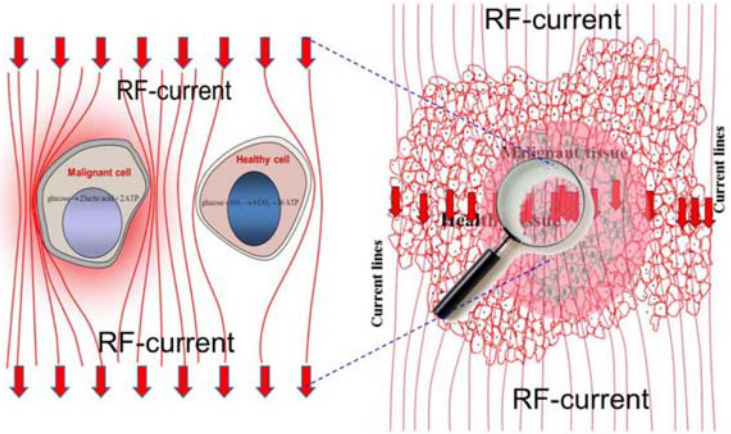

Figure 4. The radiofrequency currect is focused on the tumor lesion, and microscopically flows into the extracellular electrolytes around the malignant cells

This gives us a possibility to distinguish the malignant cells automatically and individually, see Figure 5. This automatic focusing makes it possible for the current density to follow any movements (breathing, heart-beats, muscle-movements) in the target tissue.

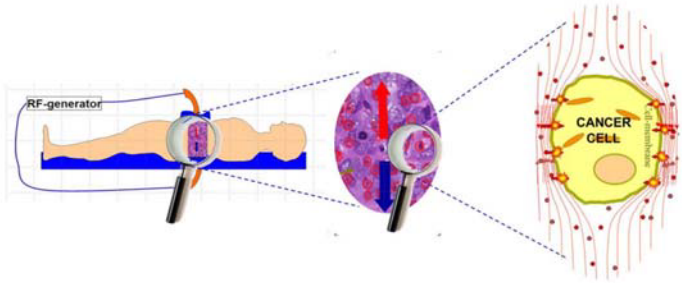

Figure 5. The microscopic heating of the extracellular electrolyte around the malignant cells excite the membrane and makes temperature gradient in a few nanometer distance

The above selection is based on the conductive component of tissue impedance. The permittivity component is also selective. Malignant cells differ from their healthy counterpart not only by their metabolic processes, but their collective behavior sharply identifies them. The malignant cells are autonomic, they are individual ”fighters”, having no collective driving of their activity, while the healthy cells have social signals [61]. These connections commonly regulate and control their life.
These cells are specialized for work-division in the organism, and their life-cycle is determined by the collective “decisions”. This requests definite order in the connective electrolytes. Indeed, the order was proven, [62], [63], [64], [65]. Contrary, the malignant cells which have no such order in their immediate extracellular connections, Figure 6. The disorder increases the electric permeability of the electrolyte near the malignant cells, [66]. The higher permittivity is also a selection factor, which is used to distinguish the malignancy by Szent-Gyorgyi’s cellular categories alpha- and beta-states, [67], [68].

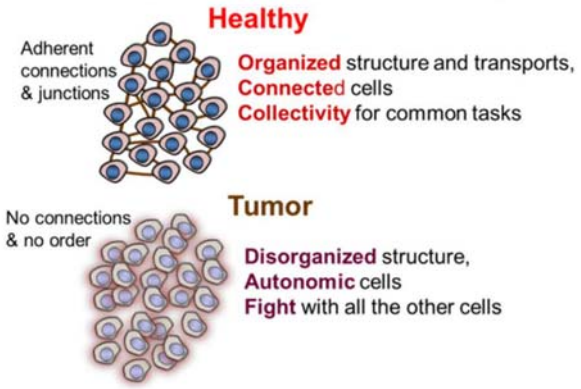

Figure 6. The difference of the healthy and malignant tissue is well observable by their organization structure

This dielectric differences are well completed by the specialties of the cell-membrane of the malignant cells.

- The efficacy of the ATP production in cancerous cell is low. The large ATP demand for the proliferative energy-consumption allows less ATP for active membrane stabilization by K+ & Na+ transport, so the membrane potentiating weakens [69].
- The cellular membrane of cancerous cells differ electrochemically also from the normal, its charge-distribution also deviates [70].
- The membrane of the cancerous cell differs in its lipid and sterol content from their healthy counterpart [71].

The membrane-permeability is changed by the above differences. In consequence of these the efflux of the K+, Mg++ and Ca++ ions increases, while the efflux of Na+ decreases together with the watertransport from the cell. Consequently, the cell swallows, its membrane potential decreases further [72]. (The efflux of K+ regulates the pH of the cell, takes the protons out from the cytosol.) The concentration of Na+ increases in the cytosol, and parallel to this the negative ion-concentration also grows on the glycocalyx shell, decreasing the membrane potential and the tumor will be negatively polarized on average, [73]. This fact was well used for direct current treatment (electro-

chemical cancer therapy (ECT)) by Nordenstrom [74], [75], and others [76], [77], [78].
There is a further selection based on complex impedance, the β -dispersion [79] (Maxwell-Wagner effect). [80]. The bound water to the membrane has the upper part of the β-dispersion, (denoted by δ, [81]), which has a further selection role in oncothermia. The treatments have to be chosen in the frequency-range of β-dispersion, promoting it with amplitude modulated pink-noise, expecting most of the changes in the complex system [82]. The carrier frequency and its modulation are selected by the membrane properties difference between the malignant and healthy cells [83], [84], [85].
Oncothermia selects by the above electromagnetic differences, and heats up the membrane of the malignant cells. The RF-current, which flows through the cancerous lesion is automatically focused by its lower complex impedance [86], it will flow mainly in the extracellular electrolyte (see Figure 7/a.), because the cells are electronically capsulated (isolated) by their membrane by more than one-million V/m fieldstrength. (The membrane is a good isolating lipid (fatty) layer). The membrane disruption is one of the targeted aims [87], [88], [89], so that is why many research groups deal with the electric field action on the cellular divisions [90], [91], [92], [93]. The main advantage of the electric field application is the missing control of the organism, physiology control over this effect; no physiology feedback limits directly the electric field, only its consequences could be regulated. The process made by oncothermia has its main energy delivery into the extracellular liquid, heating it up, and creating a little (1/1000 ^{o}C) difference between the inner and outer temperature of the cell. This looks only a small difference, but regarding the very tiny membrane layer (5 nm), the small difference in standard conditions is high: ~200,000 ^{o}C/m! The system is far from thermal equilibrium [94]. This starts a prompt heat-flow from outside to the cell through the membrane, and permanently acts till the temperature difference exists. Despite the quick heat-flow through this tiny membrane, the heat-current is long-lasting, till the full cellular interior is not heated up to the same temperature as outside. The not so high radiofrequency (13.56 MHz) is absorbed in all the electrolytes, but the main energy absorption is in the membrane and the extracellular electrolyte [95]. This creates an extreme SAR between the cells, which makes temperature gradient through the membrane [53]. The treated tissue will be inhomogeneously heated, the heat flows from the extracellular to the cytosol through the membrane, accompanied with definite other thermodynamical and chemical changes [53]. These definite thermal currents will be continued till the extra- and intracellular temperature reaches equilibrium, so the intracellular electrolyte is heated up to the equal level (see Figure 7/b.).

