

# COLLECTION OF PUBLICATIONS OF ONCOTHERMIA

Oncotherm is keen to prepare studies and publish those in relevant scientific and medical literature. Our philosophy covers a complex interaction between the various levels of research and applications. The basic researches (theoretical considerations and in-silico models) are followed by the laboratory experiments in-vitro and in-vivo completed with preclinical and afterwards clinical studies. All steps are interacting not only with the next forward, but could affect the previous research steps for corrections, modifications and further developments. This complex research scheme allows us being ready to absorb the latest results from the worldwide literature and making own development on the available top of the state-of-art. Herewith we demonstrate our actual results with our publications from the laboratories until the clinical applications. Many PubMed registered publications are in harmony with the topics which are too technical or simple submitted to the not NCI registered publishers.

To be active for the training of our oncotherm community, we issue informative newsletters each month and we publish our Oncothermia Journal (ISSN 2191-6438) three times a year [1], sharing the hot topics in the oncothermia research field with our community members and with other interested researchers, too. There are quite a large number of publications in the journal which can be found on its website.

Oncothermia is the special method of Oncotherm Kft., became the trade-name of the treatment modality of modulated electro-hyperthermia (mEHT), and is nowadays mentioned as nanothermia in the relevant literature.

# Clinical studies

## Gliomas (advanced)

- A phase II clinical study on relapsed malignant gliomas treated with electro-hyperthermia [2],
- Transcranial electro-hyperthermia combined with alkylating chemotherapy in patients with relapsed high-grade gliomas [3],
- Clinical and economic evaluation of modulated electrohyperthermia concurrent to dose-dense temozolomide 21/28 days regimen in the treatment of recurrent glioblastoma: a retrospective analysis of a two-centre German cohort trial with systematic comparison and effect-to-treatment analysis [4],
- The induction of immunogenic cell death (ICD) during maintenance chemotherapy and subsequent multimodal immunotherapy for glioblastoma (GBM) [5],
- Glioblastoma multiforme Grad IV: Regionale Tiefenhyperthermie, Antiangiogenese mit Thalidomid, Hochdosis-Ascorbinsäureinfusionen und komplementäre Therapie [6],
- Prospective phase II trial for recurrent high-grade malignant gliomas with capacitive coupled low radiofrequency (LRF) deep hyperthermia [7],
- Retrospective clinical study of adjuvant electro-hyperthermia treatment for advanced brain-gliomas [8],
- Hyperthermia in combination with ACNU chemotherapy in the treatment of recurrent glioblastoma [9],
- The treatment of patients with high-grade malignant gliomas with RF-hyperthermia [10],
- Modulated electrohyperthermia in integrative cancer treatment for relapsed malignant glioblastoma and astrocytoma: Retrospective multicenter controlled study [11],
- Nanoparticles and nanothermia for malignant brain tumors, a suggestion of treatment for further investigation [12],

## **Gastrointestinal (advanced)**

- Deep hyperthermia with radiofrequencies in patients with liver metastases from colorectal cancer [13],
- Sorafenib and locoregional deep electro-hyperthermia in advanced hepatocellular carcinoma. A phase II study [14],

## **Lung**

- Current status of oncothermia therapy for lung cancer [15],
- Definitive radiotherapy with concurrent oncothermia for stage IIIB non-small-cell lung cancer: A case report [16],
- The safety and pharmacokinetics of high dose intravenous ascorbic acid synergy with modulated electrohyperthermia in Chinese patients with stage III-IV non-small cell lung cancer [17],
- The Outcome of the Chemotherapy and Oncothermia for Far Advanced Adenocarcinoma of the Lung: Case reports of four patients [18],
- Oncothermia with chemotherapy in the patients with Small Cell Lung Cancer [19],
- Clinical study for advanced non-small-cell lung-cancer treated by oncothermia [20],

