Principles of modulated electro-hyperthermia (mEHT) (Oncothermia)

Presentation from "Oncotherm in Italy" conference 2025.04.02.

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https://www.youtube.com/watch?v=MwHAst5Wsq0&list=PLEaAiXVgvMsGMMHSufONT8E7zYBSSDNO4

Oncothermia Journal 37, September 2025., 9-23.
https://oncotherm.com/SzaszA_2025_Oncotherm_in_Italy_20250402

Principles of modulated electrohyperthermia (mEHT) (Oncothermia®)

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Rome, Italy. Apr. 2. 2025

MATE

Oncotherm
HYPERTHERMIC IMMUNO-ONCOLOGY

Outline

- Strategy of mEHT – the immune activation
- mEHT concept and principles
- mEHT verification (preclinical)
- mEHT validation (clinical)

Change the strategy against cancer

We are in a war against cancer: attack the enemy's weakest point!

Conventional oncotherapies attack the **strongest** side of malignancy: the **proliferation**

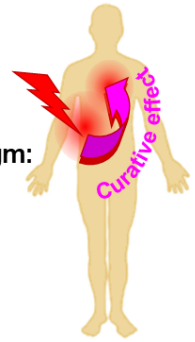
Change is necessary, attack the **weakest** side:

- **missing networking and**
- **compulsion of permanent adaptation**

- **activate the immune system,**
- **use the homeostatic processes**

Concept of the immune activation (abscopal effect)

Change of paradigm: local ⇒ systemic



Tumor-Specific Immune Activation

Outline

- ✓ Strategy of mEHT – the immune activation
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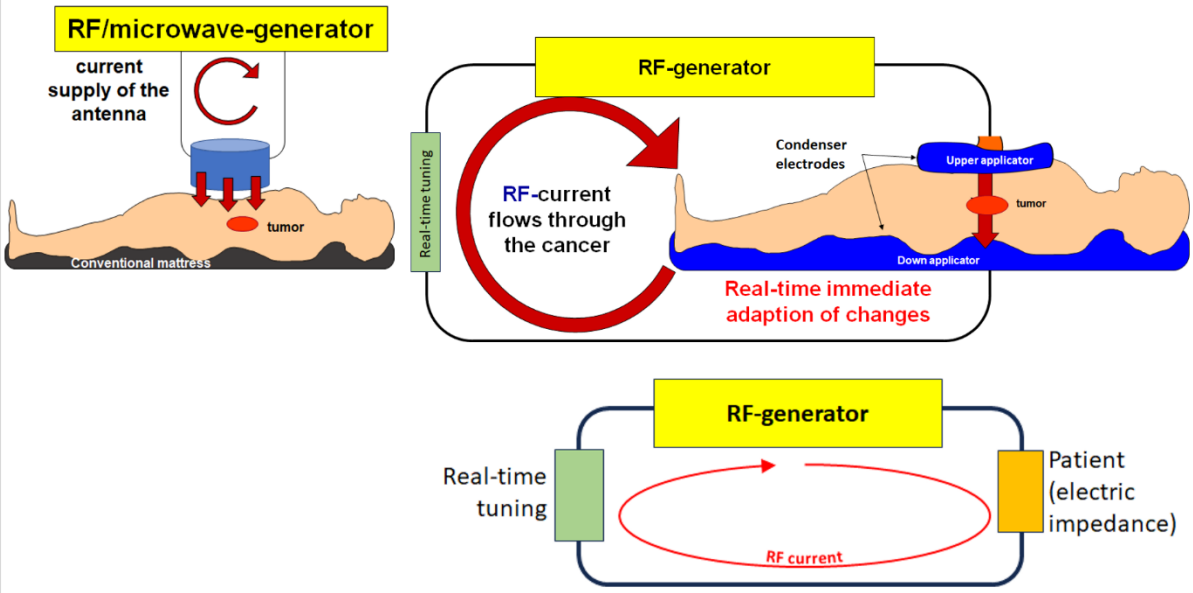
How to recognize the cancer cells?

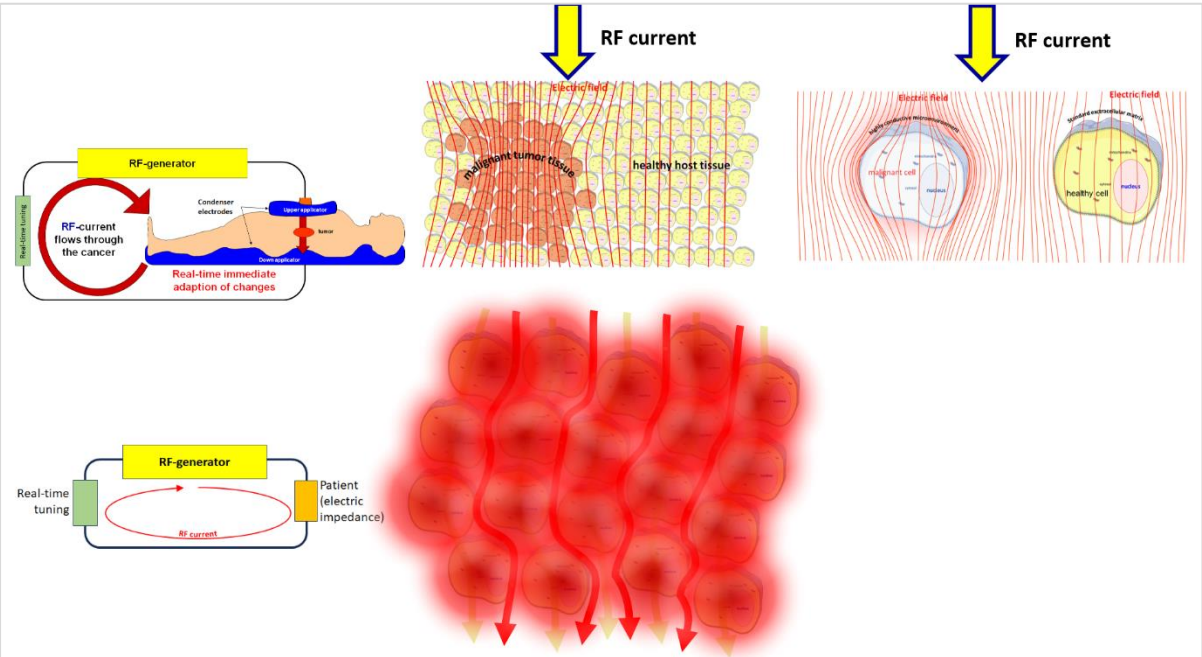
The biophysical properties of malignancy differ from its healthy surroundings

