Electro-hyperthermia: a new paradigm in cancer therapy

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Introduction

Use of hyperthermia for cancer therapy has been documented for thousands of years. The first provable application was attributed to Hippocrates for the healing of breast tumors. This healing technique revived around the end of the last century when it was possible to solve the problem of deep penetrating energy transfer. Many believe in oncological thermo-therapy, and many regard it as quackery. Fortunately, science is not the question of belief. In this article we tried to put an end to this mystification, and shortly summarise the actual scientific achievements and the open questions.

There are intensive discussions in scientific communities on the mechanism of oncological hyperthermia \cite{1}, and so not a surprise, that nowadays most oncological conferences deal with hyperthermia. There are increasing number of the relevant published books \cite{2} and periodicals \cite{3} as well as a large number of scientific articles are published in high ranked, good impact factor journals \cite{4}. The increasing number of applications and clinical trials at universities, clinics, hospitals and institutes prove the feasibility and applicability of clinical hyperthermia in cancer therapies. Some of the clinical trials are collected in the Table 1.

Hyperthermia for tumor treatment

The present situation of oncological hyperthermia is similar to that of the start of the radiology, when the ionising radiation was discovered: we know, this is a well applicable method, however, its exact dose, its contraindications and limits, the conditions of optimal treatment have not been clarified yet in details. Additional typical feature of hyperthermia as for any early-stage therapies is the lack of adequate treatment experience and long-range and comprehensive statistics.

Some well-established milestones can help to clarify in details the effects. These are briefly summarized in the following nine points below.

1. At the increase of temperature, the blood supply of tumor tissues decreases while that of healthy tissue increases \cite{24}. This is a certain selection to heating procedure: the healthy tissue temperature is regulated by the blood perfusion, while the tumor tissue could be effectively heated, without the thermo-regulation of the blood \cite{25}. The missing collectivity of the tumor tissue, its uncontrolled, relatively isolated growth works also against the heat equalisation.

2. As the metabolism of tumor tissues is more active than that of the healthy ones (their continuous proliferation requests a massive energy consumption), so their heat production is relatively high. Consequently, the tumor tissue is usually warmer than the healthy one \cite{26}. This additionally "trapped" heat enforces the tumor tissue to further increase their metabolism with a result of an additional increase of temperature. Consequently, this is a self-exciting, positive feedback process.

3. However, there is not enough oxygen available for the increased metabolism: resulting in hypoxia and anaerobe metabolism and produces acidosis \cite{27}. The cell destructive effect of acidosis is well-known.

4. Furthermore, the increased metabolism significantly decreases the ATP content of cells, therefore their metabolism gets into a self-restrictive phase resulting in increased cell destruction \cite{27}.

5. The DNS replication can be blocked by means of heat effect slowing down the reproduction processes \cite{28}.

6. The advantage of combining hyperthermia with the classical ionising-radiation is unambiguous. Principally, the heat affects the anyhow hypoxic tissues automatically as opposed to the ionising-radiation effecting on the tissues with good oxygen supply.

Summary

Hyperthermia is a rapidly developing treatment method in tumor therapy. The classical effect is based on well-focused energy absorption targeting the malignant tissue. The treatment temperature has been considered as the main technical parameter. Unfortunately, the heat-shock protein (HSP) synthesis may considerably suppress the treatment's efficiency, adapting cells to survive the shock.

Electro-hyperthermia heats up the targeted tissue by means of electricity, producing less HSP-synthesis in the cells than a usual hyperthermia process. The main idea is to keep the energy absorption in the extracellular liquid and, by heating it, increase the ion mobility, intensify the metabolic rate of the cells, and destroy the cell membrane before the heat-shock activates the intra-cellular HSP mechanisms.

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founded contra-indication for the actually required radiation-dose, the same result may be obtained by use of smaller radiation dose combined with hyperthermia. So, the hyperthermia well completes the ionising radiation. (Tabl. 2).

