Oncothermia and the paradigm shift in integrative oncology

Alfred J. Barich¹, Lazaros Daniilidis², Michael Marangos³, Aias Papastavrou⁴, John Vakalis⁵, Petros Kouridakis⁶, Valentini Natsouki⁷

¹President Hellenic Society for Integrative Oncology/AHEPA University Hospital/Oncothermia Center Thessaloniki
²Oncothermia Center Thessaloniki
³Radiation Oncologist/ Oncothermia Center Thessaloniki
⁴Oncothermia Center Athens
⁵Oncothermia Center Thessaloniki/ 424 Military Hospital
⁶Oncothermia Center Thessaloniki /424 Military Hospital
⁷Oncothermia Center Thessaloniki

Presented at 36th ICHS, Budapest, 2018

Cite this article as:
Barich AJ. (2018): Oncothermia and the paradigm shift in integrative oncology; Oncothermia Journal 24:373-404
Oncothermia and the paradigm shift in integrative oncology

Dr. Alfred J. Barich\textsuperscript{1}, Dr. Lazaros Daniilidis\textsuperscript{2}, Dr. Michael Marangos\textsuperscript{3}, Dr. Aias Papastavrou\textsuperscript{4}, Dr. John Vakalis\textsuperscript{5}, Dr. Petros Kouridakis\textsuperscript{6}, Dr. Valentini Natsouki\textsuperscript{7}

\textsuperscript{1}President Hellenic Society for Integrative Oncology/AHEPA University Hospital/Oncothermia Center Thessaloniki
\textsuperscript{2}Oncothermia Center Thessaloniki
\textsuperscript{3}Radiation Oncologist/ Oncothermia Center Thessaloniki
\textsuperscript{4}Oncothermia Center Athens
\textsuperscript{5}Oncothermia Center Thessaloniki/ 424 Military Hospital
\textsuperscript{6}Oncothermia Center Thessaloniki /424 Military Hospital
\textsuperscript{7}Oncothermia Center Thessaloniki

Abstract
We are all aware of the Phase III trials with chemotherapy and Hyperthermia vs chemotherapy alone and radiation therapy with Hyperthermia vs radiation therapy alone. All the trials indicated statistically significant differences (almost doubling of the response rates) in favor of the combination arm. The difference with Conventional vs Integrative approach to cancer treatment is similar to the differences of Conventional Hyperthermia and Oncothermia. What do we expect to see when we combine Integrative Oncology with Oncothermia? This is an analysis of the results of an Integrative Oncology Center, using an Oncothermia flagship in conjunction with a quantitative molecular/genetic analysis of the patients’ cancer cells. Integrative Oncology is forcing a paradigm shift in the treatment of cancer. When Oncothermia is included in the therapeutic strategy as a flagship for the integrative therapeutic strategy, the shift is intense. Patients are demanding more from their Oncologists beyond the Triad of Surgery, Radiation therapy and Chemotherapy. This is true for the other fields of Medicine as well, and this led to the creation of CAHCIM (Consortium of Academic Health Centers for Integrative Medicine). The demand of not only patients, but Medical Students as well, led to the formation of this Organization which has enlisted High profile institutions such as Harvard Univ., Dukes Univ., Mayo Clinic, Stanford University and many more. The establishment of CTCA (Cancer Treatment Centers of America) all across the USA, is proof of this Paradigm Shift. The combination of modulated electro Hyperthermia (Oncothermia) with a targeted approach to cancer cell kill based on molecular/genetic sensitivities, as well as targeting the cancer cell microenvironment by oxygen perfusion of the tissues (autologous ozonated blood transfusion) and tissue alkalynization (IV bicarbonate infusion) in conjunction with high doses of IV vitamin C has led to unprecedented increase of response rates and TTP. Herein we analyze these findings and propose multicentric randomized trials in centers that use mEHT.
HELLENIC SOCIETY FOR INTEGRATIVE ONCOLOGY
ONCOTHERMIA AND THE PARADIGM SHIFT IN INTEGRATIVE ONCOLOGY