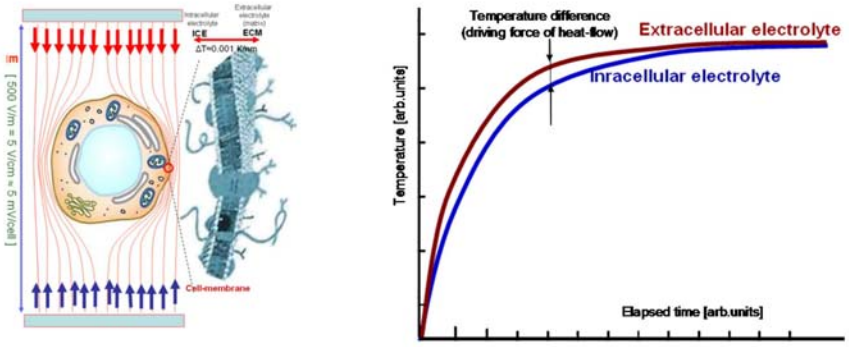

Figure 7. Oncothermia delivers its energy mainly into the extracellular electrolyte, creating a temperature gradient through the cellular membrane (a). The thermal gradient action due to the non-homogenous heating is active until the thermal equilibrium equalizes the temperature (b)

The cell killing needs energy, and afterwards the overall energy of the system would be decreased from a well ordered (bounded) state (which was in the case of the living cell) to a disordered chemical state with some broken chemical bonds. The transition from the ordered (chemically higher energy) state to the disordered (chemically lower state) arrangement of the well- known gap energy must be pumped. This gap-energy has different components. For hyperthermia, the heat energy gives the full energyconsumption, however, in oncothermia, a significant field effect takes part in the distortion mechanism [53].
This simple method allows easier cell-destruction by oncothermia, (see Figure 8.); similar to the wellknown catalytic reactions.

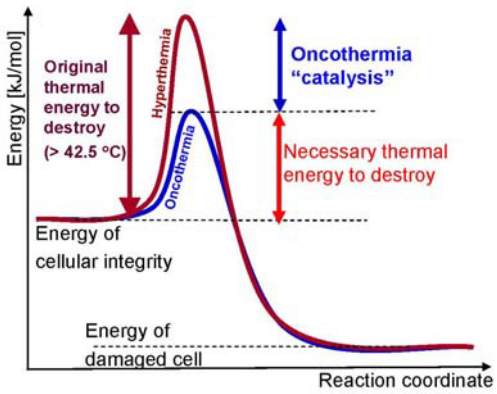

Figure 8. Oncothermia needs less thermal energy to make the same distortion as the classical hyperthermia does

The missing connections (adherent bonds, junctions) are selected not only by the dielectric properties of the cells, but they also affect the energy-absorption and the cellular protections against the energy overload. The absorbed energy by a healthy cell can easily be shared by the connections with the neighboring cells, damping the effect of the energy-overload. The malignant cells have no such possibility, the no network distribution could protect them from the energy-overload.

The large extracellular SAR makes not only thermal, but also the electric inhomogeneity in the tissue; the extracellular matrix has higher current density than the other electrolytes. The current density gradient is accompanied with the gradient of the electric field, which could reorient the high-dielectric constant proteins in the extracellular liquid. The orientation of these protein molecules would be constrained perpendicular on the membrane surface. By this effect, the lost adherent connections could be rebuilt between the malignant cells, which were indeed shown experimentally, [96]. This effect helps to suppress the metastatic dissemination and it also promotes the intercellular signals to activate the natural cellkilling mechanisms. Not only the heating makes the effect, but also the electric field itself has a strong synergy with this [97].

An important and unique specialty of oncothermia is the modulation of the carrier frequency. This timefractal pattern carried by the basic frequency distinguishes in similar way as the pathological evaluation does. The famous Adey-window was the first proof of the special modulation effects [98], [99], published in the early 1990s. The modulation of RF-carrier frequency started to be used [100], and became an important new method for cancer therapies [101]. Numerous clinical results show its efficacy [102], [103], [104], [105],[106], [107], and oncothermia has been applying it since the beginning. Biopsy specimens are evaluated by pattern-recognition of the experienced pathologist. One of the modern pattern-description is measuring the fractal dimension of the actual pattern. The malignancy has characteristic fractal dimension differences, the cancer has its own fractal structure, [108]. The analysis of fractal structures could even indicate the stage of the disease [109]. Careful fractal analysis can make predictive information, making a significant prognostic value, [110].

The fractals in patterns are accompanied by fractal dynamics. This new discipline is the "Fractal Physiology", ([111], [112], [113], [114]), which has a fundamental role in the structure of the healthy organism and is a basis of the self-similarity in biology, which is well-recognizable in the scaling behavior of the living objects, [115], [116], [117].The time fractal which characterizes the healthy tissue is the 1/f fractal-fluctuation. This is the modulation which we apply in the tumor-cure. The effect is simple: the system, which easily emits a frequency fluctuation can easily absorb it as well. So the applied modulation helps to localize the tumor-boarder, helps to "clear" the contours, and (most importantly) helps to select (self-focus) the energy-intake. Simply speaking, it works like the hammer on the drill, when you would like to make a hole in the concrete wall: it makes the action more effective. You may also switch off this modulation. Why? Because, you must not use the modulation in the sensitive organs (like the brain) from the very beginning. It causes head-ache and severe pain. In these cases from the third treatment the doctor starts the modulation in subsequently increased time, reaching the permanent modulation regime at the 8th treatment (if the patient has not complained). I propose to use the modulation in all the "usual" cases, but be careful when treating brain, spinal-cord, and head-and-neck cases. In non-tumorous applications the modulation has no role at all.

The fractal modulation, which is applied by oncothermia selects and re-establishes the apoptotic path-way functions. A day after oncothermia a definite difference can be detected between the anyway identical oncothermia treatments which are different only in the application of the modulation. Both

treatments cause the same effect immediately after the application, however a day later definite differences appear. The treated lesion by non-modulated signal started to re-grow, the ratio of dead-volume in the tumor decreased. At the same time the modulated treatment caused the opposite: the dead volume increased and in two days the complete tumor was almost destroyed after a single shot treatment reaching 42 °C in average in both the modulated and non-modulated cases.
Oncothermia selects the malignant cells and acts differently from the physiological homeostatic reactions (heat-flow on the membrane is supported by the electric field effects). It is natural, it is not against the homeostasis, physiology does not work against the action [118]. The main task is to direct the physiology in the standard way, and act on such normal line. The positive feedback loops (the avalanche effects), which may destroy the normal homeostatic equilibrium have to be stopped.

Results

Using the modern achievements of the physiology, oncothermia answers positively on the doubts about the conventional hyperthermia. The experimental and preclinical results are described in other articles presented in this conference [119], [120], [121], [122], [123], [124], [125], [126], so I summarize the clinical results only. Remarkable amount of retrospective and prospective clinical studies are available to indicate the oncothermia effect in humans [127], [128]. 62 studies were performed with altogether 3790 patients, from six countries (Hungary, Germany, Korea, China, Italy, Austria). The collection outlook is shown in Table 1, 2.

Study	Number of studies	Number of patients (n)	1st year survival (%)	Median overall survival (m)	Resposnding patients/ratio (%)	Median overall survival of responding patients (m)	Median overall survival of non-responding patients (m)
Brain studies	10	521	73.99	22.19	44.09	51.31	15.88
Pancreasa studies	6	184	47.04	11.02	53.05	28.09	7.58
Lung studies	5	636	64.76	15.79	25.73		
Bone	3	79		40.10	90.90		
Liver metastasis	7	267	86.00	18.06	80.00		
Colorectal	7	447			63.18	109.80	23.20
Gynecology (pelvic)	5	100	93.22	33.25	44.82	89.36	21.70
Breast	1	103	97.10	52.10	45.00	274.80	10.90
Esophagus	2	19	41.70	55.64	35.00	29.40	8.50
Somach study	1	68	58.90	14.40			
Kidney cancer	1	39	84.60	35.90	48.00	78.40	33.70
Urinary bladder cancer	1	18	85.00	36.50	73.00	42.00	22.60
Head and neck	1	64	92.20	26.10			
Soft tissue sarcoma	1	16	100.00	35.90	31.00	115.30	31.30
Prostate	3	135	88.90	38.80	72.00	53.40	7.60
SUM	54	2796			51.63		

Table 1. Collection of the studies (Phase II) made by oncothermia in combinantions with various conventional oncotherapies. (Data are wighted avarages of the study-results)

Miscelleonous Study	Number of patients (n)
Borreliosis	12
General oncology	277
TCM general oncology	306
Abdominal effusion	49
Peyronie's disease	25
Chronic pelvic inflammation	283
Asthma	7
Chronic bronhitis	35
SUM patients	994

Table 2. Collection of the miscellaneous studies made by oncothermia in combinantions with various other therapies

The survival time connected data, response rate connected data, the quality of life connected data, and tumor-maker connected data are collected in Tables 3, 4, 5 and 6., respectively.