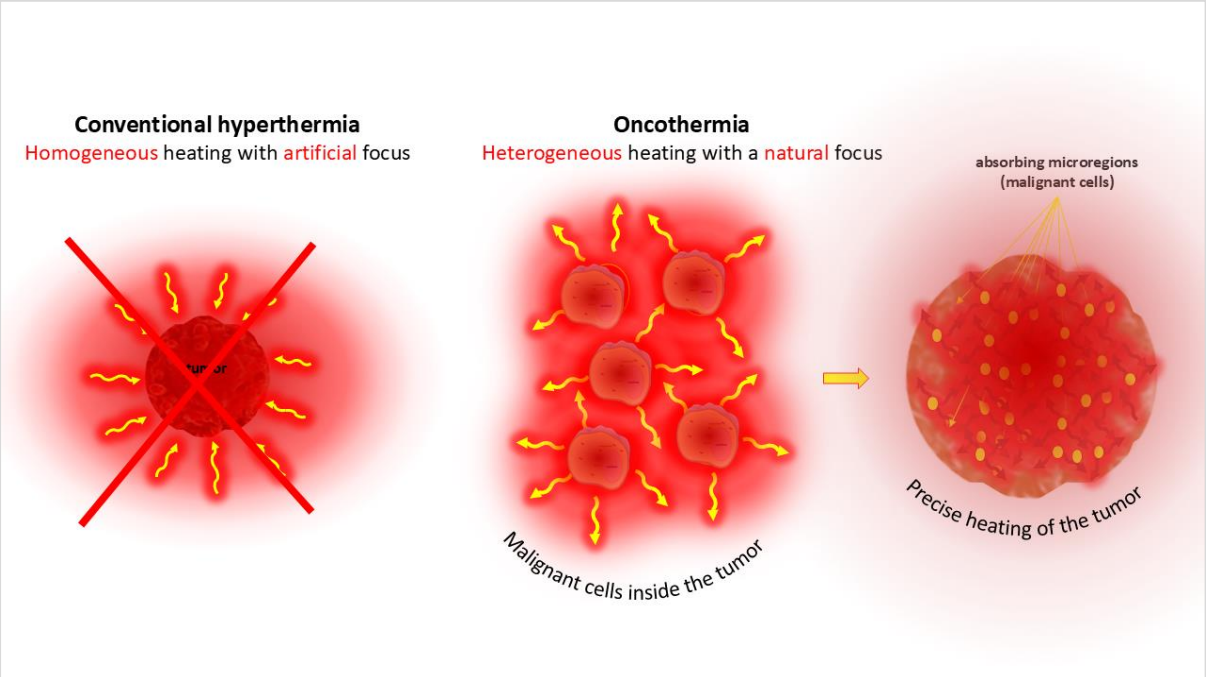
Nonthermal difference:
Malignant cells have higher metabolic rate (PET detects it) so their complex conductivity is higher than of the healthy tissue
(Example: Tumor-treating Fields)

Thermal difference:
Malignant cells are more sensitive to heat due to their high stress and autonomy
(Example: oncological hyperthermia)

Oncothermia® uses the synergy




RF current
RF current
electric field
malignant tumor tissue
healthy host tissue
Electric field
Electric field
malignant cell
healthy cell
nucleus
RF-generator
RF-current flows through the cancer
Condenser electrodes
Upper applicator
tumor
Lower applicator
Real-time immediate adaption of changes
Real-time tuning
RF-generator
Real-time tuning
RF current
Patient (electric impedance)


Conventional hyperthermia
Homogeneous heating with artificial focus
Oncothermia
Heterogeneous heating with a natural focus
absorbing microregions (malignant cells)
Malignant cells inside the tumor
Precise heating of the tumor

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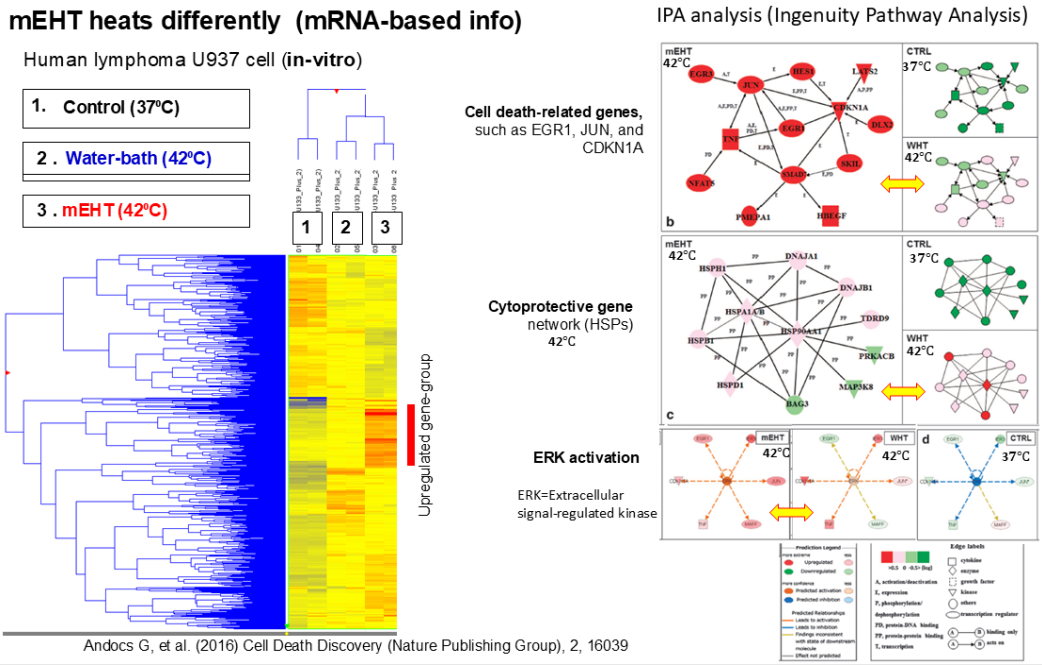
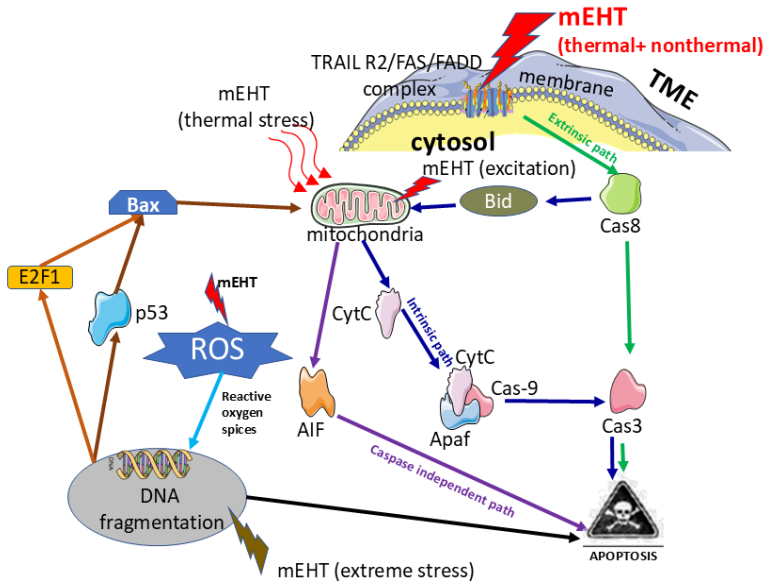


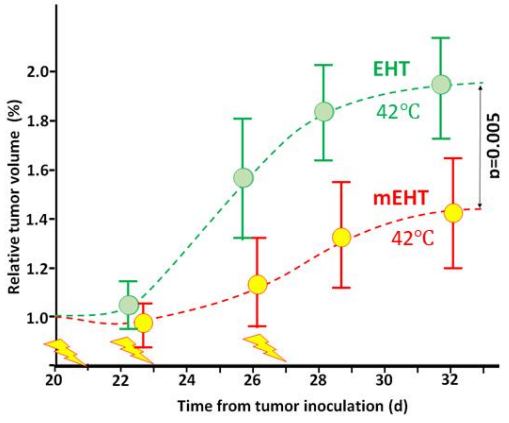
Andocs G, et al. (2016) Cell Death Discovery (Nature Publishing Group), 2, 16039