Dr. Alfred J. Barich (President Hellenic Society for Integrative Oncology/AHEPA University Hospital/Oncothermia Center Thessaloniki)
Dr. Lazaros Daniilidis (Oncothermia Center Thessaloniki)
Dr. Michael Marangos (Radiation Oncologist/ Oncothermia Center Thessaloniki)
Dr. Aias Papastavrou (Oncothermia Center Athens/BIOMED AID)
Dr. John Vakalis (Oncothermia Center Thessaloniki/ 424 Military Hospital)
Dr. Petros Kouridakis (Oncothermia Center Thessaloniki/424 Military Hospital)
Dr. Valentini Natsouki (Oncothermia Center Thessaloniki)
We are all aware of the Phase III trials with chemotherapy and Hyperthermia vs chemotherapy alone and radiation therapy with Hyperthermia vs radiation therapy alone. All the trials indicated statistically significant differences (almost doubling of the response rates) in favor of the combination arm. The difference with Conventional vs Integrative approach to cancer treatment is similar to the differences of Conventional Hyperthermia and Oncothermia. What do we expect to see when we combine Integrative Oncology with Oncothermia? This is an analysis of the results of an Integrative Oncology Center, using an Oncothermia flagship in conjunction with a quantitative molecular/genetic analysis of the patients cancer cells. Integrative Oncology is forcing a paradigm shift in the treatment of cancer. When Oncothermia is included in the therapeutic strategy as a flagship for the integrative therapeutic strategy, the shift is intense. Patients are demanding more from their Oncologists beyond the Triad of Surgery, Radiation therapy and Chemotherapy. This is true for the other fields of Medicine as well, and this led to the creation of CAHCIM (Consortium of Academic Health Centers for Integrative Medicine). The demand of not only patients, but Medical Students as well, led to the formation of this Organization which has enlisted High profile institutions such as Harvard Univ., Dukes Univ., Mayo Clinic, Stanford University and many more. The establishment of CTCA (Cancer Treatment Centers of America) all across the USA, is proof of this Paradigm Shift. The combination of modulated electro Hyperthermia (Oncothermia) with a targeted approach to cancer cell kill based on molecular/genetic sensitivities, as well as targeting the cancer cell microenvironment by oxygen perfusion of the tissues (autologous ozonated blood transfusion) and tissue alkalinization (IV bicarbonate infusion) in conjunction with high doses of IV vitamin C has led to unprecedented increase of response rates and TTP. Herein we analyze these findings and propose multicentric randomized trials in centers that use mEHT.

CONFLICT OF INTEREST

THE AUTHORS HAVE CONFLICT OF INTEREST WITH THE PREVAILING MENTALITY OF CANCER TREATMENT
WHAT IS INTEGRATIVE ONCOLOGY AND HOW DOES ONCOTHERMIA CONTRIBUTE TO PATIENT RESPONSE

DR. ALFRED J. BARICH
Surgeon – Integrative Oncologist
President Hellenic Society for Integrative Oncology
Member of New York Academy of Sciences
Member of European Association for Cancer Research

A NEW START WITH A NEW PHILOSOPHY AND A NEW PARADIGM WILL PREVAIL

Calling... Time to Rethink Everything Everyone!
http://www.globalcreativitynetwork.net
PROGRESS COMES FROM THINKING OUT OF THE BOX

As the world thinks, so is its state of affairs.

QUESTION:

Is it satisfactory?

CURRENT MEDICINE FAVORS PROTOCOLS AND NOT PATIENTS

"We shall require a substantially new manner of thinking if mankind is to survive."

Albert Einstein
THINKING GLOBALLY AND ACTING LOCALLY

WE MUST LEARN FROM OUR MISTAKES
MEDICINE MUST BE INCLUSIVE AND NOT EXCLUSIVE
WE MUST COMPLEMENT NATURE AND NOT FIGHT IT

THE PATIENT MUST BE AT THE CENTER OF OUR FOCUS
A TOAST TO HEALTH

BOWL OF HYGEIA

The bowl with a snake coiled around it is called the bowl of Hygeia with the serpent of Epidaurus, and is a variant on the above. Hygeia was Aesculapius’s daughter and a Greek Goddess of health. Her symbol was a serpent drinking from a bowl. The vessel is usually depicted with a long stem and a shallow, wide bowl as seen here. It also is considered suitable for pharmacy. The bowl of Hygeia with serpent of Epidaurus shown here is the symbol for Hungarian pharmacists.

