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Imprint

Editorial

Dear reader, Dear colleagues, Dear hyperthermia experts,

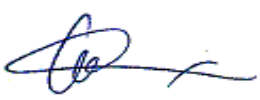
The Hungarian Embassy in Rome, Italy, organized a conference on Oncothermia and its potential in cancer treatments on April 2, 2025. This was a significant recognition of our method. The notable event showcased the latest clinical results of modulated electro-hyperthermia (mEHT) for the participating Italian experts, including decision makers. A series of presentations were given about the clinical results. This volume of our Oncothermia Journal features the presentations of recognized oncologists. The event was opened by His Excellency Adam Zoltan, Hungarian ambassador, and Balazs Acs provided a general overview of the company and its achievements, highlighting the strategic goals for future activities.

The professional program which is published here, was as follows:

- Prof. Dr. András Szász, (The Hungarian University of Agriculture and Life Sciences, Gödöllő, Hungary), founder of Oncotherm presented: Principles of modulated electro-hyperthermia (mEHT)
- Prof. Giammaria Fiorentini (Società Italiana Ipertermia Oncologica (SIIO), Rome, Italy) Oncologist, specialist in oncological radiotherapy, described the 15+ years of Oncothermia treatment results in Italy
- Dr. Carrie Minnaar, (University of Witwatersrand, Johannesburg, South Africa) Oncologic hyperthermia specialist, spoke about the mEHT added to chemoradiotherapy improves five-year survival: final results of a phase III randomised controlled trial.
- Prof. Dr. Elisabeth Arrojo (University Hospital Marqués de Valdecilla, Santander, Spain), Radiation Oncologist presented the results of Oncothermia treatments from almost a decade.

The high-level program was closed by Mr. Francesco Giaretta (Coris Medica, Italy), Oncotherm representative in Italy.

I am convinced that this material provides a perfect update on the successes of the mEHT method, and you will find this current issue of Oncothermia Journal both useful and interesting to read, applying this information in your daily medical practice. I am sure this information further supports clinicians using mEHT. The recent clinical data reinforces the superiority of mEHT, confirming the method's promised advantages and validating its applicability in oncology. I am grateful to the presenters of the successful meeting, whose collected presentations are featured in this volume of the Oncothermia Journal.



Dr. Andras Szasz
Professor, Chair, Biotechnics Department of Hungarian University of Agriculture and Life Sciences

Liebe Leser, liebe Kollegen, liebe Hyperthermie-Experten,

Die Ungarische Botschaft in Rom organisierte am 2. April 2025 eine Konferenz über Oncothermie und ihr Potenzial in der Krebsbehandlung. Diese Veranstaltung war eine bedeutende Anerkennung unserer Methode. Vor italienischen Fachleuten, darunter auch Entscheidungsträger, wurden die neuesten klinischen Ergebnisse der modulierten Elektro-Hyperthermie (mEHT) vorgestellt. Mehrere Vorträge präsentierten aktuelle wissenschaftliche Erkenntnisse, die in dieser Ausgabe des Oncothermia Journal veröffentlicht sind. Eröffnet wurde die Konferenz von S.E. Ádám Zoltán, Botschafter von Ungarn. Im Anschluss gab Balázs Ács einen Überblick über das Unternehmen, seine bisherigen Erfolge sowie die strategischen Ziele für die Zukunft.
Das hier dokumentierte Fachprogramm gestaltete sich wie folgt:

- Prof. Dr. András Szász (Ungarische Universität für Landwirtschaft und Biowissenschaften, Gödöllő, Ungarn), Gründer von Oncotherm: Grundlagen der modulierten Elektro-Hyperthermie (mEHT)
- Prof. Giammaria Fiorentini (Società Italiana Ipertermia Oncologica, Rom, Italien), Onkologe und Spezialist für Strahlentherapie: Über 15 Jahre Behandlungsergebnisse mit Oncothermie in Italien
- Dr. Carrie Minnaar (University of Witwatersrand, Johannesburg, Südafrika), Expertin für onkologische Hyperthermie: mEHT zusätzlich zu Chemo- und Radiotherapie verbessert das Fünf-Jahres-Überleben – Endergebnisse einer randomisierten Phase-III-Studie
- Prof. Dr. Elisabeth Arrojo (Universitätsklinikum Marqués de Valdecilla, Santander, Spanien), Fachärztin für Radioonkologie: Ergebnisse der Oncothermie-Behandlungen aus nahezu einem Jahrzehnt

Den Abschluss des hochkarätigen Programms bildete Herr Francesco Giaretta (Coris Medica, Italien), Oncotherm-Repräsentant in Italien.
Ich bin überzeugt, dass dieses Material einen hervorragenden Überblick über die Erfolge der mEHT-Methode bietet. Diese Ausgabe des Oncothermia Journal wird für Ihre tägliche medizinische Praxis nützlich und interessant sein. Die aktuellen klinischen Daten unterstreichen die Überlegenheit der mEHT, bestätigen ihre prognostizierten Vorteile und belegen ihre Anwendbarkeit in der Onkologie. Mein Dank gilt allen Referenten der erfolgreichen Veranstaltung, deren Beiträge in diesem Heft des Oncothermia Journal veröffentlicht sind.