Study	Number of patients	1st year survival (%)	Median overall survival (m)	Responding patients/ratio (%)	Median overall survival of responding patients (m)	Median overall survival of non-responding patients (m)	Reference
Brain gliomas	27	86.2	23.6	43	66.2	18.2	[129], [130]
Brain-glioma study Phase II,	140	71.7					[131], [132]
Astrocytoma	40		25.8	80	40.2	20.2	
Glioblastoma	92		16	73	21.*9	13.1	
Diffuse astrocytoma	8		52.9				
Glioma (WHO IV) Study, Phase II, prospective, two arms	45		15				[133], [134]
Passive arm	36	40	11				
Active arm	9	65	14.5	43	66.2	18.2	
Recurrent glioblastoma study, Phase II	19	68.0	21.8	59	32.6	12.4	[135]
Glioma study, Phase II,.	36	60.0					[136]
Astrocytoma	9		106				
Glioblastoma	27		20				
Glioma study, Phase II,.	179						[137]
Astrocytoma	53	100	103				
Glioblastoma	126	76	16				
Advanced, relapsed brain gliomas, Phase II	12		10	25			[138]
Advanced, relapsed brain gliomas, Phase II	24	55	12	25			[139]
Brain glioma WHO III-IV, Phase I, safety prospective	24						[140],[141], [142], [143]
Metastatic brain tumors study, Phase II	15	90.0	46.2	73	48.2	16.1	[138]
Head and neck study, Phase II.	64	92.2	26.1				**[133]**, [144]
Bone-metastases, monotherapy, Phase II	6	100	40.1				**[133]**, [144]
Refractory bone-metastases study, Phase II	11			90.9			[145]
Kidney cancer study, Phase II	39	84.6	35.9	48	78.4	33.7	**[133]**, [144]
Urinary bladder cancer study, Phase II	18	85.0	36.5	73	42.0	22.6	**[133]**
Non-small cell lung cancer meta-analysis.	311						[146]
Passive arm	53	26.5	14				
Active arm	258	67.0	15.8	21	53.4	18.1	
Non-advanced (WHO<III)	77		11	17			
Advanced (WHO≥III)	140		14.7	88			
Small-cell lung cancer	28						
Passive arm	9	29					[147]
Active arm	19	58					
Lung carcinoma study, Phase II	61	67.2	16.4				**[133]**, [148]
Breast cancers	103	97.1	52.1	45	274.8	10.9	**[133]**, [144]
Soft tissue sarcoma study, Phase II	16	100	35.9	31	115.3	31.3	**[133]**
Esophagus study, Phase II	12	41.7	28.5	35	29.4	8.5	**[133]**, [149]
Esophagus study, Phase II	7		6.8	100			[150]
Liver metastases from various origin, Phase II	25		20.5				[151]
Liver metastases from various origin, Comparative study, Phase II,	28						[145]
With radiotherapy	16			81			
With chemotherapy	8			38			
Monotherapy	4			25			
Liver metastasis form colorectal origin, Phase II,	80	86.0	24.1				[152]
Passive arm		53	11				
Active arm	80	91	24.1				
With chemotherapy	30	80	21.5				
Monotherapy	50	92	24.4				
Liver metastasis form colorectal origin, Phase II	15		23	80			[153]
Liver metastasis form colorectal origin, Phase II	22		28				[154]

Liver metastasis	29			86			
Liver metastasis form colorectal origin, Phase II	30		22				[155]
Pancreas tumor study, Phase II	26	46.2	11.6				[156]
Pancreas tumor study, Phase II,	107						
Passive arm	34		6.5				[148]
Active arm	73	52.1	9.93	58	25.5	8.4	
Pancreas tumor study, Phase II	30	31.0		41	34.4	5.6	[157], [158]
Pancreas tumor study, Phase II	42	52.4	12.3				[159]
Pancreas tumor study, Phase II	13	40.0	11.9				[160]
Stomach cancer study, Phase II	68	58.9	14.4				**[133]**
Colorectal cancer ()	218	84.9	28.5				**[133]**,
sigma	12			34.1			[144]
rectum	92			57.1	58	21	
colon	114			44.2	109.8	23.2	
Colon cancer study, Phase II, prospective, three arms, randomized	154						
Clifford TCM	53			75			[161] [162]
Monotherapy	50			81			
Combined therapy	51			91			
Rectum cancer study, Inoperable→operable, Phase II	7			71			[150]
Rectal cancer, non-operable, Phase II	65			96			[163]
Pelvic gynecological cancer studies, Phase II	74						
Cervix	38	86.8	27.6	25	63.5	20.9	[164]
Ovary	27	100	37.8	67	132.7	19.4	
Uterus	9	100	61.5	62	68.5	32.0	
Ovary, advanced, relapsed	26						[165]
Heavily pretreated	13		14.3				
Not heavily pretreated	13		27				
Prostate cancer study, Phase II	18	88.9	38.8	72	53.4	7.6	[149]

Table 3. Summary of the studies made by oncothermia treatment (End-points are survival connected)

Study	Number of patients	Complete remission (CR) [%]	Partial remission (PR) [%]	No change (NC) Stable disease (SD) [%]	Overall response rate (CR+PR+SD) [%]	Reference
Colorectal inoperable, liver metastasis	60					
CDDP	28	0	3.57	3.57	7.14	[166]
OXALI	32	0	15.63	15.63	31.25	
Ovary (relapsed, advanced epithelial	26					[165]
Heavily pretreated	13	0.00	23.08	38.46	61.54	
Not heavily pretreated	13	30.77	23.08	38.46	92.31	
General oncology	277		21.50	37.00	58.50	[167]
TCM general oncology	306					
Oncothermia + TCM	75	6.67	57.33	26.67	90.67	[168]
Oncothermia+TCM+i.v.CTx	65					
Passive arm	51	7.84	60.78	15.69	84.31	[168]
Active arm	14	14.29	64.28	21.43	100.00	

Oncothermia+TCM+bladder perfusion	37					
Passive arm	24	0	50	12.5	62.50	[168]
Active arm	13	7.69	53.85	30.77	92.31	
Oncothermia+TCM+RTx	42					
Passive arm	30	3.33	50	16.67	70.00	[168]
Active arm	12	8.33	66.67	16.67	91.67	
Abdominal effusion +oncothermia	49	4.08	53.06	16.38	73.52	[168]
Chronic pelvic inflammation	283					[169]
Passive arm	143					
Active arm	140	46.10	29.40	19.60	95.10	
Chronic bronhitis, TCM + oncothermia	35	30.00	24.30	25.70	80.00	[169]
Colon cancer study, , Phase II, prospective, three arms, randomized	154					[168]
Clifford TCM	53	5.7	28.3	18.9	52.90	
Monotherapy	50	10	26	26	62.00	
Combined therapy	51	13.7	45.1	23.5	82.30	
Colon operability	7	71			71.00	[170]
Prostatitis	72					[169]
Passive arm	36	16.70	27.80	19.40	63.90	
Active arm	36	41.70	36.10	22.20	100.00	
Prostate study	184	49.5	15.2	15.8	80.50	[171]
Prostate cancer (Kleef) (Gleason Score 2-6	16					[172]
Oncothermia +hormone therapy	8				50	
Oncothermia monotherapy	8				37.5	
Prostate cancer (Kleef) (Gleason Score 7-9	17					[172]
Oncothermia +hormone therapy	11				81.82	
Oncothermia monotherapy	6				33.33	
Peyronie's disease	25				100	
Pancreas	42		23.8	31	54.80	[159]
Pancreas	30	3.3	33.3	40	76.60	[157], [158]
Esophagus		8	50	42	100.00	[150]
CRC - liver	22	5		23	28	[154]
CRC liver	15		20	60	80.00	[153]
CRC liver Oxalyplatin	12				8.3	[155]
CRC liver cisplatin	18				27.8	
Advancer liver	28					[173]
Oncothermia + RTx	16		31	50	81	
Oncothermia + CTx	8		13	25	38	
Oncothermia monotherapy	4			25	25	
Brain	19		11	32	43	[135]
Asthma	7		75	10	85	[174]
Small-cell lung cancer (SCLC)	38		44.7	15.8	60.5	[175]
Benign tumors oncothermia+TCM	35	54.3	25.7		80.00	[169]

