Review of the Clinical Evidences of Modulated Electro-Hyperthermia (mEHT) Method

Magdolna Dank¹, Gyonygyver Szentmartoni¹, Gyula Peter Szigeti³, Carrie Minnaar², Marcell A. Szasz¹

¹ Cancer Center, Semmelweis University, Budapest, Hungary
² University of the Witwatersrand, Radiobiology, Johannesburg, South Africa
³ Institute of Human Physiology and Clinical Experimental Research, Semmelweis University, Budapest, Hungary

Presented at 36th ICHS, Budapest, 2018

Cite this article as:
Review of the Clinical Evidences of Modulated Electro-Hyperthermia (mEHT) Method

Magdolna Dank¹, Gyonygver Szentmartoni¹, Gyula Peter Szigeti³, Carrie Minnaar², Marcell A. Szasz¹

¹Cancer Center, Semmelweis University, Budapest, Hungary
²University of the Witwatersrand, Radiobiology, Johannesburg, South Africa
³Institute of Human Physiology and Clinical Experimental Research, Semmelweis University, Budapest, Hungary

Introduction
Modulated electro-hyperthermia (mEHT) is a new kind of hyperthermia in oncology. It is a further development of the conventional heating methods utilizing the capacitive setting. Thus, mEHT heats the malignant cells selectively instead of the complete isothermal heating of the tumor mass. The mEHT is widely accepted and applied, however, traditionally considered clinical indications are still in progress.

Aim
However, evidence is emerging, the proofs are of various evidence levels. Our overview in this presentation shows the clinical achievements, presenting the results of case presentations and clinical trials utilizing the mEHT method.

Methods
Our review on data presents the collected experience with capacitive hyperthermia treatments with the EHY-2000+ device (OncoTherm Ltd., Germany). The essence of case reports with primary and metastatic tumors treated with mEHT (grouped into carcinomas of organ systems, and sarcomas of bone and soft tissues), case presentations of immunotherapeutic combinations with mEHT and also clinical trials of various natures were summarized and evidence is provided.

Results
Based on clinical studies, the method mEHT is a feasible hyperthermia technology for oncological applications. Concomitant utilization of capacitive hyperthermia is now supported by the data from series of case reports up to randomized Phase III clinical trials.

Grant support: NVKP_16-1-2016-0042
Review of the Clinical Evidences of Modulated Electro-Hyperthermia (mEHT) Method

Dank M1, Szentmártoni Gy1, Szigeti GP3, Minnaar C2, Szasz AM1

(1) Cancer Center, Semmelweis University, Budapest, Hungary
(2) University of the Witwatersrand, Radiology, Johannesburg, South Africa
(3) Institute of Human Physiology and Clinical Experimental Research, Semmelweis University, Budapest, Hungary

Presenter’s name: Magdolna Dank MD, PhD
I have the Relationships with commercial interests:
Advisory Board: Lilly, Novartis, Pfizer
Research: Celltrion

CONFLICT OF INTEREST
mEHY treatment – easy to use and safe

The Stories

Case-reports
HCC

(61 y/m), Feb/2011, oncotherapy 24 times, Monotherapy

Investigator: Prof. Dr. Taesing Jeung
Institute: Department of Radiation Oncology, Kosin University, College of Medicine & Kosin University Gospel Hospital. Published: 31st ICBO Oct. Budapest, 2012

2 Ms before oncotherapy

Before oncotherapy

Oncotherapy 24 times

7 Ms after oncotherapy
Hepatocellular carcinoma (HCC)

Wang Y-S, Chi K-W, Shih-Kong Hospital, Taipei, Taiwan (11.2017; unpublished yet)

RT 46 Gy/23fx + Oncothermia x 5 (1/week) + Lipodox 20mg x3
Advanced hepatoma
Wang Y-S, Chi K-W, Shih-Kong Hospital, Taipei, Taiwan (11.2017; unpublished yet)

Dose-de-escalation is available (?)
Time of the infusion (?) 30 min or less? More?