Rules of submission

As the editorial team we are committed to a firm and coherent editorial line and the highest possible printing standards. But it is mainly you, the author, who makes sure that the Oncothermia Journal is an interesting and diversified magazine. We want to thank every one of you who supports us in exchanging professional views and experiences. To help you and to make it easier for both of us, we prepared the following rules and guidelines for abstract submission.

Als redaktionelles Team vertreten wir eine stringente Linie und versuchen, unserer Publikation den höchst möglichen Standard zu verleihen. Es sind aber hauptsächlich Sie als Autor, der dafür Sorge trägt, dass das Oncothermia Journal zu einem interessanten und abwechslungsreichen Magazin wird. Wir möchten allen danken, die uns im Austausch professioneller Betrachtungen und Erfahrungen unterstützen. Um beiden Seiten die Arbeit zu erleichtern, haben wir die folgenden Richtlinien für die Texterstellung entworfen.

1. Aims and Scope

The Oncothermia Journal is an official journal of the Oncotherm Group, devoted to supporting those who would like to publish their results for general use. Additionally, it provides a collection of different publications and results. The Oncothermia Journal is open towards new and different contents but it should particularly contain complete study-papers, case-reports, reviews, hypotheses, opinions and all the informative materials which could be helpful for the international Oncothermia community. Advertisement connected to the topic is also welcome.

- Clinical studies: regional or local or multilocal Oncothermia or electro cancer therapy (ECT) treatments, case-reports, practical considerations in complex therapies, clinical trials, physiological effects, Oncothermia in combination with other modalities and treatment optimization
- Biological studies: mechanisms of Oncothermia, thermal- or non-temperature dependent effects, response to electric fields, bioelectromagnetic applications for tumors, Oncothermia treatment combination with other modalities, effects on normal and malignant cells and tissues, immunological effects, physiological effects, etc.
- Techniques of Oncothermia: technical development, new technical solutions, proposals
- Hypotheses, suggestions and opinions to improve Oncothermia and electro-cancer-therapy methods, intending the development of the treatments

Further information about the journal, including links to the online sample copies and content pages can be found on the website of the journal: www.oncothermia-journal.com

Umfang und Ziele

Das Oncothermia Journal ist das offizielle Magazin der Oncotherm Gruppe und soll diejenigen unterstützen, die ihre Ergebnisse der Allgemeinheit zur Verfügung stellen möchten. Das Oncothermia Journal ist neuen Inhalten gegenüber offen, sollte aber vor allem Studienarbeiten, Fallstudien, Hypothesen, Meinungen und alle weiteren informativen Materialien, die für die internationale Oncothermie-Gemeinschaft hilfreich sein könnten, enthalten. Werbung mit Bezug zum Thema ist ebenfalls willkommen.

- Klinische Studien: regionale, lokale oder multilokale Oncothermie oder Electro Cancer Therapy (ECT) Behandlungen, Fallstudien, praktische Erfahrungen in komplexen Behandlungen, klinische Versuche, physiologische Effekte, Oncothermie in Kombination mit anderen Modalitäten und Behandlungsoptimierungen

- Biologische Studien: Mechanismen der Oncothermie, thermale oder temperaturunabhängige Effekte, Ansprechen auf ein elektrischesFeld, bioelektromagnetische Anwendungen bei Tumoren, Kombination von Oncothermie und anderen Modalitäten, Effekte auf normale und maligne Zellen und Gewebe, immunologische Effekte, physiologische Effekte etc.
- Oncothermie-Techniken: technische Entwicklungen, neue technische Lösungen
- Hypothesen undMeinungen, wie die Oncothermie- und ECT-Methoden verbessert werden können, um die Behandlung zu unterstützen

Weitere Informationen zum Journal sowie Links zu Online-Beispielen und Inhaltsbeschreibung sind auf der Website zu finden: www.oncothermia-journal.com

2. Submission of Manuscripts

All submissions should be made online via email: info@oncotherm.org

Manuskripte einreichen

Manuskripte können online eingereicht werden: info@oncotherm.org

3. Preparation of Manuscripts

Manuscripts must be written in English, but other languages can be accepted for special reasons, if an English abstract is provided.
Texts should be submitted in a format compatible with Microsoft Word for Windows (PC). Charts and tables are considered textual and should also be submitted in a format compatible with Word. All figures (illustrations, diagrams, photographs) should be provided in JPG format.

Manuscripts may be any length, but must include:

- Title Page: title of the paper, authors and their affiliations, 1-5 keywords, at least one corresponding author should be listed, email address and full contact information must be provided
- Abstracts: Abstracts should include the purpose, materials, methods, results and conclusions.
- Test: unlimited volume
- Tables and Figures: Tables and figures should be referred to in the text (numbered figures and tables). Each table and/or figure must have a legend that explains its purpose without a reference to the text. Figure files will ideally be submitted as a jpg-file (300dpi for photos).
- References: Oncothermia Journal uses the Vancouver (Author-Number) system to indicate references in the text, tables and legends, e.g. [1], [1-3]. The full references should be listed numerically in order of appearance and presented following the text of the manuscript.