Integrative Medicine

Integrative medicine combines biomedical care with appropriate complementary therapies, to heal and preserve the health of the patient’s body, mind, and spirit.
It emphasizes the individual’s capacity for self-healing and offers an approach to care that is personalized, collaborative, and comprehensive. This approach is interdisciplinary and utilizes the skills of other health care disciplines and professionals through referral and consultation.

Consortium of Academic Health Centers for Integrative Medicine
CAHCIM Members

- Albert Einstein/Beth Israel
- Columbia University
- Duke University
- George Washington
- Georgetown
- Harvard
- Laval University
- Mayo Clinic
- OHSU
- Stanford University
- Yale University
- Wake Forest University
- University of Alberta
- University of CA/Irvine
- Thomas Jefferson
- UMDNJ
- University of Arizona
- University of Calgary
- University of Hawaii
- University of Washington
- University of California/LA
- University of California/SF
- University of Colorado
- University of Connecticut
- University of Kansas
- University of Maryland
- University of Massachusetts
- University of New Jersey
- University of New Mexico
- University of North Carolina-Chapel Hill
- University of Michigan
- University of Minnesota
- University of Pennsylvania
- University of Pittsburgh
- University of Texas-Galveston
- University of Vermont
- University of Wisconsin
INTEGRATIVE ONCOLOGY

.. Because humans are different!

The Phases of Integrative Oncology
THE STRUGGLE TO INTRODUCE NEW IDEAS AND APPROACHES IS OFTEN UNEVEN

TRYING TO INTRODUCE NEW IDEAS IS OFTEN MET WITH HOSTILITY
YOU CAN FIGHT PROGRESS AND CHANGE ... BUT YOU CAN’T STOP THEM!!
TODAY, BASTIONS OF CONSERVATIVISM ARE SLOWLY INCLUDING DEPARTMENTS OF INTEGRATIVE ONCOLOGY IN THEIR HOSPITALS...
THE PARADIGM SHIFT HAS BEGUN

COMPLEMENTARY AND ALTERNATIVE MEDICINE... LEADING TO INTEGRATIVE ONCOLOGY

• “Complementary and Alternative Medicine is a Group of Diverse Medical and Health Care Systems, Practices, and Products That are Not Presently Considered Part of Conventional Medicine”
National Center for Complementary and Alternative Medicine
ONCOTHERMIA – A STRATEGICAL ADDITION TO THE ARSENAL AGAINST CANCER

[Image of chess pieces on a board]

<table>
<thead>
<tr>
<th>Control (37°C)</th>
<th>Hyperthermia (42°C)</th>
<th>Oncothermia (42°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Immersion to waterbath)</td>
<td>(capacitiv coupling)</td>
<td></td>
</tr>
<tr>
<td>Cell count: 34,000/ml ± 2,700/ml</td>
<td>Cell count: 25,000/ml ± 2,000/ml</td>
<td>Cell count: 18,000/ml ± 1,450/ml</td>
</tr>
</tbody>
</table>
Overall, there is increasing evidence that CTCs reflect cancer progression in real time and that this information may be particularly helpful in the context of systemic therapies. In the future, CTC characterization is expected to contribute to guiding specific targeted therapies to a defined population of cancer patients within a certain therapeutic window—which is the hallmark of personalized medicine.
### COMPARATIVE METHODS