Keytruda 50mg Q3W +
Lipodox 20mg Q2W + liver RT

10/16/2016 CT

05/25/2017 CT

Oncothermia for liver 15 times
Cholangiocarcinoma

Wang Y-S, Chi K-W, Shih-Kong Hospital, Taipei, Taiwan (11.2017; unpublished yet)

D1: Avastin 200MG
D2: Gemzar 500MG/M2,  D2~D4: 5-FU 500MG/M2
D5: Keytruda 150mg
RT (Cholangiocarcinoma): from 6/15 to 7/5, total 30Gy/15Fx.
Oncothermia: from 6/28 to 7/31, total 10 times
Brain metastasis from breast cancer

Investigator: Dr. Marwan Akasheh, Institute: Dar Alhefa' Tumors Treatment Center, Amman, Jordan, Patient: female 53 y.
mEHT Monotherapy

Before mEHT

After mEHT

Stomach Carcinoma, Stage IV; pts’ preference

Investigator: Prof. Dr. Taesing Jeung
Institute: Department of Radiation Oncology, Kosin University, College of Medicine & Kosin University Gospel Hospital. Patient: (54/y/F)
Published: 31st ICHO Oct. Budapest; 2012

No chemoTx, oncothermia monotherapy

Before oncothermia

Oncothermia 36 sessi...
Stomach Carcinoma, Stage IV; pts’ preference

**Investigator:** Prof. Dr. Taesig Jeung  
**Institute:** Department of Radiation Oncology, Kosin University, College of Medicine & Kosin University Gospel Hospital  
**Patient:** (54y/F)  
**Published:** 31st ICHO Oct. Budapest; 2012

Pancreatic cancer and liver metastasis

**Investigator:** Prof. Dr. Taesig Jeung  
**Institute:** Department of Radiation Oncology, Kosin University  
**Patient:** male 58 y;**  
**Therapy:** Oncothermia monotherapy, 42 times
Pancreatic cancer and liver metastasis

Investigator: Prof. Dr. Taesim Jeung; Institute: Department of Radiation Oncology, Kosin University, Patient: male 58 y., Therapy: Oncothermia monotherapy. 42 times

Recurrence of uterine sarcoma with peritoneal seedings

Investigator: Prof. Chi K-W, Shih-Kong Hospital, Taipei, Taiwan
Presented on 35th ICHS Conference, Guangzhou, China; Nov. 2017

refractory to chemotherapy and salvage with combined radiotherapy (45Gy/30fx)
Recurrent uterine sarcoma with peritoneal seedings

Investigator: Prof. Chi K-W, Shih-Kong Hospital, Taipei, Taiwan
Presented on 35th ICHS Conference, Guangzhou, China; Nov. 2017

Refractory to chemotherapy and salvage with combined radiotherapy (45Gy/30fx)

Before treatment

After treatment

Evolution of partners in the combo

Intratumoral ipilimumab 2.5 mg, i.v. nivolumab 50 mg and complementary with Oncothermia 6x times (1 time/week)

Abscopal effect

Investigator: YH Kim, Enha Womans University Mokdang Hospital, Seoul, Korea

Recurrent refracter progressive ovarian cancer (55y).

Op + multiple CTx

CTx + mEHT

4/11/2011

2/27/2012

Invasive adenocarcinoma of ovary (grade 2) (33y). Vaginal bleeding: G5P2

Metastatic non-small-cell lung cancer (55y).