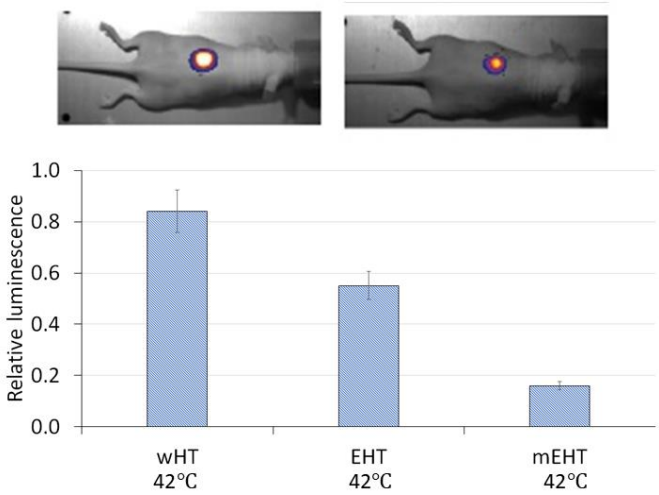


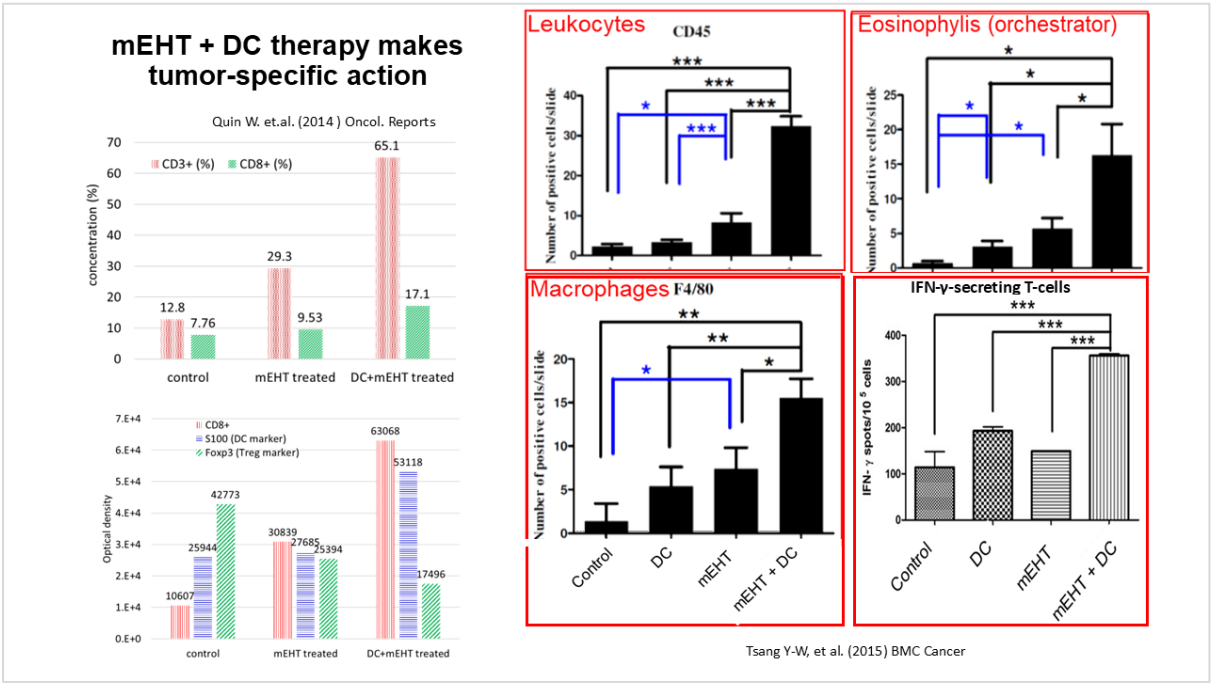
All steps are measured & published

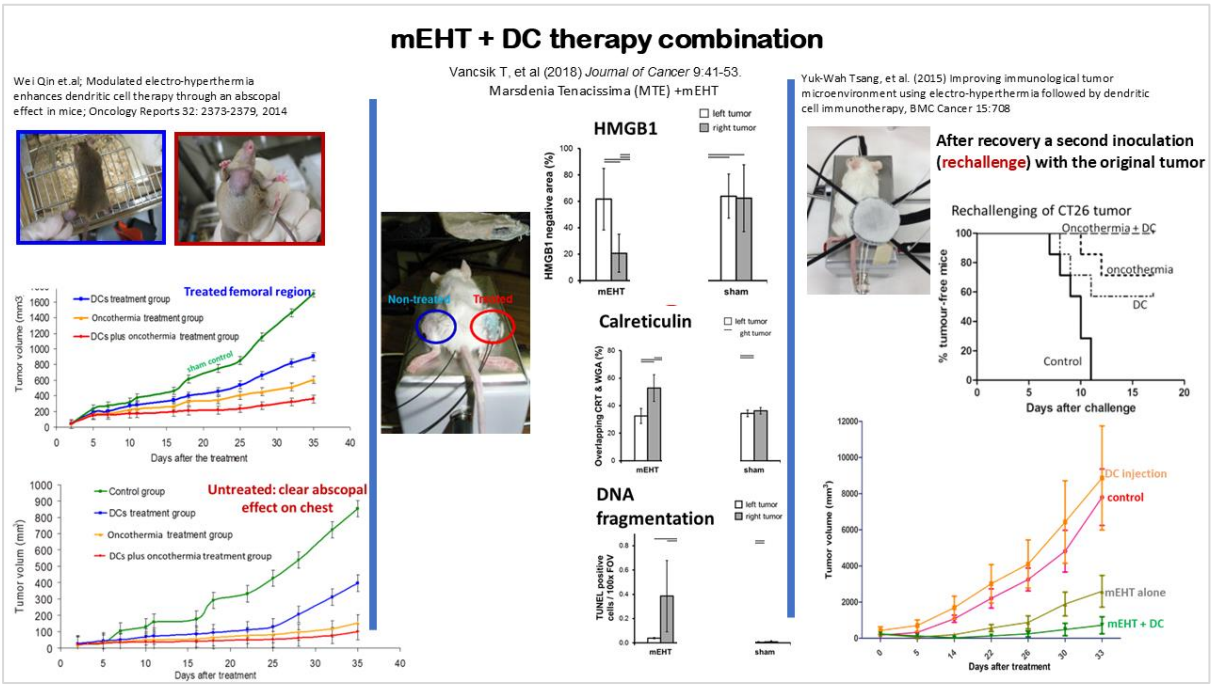
Effect of modulation in vivo

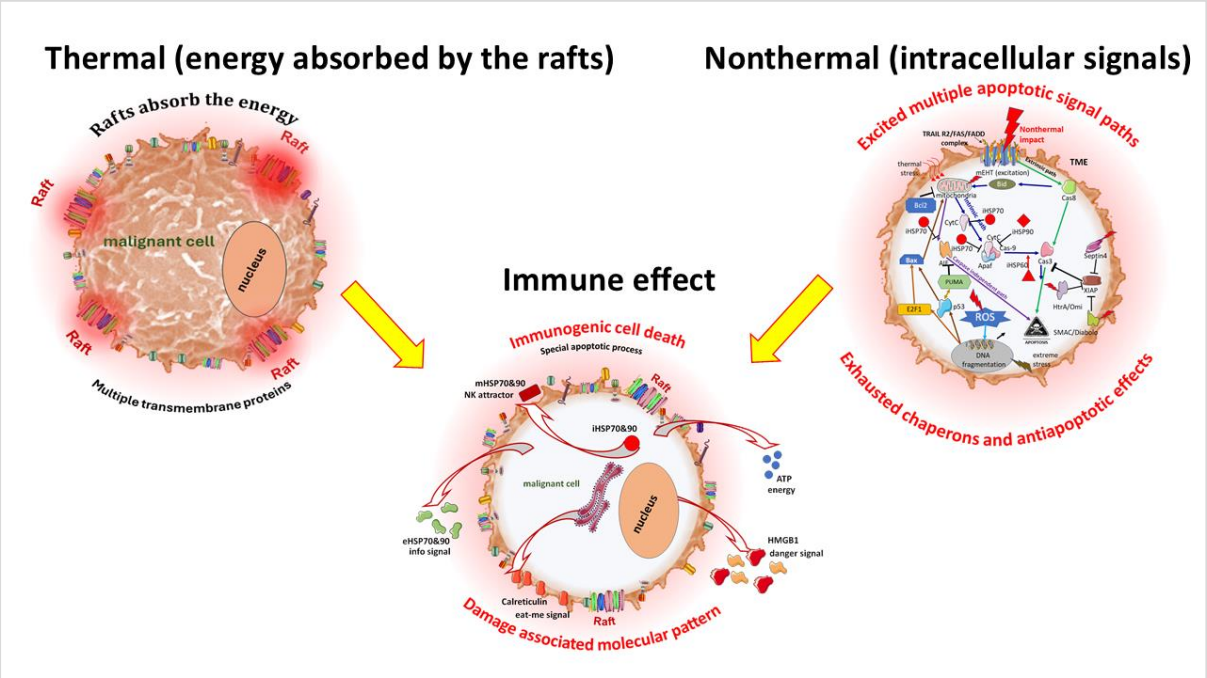
Wust P. et.al. (2022) Cancers

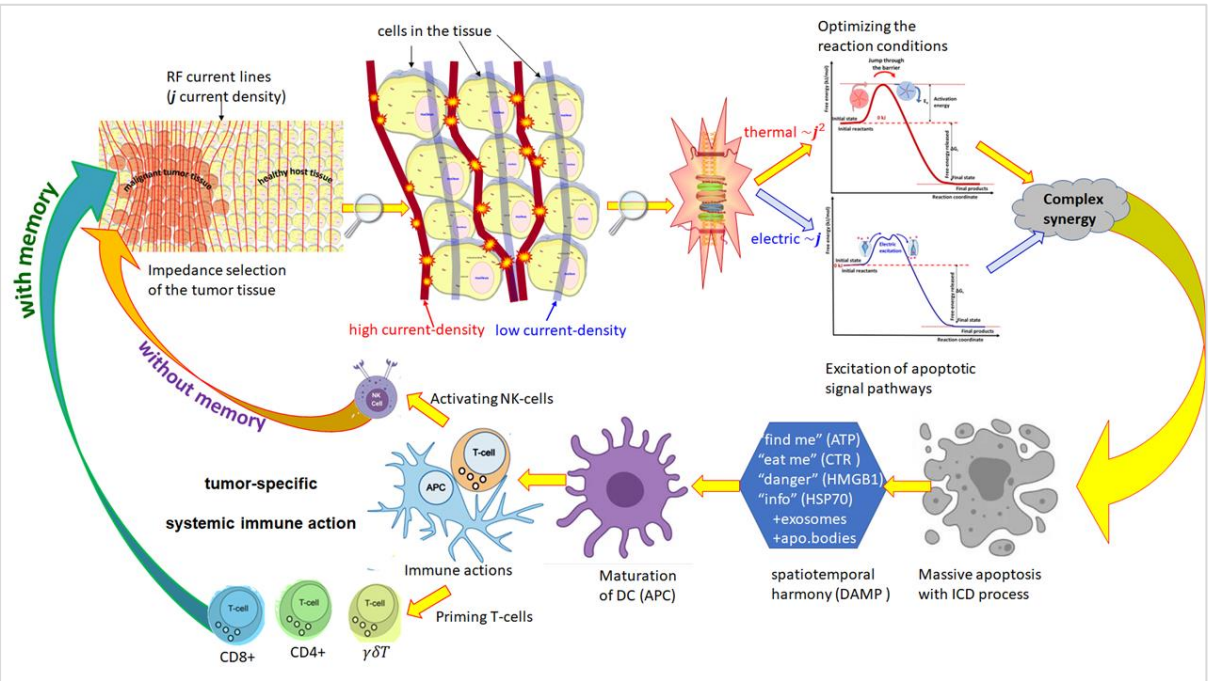





mEHT + DC therapy makes tumor-specific action
Quin W. et.al. (2014) Oncol. Reports
CD3+ (%)
CD8+ (%)
concentration (%)
12.8
7.76
29.3
9.53
65.1
17.1
control
mEHT treated
DC+mEHT treated
CD8+
S100 (DC marker)
Foxp3 (Treg marker)
Optical density
10607
25944
42773
30839
27685
25394
63068
53118
17496
Leukocytes
CD45
Number of positive cells/slide
Eosinophylis (orchestrator)
Macrophages F4/80
IFN-γ-secreting T-cells
IFN- γ spots/10 5 cells
Control
DC
mEHT
mEHT + DC
Tsang Y-W, et al. (2015) BMC Cancer


mEHT + DC therapy combination
Wei Qin et.al; Modulated electro-hyperthermia enhances dendritic cell therapy through an abscopal effect in mice; Oncology Reports 32: 2373-2379, 2014
Treated femoral region
DCs treatment group
Oncothermia treatment group
DCs plus oncothermia treatment group
sham control
Tumor volume (mm3)
Days after the treatment
Non-treated
Treated
Control group
Untreated: clear abscopal effect on chest
Tumor volum (mm3)
Days after treatment
Vancsik T, et al (2018) Journal of Cancer 9:41-53.
Marsdenia Tenacissima (MTE) +mEHT
HMGB1
left tumor
right tumor
HMGB1 negative area (%)
mEHT
sham
Calreticulin
Overlapping CRT & WGA (%)
DNA fragmentation