Table 4. Summary of the studies made by oncothermia treatment. (End-points are response connected)

Study	Number of patients	Pain-reduction [%]	increasing performances [%]	better overal QoL [%]	Reference
Colorectal inoperable, liver metastasis	60				
CDDP	28	17.86	39.29	57.14	[166]
OXALI	32	46.88	7.86	100.00	
Borreliosis	12		100.00	100.00	[176]
Abdominal effusion +oncothermia	49	88.88	73.91	85.70	[168]

Colon cancer study, , Phase II, prospective, three arms, randomized	154				[168]
Clifford TCM	53	37.7	13.73	58.49	
Monotherapy	50	36	23.53	60	
Combined therapy	51	58.8	62.75	86.28	
Prostate study	184				[171]
Prostate study	115		76.2	94.1	[177]
Colon operability	7		86	43	[170]
CRC liver	15				[153]
CRC liver Oxalyplatin	12	66.7		83.3	[155]
CRC liver cisplatin	18	11.1		27.8	

Table 5. Summary of the studies made by oncothermia treatment. (End-points are quality of life connected)

Study	Number of patients	Tumor-marker decrease [%]	References
Colorectal inoperable, liver metastasis	60		[166]
CDDP	28	14.29	
OXALI	32	37.50	
CRC liver Oxalyplatin	12	58.30	[155]
CRC liver cisplatin	18	5.60	

Table 6. Summary of the studies made by oncothermia treatment. (End-points are tumor-marker connected) Further clinical trials are in progress on advanced ovary, esophagus, breast, and pancreas tumors

Conclusion

Oncothermia is the cellular selective, highly effective nanoscopic heating of malignant cells. It is a feasible treatment for oncology in all phases of malignant diseases. This nanothermia application solved the uncontrolled controversies of the conventional hyperthermia in oncology. Numerous new ways of research can be initialized by the presently achieved results. Further basic research and clinical studies are in progress.

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References

[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. 2: Clinical Applications, Springer Verlag, Berlin, pp. 3-46

[2] Vaupel, P.W., Kelleher, D.K.: Metabolic status and reaction to heat of Normal and tumor tissue. In: Seegenschmiedt, M-H, Fessenden, P. Vernon, C.C. (eds) Thermo-radiotherapy and Thermo-chemiotherapy. Biology, physiology and physics, Vol 1, pp. 157-176, Springer Verlag, Berlin Heidelberg (1996)

[3] Busch W (1866) Uber den Einfluss welche heftigere Erysipeln zuweilig auf organisierte Neubildungenausuben. Vrh. Naturhist. Preuss Rhein Westphal 23:28-30

[4] Muller C (1912) Therapeutische Erfahrungen an 100 mit kombination von Rontgenstrahlen un Hochfrequenz, resp. Diathermie behandeleten bosartigen Neubildungen, Munchener Medizinische Wochenschrift 28:1546-1549

[5] Bauer KH, (1949) Das Krebsproblem: Einführung in die allgemeine Geschwulstlehre für Studierende, Ärzte und Naturwissenschaftler; Springer (pp.758)

[6] LeVeen HH, Wapnick S, Piccone V et al (1976) Tumor eradication by radiofrequency therapy. JAMA 235(20):2198-2200

[7] Short JG, Turner PF (1980) Physical Hyperthermia and Cancer Therapy. Proc. IEEE 68:133-142

[8] Storm FK, Morton DL, Kaiser LR (1982) Clinical radiofrequency hyperthermia: a review. Natl Cancer Inst Monogr 61:343-50

[9] Jo S, Sugahara T, Yamamoto I (1994) Clinical response of hyperthermia using heating equipment Thermotron-RF8 in Japan. Biomed. Eng. – Appl. Basis & Commun. 6:340-362

[10] Hiraki Y, Nakajo M (1998) Effectiveness of RF capacitive hyperthermia combined with radiotherapy for stages III and IV orohypopharyngeal cancers: a non-randomized comparison between thermoradiotherapy and radiotherapy. Int J Hyperthermia 14(6):593-594