Manuskripte vorbereiten

Manuskripte müssen in englischer Sprache vorliegen. Andere Sprachen können in Ausnahmefällen akzeptiert werden, wenn ein englisches Abstract vorliegt.
Texte sollten in einem mit Microsoft Word für Windows (PC) kompatiblen Format eingereicht werden. Tabellen sollten in einem Word-kompatiblen Format eingefügt werden. Alle Graphiken (Illustrationen, Diagramme, Photographien) sollten im jpg Format vorliegen.

Manuskripte können jede Länge haben, müssen aber die folgenden Punkte erfüllen:

- Titelseite: Titel der Arbeit, Autor, Klinikzugehörigkeit, 1-5 Schlüsselworte, mindestens ein Autor muss genannt werden, E-Mail-Adresse und Kontaktdetails des Autors
- Abstracts: Abstracts müssen Zielsetzung, Material und Methoden, Ergebnisse und Fazit enthalten.
- Text: beliebige Länge

- Abbildungen und Tabellen: Abbildungen und Tabellen sollten im Text erläutert werden (nummeriert). Jede Abbildung / Tabelle muss eine erklärende Bildunterschrift haben. Bilder sollten als jpg eingereicht werden (300 dpi).
- Zitate: Das Oncothermia Journal verwendet die Vancouver Methode (Autornummer), um Zitate auszuweisen, z.B. [1], [1-3]. Die Bibliographie erfolgt numerisch in Reihenfolge der Erwähnung im Text.

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Das Oncothermia Journal akzeptiert Werbeanzeigen in allen Sprachen, bevorzugt, aber die zumindest teilweise Gestaltung in englischer Sprache. Die Werbung muss eine Beziehung zu den Themen des Oncothermia Journals haben und der Wahrheit entsprechende Inhalte aufweisen.

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Die Autoren aller im Oncothermia Journal veröffentlichten Artikel sind in vollem Umfang für ihre Texte verantwortlich. Das Oncothermia Journal übernimmt keinerlei Haftung für die Artikel der Autoren. Die Redaktion hat das Recht Artikel abzulehnen.

9. Reviewing

The Oncothermia Journal has a special peer-reviewing process, represented by the editorial board members and specialists, to whom they are connected. To avoid personal conflicts the opinion of the reviewer will not be released and her/his name will be handled confidentially. Papers which are not connected to the topics of the journal could be rejected without reviewing.

Bewertung

Die Texte für das Oncothermia Journal werden durch die Redaktion kontrolliert. Um Konflikte zu vermeiden, werden die Namen des jeweiligen Korrektors nicht öffentlich genannt. Artikel, die nicht zu den Themen des Journals passen, können abgelehnt werden

Content

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

Presentation from "Oncotherm in Italy" conference 2025.04.02.

Prof. Dr. András Szász

Department of Biotechnics, MATE, Hungarian University of Agriculture and Life Sciences, 2100 Gödöllő, Hungary; biotech@gek.szie.hu

Citation

Szasz, A. (2025) Principles of modulated electro-hyperthermia (mEHT) (Oncothermia) – Oncotherm in Italy, 2025.04.02.
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®)

Andras Szasz
Professor on biophysics
MATE, Hungarian University of Agriculture and Life Sciences
Founder & Scientific Consultant of Oncotherm Group

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**

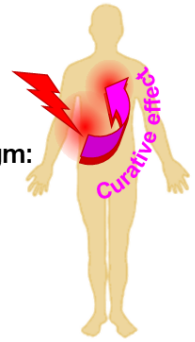
Change is necessary, attack the **weakest** side:

- **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
- mEHT concept and principles
- mEHT verification (preclinical)
- mEHT validation (clinical)