7. The applied drugs delivered into the tumor tissues through the blood circulation. Therefore the effect of chemotherapy is more reactive beside the arteries. In this respect the same area is affected by chemotreatment as in the case of ionising radiation. Consequently the chemotherapies (systemic, regional or local) can be complemented by hyperthermia (Table 3). Moreover, a robust synergy prefers the combination of chemotherapy with hyperthermia: the thermally increased metabolism means enhanced reaction rate of drugs, increased absorption of cytotoxines. In case, when the patient is not allowed to take big doses of drugs (for example at renal or liver insufficiency) the same results may be achieved by the combination of decreased chemo-dose and hyperthermia.

8. Significant pain-reduction and few side-effects are the specific advantages of hyperthermia [29]. These facts may contribute to a considerable improvement of life quality.

9. Hyperthermia enhances the efficiency of the immune-reactions as well [28].

There are considerable discussions on the relevant treatment parameters and optimization of the treatment. Most of the physicians are convinced: the single important factor is the temperature

Table 1. Some clinical trial on hyperthermia

<table>
<thead>
<tr>
<th>Localization</th>
<th>Trial phase</th>
<th>Radiodose [Gy]</th>
<th>Chemo</th>
<th>Response conventional alone [%]</th>
<th>Response with hyperthermia [%]</th>
<th>Number of patients</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head- and neck CA</td>
<td>Ph. I/II</td>
<td>70-77</td>
<td>no</td>
<td>92</td>
<td>27</td>
<td>[5]</td>
<td></td>
</tr>
<tr>
<td>Head- and neck CA</td>
<td>Ph. III</td>
<td>40</td>
<td></td>
<td>15</td>
<td>20</td>
<td>184</td>
<td>[6]</td>
</tr>
<tr>
<td>Malignant non-Hodgkin</td>
<td>Ph. III</td>
<td>61</td>
<td></td>
<td>64</td>
<td>172</td>
<td>[7]</td>
<td></td>
</tr>
<tr>
<td>Recurrent Breast CA</td>
<td>Ph. III</td>
<td></td>
<td></td>
<td>101</td>
<td></td>
<td>[8]</td>
<td></td>
</tr>
<tr>
<td>Cervical CA</td>
<td>Ph. III</td>
<td>10.8</td>
<td>no</td>
<td>52.5</td>
<td>83.3</td>
<td>37</td>
<td>[9]</td>
</tr>
<tr>
<td>Cervical CA</td>
<td>Ph. III</td>
<td></td>
<td>high brachy</td>
<td>50</td>
<td>80</td>
<td>40</td>
<td>[10]</td>
</tr>
<tr>
<td>Esophageal CA</td>
<td>Ph. III</td>
<td></td>
<td></td>
<td>24.2</td>
<td>50.4</td>
<td>66</td>
<td>[11]</td>
</tr>
<tr>
<td>Malignant melanoma</td>
<td></td>
<td>27</td>
<td></td>
<td>28</td>
<td>46</td>
<td>70</td>
<td>[12], [13]</td>
</tr>
<tr>
<td>Rectal CA</td>
<td>Ph. II</td>
<td>45</td>
<td>yes</td>
<td>60</td>
<td>40</td>
<td>[14]</td>
<td></td>
</tr>
<tr>
<td>Gastric Tumor</td>
<td></td>
<td>20</td>
<td></td>
<td>35.5</td>
<td>57.6</td>
<td>293</td>
<td>[15]</td>
</tr>
<tr>
<td>Breast CA (superf.)</td>
<td>Ph. III</td>
<td></td>
<td>no</td>
<td>41</td>
<td>61</td>
<td>148</td>
<td>[16]</td>
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<tr>
<td>Glioblastoma mf.</td>
<td>Ph.I/III</td>
<td>59.4</td>
<td>no</td>
<td>15</td>
<td>31</td>
<td>112</td>
<td>[17]</td>
</tr>
<tr>
<td>Soft tissue sarcoma</td>
<td>Ph II</td>
<td></td>
<td>no</td>
<td>59</td>
<td></td>
<td></td>
<td>[18]</td>
</tr>
<tr>
<td>Superfically located CA</td>
<td>Ph II</td>
<td></td>
<td>yes</td>
<td>62.6</td>
<td>82.8</td>
<td>92</td>
<td>[19]</td>
</tr>
<tr>
<td>Lung CA</td>
<td>Ph II</td>
<td></td>
<td>yes</td>
<td>31</td>
<td></td>
<td></td>
<td>[20]</td>
</tr>
<tr>
<td>Nonsmall Lung CA</td>
<td></td>
<td>yes</td>
<td>no</td>
<td>20</td>
<td>73</td>
<td>49</td>
<td>[21]</td>
</tr>
<tr>
<td>Esophageal CA</td>
<td></td>
<td>60</td>
<td></td>
<td>59</td>
<td>81.2</td>
<td>66</td>
<td>[22]</td>
</tr>
<tr>
<td>Bladder CA, Cervical CA, Rectal CA</td>
<td>Ph. III</td>
<td>65</td>
<td>no</td>
<td>39</td>
<td>55</td>
<td>358</td>
<td>[23]</td>
</tr>
</tbody>
</table>