Investigator: Prof. Dr. Seong Min Yoon,
Division of Hematology-Oncology, Department of Internal Medicine, Samsung Changwon Hospital, Sungkyunkwan University, Korea
Patient: 72y, male. Primary tumor: NSCLC, Size: 9.5 cm right middle lobe. Metastases: in sentinel and distant lymph-nodes. Tumor classification: cT2 cN2 M1, stage IIIb
Treatment: 28x1.7 Gy; support: 250 microgram Leukine and Oncothermia 6x
Clinical studies

Randomized study (n=6+6) for pharmacokinetics

mEHT (with Nefopam)  Lee SY, Kim M-G (2015); Int J Hyp, 31:869; 2015

![Graph showing blood concentration over time with and without mEHT effect]
Oncothermia is safe in heavily escalated dose too

Institute: Neurology Clinic, Regensburg University, Germany,
Investigators: Prof. Dr. U. Bogdahn & P.D.Dr. P.Hau

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of Patients</th>
<th>Chemotherapy (single close of a 6 week cycle)</th>
<th>Oncothermia (4 of 6 week cycle)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3 (6)</td>
<td>ACNU 90 mg/m2</td>
<td>Oncothermia 2x/week</td>
</tr>
<tr>
<td>2</td>
<td>3 (6)</td>
<td>ACNU 90 mg/m2</td>
<td>Oncothermia 3x/week</td>
</tr>
<tr>
<td>3</td>
<td>3 (6)</td>
<td>ACNU 90 mg/m2</td>
<td>Oncothermia 4x/week</td>
</tr>
<tr>
<td>4</td>
<td>3 (6)</td>
<td>ACNU 90 mg/m2</td>
<td>Oncothermia 5x/week</td>
</tr>
</tbody>
</table>

Advanced glioma (3rd & 4th line)
Dose escalation study (Ph1)
Number of patients: 24

No additional side effect of oncothermia was observed. (Side effects were not more than with Nimustine alone!)

Recurrent glioblastoma multiforme meta-analysis
Comparison by international trials

Glioblastoma multiforme (WHO IV) clinical trial-results

- Median survival (m)
  - MRC RT: 9.5 m
  - MRC RT+PCV: 9.5 m
  - SEER: 10.2 m
  - RTOG <50 y: 13.7 m
  - RTOG >50 y: 9.7 m
  - Oncothermia study <50 y: 16 m
  - Oncothermia study >50 y: 19 m
  - Oncothermia study: 14.4 m

Patient no

Clinical study


Relapsed gliomas survival (n=24)

Investigator: Prof. Dr. Fiorentini G.; Department of Oncology, Azienda Ospedaliera Marche Nord, Pesaro, Italy

Patients: n=25, 19 glioblastoma, 6 astrocytoma.

Pretreatments: all temozolomide & radiotherapy, 22/24 surgery.

Published: Fiorentini G. Oncothermia in brain tumors, invited lecture on 35th annual conference of the International Clinical Hyperthermia Society (ICHS), November 25-26, 2017, Guangzhou, China

Overall survival

Response | No. | %
--- | --- | ---
CR | 2 | 8
PR | 6 | 24
SD | 8 | 32
PD | 9 | 36

Clinical benefit in pretreated pts.
Glioblastoma multiform

Investigator: Dr. Gurdev Parmar
Institute: Integrated Health Clinic, Cancer care center, Fort Langley, British Columbia, Canada.
Published: 33rd ICHS Nidda, Germany; 2015

Overall survival

Probability Curve

\[ N = 18, \text{ Event}=12 \]

Survival Probability

Time from Diagnosis (years)

\[ \text{mEHT} \]

\[ \approx 3x \]

\[ \text{NCI USA database; (SEER)} \]

\[ \approx 5x \]

\[ 5 \text{ year survival} \]

Glioblastoma multiform – comparison of three survival results

Overall survivals

Investigator: Dr. Gurdev Parmar
Institute: Integrated Health Clinic, Cancer care center, Fort Langley, British Columbia, Canada.
Published: 33rd ICHS Nidda, Germany; 2015

Investigator: Dr. Dieter Hager
Institute: Biomed Clinic, Bad Bergzabern, Germany,

Investigator: Prof. Dr. Giannarina Fiorentini
Institute: Department of Onco-hematology, Azienda Ospedaliera Marche Nord, Pesaro, Italy.
Published: 35th ICHS Guangzhou, China; 2017