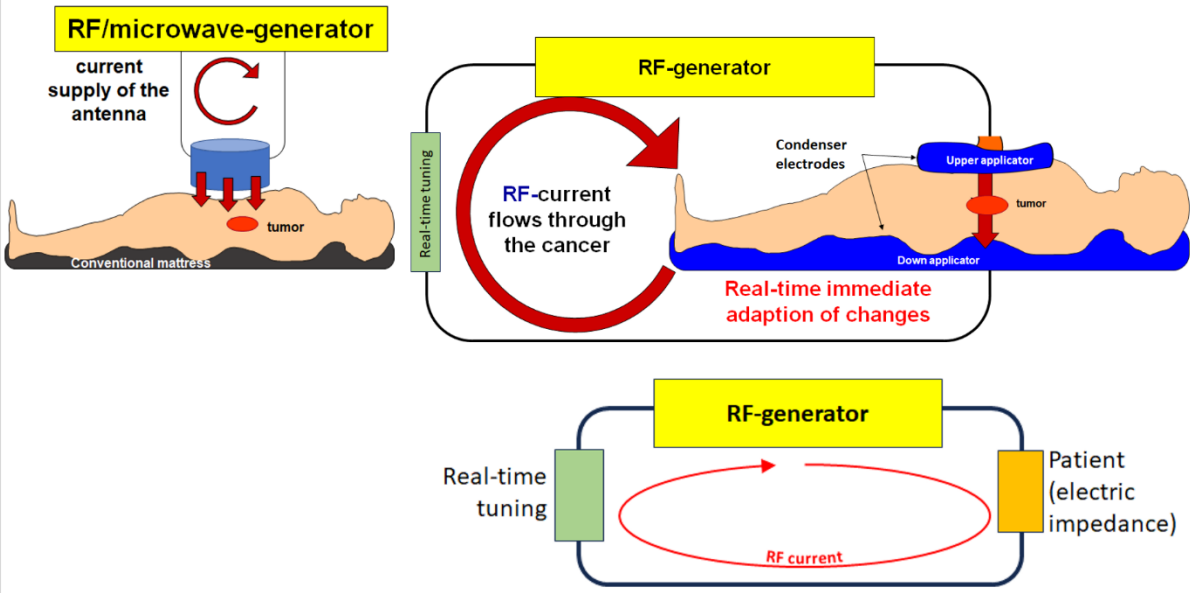
How to recognize the cancer cells?

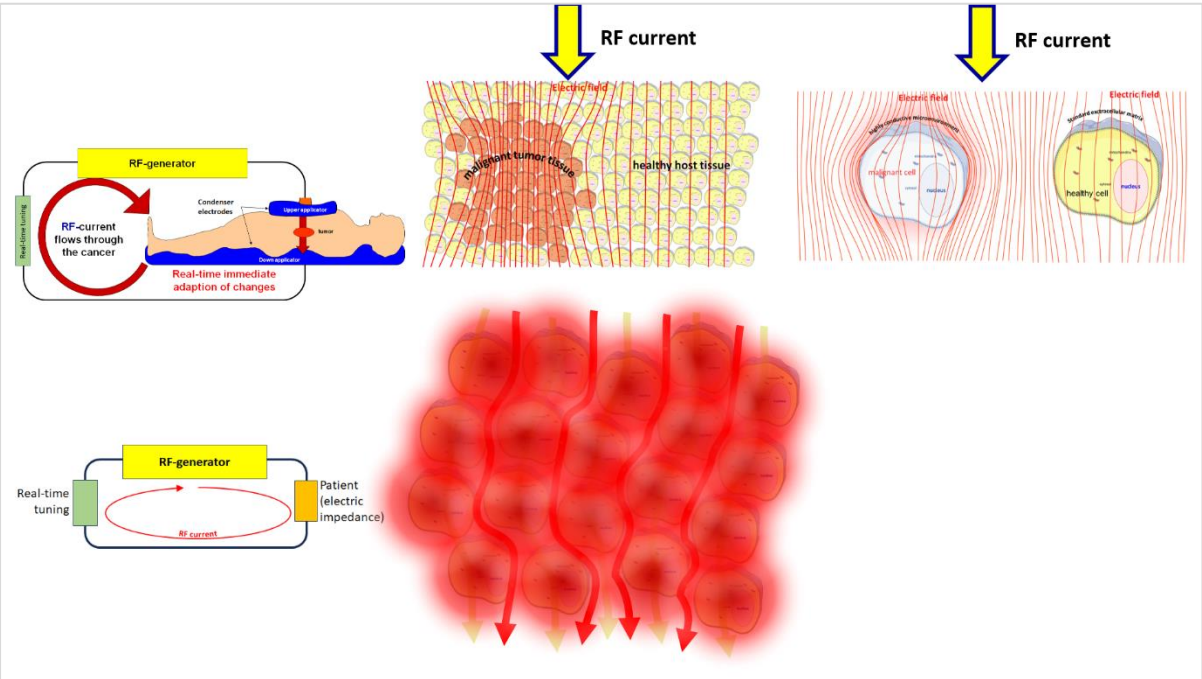
The biophysical properties of malignancy differ from its healthy surroundings