TUNEL positive cells / 100x FOV
Yuk-Wah Tsang, et al. (2015) Improving immunological tumor microenvironment using electro-hyperthermia followed by dendritic cell immunotherapy, BMC Cancer 15:708
After recovery a second inoculation (rechallenge) with the original tumor
Rechallenging of CT26 tumor
Oncothermia + DC
oncothermia
DC
Control
% tumour-free mice
Days after challenge
DC injection
control
mEHT alone
mEHT + DC
Tumor volume (mm3)
Days after treatment


Thermal (energy absorbed by the rafts)
Nonthermal (intracellular signals)
Rafts absorb the energy
Raft
malignant cell
nucleus
Multiple transmembrane proteins
Immune effect
Excited multiple apoptotic signal paths
Exhausted chaperons and antiapoptotic effects
Immunogenic cell death
Special apoptotic process
mHSP70&90
NK attractor
iHSP70&90
ATP
energy
eHSP70&90
info signal
HMGB1
danger signal
Calreticulin
eat-me signal
Damage associated molecular pattern


cells in the tissue
RF current lines
(j current density)
Optimizing the
reaction conditions
thermal ~j²
electric ~j
Complex
synergy
with memory
Impedance selection
of the tumor tissue
high current-density
low current-density
Excitation of apoptotic
signal pathways
without memory
Activating NK-cells
tumor-specific
systemic immune action
find me" (ATP)
"eat me" (CTR)
"danger" (HMGB1)
"info" (HSP70)
+exosomes
+apo.bodies
Immune actions
Maturation
of DC (APC)
spatiotemporal
harmony (DAMP)
Massive apoptosis
with ICD process
Priming T-cells
CD8+
CD4+
γδT