<table>
<thead>
<tr>
<th>Method of isolation</th>
<th>Beads Based Method</th>
<th>PCR Based Method</th>
<th>R.G.C.C.</th>
<th>Microscopy Based Method</th>
<th>Gradient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnetic beads (antibodies with iron particles)</td>
<td>Magnetic beads (antibodies with iron particles)</td>
<td>Magnetic beads (antibodies with iron particles)</td>
<td>Magnetic beads (antibodies with iron particles)</td>
<td>Magnetic beads (antibodies with iron particles)</td>
<td>Magnetic beads (antibodies with iron particles)</td>
</tr>
<tr>
<td>Enrichment method and isolation method</td>
<td>PCR based method which need to destroy the cells in order to identify one maker (mainly panCK or EpCAM)</td>
<td>Flow cytometric sorting with interrogation in droplets in ratio of drop-lot per cell (1:1)</td>
<td>Immobilizing cells on a slide and staining</td>
<td>The cells are isolated based on size</td>
<td></td>
</tr>
<tr>
<td>No cells</td>
<td>No cells</td>
<td>No cells</td>
<td>Purity is higher than 97.00% (isolation method)</td>
<td>The CTCs are simply stained not isolated</td>
<td></td>
</tr>
<tr>
<td>70-85%</td>
<td>Viability &gt; 99%</td>
<td>No viable cells remain</td>
<td>Questionable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inappropriate for further molecular analysis due to lymphocyte contamination</td>
<td>Limited for further molecular analysis</td>
<td>Appropriate for further molecular analysis since there is no noise</td>
<td>The CTCs are no longer visible</td>
<td>Not recommended for further studies</td>
<td></td>
</tr>
<tr>
<td>Based mainly in positive selection of CTCs in a few number of markers</td>
<td>Based on positive selection</td>
<td>Based on negative and positive selection in order to identify and secondly Immunophenotyping CTCs</td>
<td>Possible selection method</td>
<td>Based on size</td>
<td></td>
</tr>
<tr>
<td>Identification of heterogeneity of CTCs</td>
<td>Identification of heterogeneity of CTCs</td>
<td>The identification of heterogeneity of the selected marker(s)</td>
<td>Identification of heterogeneity of CTCs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Method only to enumerate CTCs</td>
<td>Method to enumerate CTCs and identify only very limited features of CTC</td>
<td>Method which allows to perform gene expression assays and determine features vital for therapy scheduling</td>
<td>A method for detection and enumeration only</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### ASSESSMENT REPORT

**R.G.C.C.-RESEARCH GENETIC CANCER CENTRE LTD**

**Assessment of the results:**

**Patient Name:** Mo Jungra Cota

**Type of cancer:** breast

**Physician:** Dr. Schilling Florian

**Stage:** N/A

**Risk of relapse:**
- CTC concentration
- Measured: isolated 9.4 cells/7.4 ml, SD ±: 0.3 cells
- Cut off point: 5 cells/7.5 ml

**Resistance markers:**
- MDR: 65%
- MRP: 35%
- LRP: 2%
- GST: 25%

**Metastases/angiogenesis risk related markers:**

<table>
<thead>
<tr>
<th>FUNCTION</th>
<th>CLINICAL RISK</th>
<th>MARKERS</th>
<th>RESULTS</th>
<th>OUTCOME</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migration-invasion</td>
<td>HIGH RISK</td>
<td>MDR, N</td>
<td>35%</td>
<td>LOW RISK</td>
</tr>
<tr>
<td>Angiogenesis</td>
<td>HIGH RISK</td>
<td>N22</td>
<td>35%</td>
<td>LOW RISK</td>
</tr>
<tr>
<td></td>
<td>HIGH RISK</td>
<td>FGFR</td>
<td>35%</td>
<td>LOW RISK</td>
</tr>
<tr>
<td></td>
<td>HIGH RISK</td>
<td>PIK3</td>
<td>35%</td>
<td>LOW RISK</td>
</tr>
</tbody>
</table>

**Proliferation related markers:**

<table>
<thead>
<tr>
<th>SIGNAL transduction pathways</th>
<th>CLINICAL RISK</th>
<th>MARKERS</th>
<th>RESULTS</th>
<th>OUTCOME</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ras/raf/MEK/Erk1-2</td>
<td>HIGH PROLIFERATIVE SIGNAL</td>
<td>35%</td>
<td>HIGH RISK</td>
<td></td>
</tr>
<tr>
<td>mTOR</td>
<td>HIGH PROLIFERATIVE SIGNAL</td>
<td>35%</td>
<td>HIGH RISK</td>
<td></td>
</tr>
<tr>
<td>EGF</td>
<td>HIGH PROLIFERATIVE SIGNAL</td>
<td>35%</td>
<td>HIGH RISK</td>
<td></td>
</tr>
<tr>
<td>TGF-β2</td>
<td>HIGH PROLIFERATIVE SIGNAL</td>
<td>35%</td>
<td>HIGH RISK</td>
<td></td>
</tr>
<tr>
<td>Estrogen Receptor</td>
<td>HORMONE INDEPENDENT</td>
<td>normal</td>
<td>LOW RISK</td>
<td></td>
</tr>
<tr>
<td>Progesterone Receptor</td>
<td>normal</td>
<td>LOW RISK</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NC1R4-A</td>
<td>normal</td>
<td>LOW RISK</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NC1R4-B</td>
<td>normal</td>
<td>LOW RISK</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cell cycle rate</td>
<td>RAPID</td>
<td>P16</td>
<td>35%</td>
<td>LOW RISK</td>
</tr>
<tr>
<td></td>
<td>RAPID</td>
<td>P53</td>
<td>35%</td>
<td>LOW RISK</td>
</tr>
</tbody>
</table>