Oncothermia Journal, Volume 24, October 2018
Small-cell-lung-cancer (n=9+10) double arm prospective study 2L

Investigator: Professor DY Lee, Kangnam Severance Hospital, Yonsei University, Seoul, S.Korea

Prospective, monocenter, cohort double-arm study of chemotherapy with and without complementary oncothermia
Chemotherapy 1st line (n=28): Irinotecan (60 mg/m²), Cisplatin (60 mg/m²) three times.
Chemotherapy 2nd line (n=19): Etoposide, (110 mg/m²) Cisplatin (70 mg/m²)

Additional oncothermia in 2nd line combination (n=9): 150 Watt, 1,490.5 kJ, 60 min, every second day, with rise in temperature to 38.5°C–42.5°C. Electrode 30 cm diameter at least 12 sessions were in 1 cycle.

Overall survival

Metastatic lung

Investigator: Dr. Gurdev Parmar
Institute: Integrated Health Clinic, Cancer care center, Fort Langley, British Columbia, Canada.
Published: 33rd ICHS Nidda, Germany; 2015

Probability Curve

N=30, Event=21

Survival Probability

Median survival

≈2x

oncothermia

NCI USA database (SEER)

≈4x

5 years survival

Time from Diagnosis (Years)

IHC SEER
Recurrent cervix double arm (n=20+18), randomized study


Patients received conventional chemotherapy alone (n=20) compared to the combination to mEHT (n=18). Every patient had chemotherapy [paclitaxel + cisplatin (n=14), paclitaxel + carboplatin (n=10), cisplatin + 5-fluorouracil (n=12), cisplatin alone (n=2)]. Radiotherapy was not permitted in this cohort.

Both the local control and the overall survival are improved

Phase III randomised cervix trial (n=236) of mEHT with CHRT (interim results (n=160), follow-up is ongoing)

Investigators: Minnaar CA, Kotzen JA, Baeyens A. Charlotte Maxeke Johannesburg Academic Hospital, S.Africa. Aim: to enrol 236 participants with FIGO stage IIB (initial distal parametrium involvement) to IIB cervical cancer

Radiation: 25x2Gy external and 3x8Gy brachytherapy
Chemotherapy: 3x 80mg/m2 Cisplatin
mEHT (oncothermia), 2x 55min/week (4 weeks)

Local control
Until now: 6 month Local Disease Control 160 patients completed 6 month PET scan.

<table>
<thead>
<tr>
<th>Measured</th>
<th>Radio-chemotherapy</th>
<th>Gain by mEHT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>with mEHT</td>
<td>without mEHT</td>
</tr>
<tr>
<td>Complete response</td>
<td>33</td>
<td>47%</td>
</tr>
<tr>
<td>6 months survival (n=160)</td>
<td>70</td>
<td>91%</td>
</tr>
<tr>
<td>24 months survival (n=114)</td>
<td>55</td>
<td>78%</td>
</tr>
</tbody>
</table>

Survival time control

p=0.02, HR=0.33 (0.293 - 0.378)

Until now, both the local control and the overall survival are improved

Interim report by HIV infection (subgroups)
Non-resectable pancreatic adenocarcinoma

Investigator: Dr. Gurdev Parmar
Institute: Integrated Health Clinic, Cancer care center, Fort Langley, British Columbia, Canada.
Published: 33rd ICHS Nidda, Germany; 2015

Probability Curve

\[ N = 16, \text{Event} = 11 \]

Survival Probability

\[ \text{Median survival} \approx 1.3x \]

NCI USA database, SEER

\[ \text{oncothermia} \]

\[ \approx 4x \text{ survival} \]

Own study – real life data at Cancer Center, Semmelweis University (poster at ESHO 2018)
Non-resectable pancreatic adenocarcinoma

Preliminary results of an prospective trial with 2L GEMOX+mEHT (n=26)