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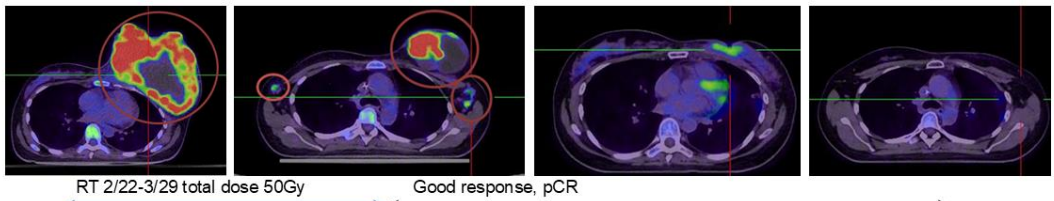
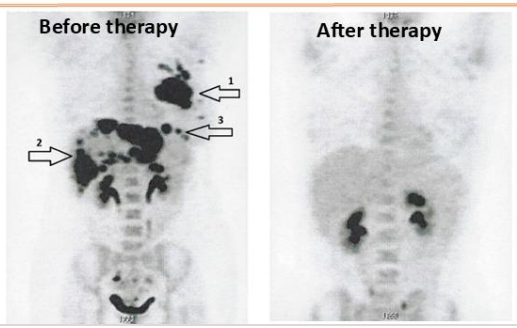
Marked local and distant response (immunogenic action)



Chi M-S. et.al. (2021) Marked local and distant response of heavily treated breast cancer with cardiac metastases treated by combined low dose radiotherapy, low dose immunotherapy and hyperthermia, Ther Radiol Oncol 2021;5:17

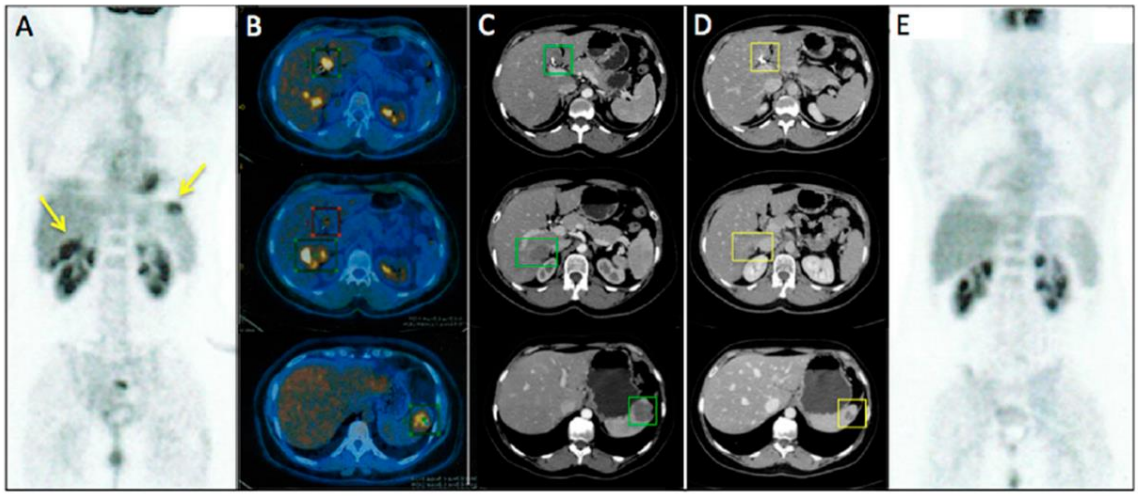
Stage IV Triple-Negative Breast Cancer



İyikesici MS, Slocum AK, Slocum A, Berkarda FB, Kalamian M, Sey\\fried TN; (2017) Efficacy of Metabolically Supported Chemotherapy Combined with Ketogenic Diet, Hyperthermia, and Hyperbaric Oxygen Therapy for Stage IV Triple-Negative Breast Cancer; Cureus 9(7): e1445. DOI 10.7759/cureus.1445

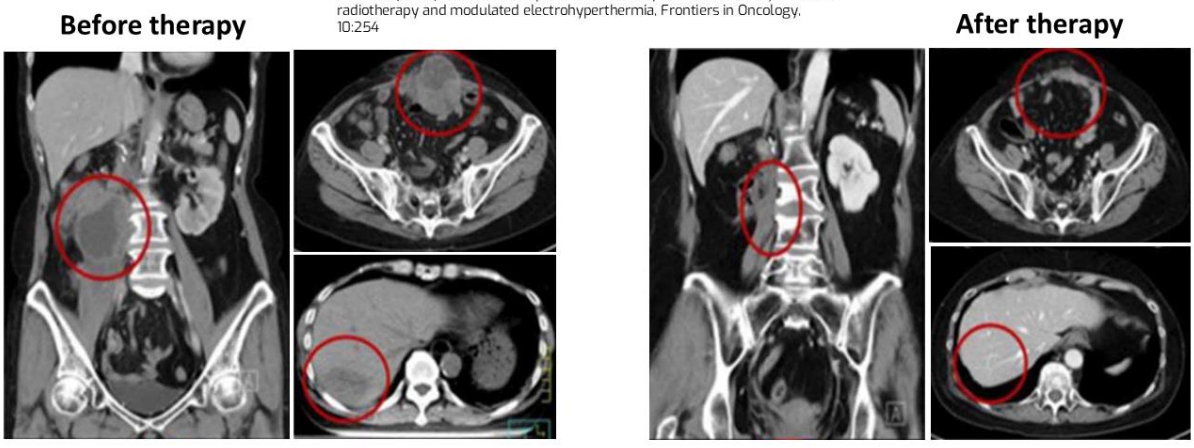
Ovarian cancer with liver and spleen metastasis

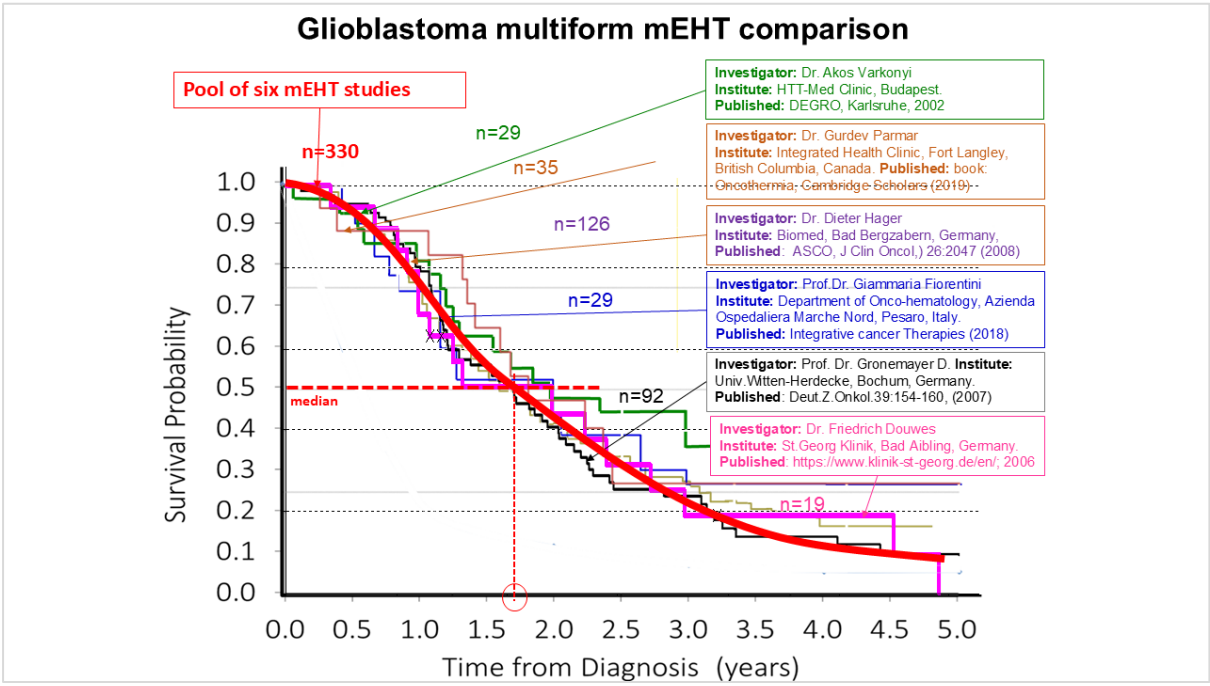
Ranieri G et al.; (2017) Bevacizumab-Based Chemotherapy Combined with Regional Deep Capacitive Hyperthermia in Metastatic Cancer Patients: A Pilot Study;, Int. J. Mol. Sci. 18: 1458; doi:10.3390/ijms18071458