## **Gynecology**

- Successful treatment of advanced ovarian cancer with thermochemotherapy and adjuvant immune therapy [21],
- Positive response of a primary leiomyosarcoma of the breast following salvage hyperthermia and pazopanib [22],
- Long-term survival of a breast cancer patient with extensive liver metastases upon immune and virotherapy: a case report [23],
- Treatment outcome analysis of chemotherapy combined with modulated electro-hyperthermia compared with chemotherapy alone for recurrent cervical cancer, following irradiation. [24],
- Oncothermia in HIV positive and negative locally advanced cervical cancer patients in South Africa [25],
- Treatment of advanced cervical cancer with complex chemoradio – hyperthermia [26],

- Update on phase III randomized clinical trial investigating the effects of the addition of electro-hyperthermia to chemoradio-therapy for cervical cancer patients in South Africa [27],
- Combined treatment with modulated electro-hyperthermia and an autophagy inhibitor effectively inhibit ovarian and cervical cancer growth [28],
- Efficacy of metabolically supported chemotherapy combined with ketogenic diet, hyperthermia, and hyperbaric oxygen therapy for stage IV triple-negative breast cancer [29],

## **Bone**

- Posttreatment histology and microcirculation status of osteogenic sarcoma after a neoadjuvant chemo- and radiotherapy in combination with local electromagnetic hyperthermia [30],
- Successful treatment of solitary bone metastasis of non-small cell lung cancer with combination of bevacizumab and hyperthermia [31],

## **Prostate**

- Long-term remission of prostate cancer with extensive bone metastases upon immuno- and virotherapy: A case report [32],
- Androtherm application for the Peyronie's Disease [33],
- Prostatakarzinom: Neue Aspekte für Diagnostik und Therapie [34],
- Für und Wider des Prostata-Karzinom-Screenings [35],
- Neue Studie heizt Diskussion über den Wert von PSA-Tests an [36],
- Sanfte Hilfen für die Prostata [37],
- Bestrahlung der Prostata erhöht Rektum-Ca-Risiko [38],
- Rebell gegen den Krebs. Biologische Intensivtherapie – Neue Hoffnung für Patienten? [39],
- Radiofrequency Transurethral Hyperthermia and complete Androgen Blockade. A Nonsurgical Approach to Treating Prostate Cancer [40],
- Transurethral hyperthermia in early stage prostate cancer [41],
- Adjuvante Radiotherapie: Welcher Patient mit Prostatakarzinom profitiert? [42],

- Hoffnung bei Prostata-Beschwerden. Die neue Therapie ohne Messer [43],
- Malignus és benignus prosztatadaganatok hyperthermiája [44],

### **Multiple**

- Bevacizumab-Based Chemotherapy Combined with Regional Deep Capacitive Hyperthermia in Metastatic Cancer Patients: A Pilot Study [45],

### **Temperature**

- The effect of modulated electro-hyperthermia on the pharmacokinetic properties of nefopam in healthy volunteers: A randomised, single-dose, crossover open-label study [46],
- Effect of modulated electrohyperthermia on the pharmacokinetics of oral transmucosal fentanyl citrate in healthy volunteers [47],
- The effect of modulated electro-hyperthermia on temperature and blood flow in human cervical carcinoma [48],

### **Immuno-oncology**

- Oncolytic Newcastle disease virus as a prospective anti-cancer therapy. A biologic agent with potential to break therapy resistance [49],
- Hypoxia Immunity, Metabolism and Hyperthermia [50],
- Stage IV Wilms tumor treated by Korean medicine, hyperthermia and thymosin- $\alpha$ 1: A case report [51],
- A new strategy of cancer immunotherapy combining hyperthermia/oncolytic virus pretreatment with specific autologous anti-tumor vaccination - a review [52],
- Role of HIF-1 $\alpha$  in response of tumors to a combination of hyperthermia and radiation in vivo [53],

### **Non-oncology**

- Oncothermia-Booster (Targeted Radiofrequency) Treatment – in Some Non-Oncological Diseases as Special Physiotherapy [54],
- Synergy between Oncothermia and Traditional Chinese Medicine [55],

- Low back pain – complex approach of treatment by different CAM modalities (Acupuncture and other type of dry-needling, “Targeted RF non invasive physiotherapy” for low back pain). [56],
- Newer application of oncothermia to non-malignant diseases such as Dupuytren's contracture of the hand and chronic lower back pain lasting more than 4 weeks [57],
- Fluctuations hypothesize the new explanation of meridians in living systems [58],