Metastatic pancreatic cancer after 1L gemcitabine treatment. In the 2nd line the patients received gemcitabine 1000mg/m² IV and oxaliplatin 100mg/m² IV day 1 (GEMOX) combined with mEHT days 1, 3 and 5 all repeated at 14 days.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Enrolled (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>9</td>
</tr>
<tr>
<td>Female</td>
<td>17</td>
</tr>
<tr>
<td>ECOG Performance status</td>
<td>15</td>
</tr>
<tr>
<td>ECOG 1</td>
<td>5</td>
</tr>
<tr>
<td>ECOG 2</td>
<td>12</td>
</tr>
<tr>
<td>Stage at study entry</td>
<td></td>
</tr>
<tr>
<td>Liver metastasis</td>
<td>6</td>
</tr>
<tr>
<td>Lung metastasis</td>
<td>4</td>
</tr>
<tr>
<td>Lymph node metastasis</td>
<td>6</td>
</tr>
<tr>
<td>Peritoneal carcinomatous</td>
<td>4</td>
</tr>
<tr>
<td>Bone metastasis</td>
<td>6</td>
</tr>
<tr>
<td>Ascites/plural effusion</td>
<td>8</td>
</tr>
<tr>
<td>No. of prior chemotherapy cycles (GEMI - medium)</td>
<td>5.4</td>
</tr>
<tr>
<td>Histopathologic types</td>
<td></td>
</tr>
<tr>
<td>O Hered cell carcinoma</td>
<td>11</td>
</tr>
<tr>
<td>Acinar cell carcinoma</td>
<td>1</td>
</tr>
<tr>
<td>Papillary endocrine carcinoma</td>
<td>2</td>
</tr>
<tr>
<td>Signet ring carcinoma</td>
<td>1</td>
</tr>
<tr>
<td>Adenoid cystic carcinoma</td>
<td>1</td>
</tr>
<tr>
<td>Undifferentiated carcinoma</td>
<td>1</td>
</tr>
<tr>
<td>Prior regional therapy</td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>6</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>5</td>
</tr>
</tbody>
</table>

OS: 8.9 months
PFS: 3.9 months

SEER: median survival for all the pancreatic patients is 7.5 months

Advanced, metastatic pancreas study (n=99)

Retrospective, 2centers [A & B], single-arm clinical trial (n=99) for advanced pancreas cancer treated by oncothermia [1]. Most of the patients had distant mets (77.78%, A:23.88.7%, B:54.74%) and more than 40% had multiple mets. The trial includes a cohort of heavily pretreated patients (3+ lines), and due to the refractory or another fail of the conventional therapies, in this study mEHT was applied as monotherapy. The first and subsequent year survivals were: 1st: 50.5%, 2nd: 27.3%, 3rd: 15.2%, 4th: 8.1%, 5th: 3%. These values are significantly higher than the values from the large databases (SEER and Eurocare). The center B had the historical arm of conventional therapies (and palliation) of the cohort, with median overall survival 6.5 m, while the median in study arm was 12.7 m.

Comparison of pancreas studies

Metastatic pancreas CA 1y survival [%]

mEHT treatments

<table>
<thead>
<tr>
<th>NCI (USA) database</th>
<th>European database</th>
</tr>
</thead>
<tbody>
<tr>
<td>All stages, all lines, all patients</td>
<td>Advanced stages, multiple lines, dismaul patients, “gold standards” fall patients</td>
</tr>
</tbody>
</table>

Advanced, metastatic pancreas study (n=99)

Retrospective, 2centers [A & B], single-arm clinical trial (n=99) for advanced pancreas cancer treated by oncothermia [1]. Most of the patients had distant mets (77.78%, A:23.88.7%, B:54.74%) and more than 40% had multiple mets. The trial includes a cohort of heavily pretreated patients (3+ lines), and due to the refractory or another fail of the conventional therapies, in this study mEHT was applied as monotherapy. The first and subsequent year survivals were: 1st: 50.5%, 2nd: 27.3%, 3rd: 15.2%, 4th: 8.1%, 5th: 3%. These values are significantly higher than the values from the large databases (SEER and Eurocare). The center B had the historical arm of conventional therapies (and palliation) of the cohort, with median overall survival 6.5 m, while the median in study arm was 12.7 m.