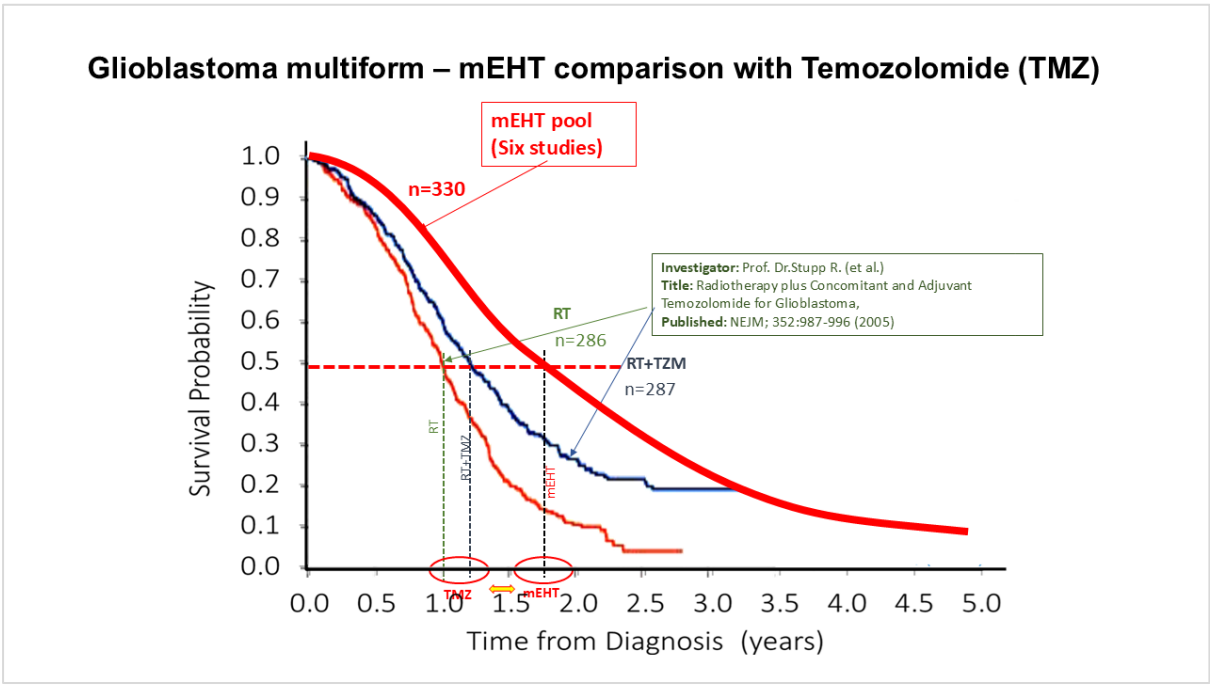


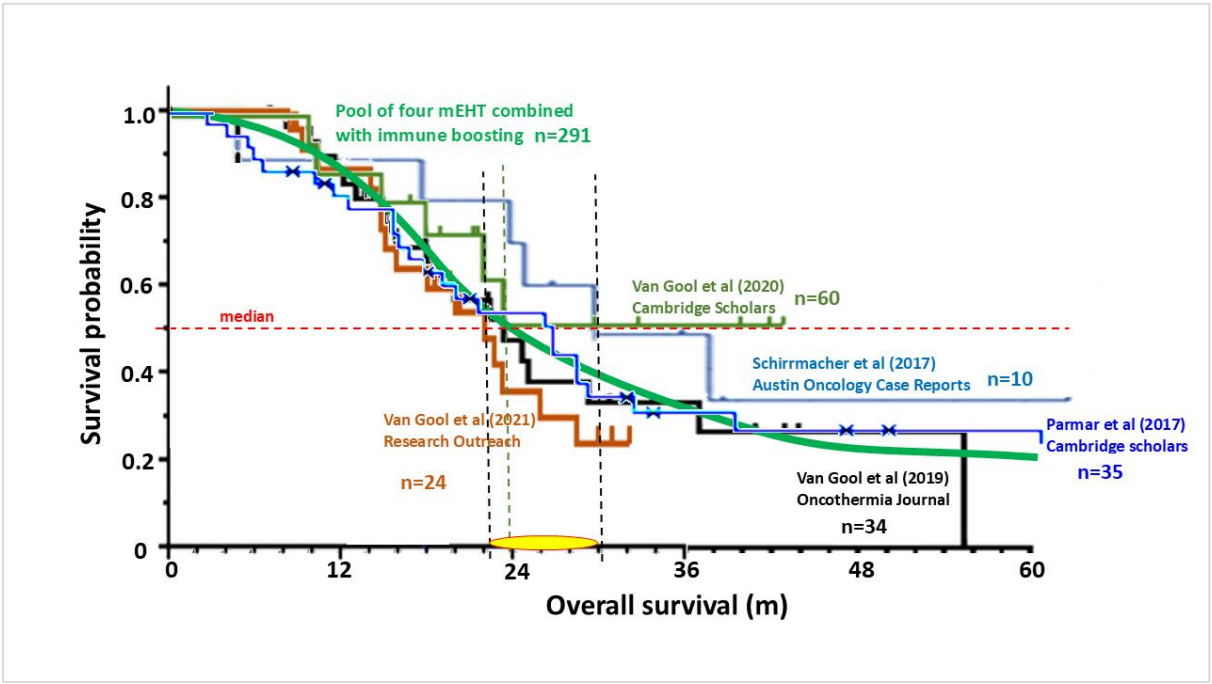
Metastatic urothelial carcinoma with abscopal tumor effect on liver metastases