Table 2. Completing of radio-effects by hyperthermia

<table>
<thead>
<tr>
<th>Effect/Method</th>
<th>Ionising radiation acts</th>
<th>Hyperthermia acts</th>
</tr>
</thead>
<tbody>
<tr>
<td>action of cell division</td>
<td>in M+G1 phase</td>
<td>in S phase</td>
</tr>
<tr>
<td>pH-dependence</td>
<td>in alkaline phase</td>
<td>in acidic regions</td>
</tr>
<tr>
<td>oxygenation</td>
<td>in well oxygenated</td>
<td>in hypoxic tissue</td>
</tr>
</tbody>
</table>

Table 3. Completing of chemo-effects by hyperthermia

<table>
<thead>
<tr>
<th>Effect/Method</th>
<th>Chemo-therapy</th>
<th>Hyperthermia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell division</td>
<td>acts in M+G1 phase</td>
<td>acts in S phase</td>
</tr>
<tr>
<td>Chemo penetration</td>
<td>low, due to high pressure</td>
<td>gained by electro osmosis</td>
</tr>
<tr>
<td>Chemo metabolism</td>
<td>weak</td>
<td>good</td>
</tr>
<tr>
<td>Place of activity</td>
<td>at arteries</td>
<td>far from arteries</td>
</tr>
<tr>
<td>Reaction rate</td>
<td>low</td>
<td>enhanced</td>
</tr>
</tbody>
</table>

Deutsche Zeitschrift für Onkologie, 2001; 33:91–99
itself. However, there are strong opposing opinions, which declare the delivered heat (absorbed energy) or applied field (electro-magnetic influence) are the primary effects. The temperature idea is well confirmed by the phase transition (at about 42.5°C) behavior [30], and the surprisingly good fitting of Arrhenius-plot to the experimental results [31].

On the other hand, there are no doubts about the strong heat-dose (energy absorption) dependence, which is shown by the treatment-time relevance in laboratory and clinical results [32]. Also the cell destruction results support the heat-centred idea: the results are not as good as expected in the case of the systemic heating, where the homogeneous temperature could be guaranteed. The loco-regional hyperthermia, which has a little lower and inhomogeneous temperature distribution, looks more successful.