Comparison of pancreas studies

Metastatic pancreas CA 1y survival [%]

mEHT treatments

<table>
<thead>
<tr>
<th>NCI (USA) database</th>
<th>European database</th>
</tr>
</thead>
<tbody>
<tr>
<td>All stages, all lines, all patients</td>
<td>Advanced stages, multiple lines, dismaul patients, “gold standards” fall patients</td>
</tr>
</tbody>
</table>

Advanced, metastatic pancreas study (n=99)

Retrospective, 2centers [A & B], single-arm clinical trial (n=99) for advanced pancreas cancer treated by oncothermia [1]. Most of the patients had distant mets (77.78%, A:23.88.7%, B:54.74%) and more than 40% had multiple mets. The trial includes a cohort of heavily pretreated patients (3+ lines), and due to the refractory or another fail of the conventional therapies, in this study mEHT was applied as monotherapy. The first and subsequent year survivals were: 1st: 50.5%, 2nd: 27.3%, 3rd: 15.2%, 4th: 8.1%, 5th: 3%. These values are significantly higher than the values from the large databases (SEER and Eurocare). The center B had the historical arm of conventional therapies (and palliation) of the cohort, with median overall survival 6.5 m, while the median in study arm was 12.7 m.

Comparison of pancreas studies

Metastatic pancreas CA 1y survival [%]

mEHT treatments

<table>
<thead>
<tr>
<th>NCI (USA) database</th>
<th>European database</th>
</tr>
</thead>
<tbody>
<tr>
<td>All stages, all lines, all patients</td>
<td>Advanced stages, multiple lines, dismaul patients, “gold standards” fall patients</td>
</tr>
</tbody>
</table>

Advanced, metastatic pancreas study (n=99)

Retrospective, 2centers [A & B], single-arm clinical trial (n=99) for advanced pancreas cancer treated by oncothermia [1]. Most of the patients had distant mets (77.78%, A:23.88.7%, B:54.74%) and more than 40% had multiple mets. The trial includes a cohort of heavily pretreated patients (3+ lines), and due to the refractory or another fail of the conventional therapies, in this study mEHT was applied as monotherapy. The first and subsequent year survivals were: 1st: 50.5%, 2nd: 27.3%, 3rd: 15.2%, 4th: 8.1%, 5th: 3%. These values are significantly higher than the values from the large databases (SEER and Eurocare). The center B had the historical arm of conventional therapies (and palliation) of the cohort, with median overall survival 6.5 m, while the median in study arm was 12.7 m.

Comparison of pancreas studies

Metastatic pancreas CA 1y survival [%]

mEHT treatments

<table>
<thead>
<tr>
<th>NCI (USA) database</th>
<th>European database</th>
</tr>
</thead>
<tbody>
<tr>
<td>All stages, all lines, all patients</td>
<td>Advanced stages, multiple lines, dismaul patients, “gold standards” fall patients</td>
</tr>
</tbody>
</table>

Advanced, metastatic pancreas study (n=99)

Retrospective, 2centers [A & B], single-arm clinical trial (n=99) for advanced pancreas cancer treated by oncothermia [1]. Most of the patients had distant mets (77.78%, A:23.88.7%, B:54.74%) and more than 40% had multiple mets. The trial includes a cohort of heavily pretreated patients (3+ lines), and due to the refractory or another fail of the conventional therapies, in this study mEHT was applied as monotherapy. The first and subsequent year survivals were: 1st: 50.5%, 2nd: 27.3%, 3rd: 15.2%, 4th: 8.1%, 5th: 3%. These values are significantly higher than the values from the large databases (SEER and Eurocare). The center B had the historical arm of conventional therapies (and palliation) of the cohort, with median overall survival 6.5 m, while the median in study arm was 12.7 m.