[11] Harima Y, Nagata K, Harima K et al (2000) Bax and Bcl-2 Protein Expression following Radiation Therapy versus Radiation plus Thermoradiotherapy in Stage IIIB Cervical Carcinoma. Cancer 88(1):132-138
[12] Lee CK, Song CW, Rhee JG et al (1995) Clinical experience using 8 MHz radiofrequency capacitive hyperthermia in combination with radiotherapy: results of a phase I/II study. Int J Radiat Oncol Biol Phys 32(3):733-45
[13] Masunaga SI, Hiraoka M, Akuta K et al (1994) Phase I/II trial of preoperative thermoradiotherapy in the treatment of urinary bladder cancer. Int J Hyperthermia 10(1):31-40
[14] Weiss TF (1996) Cellular Biophysics. Bradford Book, MIT Press, Cambridge, MA, USA
[15] Rand RW, Snow HD, Brown WJ (1982) Thermomagnetic Surgery for Cancer. J Surg Res 33:177-183
[16] Matsuki H, Satoh T, Murakami K (1990) Local hyperthermia based on soft heating method utilizing temperature sensitive ferrite-rod. IEEE Trans Magn 26:1551-1553
[17] Gilchrist RK, Medal R, Shorey WD et al (1957) Selective inductive heating of lymph nodes. Ann Surg 146(4):596-606
[18] Nishide Oleson JR (1985) The role of magnetic inductiontechniques for producing hyperthermia. In: Anghileri LJ, Robert J (eds) Hyperthermia in Cancer Treatment, Vol. II. CRC Press, Boca Roton, Fla, USA. pp. 141-154
[19] Nishide SM, Ueno S (1993) A method of localized hyperthermia by using a figure-of-eight coil and short-circuit rings. Eng Med Biol Soc Proc 15th Ann Int Conf IEEE, pp 1447-1448
[20] Jojo M, Murakami A, Sato F et al (2001) Consideration of handy excitation apparatus for the inductive hyperthermia. IEEE Trans Magn 37(1):2944-2946
[21] Jordan A, Scholz R, Wust P, Faehling H., Felix R. (1999) Magnetic fluid hyperthermia (MFH): Caner treatment with AC magnetic field induced excitation of biocompatible supermegnetic nanoparticles, J. Magn. Magnetic Materials, 201:413-419
[22] Taylor LS (1978) Devices for microwave hyperthermia. In: Streffer C, vanBeuningen D, Dietzel F (eds) Cancer Therapy by Hyperthermia and Radiation, Urban & Schwarzenberg, Baltimore, Munich, pp 115-121
[23] Turner PF (1984) Regional hyperthermia with an annular phase array. IEEE Trans Biomed Eng BME-31:106-111
[24] Gonzalez-Gonzalez D, van Dijk JDP, Oldenburger F (1992) Results of combined treatment with radiation and hyperthermia in 111 patinets with large of deep-seated tumors. In: Germeg EW (ed) Hyperthermia Oncology, Vol. 1, Vol. 2. Ticson, AZ, USA, p 415
[25] Myerson RJ, Leybovich L, Emami B et al (1991) Pahntom studies and preliminary clinical experience with the BSD2000. Int J Hyperthermia 7(6):937-951
[26] Wust, P., Fahling, H., Wlodarczyk, W.: Antenna arrays in the sigma-eye applicator: Interactions and transforming networks. Med. Phys 28, 1793-1805 (2001)
[27] Wust P, Felix R, Deuflhard P (1999) Kunstliches Fieber gegen Krebs. Spektrum der Wissenschaft Dezember 78-84
[28] Issels R (1999) Hyperthermia combined with chemotherapy – biological rationale, clinical application, and treatment results. Onkologie 22(5):374-381
[29] Issels RD, Adbel-Rahman S, Wendtner C-M et al (2001) Neoadjuvant chemotherapy combined with regional hyperthermia (RHT) for locally advanced primary or recurrent high-risk adult soft-tissue sarcomas (STS) of adults: long-term results of a phase II study. European Journal of Cancer 37:1599-1608
[30] Wust P, Hildebrandt B, Sreenivasa G et al (2002) Hyperthermia in combined treatment of cancer. Lancet Oncol 3(8):487-497
[31] Shah SA, Jain RK, Finney PL (1983) Enhanced metastasis formation by combined hyperthermia and hyperglycemia in rats bearing Walker 256 carcinosarcoma. Cancer Lett. 19(3):317-23
[32] Nathanson SD, Nelson L, Anaya P, Havstad S, Hetzel FW (1991) Development of lymph node and pulmonary metastases after local irradiation and hyperthermia of footpad melanomas, Clinical and Experimental Metastasis 9:377-392
[33] Oliveira-Filho RS, Bevilacqua RG, Chammas R, (1997) Hyperthermia increases the metastatic potential of murine melanoma, Brazilian Journal of Medical and Biological Research, 30:941-945
[34] Storm FK (1993) What happened to hyperthermia and what is its current status in cancer treatment? J Surg Oncol 53:141-143
[35] Nielsen OS, Horsman M, Overgaard J (2001) A future of hyperthermia in cancer treatment? (Editorial Comment), European Journal of Cancer, 37:1587-1589
[36] Smythe WR, Mansfield PF (2003) Hyperthermia: has its time come? Ann Surg Oncol 10:210-212
[37] van der Zee J, Gonzalez Gonzalez D, van Rhoon GC et al (2000) Comparison of radiotherapy alone with radiotherapy plus hyperthermia in locally advanced pelvic tumors: a prospective, randomised, multicentre trial. Dutch Deep Hyperthermia Group. Lancet 355(9210):1119-1125
[38] Stauffer PR (2005) Evolving technology for thermal therapy of cancer. Int. J. Hyperthermia, 21:731-744
[39] Vasanthan A, Mitsumori M, Part JH et al (2005) Regional hyperthermia combined with radiotherapy for uterine cervical cancers: a multiinstitutional prospective randomized trial of the international atomic energy agency. Int. J. Rad. Oncol. Biol. Phys. 61:145-153
[40] Szasz A (2006) What is against the acceptance of hyperthermia? Die Naturheilkunde Forum-Medizine 83:3-7
[41] Gellermann J, Wlodarczyk W, Hildebrandt B, Ganter H, Nicolau A, Rau B, Tilly W, Fähling H, Nadobny J,

Felix R, Wust P, (2005) Noninvasive Magnetic Resonance Thermography of Recurrent Rectal Carcinoma in a 1.5 Tesla Hybrid System Cancer Res 65:5872-5880
[42] P Wust, B Hildebrandt, G Sreenivasa, B Rau, J Gellermann, H Riess, R Felixand PM Schlag (2002) Hyperthermia in combined treatment of cancer. Lancet Oncol 3(8):487-497
[43] Gellerman J: (2006) Nichtinvasive Thermometrie bei lokoregionaler Tiefenhyperthermie Invited presenation, Key-note, Hyperthermia Seminar Cologne,
[44] Wlodarczyk W. Wust P, Seebass M, Gellermann J, Nadobny J. (Charite University Clinic, Berlin); Recent advances in technology and technique of rf hyperthermia, www.ursi.org/Proceedings/ProcGA02/papers/p0835.pdf (accessed 2012 Aug.)
[45] P. Wust, J Gellermann Nichtinvasives MR-Monitoring von Weichteilsarkom en unter regionale Hyperthermie. http://ebookbrowse.com/wust-gellermann-20-5-08-pdf-d67803854
[46] J. Gellermann, B. Hildebrandt, R. Issels, H. Ganter, W. Wlodarczyk, V. Budach, R. Felix, P.-U. Tunn, P. Reichardt, and P. Wust, \Noninvasive magnetic resonance thermography of soft tissue sarcomas during regional hyperthermia: correlation with response and direct thermometry," Cancer 107(6), 1373{1382 (2006),
[47] Brochure of Thermotron RF-8. (Yamamoto Vinita, Osaka, Japan)
[48] Sugarbaker PH, Siugarbeker C, Chang D, (2001) Radiofrequency Hyperthermia Alone in the palliative treatment of mucinous Carcinomatosis: Optimizing and Monitoring Heat delivery, in book: Thermotherapy for Neoplasia, Inflammation, and Pain, Eds: Kosaka M, Sugahara T, Schmidt KL, Simon E, Springer-Verlag Tokyo, pp. 456-463
[49] Osinsky S, Ganul V, Protsyk V et al (2004) Local and regional hyperthermia in combined treatment of malignant tumors: 20 years experience in Ukraine, The Kadota Fund International Forum 2004, Awaji Japan, June 15-18
[50] van der Zee J, (2005) Presentation on Conference in Mumbai India (http://www.google.com/#sclient=psy&hl=en&site=&source=hp&q=%22van+der+Zee%22+Mumbai+ext:ppt&btnG=Google+Search&aq=&aqi=&aql=&oq=&pbx=1&bav=on.2,or.r_gc.r_pw.&fp=e7df6ea8d325b7b2, accessed Apr. 2011)
[51] Fatehi D, van der Zee J, van der Wal E et al (2006) Temperature data analysis for 22 patients with advanced cervical carcinoma treated in Rotterdam using radiotherapy, hyperthermia and chemotherapy: a reference point is needed. Int J Hyperthermia 22:353-363
[52] Szasz A, Szasz O, Szasz N (2001) Electro-hyperthermia: a new paradigm in cancer therapy. Deutsche Zeitschrift fur Onkologie 33:91-99
[53] Szasz A, Vincze Gy, Szasz O, Szasz N (2003) An energy analysis of extracellular hyperthermia. Magneto- and electrobiology, 22:103-115
[54] Andocs G et al (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
[55] Szasz A, Szasz N, Szasz O (2010) Oncothermia: Principles and Practices. Springer Verlag GmbH, Heidelberg
[56] Szasz A., “Quo vadis” oncologic hyperthermia? XXXI. Conference of the International Clinical Hyperthermia Society (ICHS), 12-14 October, 2012, Budapest, Hungary
[57] Otto Warburg - Nobel Lecture: The oxigen-transferring ferment of respiration, Nobel Lecture, December 10, 1931
[58] Mikac U, Demsar F, Beravs K, Sersa I: Magnetic Resonance Imaging of alternating electric currents, Magnetic Resonance Imaging 19:845-856, 2001
[59] Scholz B, Anderson R: On Electrical Impedance Scanning – Principles and Simulations, electromedica 68 – onco 2000, pp.35-44
[60] Muftuler TL, Hamamura MJ, Birgul O, Nalcioglu O: In Vivo MRI Electrical Impedance, Tomography (MREIT) of Tumors, Technology in Cancer Research and Treatment, 5(4):381-387, 2006
[61] Raff MC (1992) Social controls on cell survival and death. Nature 356(6368):397-400
[62] Damadian R (1971) Tumor detection by nuclear magnetic resonance. Science 171(3976):1151-1153
[63] Cope FW (1975) A review of the applications of solid state physics concepts to biological systems. J. Biol. Phys. 3(1):1-41
[64] Hazlewood CF, Nichols BL, Chamberlain NF (1969) Evidence for the existence of a minimum of two phases of ordered water in skeletal muscle. Nature 222(195):747–750
[65] Hazlewood CF, Chang DC, Medina D et al (1972) Distinction between the Preneoplastic and Neoplastic State of Murine Mammary Glands. Proc Natl Acad Sci USA 69(6):1478-1480
[66] Szentgyorgyi, A.: The living state and cancer. Physiological Chemistry and Physics 12, 99-110 (1980)
[67] Szentgyorgyi A (1968) Bioelectronics, A Study on Cellular Regulations, Defense and Cancer. Acad. Press, New York, London
[68] Szentgyorgyi A (1998) Electronic Biology and Cancer. Marcel Dekkerm New York
[69] Marino AA, Iliev IG, Schwalke MA, Gonzalez E, Marler KC, Flanagan CA (1994) Association between cell membrane potential and breast cancer. Tumour Biol, 15:82-89
[70] Cure JC (1995) On the electrical charateristics of cancer. II. International Congress of Electrochemical Treatment of Cancer. Jupiter, Florida