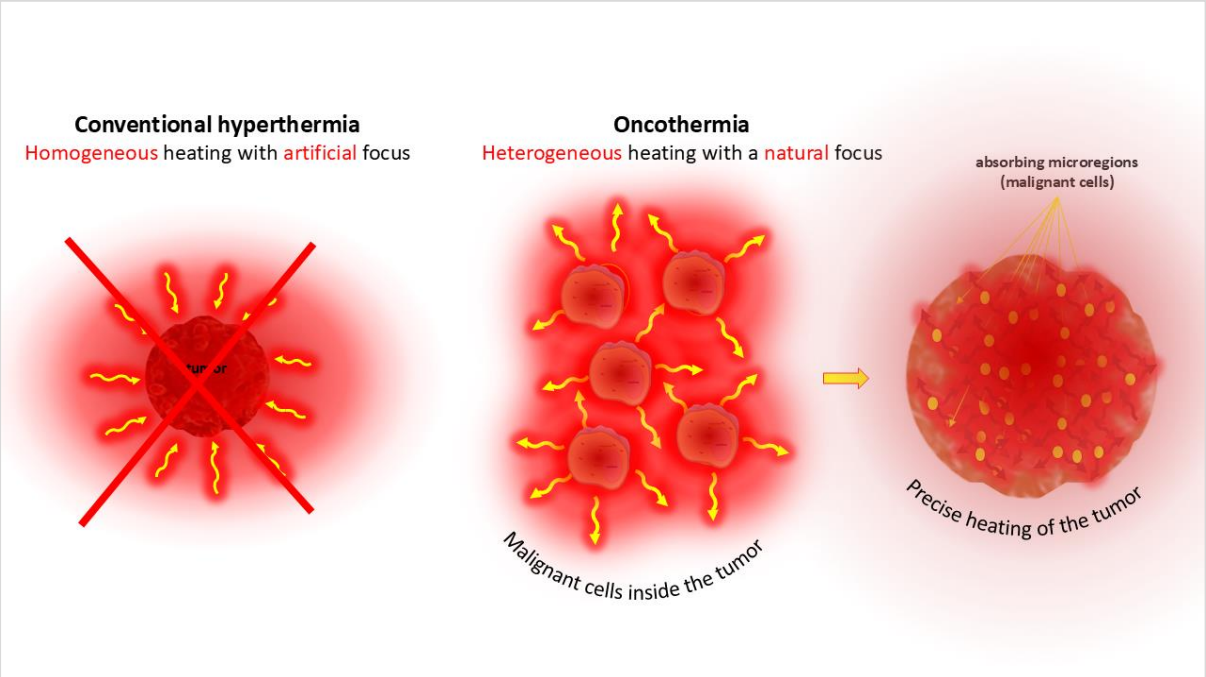
Nonthermal difference:
Malignant cells have higher metabolic rate (PET detects it) so their complex conductivity is higher than of the healthy tissue
(Example: Tumor-treating Fields)

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

Oncothermia® uses the synergy

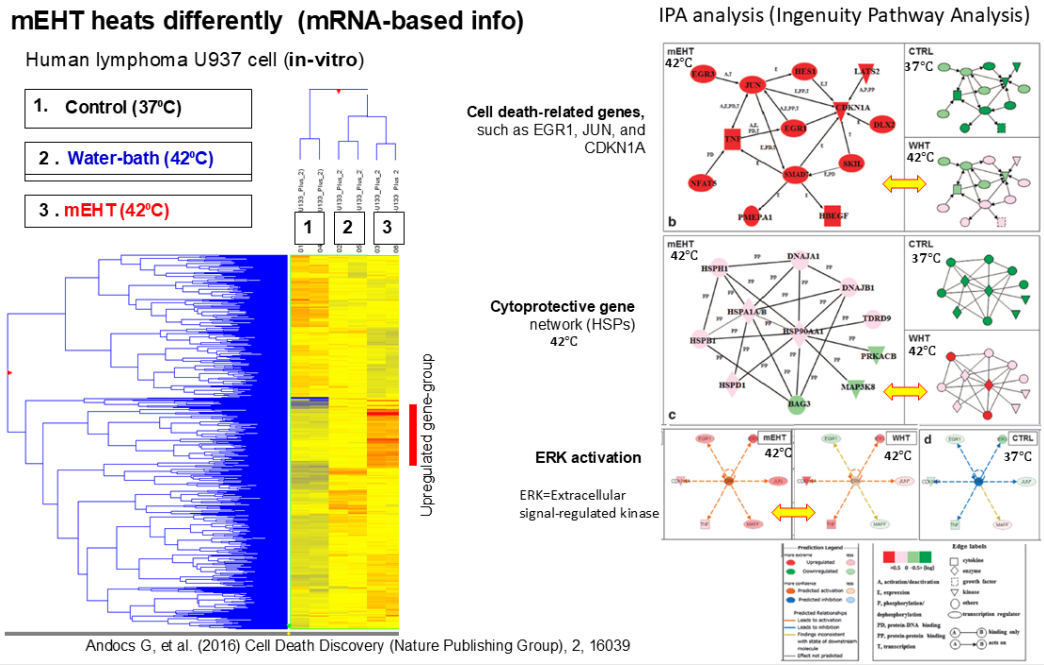



RF current
RF current
Electric field
malignant tumor tissue
healthy host tissue
Electric field
Electric field
RF-generator
RF-current flows through the cancer
Condenser electrodes
Upper applicator
tumor
Lower applicator
Real-time immediate adaption of changes
RF-generator
Real-time tuning
RF current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