Comparison of pancreas studies

Metastatic pancreas CA 1y survival [%]

mEHT treatments

<table>
<thead>
<tr>
<th>NCI (USA) database</th>
<th>European database</th>
</tr>
</thead>
<tbody>
<tr>
<td>All stages, all lines, all patients</td>
<td>Advanced stages, multiple lines, dismaul patients, “gold standards” fall patients</td>
</tr>
</tbody>
</table>

Advanced, metastatic pancreas study (n=99)

Retrospective, 2centers [A & B], single-arm clinical trial (n=99) for advanced pancreas cancer treated by oncothermia [1]. Most of the patients had distant mets (77.78%, A:23.88.7%, B:54.74%) and more than 40% had multiple mets. The trial includes a cohort of heavily pretreated patients (3+ lines), and due to the refractory or another fail of the conventional therapies, in this study mEHT was applied as monotherapy. The first and subsequent year survivals were: 1st: 50.5%, 2nd: 27.3%, 3rd: 15.2%, 4th: 8.1%, 5th: 3%. These values are significantly higher than the values from the large databases (SEER and Eurocare). The center B had the historical arm of conventional therapies (and palliation) of the cohort, with median overall survival 6.5 m, while the median in study arm was 12.7 m.

Comparison of pancreas studies

Metastatic pancreas CA 1y survival [%]

mEHT treatments

<table>
<thead>
<tr>
<th>NCI (USA) database</th>
<th>European database</th>
</tr>
</thead>
<tbody>
<tr>
<td>All stages, all lines, all patients</td>
<td>Advanced stages, multiple lines, dismaul patients, “gold standards” fall patients</td>
</tr>
</tbody>
</table>

Advanced, metastatic pancreas study (n=99)

Retrospective, 2centers [A & B], single-arm clinical trial (n=99) for advanced pancreas cancer treated by oncothermia [1]. Most of the patients had distant mets (77.78%, A:23.88.7%, B:54.74%) and more than 40% had multiple mets. The trial includes a cohort of heavily pretreated patients (3+ lines), and due to the refractory or another fail of the conventional therapies, in this study mEHT was applied as monotherapy. The first and subsequent year survivals were: 1st: 50.5%, 2nd: 27.3%, 3rd: 15.2%, 4th: 8.1%, 5th: 3%. These values are significantly higher than the values from the large databases (SEER and Eurocare). The center B had the historical arm of conventional therapies (and palliation) of the cohort, with median overall survival 6.5 m, while the median in study arm was 12.7 m.
Oncothermia Journal, Volume 24, October 2018

Advanced, high risk recurrent sarcoma (n=24)

After recurrence of 1L CHT with doxorubicin 2L CHT (ifosfamide 3000mg/m², day 1–3) and mEHT (1 hour application with temperature between 41.5°C and 42°C, 3 days/week).

The response 88% (partial response 44% patients for 4 m; stable disease 44% patients for 4 m and 5% only 1 m).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Nr. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Performance status</td>
<td></td>
</tr>
<tr>
<td>ECOG 2</td>
<td>4</td>
</tr>
<tr>
<td>ECOG 3</td>
<td>14</td>
</tr>
<tr>
<td>Site of metastasis</td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>8</td>
</tr>
<tr>
<td>Liver</td>
<td>11</td>
</tr>
<tr>
<td>Bone</td>
<td>7</td>
</tr>
<tr>
<td>Hystopathologic Type</td>
<td></td>
</tr>
<tr>
<td>Fibrosarcoma</td>
<td>5</td>
</tr>
<tr>
<td>Malignant fibrous tumor</td>
<td>2</td>
</tr>
<tr>
<td>Synovial sarcoma</td>
<td>3</td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
<td>2</td>
</tr>
<tr>
<td>Epithelioid Sarcoma</td>
<td>2</td>
</tr>
<tr>
<td>Angiosarcoma</td>
<td>3</td>
</tr>
</tbody>
</table>