More recently, numerous scientific theories concentrate on the vital significance of the thermally induced but basically non-thermal effects, [33]. They back up their view by the thermally and non-thermally generated chaperone proteins, which are most of the case heat-shock proteins (HSP) [34], Intensive research shown those proteins modify the stress tolerance their action in the programmed cell death (apoptosis) [35], and refer to the observed data of angiogenetic blockage, [36]. However, there are only a few studies about the field-effects in hyperthermia [37]. Nevertheless, in connection with the applied electromagnetic effects various technical questions arise: how to choose the various frequencies, which applicators and couplings could be the most effective for the energy transfer. The applied electromagnetic field in hyperthermia can affect the chaperones (stress-proteins) expression [38] and therefore it may have an intensive impact on the immune response of the tissue [39]. Considering the mainly completing application of the hyperthermia to classical oncological methods, the potentiality of the parallel chemo- or radiotherapy as well as pre- and post-operative synergy is also influenced by electromagnetic fields.

Hereafter in our present paper, we concentrate on the electromagnetic-effects of the electro-hyperthermia method.

**Chaperones production**

Chaperones (stress- or heat-shock-proteins) are highly conserved proteins, which are vital in almost every living cells and on their surfaces during their whole lifetime, regardless their stage in the evolution, [40]. Any kind of change the dynamic equilibrium of the cell life (environmental stresses, various pathogen processes, diseases, etc.) activate their synthesis [41]. Excretion of the chaperones is the stress-answer of the cells to accommodate themselves to the new challenges. As a consequence of the stressful life of malignant cells, the molecular chaperones are present in all the cancerous cells [42], [43], [44] to adapt the actual stress to help tumor-cell survival.

Moreover the shock-proteins are induced by every oncological treatment methods, which are devoted to eliminate the malignancy: after conventional hyperthermia [45], [46], after chemotherapy [47], after radiotherapy [48] or even after photo-therapy [49] was shown the intensive HSP synthesis. On the way of the stress adaptation the induction or over-expression of the stress proteins generally provide effective protection of the cell against apoptosis [50].

Furthermore, induction of various HSPs (HSP27, HSP70, HSP90) was observed in numerous metastases and the HSP90 homologue, GRP94 may act as a mediator of metastasis generation. HSP generally degrades the effect of the hyperthermia therapy because it may increase the tumor cell survival, and its massive induction may generate the tumor thermo-tolerance and in parallel drug- and radio-tolerance. Heat treatment can also lead to a multi-drug resistance [51].

Non-thermal effects (mainly field stresses) could also produce chaperone-synthesis [52]. The HSP manifestation in the biopsies could give a good clinical indication for the treatment response [35].

On the other hand, the chaperone HSP70 assists to freeze the actual dynamic equilibrium (the "status-quo") and so try to reestablish the cellular communication in the extra-cellular electrolyte [53]. It is shown that their expression on the cell-membrane gains the apoptotic signals and enhances the immune reactions, [53]. HSP participates in the activation of the p53 tumor-suppresser [54] and has been associated with the tumor-suppresser retinoblastoma protein [55].

Summarizing: stress-proteins have an important role in immunology, having two apparently opposite actions:

- their induction in the cell interior elongates the cell survival, the malignant cell with their assistance can be more resistant against apoptosis, anticancer drugs, immune attacks or even for hyperthermia, as well as may their massive presence increases the metastatic potential
- however, due to their helper capability in the extracellular matrix HSP could defeat the cancer-process, (helping reestablish the cell communications) even could be the basic of the anti-tumor vaccination [56] as well.

**Electro-hyperthermia**

Conventional hyperthermia applies heat to achieve curative influence. Starting from the methods used in ancient cultures, various procedures have been applied to deliver heat into the malignant area [57]; for example hot-bath (water or wax) or surface heaters (heat-blanket, heat-radiators), etc. The expected effect was mainly to change the pH-environment of the malignant tissue by the elevated temperature, based on the higher rate of metabolism, to cause acidosis and to unsettle the tumor from the state of equilibrium growth.