**Resistance phenotype markers:**

<table>
<thead>
<tr>
<th>MARKERS</th>
<th>RESULTS</th>
<th>OUTCOME</th>
<th>PHENOTYPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>-normal</td>
<td>normal</td>
<td>LOW RISK</td>
<td></td>
</tr>
<tr>
<td>P66</td>
<td>normal</td>
<td>LOW RISK</td>
<td></td>
</tr>
<tr>
<td>Histone deacetylase</td>
<td>normal</td>
<td>LOW RISK</td>
<td>NON RESISTANT</td>
</tr>
</tbody>
</table>
**Radiotherapy/Hyperthermia sensitivity:**

<table>
<thead>
<tr>
<th>Marker</th>
<th>Result (%)</th>
<th>Clinical outcome per marker</th>
<th>Clinical outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSP90</td>
<td>-35%</td>
<td>SENSITIVE</td>
<td>SENSITIVE</td>
</tr>
<tr>
<td>HSP72</td>
<td>-10%</td>
<td>SENSITIVE</td>
<td></td>
</tr>
<tr>
<td>HSP27</td>
<td>-25%</td>
<td>SENSITIVE</td>
<td></td>
</tr>
</tbody>
</table>

**Follow-up options:**

<table>
<thead>
<tr>
<th>YES</th>
<th>✓</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td></td>
</tr>
</tbody>
</table>

Time interval (when)

<table>
<thead>
<tr>
<th>After 3 months</th>
<th>After 6 months</th>
<th>After 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Steps of therapy**

1. Bring down resistance
2. Introduce cytotoxic procedures
3. Take care of the immune system
RESISTANCE

Antisense
Metabolic inhibitors
KD
HDS
Quercetin
Piperin

CYTOTOXIC PROCEDURES

IPT
TACE
TACP
Biological substances

IMMUNOTHERAPY

DC
MOAB
GcMAF

RGCC/ BIOMED AID

RGCC technology enables the application of Integrative Oncology to our patients, giving them completely Targeted Therapeutic Strategy Options

Integrative Oncology without RGCC molecular profile places us in the position of Conventional Oncology (giving our patients therapeutic options based soley on STATISTICS but never knowing before hand on which side of the statistics they will be...).

RGCC technology is revolutionizing the practice of Oncology and BIOMED AID enables application of advanced Biotechnology.
CONCLUSIONS

THERE IS A PARADIGM SHIFT IN CANCER RESEARCH EMPHASIS IS BEING PLACED ON TARGETED THERAPIES
HYPERTHERMIA IS GAINING GROUND IN THE MAJORITY OF PUBLISHED STUDIES AS WELL AS CELL THERAPIES WITH DENDRITIC CELLS

ONGOING STUDIES FOCUS ON COMBINED MODALITY TREATMENTS INCLUDING COMBINATIONS OF CONVENTIONAL RT WITH HT AND CT WITH HT
LIQUID BIOPSIES GIVING US FULL MOLECULAR PROFILES OF CANCER CELLS AND EXPOSING THEIR RESISTANCE MECHANISMS AS WELL AS THEIR SENSITIVITIES HAVE MADE THE FLEETING IMAGE OF COMPLETELY TARGETED THERAPIES A REALITY. MORE AND MORE RESEARCH INTO BIOLOGICAL AND NATURAL AGENTS HAVE ENABLED LESS TOXIC APPROACHES.