Metastatic colorectal cancer

Investigator: Dr. Gurdev Parmar
Institute: Integrated Health Clinic, Cancer care center, Fort Langley, British Columbia, Canada.
Published: 33rd ICHS Nidda, Germany; 2015

Probability Curve
N=54, Event=24

Median survival
≈4x

NCI USA database; (SEER)

Time from Diagnosis (Years)

IHC

SEER

5 years survival
≈3x
Advanced ovarian cancer

**Investigator:** Dr. Gurdev Parmar  
**Institute:** Integrated Health Clinic, Cancer care center; Fort Langley, British Columbia, Canada  
**Published:** 33rd ICHS Nidda, Germany; 2015

![Probability Curve](image1)

**Probability Curve**  
\( N=16, \text{ Event}=6 \)

- Survival Probability
- Median survival
- NCI USA database; (SEER)
- \( \approx 2x \)
- \( \approx 1.5x \)
- 5 years survival

Metastatic breast cancer

**Investigator:** Dr. Gurdev Parmar  
**Institute:** Integrated Health Clinic, Cancer care center; Fort Langley, British Columbia, Canada  
**Published:** 33rd ICHS Nidda, Germany; 2015

![Probability Curve](image2)

**Probability Curve**  
\( N=19, \text{ Event}=8 \)

- Survival Probability
- Median survival
- NCI USA database; (SEER)
- \( \approx 2x \)
- 5 years survival

---

*Oncothermia Journal, Volume 24, October 2018*  
31
Hepatocellular carcinoma Phase II study (n=21)

A mono-institutional uncontrolled phase II trial was conducted on advanced HCC patients. Treatment was continued until disease progression (PD) or unacceptable drug-related toxicities. Sorafenib treatment interruptions and dose reductions (initially 200 mg twice daily, then reduced to 200 mg once daily) were allowed for drug-related toxicity.

TCM + oncothermia for intraperitoneal chemoinfusion (IPCI)

**Investigator:** Prof. Dr. Clifford LK Pang  
**Institute:** Clifford Hospital, Panyu, Guangzhou, China  
**Patient:** 260 patients in two randomized groups: IPCI control and IPCI+TCM+mEHT  
**Diagnosis:** peritoneal carcinomatosis with malignant ascites (PCMA)
TCM + oncothermia for intraperitoneal chemoinfusion (IPCI)

**Investigator:** Prof. Dr. Clifford LK Pang  
**Institute:** Clifford Hospital, Panyu, Guangzhou, China

**Published:** CLK Pang et al (2017) Local modulated electro-hyperthermia in combination with traditional Chinese medicine vs. intraperitoneal chemoinfusion for the treatment of peritoneal carcinomatosis with malignant ascites: A phase II randomized trial. MOLECULAR AND CLINICAL ONCOLOGY 6: 723-732, 2017

**Patient:** 260 patients in two randomized groups: IPCI control and IPCI+TCM+mEHT

**Diagnosis:** peritoneal carcinomatosis with malignant ascites (PCMA)

---

**Comparison of efficacy**

- **Current trial:** 78% Objective Response Rate, 64% Control Group, 22% Relative Increase
- **Prior Art (averaged):** 75% Objective Response Rate, 48% Control Group, 55% Relative Increase
- **Yin J (2007)*:** 65% Objective Response Rate, 46% Control Group, 42% Relative Increase
- **Wang H (2015)*:** 71% Objective Response Rate, 60% Control Group, 44% Relative Increase
- **Li Z (2010):** 73% Objective Response Rate, 60% Control Group, 60% Relative Increase
- **Yu X (2007):** 77% Objective Response Rate, 67% Control Group, 58% Relative Increase
- **Chen F (2011):** 87% Objective Response Rate, 69% Control Group, 49% Relative Increase

---

**Immuncells**  
**Immflammation- hot and cold tumours**  
**CHT, targeted therapy and RT induces tumor-antigens**  
**Neoangiogenesis**

---

Oncothermia Journal, Volume 24, October 2018