The delivered heat in the classical hyperthermia brings up some problems as well.
1. The already high heat shock protein concentration of tumor cells increased by the applied heat. The HSP-assisted adaptation mechanism degrades the efficacy of thermo-treatment and may generate a heat-, multi-drug- and radiation-resistance. Additional result is the HSP generating effect of magnetic field [58], which basically has to be avoided.

2. If the thermal effect is not adequately supplied and focused, this fact may increase the oxygen supply of tumor and therefore accelerate its fast increase. The not appropriate focusing may increase the risk of necrosis at the healthy tissues, and intensify the formation of metastasis.

3. Technically it is very difficult to control the heat transfer reproduction and stability therefore there is not any technical "success parameter", the retention and observation of which can be regarded as a reliable index of the successful treatment. The treatment of complex deforma
tion needs complex set of parameters therefore it is not probable that the successful treatment process can be controlled by one or two parameters.

Electro-hyperthermia is devoted to enhance the efficiency of conventional hyperthermia by additional, mainly thermally induced, non-thermal effects with the aim of suppressing the existing disadvantages of the classical thermal treatments. The electric field energy matching (capacitive coupling) has smaller penetration depth relative to the magnetic field, however, the absorbed energy is significantly increased.

On the other hand, the penetration depth of the radiative (antenna-array coupled) applications is only one third of that of the capacitive coupling. Moreover the electric field offers important selectivity factors to use. The dielectric constant is lower at ordered media than in the case of disordered ones typical to tumor areas. Therefore the electric coupling could select between the healthy and tumor-tissues. The energy absorption is more significant in the tumor. The suitably chosen frequency together with the resonant energy absorption of bound water can be used for further increase of selectivity.

The energy absorption at the applied frequency is proportional to the tissue conductivity and the square root of the dielectric constant of the targeted material. The conductivity in malignant tissue is about three times higher than that of normal tissue [59], [60]. Furthermore, the dielectric constant of the extracellular matrix at the applied frequency is also higher in the malignant tissue than in the healthy one [59], [61]. Change of the dielectric constant is even higher than the measurable value. Measurement indicates only the average of the dielectric constants in the measured volume as this tissue volume is far from homogeneous.

Non-homogeneity and disorder characterize the malignant growth observed by NMR measurements [62], [63], [64] and supported by theoretical considerations [65]. As a consequence of the bond-disorder in extracellular liquid, a high dielectric constant is to be expected at the applied frequency. As higher electric conductivity is accompanied by higher dielectric constant, the extracellular matrix in the malignant regions absorbs more energy than in healthy areas. In well-matched electro-
hyperthermia the above selective absorption works like a self-focusing mechanism. Further focusing effect can be derived from the coherent electric waves [66], [67], [68], with spontaneous breakdown of the polarization symmetries.

Other useful advantage is that the electric-coupled energy is primarily absorbed in the extracellular matrix as it is not able to penetrate through the membrane of high field strength (more than 1 million V/m) (Fig. 1). Therefore the directly heated area will be the extra-cellular liquid (Fig. 2).

The dominant extra-cellular action is the main advantage of the well-tuned (personalized and automatically matched) electro-hyperthermia. The cytoplasm of cell will be heated by heat diffusion through the membrane alone. The heat (from the absorbed energy) penetrates only into the cell by diffusion, which acts considerably slower in the cell than the direct heat does in the extra-cellular liquid [69]. Moreover, the suppressed primary intracellular field absorption reduces the non-thermal HSP synthesis.

The absorbed energy from the electric field effectively heats up the extra-cellular liquid. The temperature in the relatively small amount of extra-cellular electrolyte rapidly increases. Simple and approximate calculation can be done considering the volume ratio of the inter- and intra-cellular material from the measured average temperature of the treated mass. The speedy temperature rise at the membrane surface can rapidly reach the critical 43°C temperature to damage the membrane. Accompanying the absorbed energy induced heat-effects in the extra-cellular matrix, the applied radio-frequency electric
field stresses the highly polarized cell-membrane (from the extra-cellular side), and injures it in the same way as the heat does without prompt stress-protein synthesis in the cell interior.