[71] Revici E (1961) Research in Pathophysiology as Basis Guided Chemotherapy, with Special Application to Cancer. Princeton, NJ. D. Van Nostrand Company
[72] Seeger PG, Wolz S (1990) Succesful Biological Contol of Cancer. Neuwieder Verlagsgesellschaft Gmbh
[73] Cure JC. (1991) Cancer an electrical phenomenon. Resonant 1(1)
[74] Nordenstrom BWE (1983) Biologically Closed Electric Circuits: Clinical experimental and theoretical evidence for an additional circulatory system. Nordic Medical Publications, Stockholm, Sweden
[75] Nordenstrom BWE (1998) Exploring BCEC-systems, (Biologically Closed Electric Circuits), Nordic Medical Publications. Stockholm, Sweden
[76] Pekar R (1996) Die Perkutane Galvano-Therapie bei Tumoren- Schwachstrombehandlung von zugänglichen Neoplasmen und ihre vitale Hybridisation in Theorie und Praxis. Verlag W. Maudrich, Vienna, Munich, Berlin
[77] Pekar R (2002) Die perkutane Bio-Elektrotherapie bei Tumoren (The percutaneous bio electrical therapy for tumors). Verlag W. Maudrich; Vienna – Munich - Berlin
[78] Song Y (1994) Electrochemical Therapy in the Treatment of Malignant Tumors on the Body Surface. The European Journal of Surgery Suppl. 574:S41-43, Scandinavian University Press
[79] Cole KS (1968) Membranes, ions and impulses. University of California Press, Berkeley, Los Angeles
[80] Pethig, R., Kell, D.B.: The passive electrical properties of biological systems: their significance in physiology, biophysics and biotechnology. Phys. Med. Biol. 32, 933-977 (1987)
[81] Pennock, B.E., Schwan, H.P.: Further observations on the electrical properties of heamoglobine bound water. J. Phys. Chem. 73, 2600-2610 (1969)
[82] Schwan, H.P.: Determination of biological impedances. In: Physical Techniques in Biological Research, vol. 6, pp 323-406, Academic Press, New York (1963)
[83] Pethig R (1984) Dielectric properties of biological materials: biophysical and medical application. IEEE Transactions on Electrical Insulation E1-19(5):453-474
[84] Pliquett F, Pliquett U (1992) Tissue impedance, measured by pulse deformation. In: Lahtinen T (ed) The 8th International Conference on Electrical Bio-impedance, University of Kuopio, Finnland, 28-31 July 1992, pp 179-181
[85] Loft SM et al (1992) Bioimpedance and cancer therapy. In: Lahtinen T (ed) The 8th International Conference on Electrical Bio-impedance, University of Kuopio, Finnland, 28-31 July 1992, pp 119- 121
[86] Pethig R (1984) Dielectric properties of biological materials: biophysical and medical application. IEEE Transactions on Electrical Insulation E1-19(5):453-474
[87] Barnes F, Kwon Y (2005) A theoretical Study of the Effects of RF Fields in the vicinity of membranes. Bioelectromagnetics 26: 118-124
[88] Groves JT, Boxer SG, McConnell MH (1997) Electric field-induced reorganization of two-component supported bilayer membranes. Proc. Natl. Acad. Sci. USA 94:13390-13395
[89] Groves JT, Boxer SG, McConnell HM (1998) Electric field-induced critical demixing in lipid bilayer membranes. Proc. Natl. Acad. Sci. USA 95:935-938
[90] de Pomerai DI et al (2002) Growth and maturation of the nematode Caenorhabditis elegans following exposure to weak microwave fields. Enzyme and Microbial Technology 30:73-79
[91] de Pomerai DI et al (2003) Microwave radiation can alter protein conformation without bulk heating. FEBS Letters 543:93-97
[92] Zhao M, Forrester JV, McCaig CD (1999) A small, physiological electric field orients cell division. Proc. Natl. Acad. Sci. USA 96:4942-4946
[93] Kirson ED et al (2004) Disruption of cancer cell replication by alternating electric fields. Cancer Research 64:3288-3295
[94] Szasz A, Andocs G, Szasz O, Vincze G, Koncz T, Balogh L (2009) Effects far from equilibrium in electromagnetic heating of tissues. Annual Congress of Bioelectromagnetic Society, BEMS, Davos, Switzerland, June 14-19, 2009
[95] Kotnik T, Miklavcic D (2000) Theoretical evaluation of the distributed power dissipation in biological cells exposed to electric field. Bioelectromagnetics, 21:385-394
[96] Andocs G, Meggyeshazy N (2010) Experimental oncothermia in nude mice xenograft tumor models 1t International Oncothermia Symposium, Cologne, November 22-23
[97] Andocs G, Szasz O, Renner H, Patonay L, Balogh L, Fonyad L, Jakab Cs, Szasz A: Synergy of temperature-dependent and field-dependent effects at HT29 xenograft study in nude mice. Electromagnetic Biology and Medicine, (submitted, 2008)
[98] Adey RW (1992) Collective properties of cell membranes. In Interaction Mechanisms of Low-level Electromagnetic Fields in Living Systems, Norden B, Ramel C (eds) pp 47–77. Oxford University Press: Oxford; New York
[99] Adey RW (1993) Biological Effects of Electromagnetic Fields, Journal of Cellular Biochemistry 51:410-416
[100] Foster KR, Repachoh MH (2004) Biological effects of Radiofrequency fields. Does modulation matter? Radiation Research 162:219-225
[101] Blackman CF (2012) Treating cancer with amplitude-modulated electromagnetic fields: a potential paradigm shift, again?, British Journal of Cancer 106, 241 – 242
[102] Barbault A, Costa FP, Bottger B, Munden RF, Bomholt F, Kuster N, Pasche B (2009) Amplitude-modulated