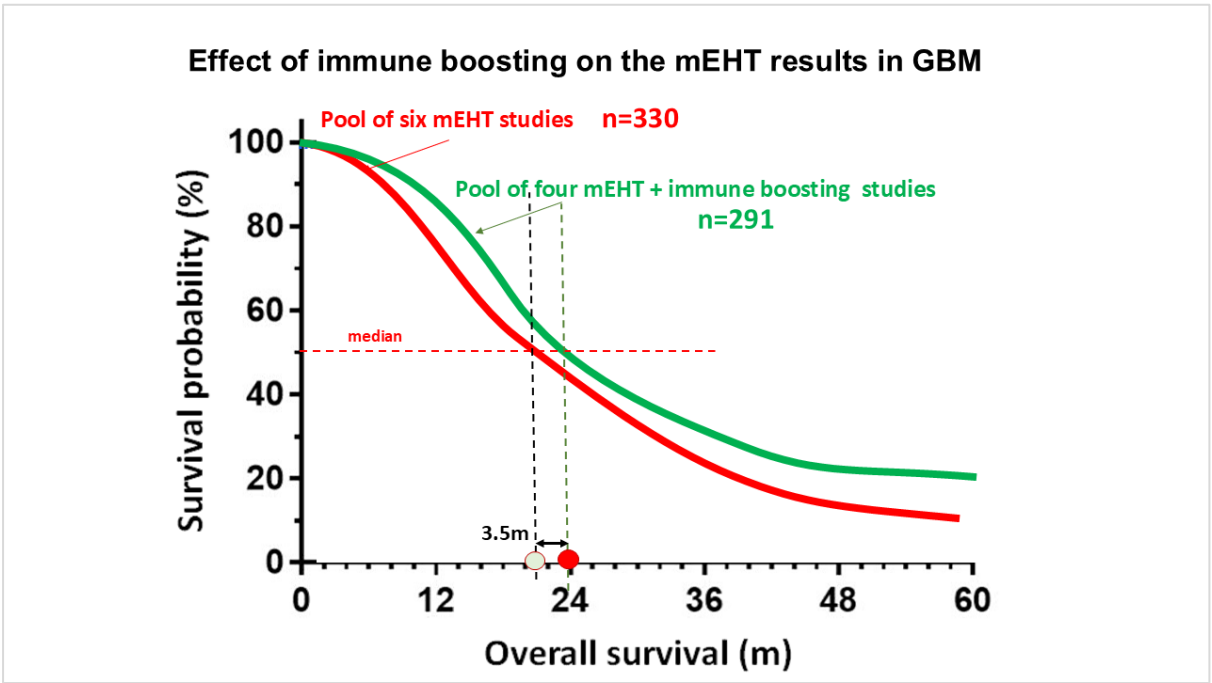
Chi et al. (2020) Putative abscopal effect in three patients treated by combined radiotherapy and modulated electrohyperthermia, Frontiers in Oncology, 10:254