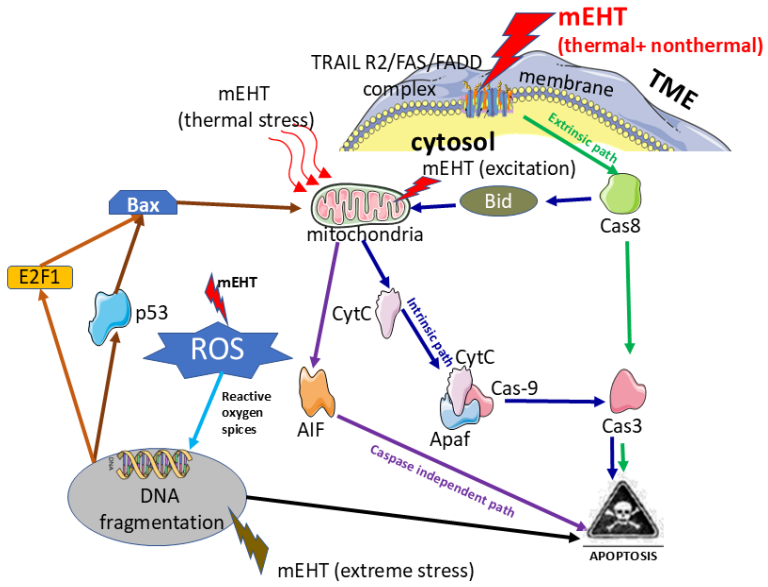

Conventional hyperthermia
Homogeneous heating with artificial focus
Oncothermia
Heterogeneous heating with a natural focus
absorbing microregions (malignant cells)
Malignant cells inside the tumor
Precise heating of the tumor

Outline

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



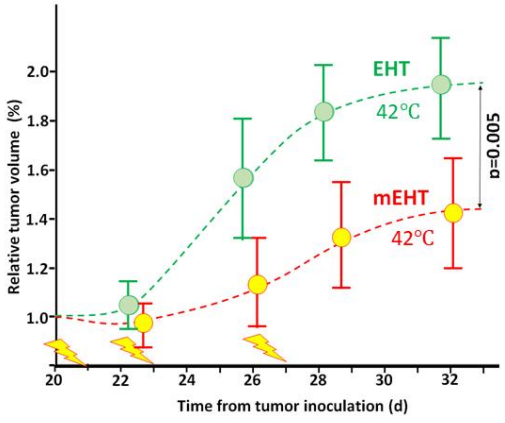
Andocs G, et al. (2016) Cell Death Discovery (Nature Publishing Group), 2, 16039