Vitamin C and Hyperthermia

Enhancement of radical intensity and cytotoxic activity of ascorbate by hyperthermia.
The combination of hyperthermia and ascorbate treatment might produce higher antitumor activity.
Oncothermia Studies at Universities II

Phase I/II studies at Roswell Park Cancer Institute Buffalo, E Repasky, W Kraybill
Phase 1· Study of Fever-Range Whole-Body Hyperthermia in Patients with Advanced Solid Tumours
⇒ Int J Hyperthermia, 2002, VOL.18, NO.3
Phase 1· Study of Doxil with Long Term Low Level WBH
⇒ Abstract STM 2007

Phase I/II studies at Univ. of Texas, Medical School at Houston, JM Bull
FR-WBH + Cisplatin (CIS) + Gemcitabine (GEM) + Metronomic, Low-Dose Interferon-alpha
CIS 24h before FR WBH/GEM
Running protocol with various tumor entities, mainly pancreatic cancer
⇒ Int J Hyperthermia, Dec 2008
⇒ http://www.uth.tmc.edu/thermaltherapy/

Breast CA (Jones et al 2007 + 2005 Duke Univ.)
randomised Phase III and Phase I Trials

109 Patients with breast CA close to skin surface
Comprehensive response rate of 68,1 % (radiation + HT) vs. 42,3% (radiation alone)

Most significant difference with patients previously radiated :
68,2% in radiation+ HT vs. 23,5 % radiation alone

(Jones et. al., Journal of Clinical Oncology Vol. 23, No 13, May 1, 2005.)
In an extension using thermo-sensitive Liposomen as carrier of Doxorubicin running as phase I trial, the authors came to a cautious concluding, that here as well hyperthermia with a liposomal-thermosensitive chemotherapy seems to enhance „anti-tumor-effects”. (Jones et al, June 2007, 24th Annual Meeting of ESHO, Prague, Abstracts S. 11)
**Cervix Tumor** (Van der Zee, Franckena et al) 2007
(randomised Phase III trial incl. Follow-Up)
Follow-Up: long time survival after 12 years
58 Patients (Rad.+HT) vs. 56 Patients (Rad. alone)

* Better lokal Control: 36 % (radiation alone) vs. 56 % (radiation + HT)

* overall Survival after 12 years: 20 % (radiation alone) vs. 37 % (radiation + HT)
  (at p= 0.02)

(Franckeno et al, June 2007, 34th Annual Meeting of ESHO, Prag, Abstracts S. 18)

Hyperthermia successes:

---

![Graph showing local responses of hyperthermia plus chemotherapy compared to chemotherapy alone.](image)

**Fig. 2.20** Local response of hyperthermia plus chemotherapy compared to chemotherapy alone. (Chemotherapy is mostly Adriamycin, Bleomycin, Cisplatin, Mitomycin, and 5Fu), (Hyperthermia 40–60 min, capacitive, 8 MHz, 4–16 lesions)
Summary of the results obtained in Japan by capacitive hyperthermia combined with radiotherapy.

Hepatocellular carcinoma and metastatic tumors of the liver.
# Trials in combination with radiation therapy

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Anzahl der Studien.</th>
<th>Anzahl Patienten/Regionen</th>
<th>Strahlentherapie allein (%)</th>
<th>Strahlentherapie + Hyperthermie (%)</th>
<th>Odds ratio (95% CI) (CI-Confidence ratio)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>2</td>
<td>143</td>
<td>67</td>
<td>68</td>
<td>1.06 (0.02–2.14)</td>
</tr>
<tr>
<td>Chest Wall</td>
<td>4</td>
<td>270</td>
<td>38</td>
<td>59</td>
<td>2.37 (1.46–3.86)</td>
</tr>
<tr>
<td>Cervix</td>
<td>4</td>
<td>248</td>
<td>52</td>
<td>77</td>
<td>3.95 (1.77–5.27)</td>
</tr>
<tr>
<td>Rectum</td>
<td>2</td>
<td>238</td>
<td>9</td>
<td>19</td>
<td>2.27 (1.08–4.76)</td>
</tr>
<tr>
<td>Bladder</td>
<td>1</td>
<td>101</td>
<td>51</td>
<td>73</td>
<td>2.61 (1.14–5.90)</td>
</tr>
<tr>
<td>Prostate</td>
<td>1</td>
<td>40</td>
<td>70</td>
<td>81</td>
<td>1.16 (0.28–4.77)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>1</td>
<td>70128</td>
<td>51</td>
<td>56</td>
<td>2.81 (1.58–3.50)</td>
</tr>
<tr>
<td>Head &amp; Neck</td>
<td>5</td>
<td>374</td>
<td>53</td>
<td>51</td>
<td>2.08 (1.28–3.39)</td>
</tr>
<tr>
<td>Diverse</td>
<td>3</td>
<td>442</td>
<td>34</td>
<td>39</td>
<td>1.34 (0.84–2.12)</td>
</tr>
<tr>
<td>All Studies</td>
<td>23</td>
<td>1861</td>
<td>38</td>
<td>52</td>
<td>1.00 (0.50–2.14)</td>
</tr>
</tbody>
</table>

The authors conclude: if taken all these clinical results (1861 Patients from 23 Studies) it shows a highly significant benefit (P< 0.0001) that confirms the rationale of a combined efficacy of radiation with hyperthermia. That result stands besides the fact that there were quite different treatment protocols in the various tumor entities (ditto p.423).