electromagnetic fields for the treatment of cancer: Discovery of tumor specific frequencies and assessment of a novel therapeutic approach. Jornal of Experimental&Clinical Cancer Research 28:51-61
[103] Zimmerman ZW, Pennison MJ, Brezovich I, Nengun Y, Yang CT, Ramaker R, Absher D, Myers RM, Kuster N, Costa FP, Barbault A, Pasche B (2012) Cancer cell proliferation is inhibited by specific modulation frequencies. Br J Cancer 106: 307–313
[104] Blackman CF, Elder JA, Weil CM, Benane SG, Eichinger DC, House DE. (1979) Induction of calcium ion efflux from brain tissue by radiofrequency radiation: effects of modulation-frequency and field strength. Radio Sci 14(6S): 93–98
[105] Blackman CF (2007) Evidence for Disruption by the modulating signal; BioInitiative Working Group
[106] Costa FP, AC de Oliveira, R Meirelles, MCC Machado, T Zanesco, R Surjan, MC Chammas, M de Souza Rocha, D Morgan, A Cantor, J Zimmerman, I Brezovich, N Kuster, A Barbault, Pasche B (2011) Treatment of advanced hepatocellular carcinoma with very low levels of amplitude-modulated electromagnetic fields, British Journal of Cancer 105:640 – 648
[107] Rakovic D, Djordjevic D (2012) Wear amplitude modulated RF EM fields for cancer treatment, Medical Review 4(1):089-092
[108] Ballerini L Franzen L, Fractal Analysis of Microscopic Images of Breast Tissue, http://www.wseas.us/elibrary/conferences/digest2003/papers/466-198.pdf (accessed Aug. 2012)
[109] Tambasco M, Magliocco AM, (2008) Relationship between tumor grade and computed architectural complexity in breast cancer specimens, Human Pathology, 39:740-746
[110] Delides et al (2005) Fractal Dimension as a Prognostic Factor for Laryngeal Carcinoma. Anticancer Research 25: 2141-2144
[111] Walleczek J (ed) (2000) Self-organized biological dynamics & nonlinear control. Cambridge Univ. Press, Cambridge
[112] Musha T, Sawada Y (eds) (1994) Physics of the living state, IOS Press, Amsterdam
[113] West BJ (1990) Fractal Physiology and Chaos in Medicine. World Scientific, Singapore, London
[114] Bassingthwaighte JB, Leibovitch LS, West BJ (1994) Fractal Physiology. Oxford Univ. Press, New York, Oxford
[115] West GB, Brown JH, Enquist BJ (1999) The Four Dimension of Life: Fractal Geometry and Allometric Scaling of Organisms. Science 284, 4 June
[116] Brown JH, West GB (2000) Scaling in Biology, SantaFe Institute studies in the sciences of complexity. Oxford University Press
[117] Calder WA (1996) Size, Function and Life History. Dover Publications Inc., Mineola, New York
[118] Hegyi G, Vincze G, Szasz A, (2012) On the dynamic equilibrium in homeostasis, Open Journal of Biophysics, 2:64-71
[119] Meggyeshazi N, Andocs G, Krenacs T. Programmed cell death induced by modulated electro-hyperthermia, XXXI. Conference of the International Clinical Hyperthermia Society (ICHS), 12-14 October, 2012, Budapest, Hungary
[120] Andocs G, Okamoto Y, Osaki T, Tsuka T, Imagawa T, Minami S, Balogh L, Meggyeshazi N, Szasz O. Oncothermia research at preclinical level, XXXI. Conference of the International Clinical Hyperthermia Society (ICHS), 12-14 October, 2012, Budapest, Hungary
[121] Kovago Cs. Proposed investigation on the possible synergic effect between high dose ascorbic acid application and oncothermia treatment, XXXI. Conference of the International Clinical Hyperthermia Society (ICHS), 12-14 October, 2012, Budapest, Hungary
[122] Fiorentini G, Dentico P, Turrisi G, Milandri C. Phase II. clinical study on relapsed malignant gliomas treated with electrohyperthermia, XXXI. Conference of the International Clinical Hyperthermia Society (ICHS), 12-14 October, 2012, Budapest, Hungary
[123] Wei Qin, Yasunori Akutsu, Yutaka Tamura, Andocs Garbor, Gulbostan Yusup, Xin Hu, Aki Komatsu-Akimoto, Isamu Hoshino, Yuka Isozaki, Naoki Akanuma and Hisahiro Matsubara; A novel dendritic cell therapy with oncothermotherapy mediated by abscopal effect, XXXI. Conference of the International Clinical Hyperthermia Society (ICHS), 12-14 October, 2012, Budapest, Hungary
[124] Jeoung T. S. Cases that respond to oncothermia monotherapy, XXXI. Conference of the International Clinical Hyperthermia Society (ICHS), 12-14 October, 2012, Budapest, Hungary
[125] Ballerini M, Baronzio G. H, Szasz O, Cassutti V. AndroTherm application for Peyrinie Disease (Phase I/II study). Additional seven cases. XXXI. Conference of the International Clinical Hyperthermia Society (ICHS), 12-14 October, 2012, Budapest, Hungary
[126] Seong Gi Min. A case of clinically complete remission of lung with hyperthermia and concurrent 5th-line chemotherapy in a dissaminated NSCLS patient, XXXI. Conference of the International Clinical Hyperthermia Society (ICHS), 12-14 October, 2012, Budapest, Hungary
[127] Dani A, Varkonyi A, Magyar T, Szasz A (2009) A retrospective study of 1180 cancer patients treated by oncothermia. Forum Hyperthermia in print (pp. 1-11).
[128] Szasz A (2009) Clinical studies evidences of modulated rf-conductive heating (mEHT) method. Paper presented at the 25th Annual Meeting of the European Society for Hyperthermic Oncology, ESHO, Verona, Italy, 4-6 June 2009
[129] Dani A, Varkonyi A: Electro-hyperthermia treatment of malignant brain tumors, Results of hyperthermia,