### **Toxicity**

- Tolerability of external electro-hyperthermia in the treatment of solid tumors [59],

### **Sarcoma**

- Results of oncothermia combined with operation, chemotherapy and radiation therapy for primary, recurrent and metastatic sarcoma [60],
- The results of combination of ifosfamid and locoregional hyperthermia (EHY 2000) in patients with advanced abdominal soft-tissue sarcoma after relapse of first line chemotherapy [61],

### **Pancreas**

- Second-line chemotherapy with gemcitabine and oxaliplatin in combination with loco-regional hyperthermia (EHY-2000) in patients with refractory metastatic pancreatic cancer - preliminary results of a prospective trial [62],
- Clinical study for advanced pancreas cancer treated by oncothermia [63],
- Behandlung des fortgeschrittenen Pankreaskarzinoms mit regionaler Hyperthermie und einer Zytostase mit Mitomycin- C und 5-Fluorouracil/ Folsäure [64],
- Thermochemotherapy of the advanced pancreas carcinoma [65],
- Thermo-Chemotherapie des fortgeschrittenen Pankreaskarzinoms. Ergebnisse einer klinischen Anwendungsstudie [66],
- Complex therapy of the not in sano respectable carcinoma of the pancreas – a pilot study [67],

### **Lyme-disease**

- Lyme Disease and Oncothermia [68],

### **Multiple**

- Oncothermia Application for Various Malignant Diseases [69],
- Oncothermia: Emerging Therapy in Oncology [70],

### **Liver**

- Lebermetastasen bei kolorektalen Karzinomen [71],
- Deep electro-hyperthermia (EHY) with or without thermo-active agents in patients with advanced hepatic cell carcinoma: phase II study [72],

### **Melanoma**

- Malignes Melanom Stadium IV: Anwendung von regionaler Tiefenhyperthermie, Tamoxifen, Interferon- $\alpha$  und komplementären Therapien [73],

### **WBH**

- Whole body hyperthermia combined with carboplatin/paclitaxel in patients with ovarian carcinoma – Phase-II-study [74],
- Whole-body hyperthermia in combination with platinum containing drugs in patients with recurrent ovarian cancer [75],

### **ECT**

- Electrochemical Therapy of Tumors [76],

## **Experimental studies**

### **Apoptosis**

- Electro-hyperthermia inhibits glioma tumorigenicity through the induction of E2F1-mediated apoptosis [77],

- Programmed cell death induced by modulated electro-hyperthermia [78],
- A modulált rádiófrekvenciás (RF) hyperthermia (oncothermia) apoptózis-indukáló hatása immunhiányos egér xenograft tumorokban [The apoptosis-inducing effect of modulated radio-frequency (RF) hyperthermia (oncothermia) on immun deficient mouse xenograft tumors] [79],
- Klinikai vizsgálatok és evidenciák a modulált vezetékes rádiófrekvenciás hyperthermia (oncothermia) alkalmazásában [Clinical trials and evidences of the application of modulated radio-frequency hyperthermia] [80],
- Modulated electrohyperthermia causes caspase independent programmed cell death in HT29 colon cancer xenografts [81],
- Modulated electro-hyperthermia induced programmed cell death in HT29 colorectal carcinoma xenograft [82],
- DNA fragmentation-driven tumor cell degradation induced by modulated electro-hyperthermia [83],

### **Apoptosis, DAMP, ICD**

- DNA fragmentation and caspase-independent programmed cell death by modulated electrohyperthermia [84],
- Upregulation of heat shock proteins and the promotion of damage-associated molecular pattern signals in a colorectal cancer model by modulated electrohyperthermia [85],

### **Abscopal effect**

- Modulated electro-hyperthermia enhances dendritic cell therapy through an abscopal effect in mice [86],
- Improving immunological tumor microenvironment using electro-hyperthermia followed by dendritic cell immunotherapy [87],
- Modulated electro-hyperthermia induced loco-regional and systemic tumor destruction in colorectal cancer allografts [88],