---

**Figure 1**
SM’s PET-Scan taken in January 2007.
The PET-Scan shows a massive infiltration in the peritoneum, the lymph nodes, liver, and spleen. The patient was at this time untreatable because of multidrug resistance.

**Figure 2**
SM after treatment at St. George Hospital with two whole body hyperthermias, local hyperthermia, and a complementary nontoxic cancer treatment program. No hot spots are visible; patient is in a complete remission. See also Figure 3.
Colon (transversum) carcinoma

Investigator: Prof. H. Kirchner
Department: Department of Hematology & Oncology, Hospital Siloah, Hannover, Germany
Patient: B.Z., 61 y, male
Surgery: Hemicolostomy.
Tumor classification: T4, pN2, M1 (Liver).
Therapy (2): Erbitux, Campto (Mar. 2006) + oncothermia on liver.
Therapy pause
Result (2): Progressive disease (PD)
Result (3): Good partial remission (PR) tumor and tumor marker regression, became normal.

Cervix carcinoma

Investigator: Prof. H. Renner
Department: Klinikum Nord, Nürnberg, Germany
Patient: H.K., 61 y, female; Cervix carcinoma; cT4 cN0 M0 G3
Histology: Squamous cell carcinoma;
Therapy: 12/06-01/07 bimodality therapy, Radiotherapy: 50.4 Gy; (5x1.8 Gy/weeks); oncothermia: 6 sessions.
Control: 3 months later hysterectomy (Wertheim).
Result: pathologically complete remission ypT0ypN0.
Intrahepatic bile-duct carcinoma

Investigator: Dr. A. Csejtey & Mr. P. Lorentz
Institution: Markusovsky Hospital, Szombathely, Hungary,
Diagnosis: Intrahepatic bile-duct carcinoma, inoperable
Therapy: Oncothermia as monotherapy with concomitant supportive vitamins only.
Due to the patient’s status, no any other therapies was possible. Oncothermia started (June 14, 2007)
Prognosis: overall median survival 6 months
Results: Complete remission (CR)
Follow up: last checkup Sept. 2009, symptom-free, tumor-free

A PATIENT OF OURS WITH MULTIPLE PULMONARY METASTASES WHO HAD A COMPLETE REMISSION IN 6 MONTHS WITH INTEGRATIVE TREATMENT AND mEHT
HIV-positive patient with multiple myeloma and Lymphoma from 2016. The role of mEHT.

Patient with multiple myeloma and Lymphoma that started from the palate, with a history of immunosuppression (AIDS). After 3 sessions of mEHT in June 2018, parallel to his chemotherapy, a remission of the disease was observed. At that point, he decides to interrupt mEHT and continue solely with chemotherapy, in the duration of stops in the middle of sessions and continue with chemotherapy. Results: The disease relapses and the extension of the disease into adjacent tissues. The patient returned in mid-August in the center of personalized Oncology and began anew his therapy with mEHT sessions. Today significant remission of the disease with mEHT as monotherapy, depicting extensive liquification of the previous tumors.

04/10/2017 status: (CT Visceral Cranium): "Invasive soft tissue CT 68 x 45 mm, with erosion of adjacent bone jaw citizens and lower parts of the sinuses. 12/02/2018 status: (CT Visceral Cranium): "Invasive CT soft tissue X22 44 mm, with erosion of adjacent maxillary bone and the lower parts of the sinuses. Multiple osteolytic masses in the bones of the skull and infiltration of soft tissue (meta-disease), the greater lesion is frontal right 29Ch 28 mm.