Thermo-statically the membrane damage by heat is not effective. Even the opposite: the membrane potential itself changes by the temperature with slope -0.22 mV/K. The temperature equalization for the cell is also very quick, about 10 ms, not allowing long-time existing instability.

However, a tremendous heat-flow, 1500 nW/μm², permanently transmits through the membrane. It is well above the natural heat-flow by metabolism, which is only 20 nW/μm². Moreover, the temperature gradient (contrary to the quick equalization) is extremely high: 1 K/μm. The great heat-gradient in the cell allows (by the Onsager relations in non-equilibrium thermodynamics) distinct membrane currents because of its definite thermodynamic driving force. The forced current is also remarkable high: 150 pA/μm², which is dominantly Na⁺ influx into the cell. These currents, however, do not conform with the natural ion currents (which is 12 pA/μm², sodium efflux) and so their presence strongly decreases the dynamic stability of cell membrane.

In addition the thermal flux induces high pressure increase in the cell, reaching 1.32 MPa. The mutant cells have an enhanced concentration of phospholipids in their membranes [70], making it rigid. Consequently the actual pressure has a selective action to destroy the malignant cells.

Helping effect to destroy the malignant cell, that the diode-like behavior of the membrane absorbs increased energy from the RF current. This effect raises more the membrane temperature, which helps to gain the diode-absorption higher. This positive feedback gains further the membrane temperature.

These processes allow a very important effect: the cell membrane of malignant cells is damaged before the heat reaches the cell-nuclei to synthesise HSP to adapt the stress of invasion. However, membrane HSP is induced by the extreme heat at the membrane, which are supporting the apoptotic signals, to eliminate the malignant cells on the natural way.

Moreover, the elevated temperature distributes tumor-specific antigens on the surface of various tumor cells [71], and assists in their secretion in the extra-cellular fluid [72]. The extra-cellular HSP90-α has a stimulatory effect on the growth of some lymphoid cells [73]. Chaperones are involved in the antigen presentation in the extracellular liquid, and that mechanism increases the immune efficiency [74], [75].

Electro hyperthermia concentrates on the resolution of these problems by keeping in mind the importance of its known advantages as well. This target may be achieved by utilising two basic effects:

1. As far as possible, this method applies solely electric field not penetrating directly into the cytoplasm. This can be achieved by the application of largely lower field strength than that of the cell membrane potential. Additional feature is the applied special modulation. In this way the energy will be primarily absorbed in the extra-cellular matrix, and penetrate into the cell by thermal diffusion through the cell membrane resulting in the damage of membrane. Consequently, the HSP synthesis starts too late to exert its retroaction and because of the locking out of field there is not any extra HSP generation. As the HSP can be regarded as a very important component in the adaptation process this effect will decrease the chance of adaptation itself.

2. The applied frequency is able to the selective heating. Mainly the tumor cells and tissues without collective connections are heated. This effect is based on the one hand on the differences between the dielectric constant and dielectric loss, on the other hand on the selective absorption features of bound water.

**Completing the modalities**

Completing of the hyperthermia methods with classical oncological modalities is very promising (Fig. 3). Magnifying a blood-vessel in the tumor, its vicinity is relatively well oxygenated compare to the tissues more far from the vessel wall. Both the radio- and chemotherapies mainly act in the vessel neighbourhood, because of their higher activity in oxygen-rich tissues and the blood-delivered drug diffusion, respectively. The electro-hyperthermia targets
the relatively hypoxic tissues, with a distance from the blood vessels, so the completing in the targeted tissue areas is also effective.