Seminar, St. IstvanUniversity, Aug. 26-27., 2003. (in Hungarian)
[130] Szasz A, Dani A, Varkonyi A (2004) Az elektro-hipertermia eredményei nagyszámú beteg retrospektív kiértékelésénektükrében Magyarországon. Magyar Klinikai Onkológiai Társaság III. Kongresszusa, Budapest, Hungary, 17–20 November 2004
[131] Sahinbas H, Baier JE, Groenemeyer DHW, Boecher E, Szasz A. (2006) Retrospective clinical study for advanced braingliomas by adjuvant oncothermia (electro-hyperthermia) treatment. www.gimtonline.de/uploads/media/Therapieergebnisse_Giloma_Studie_01.pdf
[132] Sahinbas H, Groenemeyer D, Boecher E, Szasz A (2007) Retrospective clinical study of adjuvant electrohyperthermia treatment for advanced braingliomas, Deutsche Zeitschrift fuer Onkologie, 39:154-160
[133] Szasz A, Szasz N, Szasz O (2010) Oncothermia – Principles and Practices, Springer, Heidelberg, Dodtrecht
[134] 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
[135] Douwes F, Douwes O, Migeod F, Grote C, Bogovic J (2006) Hyperthermia in combination with ACNU chemotherapy in the treatment of recurrent glioblastoma. http://www klinikstgeorg.de/pdf/hyperthermia_in_combination_with_ACNU_chemotherapy_in_the_treatment_of_recurrent_glioblastoma.pdf
[136] Hager ED et al (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
[137] Hager ED et al (2008) Prospective phase II trial for recurrent high-grade malignant gliomas with capacitive coupled low radiofrequency (LRF) deep hyperthermia. ASCO, J Clin ncol, Annual Meeting Proceedings (Post-Meeting Edition) 26:2047
[138] 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
[139] Baronzio G, Fiorentini G: Relapsed malignant gliomas treated with electro-hyperthermia: report of 24 casdes; ; 31st Conference of International Clinical Hyperthermia Society (ICHS), Budapest, Hungary, October 12-15, 2012
[140] Wismeth C et al (2006) Loco-regional hyperthermia in patients with progressive astrocytoma WHO III or glioblastoma WHO IV (RNOP-10) – a prospective single arm phase I/II study; EANO
[141] Hau P (2010) Transcranial electro-hyperthermia combined with alkylating chemotherapy in patients with relapsed high-grade gliomas: phase I clinical results. 1st International Oncothermia Symposium, 22-23 November, Cologne, Germany
[142] Wismeth C et al (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
[143] Wismeth C, Dudel C, Pascher C et al (2010) Transcranial electro-hyperthermia combined with alkylating chemotherapy in patients with relapsed high-grade gliomas – Phase I clinical results. J Neurooncol 98(3):395–405
[144] Szasz A et al (2005) Retrospective analysis of 1180 oncological patients treated by electrohyperthermia in Hungary. Jahreskongress der Deutschen Gesellschaft für Radioonkologie, DEGRO 11, Karlsruhe, 26–29 May 2005
[145] Aydin H et al (2003) Strahlen-Hyperthermie bei Lebermetastasen und bei therapieresistenten Knochenmetastasen. Hyperthermia Symposium, Cologne, Germany, 25–26. October
[146] Dani A, Varkonyi A, Magyar T, Szasz A. (2011) Clinical study for advanced non-small-cell lung cancer treated by oncothermia; Oncothermia Journal, 3:39-49
[147] Lee DY, Paik HC, Haam SJ: Hyperthermia in the patients with small cell lung cancer, 31st Conference of International Clinical Hyperthermia Society (ICHS), Budapest, Hungary, October 12-15, 2012
[148] Szasz A, Dani A et.al (2005) Retrospective analysis of 1180 oncological patients treated by electro-hyperthermia, DEGRO 11. Jahreskongress der Deutschen Gesellschaft für Radioonkologie, 26-29 Mai 2005, Kongresszentrum, Karlsruhe
[149] Dani A, Varkonyi A, Magyar T, Szasz A (2010) A retrospective study of 1180 cancer patients treated by oncothermia. Forum Hyperthermia accepted (pp. 1–11)
[150] Renner H. (2003) Simultane RadioThermoTherapie bzw. RadioChemoThermoTherapie, Hyperthermia Symposium, Cologne, Germany, October
[151] Szasz A (2009) Clinical studies evidences of modulated rf-conductive heating (mEHT) method. Paper presented at the 25th Annual Meeting of the European Society for Hyperthermic Oncology, ESHO, Verona, Italy, 4–6 June
[152] Hager ED et al (1999) Deep hyperthermia with radiofrequencies in patients with liver metastases from colorectal cancer. Anticancer Res 19(4C):3403–3408
[153] 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
[154] Ferrari VD, De Ponti S, Valcamonico F et al (2007) Deep electro-hyperthermia (EHY) with or without thermo-active agents in patients with advanced hepatic cell carcinoma: phase II study. J Clin Oncol 25:18S,

15168
[155] Fiorentini G, deGiorgi U, Turrisi G et al (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, France, Jan 30–Feb 2 2006
[156] Dani A, Varkonyi A, Nyiro I, Osvath M (2003) Clinical experience of electro-hyperthermia for advanced pancreatic tumors, Conference of European Society of Hyperthermic Oncology, (ESHO) Munich, 04-07. June
[157] Douwes F (2004) Thermo-Chemotherapie des fortgeschrittenen Pankreaskarzinoms. Ergebnisse einer klinischenAnwendungsstudie. http://www klinik-st-georg.de/publikationen/pdf/thermochemotherapie_des_fortgeschrittenen_pankreaskarzinoms htm
[158] Douwes F, Migeod F, Grote C (2006) Behandlung des fortgeschrittenen Pankreaskarzinoms mit regionaler Hyperthermie und einer Zytostase mit Mitomycin- C und 5-Fluorouracil/Folinsäure. http://www klinik-st-georg.de/pdf/pankreastherapien.pdf
[159] VeraMed Clinic, Meshede, Germany; Dr.M. Kalden, unpublished data, private information
[160] Renner H, Albrecht I (2007) Analyse der Überlebenszeiten von Patienten mit Pankreastumoren mit erfolgter kapazitativer Hyperthermiebehandlung. Internal Report of Praxis in Klinikum Nord, Nurnberg, Germany, (Prepared by: Mr. Mirko F; May 2007)
[161] Pang C (2012) Clinical Research on Integrative Treatment of Colon Carcinoma with Oncothermia and Clifford TCM Immune Booster. Oncothermia Journal 5:24-41
[162] Pang C (2010) Clinical Research on Integrative Treatment of Colon Carcinoma with Oncothermia and Clifford TCM Immune Booster. 1st International Oncothermia Symposium, 22-23 November, Cologne, Germany
[163] Vigvary Z, Mako E, Dank M (2002) Combined radiological and interventional treatment of non-operable rectal tumors and their liver metastases. Regional Radiology Conference, Maribor, Sept. 19–20, Slovenia
[164] Szasz A (2010) Oncothermia from laboratory to Clinical practice, 25th Annual Meeting of Korean Gynaecologic Oncology Group, Jeju, Korea, 29-30. April
[165] Fiorentini G, Montagnanai F, Vaira M, DeSimone M; Intraperitoneal cisplatine and paclitaxel combined with external capacitive hyperthermia in patients with relapsed epithelial ovarian cancer : a phase II clinical study, International Oncothermia Symposium, Cologne, Germany, Nov.22-23, 2010; http://www.iosymposium.com/oncothermia/2010/pres/Fiorentini2.PDF
[166] Fiorentini G, Milandri C, Dentico P, Giordani P, Catalano V, Bunkeila F: Deep electro-hyperthermia with radiofrequencies combined with thermoactive drugs in patients with liver metastases form colorectal cancer (CRC) a phase II clinical study; 31st Conference of International Clinical Hyperthermia Society (ICHS), Budapest, Hungary, October 12-15, 20122
[167] Lee Y. Outcome analysis and case reports of cancer patients, 31st Conference of International Clinical Hyperthermia Society (ICHS), Budapest, Hungary, October 12-15, 2012
[168] Pang Clifford L. K. Research progress of hyperthermia integrate with TCM in treating cancer, 31st Conference of International Clinical Hyperthermia Society (ICHS), Budapest, Hungary, October 12-15, 2012
[169] Lu Yimin, Deep Hyperthermia Combined with Traditional Chinese Medicine in Treating Benign Diseases in Clifford Hospital; 31st Conference of International Clinical Hyperthermia Society (ICHS), Budapest, Hungary, October 12-15, 2012
[170] Renner H. (2003) Simultane RadioThermoTherapie bzw.RadioChemoThermoTherapie, Hyperthermia Symposium, Cologne, Germany, October
[171] FR Douwes, S. Lieberman Radiofrequency Transurethral Hyperthermia and Complete Androgen Blockade; Journal of alternative and complementary therapies 7:149-157, 2002
[172] R. Kleef, Application of Transurethral Prostate Hyperthermia in benign and malign prostate hyperplasia and chronic prostatitis, 31st Conference of International Clinical Hyperthermia Society (ICHS), Budapest, Hungary, October 12-15, 2012
[173] Aydin H, et al. (2003) Strahlen-Hyperthermie bei Lebermetastasen und bei therapieresistenten Knochenmetastasen; Hyperthermia Symposium, Cologne, Germany, 25-26. October
[174] Babinszky E: Electrohyperthermia application in asthmatic diseases, Oncothermia Symposium, St.Istvan University, Godollo, Hungary 28. Aug., 2001
[175] Ham Seokjin Seojiwon, Kim Na Eun, Jung, Yiduyeon Hyperthermia in the patients with small cell lung cancer , Annual conference of Korean Oncothermia Study Group, Kagnam Severance hospital, Yonsei University, Seoul, Korea, Novenber 22, 2012
[176] Zais O. Lyme disease and oncothermia, 31st Conference of International Clinical Hyperthermia Society (ICHS), Budapest, Hungary, October 12-15, 2012
[177] Douwes F. R. Transurethral hyperthermia in prostate cancer: a ten year observation study, 31st Conference of International Clinical Hyperthermia Society (ICHS), Budapest, Hungary, October 12-15, 2012