Sensitivity to mEHT. Documented through measurement of levels of HSP’S (27, 72 and 90)

CONCLUSION-An Integrative Oncology Centre with hyperthermia should have very specific characteristics in order to meet the difficult challenges of the times. The ability to evaluate the molecular and genetic profile of individual cancer cells, creates a definite advantage and doubles the response rates of patients who have failed conventional treatment modalities. On the basis of our patients’ profiles it seems that 85% of the patients have sensitivity to Hyperthermia (as expressed by measuring HSP levels). Even patients undergoing chemotherapy (non targeted) continue to respond even when chemo is interrupted.
SUBJECT: the combination of ozone with mEHT in combination with blood alkalinization and high dose Vitamin C., in multiple metastatic bone disease from prostate Ca for control of disease symptoms and avoidance of the risk of further damage to the maxillary bone of Osteoradionecrosis due to RT(radiation therapy) in very extensive metastatic focus in the left mandible.

INTRODUCTION: In prostate cancer of this stage it is common to see the presence of distant metastases. The situation becomes much more difficult when metastatic foci are identified in bones of the jaw. In the stage VI of prostate Ca, therapy must be highly personalized with the best supportive care of the patient to relieve symptoms of pain and avoiding traumatic fractures and should include Hormonal manipulations, the use of bisphosphonates, Surgery, Chemotherapy and or radiotherapy. But we should not ignore and use hyperbaric oxygen (or ozone) where necessary to maintain as far as possible the quality of life in patients’ daily lives as is in this case the mastication function.

Presentation incident: Patient 65 years with meta-disease of Prostate Biopsy 20/12/2014 Ca: AdenoCa 4 + 3 = 7/10 by Gleason 4/5/2018 Stage (CT-scanning): multiple bone lesions scattered the bones of the skeleton especially in the vertebrae and the pelvis and strong fixation of radiolabled Tc on the left upper jaw, attributed to metastatic disease. Hormonal manipulations with the X-120 Geva formulations mg and 80 mg Firmagon Condition 8/8/2018 gave no response and added considerable morbidity (Medical radiological diagnosis) area #37, 38 teeth molars until the angle of the mandible and with the extended subperiosteal reaction (2.9 cm) with irregularly shaped core osteolytic imagery indicative metastatic flare.

8/8/2018 status: (CT of lumbar Spine): extensive osteoblastic and mixed lesions.

METHODS: the sensitivity to mEHT. Documented through measurement of levels HSP’S (27, 72, and 90).

Results: Date Value Comments 16/12/2014 100.20 PSA ng/ml ng/ml 05/01/2015 15.92 21/01/2015 2.18 ng/ml ng/ml 0.81 19/02/2015 18/12/2015 0.55 15/01/2016 0.27 ng/ml ng/ml 0.00 11/03/2016 0.14 ng/ml ng/ml 0.12 ng/ml 16/01/2017 04/04/2017 0.90 ng/ml ng/ml 27/04/2017 0.75 Total testosterone: 0.11 ng/ml ng/ml 09/02/2018 27.71 07/06/2018 281 ng/ml ng/ml 05/06/2018 176.5 Introduction the Oncothermia Center and starting with 2 y fields mEHT (abdominal covering prostate and lumbar areas, and the left mandible with extensive osteolytic disease) with O3 autotransfusion of Ozonated blood and Vitamin C and hormone therapy (LHRH analogue) with Bisphosphonates, in 6 weeks and impressive drop to 28 ng/ml PSA CT-scan “04/08/2018 significant improvement. Bone Scan also indicates clear response of osteolytic lesions. CURRENT PERFORMANCE STATUS: 85-95% (Karnofsky) vs 50% previously.

CONCLUSIONS: Even stage IV disease with very poor performance status can be treated with an Integrative approach using Oncothermia as a pivot point for therapeutic strategy.
We are still sailing in unchartered waters and making new maps

IT’S JUST A MATTER OF TIME...
BEFORE WE SEE HAPPY PATIENTS!!

ALL WE HAVE TO DO IS TAKE THE LEAP!!
INTEGRATIVE ONCOLOGY...THE DIFFICULT BUT RIGHT PATH

“Two roads diverged in a wood, and I—
I took the one less traveled by,
And that has made all the difference”

Robert Frost, New England Wisdom

ALWAYS KEEPING OUR GOALS SKY-HIGH AND STRIVING TO ACHIEVE THEM

KÖSZÖNÖMA FIGYELMET