### **Strong synergy**

- Strong synergy of heat and modulated electro- magnetic field in tumor cell killing, Study of HT29 xenograft tumors in a nude mice model [89],

### **Human lymphoma U937 cells**

- Comparison of biological effects of modulated electro-hyperthermia and conventional heat treatment in human lymphoma U937 cells [90],

### **Septin**

- Electro-hyperthermia up-regulates tumour suppressor Septin 4 to induce apoptotic cell death in hepatocellular carcinoma [91],

### **In vitro comparison**

- In vitro comparison of conventional hyperthermia and modulated electro-hyperthermia [92],

### **Preclinical**

- Quantitative estimation of the equivalent radiation dose escalation using radiofrequency hyperthermia in mouse xenograft models of human lung cancer [93],
- Modulated electro-hyperthermia-enhanced liposomal drug uptake by cancer cells [94],
- Temperature increase induced by modulated electrohyperthermia (oncothermia<sup>®</sup>) in the anesthetized pig liver [95],
- Oncothermia research at preclinical level [96],
- Report of the pilot-study done for the proposed investigation on the possible synergic effect between high dose ascorbic acid application and oncothermia treatment [97],
- Oncothermia basic research at in vivo level. The first results in Japan [98],
- Diagnostic and therapeutic aspects of canine malignant melanoma. Part 2. Own experiences [99],
- Transferrin as a thermosensitizer in radiofrequency hyperthermia for cancer treatment [100],

## **Temperature**

- Temperature mapping and thermal dose calculation in combined radiation therapy and 13.56 MHz radiofrequency hyperthermia for tumor treatment [101],
- Messung der Temperaturverteilung am Modell der nicht perfundierten Schweineleber bei lokaler Hyperthermie mit Kurzwellen mit 13,56 MHz [102],
- Deep temperature measurements in oncothermia processes [103],

## **Protein kinase signaling**

- Mechanical regulation of mitogen-activated protein kinase signaling in articular cartilage [104],

## **mRNA**

- Early changes in mRNA and protein expression related to cancer treatment by modulated electro-hyperthermia [105],

## **Modulation**

- Modulation effect in oncothermia [106],
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## **Nanoheating**

- Nanoheating without Artificial Nanoparticles Part II. Experimental support of the nanoheating concept of the modulated electro-hyperthermia method, using U937 cell suspension model [108],

## **Monotherapy**

- Cases that respond to oncothermia monotherapy [109],

## **Chondrocyte biosynthesis**

- Electric field regulation of chondrocyte biosynthesis in agarose gel constructs [110]

# Theoretical & In silico studies

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## Field effects

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- Effect of Curl-Free Potentials on Water [114],
- Axial vector interaction with bio-systems [115],
- Oncothermia: Complex therapy by EM and fractal physiology [116],

## From lab

- Oncothermia treatment of cancer: from the laboratory to clinic [117],

## Oncothermia general

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## **Fractal noise**

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- Internal charge redistribution and currents in cancerous lesions [125],

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## **Membrane effects**

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- An energy analysis of extracellular hyperthermia [128],
- Water states in living systems. I. Structural aspects [129],

## **Dose**

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- Hyperthermia, a Modality in the Wings [131],
- Heating, efficacy and dose of local hyperthermia [132],
- Generalization of the thermal dose of hyperthermia in oncology [133],
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- Connections between the specific absorption rate and the local temperature [135],
- Hyperthermia dosing and depth of effect [136],
- Oncological hyperthermia: The correct dosing in clinical applications [137],

## **Water-structure**

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- Appearance of collectivity in two-dimensional cellular structures [143],
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- Why modulated electrohyperthermia (mEHT) destroys the rouleaux formation of erythrocytes? [150],
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- What is against the acceptance of hyperthermia? [181],
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- Energy absorption by the membrane rafts in the modulated electro-hyperthermia (mEHT) [227],

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- Studio dei meccanismi fisiopatologici dell'ipertermia oncologica e dell'oncothermia [251]
- Studies on modulated electrohyperthermia induced tumor cell death in a colorectal carcinoma model [252]
- Preclinical investigation on the biological effects of modulated electrohyperthermia [253]

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