Furthermore, the systemic hyperthermia completes the loco-regional electro-hyperthermia, because the systematically heated blood primarily targets the vessels neighbourhood (Fig. 3). With the development of the electro-hyperthermia devices we were able to achieve that the hyperthermia could be one of the new, safe and reproducible modalities in oncological treatments with an expectable serious success. By the application of electro-hyperthermia we believe that a new era has started in hyperthermia, and this method can be one of the successful oncological treatment methods in the near future.

**Electro-hyperthermia realization**

Equipment developed by capacitive coupling for electro-hyperthermia uses a well-tuned RF (13.56 MHz) electric field. Proper automatic matching (standing-wave-ratio, SWR ≤ 1.1) guarantees the standing electric effect. In consequence of the relatively low field-strength (max. 500 V/m) applied between the electrodes of the capacitor (applicators for the coupling to the treated body volume), there is a suppressed penetration to the membrane-protected (approx. 10⁶ V/m) cell interior.

The equipment developed is specially constructed applicators (the patient is the dielectric in a condenser, and so is a part of a well tuned resonant electric circuit) and carefully matched to have the best SWR. The machine does the matching and all the personalized tuning automatically and measures the electric parameters to keep the procedure controlled. To monitor the tissue temperature, the measured absorbed energy and the impedance is used. The matching of applicators is based on electro-dynamic calculations. Relatively little total power can be applied because of the good selectivity and well-focused heat absorption.

Well-cooled condenser surfaces (for capacitive coupling on the patients) are applied to avoid burning the surface and to make the application of higher treating power possible without any overheating risk; the heat-energy is not enough to heat-up the skin over 40 °C.

The system (under the commercial name EHY2000) has been installed at numerous Clinics and Hospitals in Europe with CE/MDD (European certificate for medical devices) certification.

The capacitive coupling is not only the possibility to deliver electric field into the extracellular matrix. DC electrodes (percutane) as well as AC catheters (up to few kHz, inserted into the body cavities) could be also applied to act in the above manner.

We developed a complete set of treatment devices taking into consideration the before-mentioned results. The difference of these devices may be observed only in the relationship between the thermal effect and electric field strength, in the locality of effect and in the application way of medical therapy. These treatment devices (in growing order of their target locality) are as follows:

- **Local electro-hyperthermia, ECT 2000**: Superficial, local, invasive method applicable for the treatment of malignant and benign tumours close to the skin. Basically the applied electric field strength dominates.
- **Interstitial electro-hyperthermia, ICT2000**: This invasive, superficial treatment is in the experimental phase and provides interstitial, explicitly thermal treatments applicable even in open surgery.
- **Intra-cavity electro-hyperthermia, PCT2000**: Cavity hyperthermia method serving for the treatment (by using adequate catheter, applicator) of different cavities (for example: prostate, rectum, food-pipe, vagina, cervix).
- **Loco-regional electro-hyperthermia, EHY2000**: Regional hyperthermia method for the treatment of the deep-seated, generally organic tumours (brain, liver, kidney, lung, pancreas, etc.). It is a non-invasive, universal, simply controllable device and does not require any complicated operation. Practically, there is not any contra-indicated treatment area.
- **Systemic (whole-body) hyperthermia, WBH2000**: This was developed for the whole-body hyperthermia and can be applied when the tumour is diffused, not localizable to one or some areas, and the only treatment way is the application of a systematic method.
These devices have been implemented and work successfully in a wide range of the clinical clinical practice.

Conclusions

The hyperthermia method is one of the effective treatment methods in oncology. It becomes a new modality of cancer treatments. Its update technique, the electro-hyperthermia is highly selective, gentle and safe, providing all the positive effects of the conventional hyperthermia with additional extra advantages. Its effectiveness is mainly based on the induced chaperone expression in the extra-cellular and suppressed shock-protein induction in intra-cellular region. Furthermore, the method induces the immune surveillance to attack the malignant cells by stimulus of HS990-u in extra-cellular electrolyte. The electro-hyperthermia extends the thermal treatment efficiency by non-thermal effects.

References


Zusammenfassung