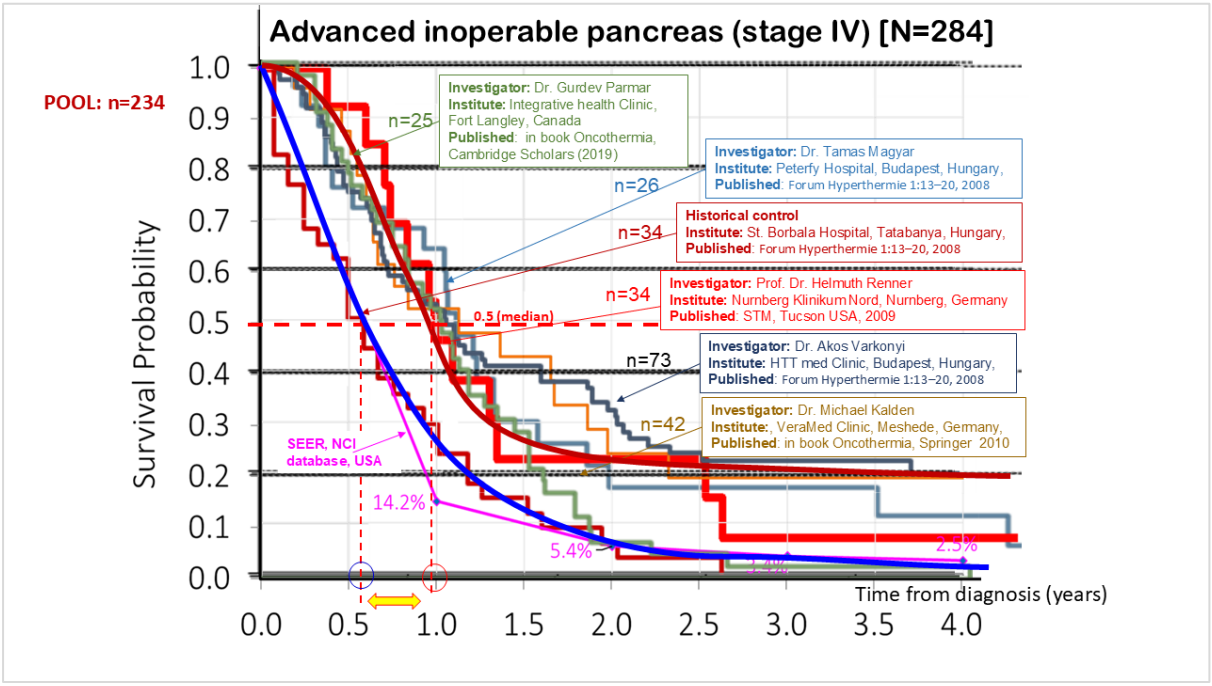


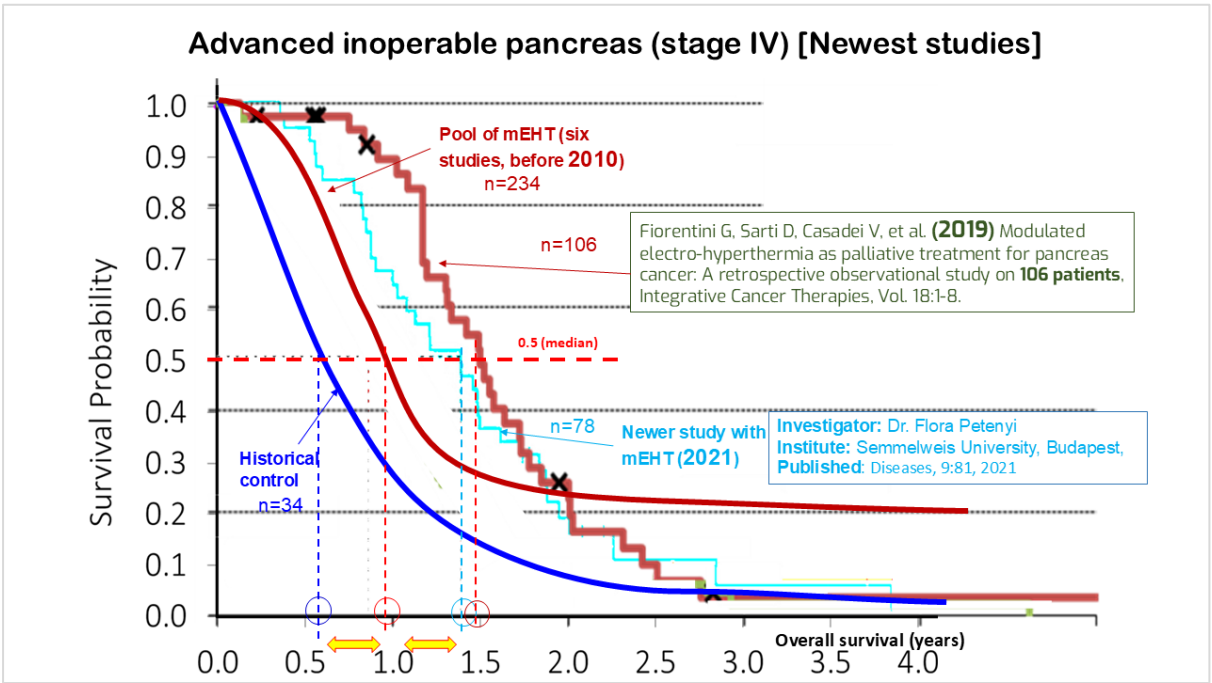

Glioblastoma multiform mEHT comparison
Pool of six mEHT studies
n=330
n=29
n=35
n=126
n=29
n=92
n=19
median
Investigator: Dr. Akos Varkonyi
Institute: HTT-Med Clinic, Budapest.
Published: DEGRO, Karlsruhe, 2002
Investigator: Dr. Gurdev Parmar
Institute: Integrated Health Clinic, Fort Langley, British Columbia, Canada. Published: book: Oncothermia. Cambridge Scholars (2019)
Investigator: Dr. Dieter Hager
Institute: Biomed, Bad Bergzabern, Germany,
Published: ASCO, J Clin Oncol,) 26:2047 (2008)
Investigator: Prof.Dr. Giammaria Fiorentini
Institute: Department of Onco-hematology, Azienda Ospedaliera Marche Nord, Pesaro, Italy.
Published: Integrative cancer Therapies (2018)
Investigator: Prof. Dr. Gronemayer D. Institute: Univ.Witten-Herdecke, Bochum, Germany.
Published: Deut.Z.Onkol.39:154-160, (2007)
Investigator: Dr. Friedrich Douwes
Institute: St.Georg Klinik, Bad Aibling, Germany.
Published: https://www.klinik-st-georg.de/en/, 2006
Survival Probability
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0.0 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0
Time from Diagnosis (years)


Glioblastoma multiform – mEHT comparison with Temozolomide (TMZ)
mEHT pool
(Six studies)
n=330
Investigator: Prof. Dr.Stupp R. (et al.)
Title: Radiotherapy plus Concomitant and Adjuvant Temozolomide for Glioblastoma,
Published: NEJM; 352:987-996 (2005)
RT
n=286
RT+TZM
n=287
RT
RT+TMZ
mEHT
TMZ
mEHT
Survival Probability
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0.0 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0
Time from Diagnosis (years)


Pool of four mEHT combined
with immune boosting n=291
Van Gool et al (2020)
Cambridge Scholars
n=60
median
Schirrmacher et al (2017)
Austin Oncology Case Reports
n=10
Van Gool et al (2021)
Research Outreach
n=24
Parmar et al (2017)
Cambridge scholars
n=35
Van Gool et al (2019)
Oncothermia Journal
n=34
Survival probability
Overall survival (m)
1.0
0.8
0.6
0.4
0.2
0
0
12
24
36
48
60

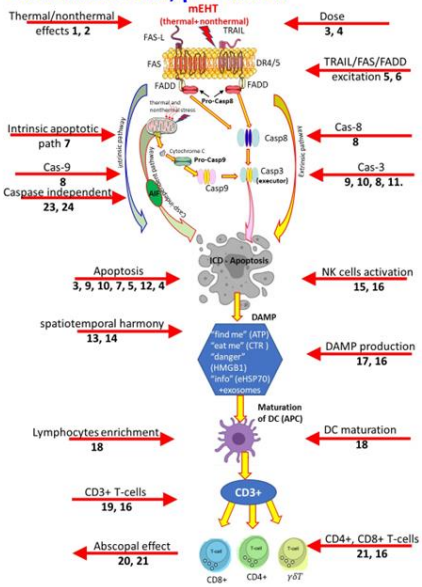

Effect of immune boosting on the mEHT results in GBM
Pool of six mEHT studies n=330
Pool of four mEHT + immune boosting studies
n=291
median
3.5m
Survival probability (%)
Overall survival (m)
100
80
60
40
20
0
0
12
24
36
48
60


Advanced inoperable pancreas (stage IV) [N=284]
POOL: n=234
Survival Probability
Time from diagnosis (years)
Investigator: Dr. Gurdev Parmar
Institute: Integrative health Clinic, Fort Langley, Canada
Published: in book Oncothermia, Cambridge Scholars (2019)
n=25
Investigator: Dr. Tamas Magyar
Institute: Peterfy Hospital, Budapest, Hungary,
Published: Forum Hyperthermie 1:13–20, 2008
n=26
Historical control
Institute: St. Borbala Hospital, Tatabanya, Hungary,
Published: Forum Hyperthermie 1:13–20, 2008
n=34
Investigator: Prof. Dr. Helmuth Renner
Institute: Nurnberg Klinikum Nord, Nurnberg, Germany
Published: STM, Tucson USA, 2009
n=34
0.5 (median)
Investigator: Dr. Akos Varkonyi
Institute: HTT med Clinic, Budapest, Hungary,
Published: Forum Hyperthermie 1:13–20, 2008
n=73
Investigator: Dr. Michael Kalden
Institute:, VeraMed Clinic, Meshede, Germany,
Published: in book Oncothermia, Springer 2010
n=42
SEER, NCI database, USA
14.2%
5.4%
2.5%
1.4%


Advanced inoperable pancreas (stage IV) [Newest studies]
Survival Probability
Overall survival (years)
Pool of mEHT (six studies, before 2010)
n=234
n=106
Fiorentini G, Sarti D, Casadei V, et al. (2019) Modulated electro-hyperthermia as palliative treatment for pancreas cancer: A retrospective observational study on 106 patients, Integrative Cancer Therapies, Vol. 18:1-8.
0.5 (median)
n=78
Newer study with mEHT (2021)
Investigator: Dr. Flora Petenyi
Institute: Semmelweis University, Budapest,
Published: Diseases, 9:81, 2021
Historical control
n=34

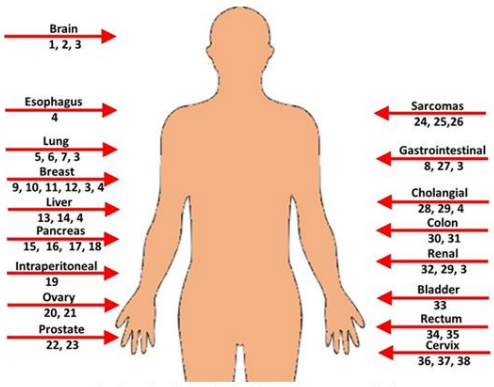
Publications

Basic molecular, preclinical



Some preclinical experiments with mEHT method. The numbers refer on the references: 1.= [42], 2.= [237], 3.= [238], 4.= [94], 5.= [202], 6.= [198], 7.= [239], 8.= [65], 9.= [207], 10.= [203], 11.= [240], 12.= [64], 13.= [207], 14.= [206], 15.= [204], 16.= [32], 17.= [205], 18.= [66], 19.= [241], 20.= [200], 21.= [33], 23.= [205].

Clinical



The clinical studies with mEHT. It contains various level of evidences including case reports and phase II/III trials. The **Oncotherm PubList** numbers denoting on the references.

1.= [243], **2.**= [244], **3.**= [245], **4.**= [246], **5.**= [247], **6.**= [248], **7.**= [249], **8.**= [250], **9.**= [251], **10.**= [252], **11.**= [253], **12.**= [254] **13.**= [255], **14.**= [256], **15.**= [257], **16.**= [258], **17.**= [259], **18.**= [260], **19.**= [261], **20.**= [262], **21.**= [263], **22.**= [264], **23.**= [265] **24.**= [266], **25.**= [267], **26.**= [268], **27.**= [269], **28.**= [270], **29.**= [254], **30.**= [271], **31.**= [272], **32.**= [273], **33.**= [274], **34.**= [275] **35.**= [276], **36.**= [277], **37.**= [278], **38.**= [20],

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Thank you for your attention

Prof.Szasz@gmail.com