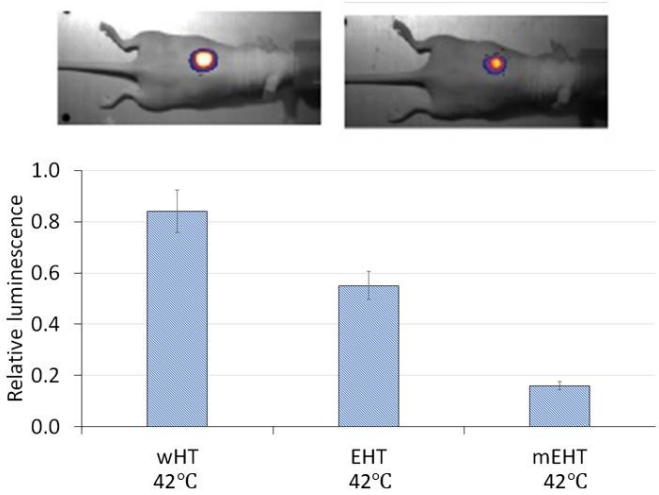


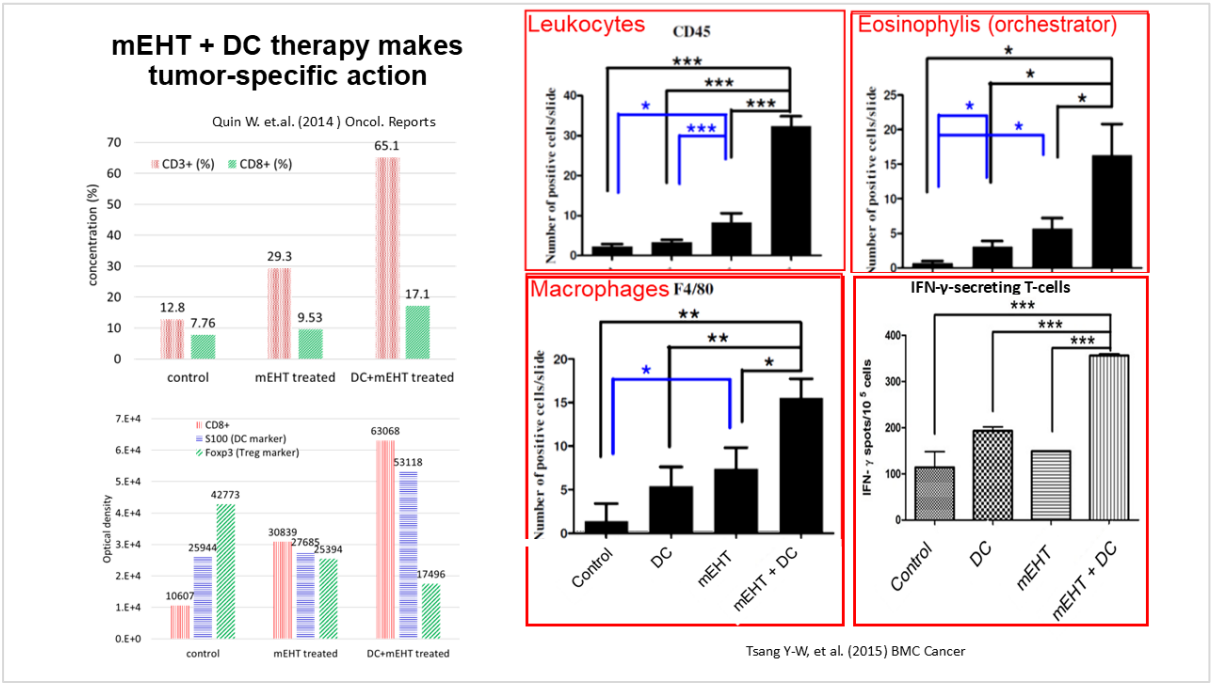
All steps are measured & published

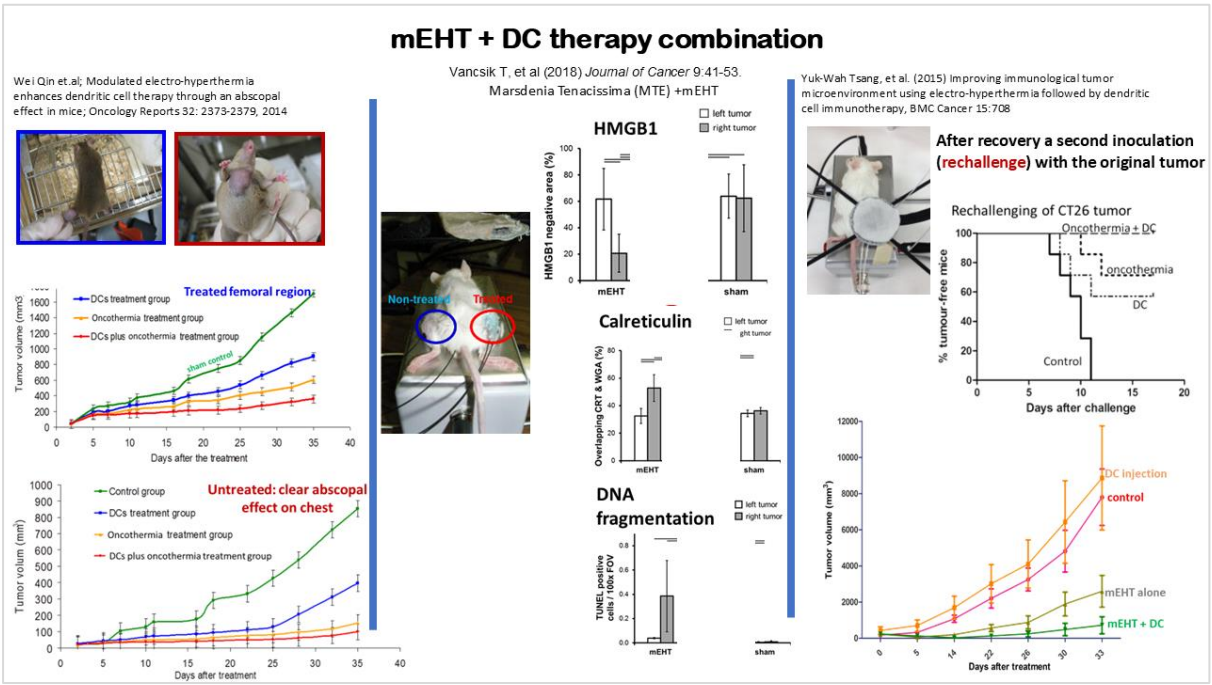
Effect of modulation in vivo

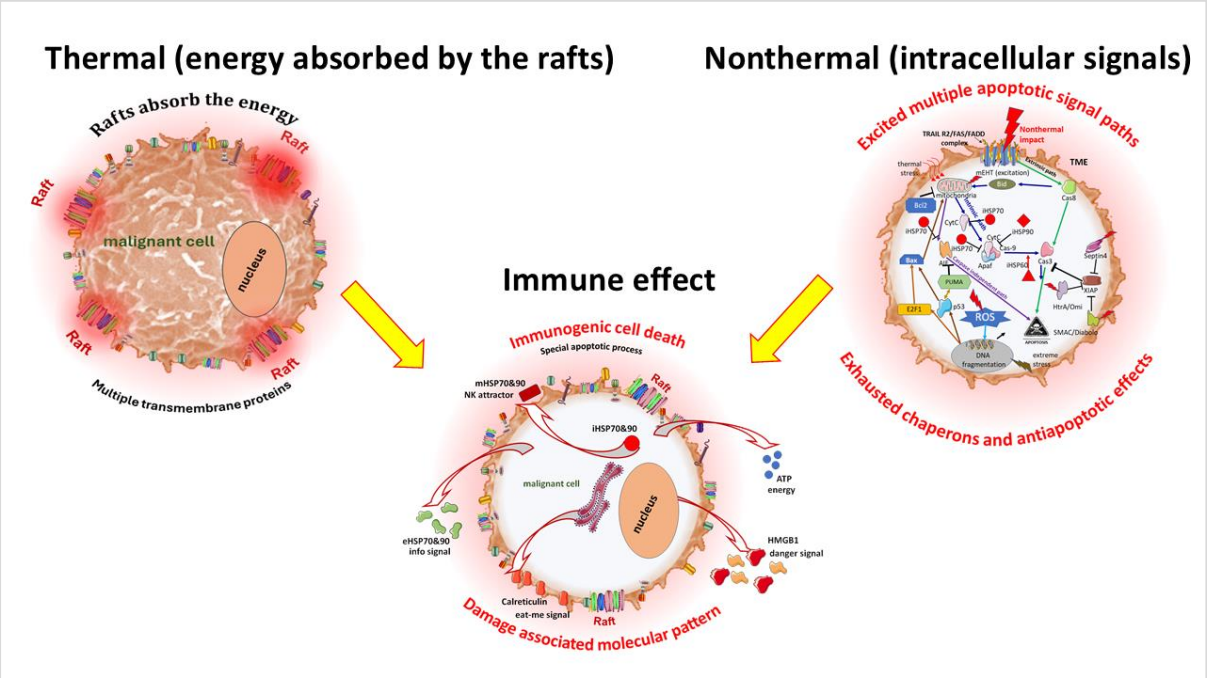
Wust P. et.al. (2022) Cancers

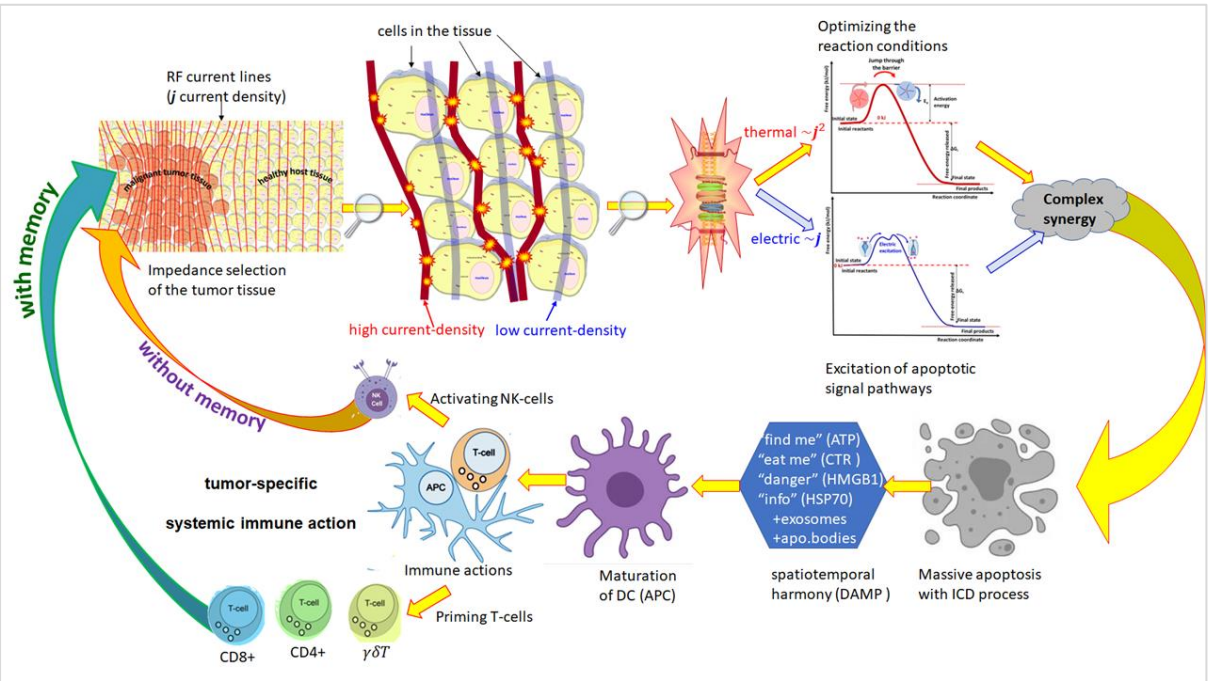





mEHT + DC therapy makes tumor-specific action
Quin W. et.al. (2014) Oncol. Reports
CD3+ (%)
CD8+ (%)
concentration (%)
12.8
7.76
29.3
9.53
65.1
17.1
control
mEHT treated
DC+mEHT treated
CD8+
S100 (DC marker)
Foxp3 (Treg marker)
Optical density
10607
25944
42773
30839
27685
25394
63068
53118
17496
Leukocytes
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
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
Non-treated
Treated
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
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
Excited multiple apoptotic signal paths
Exhausted chaperons and antiapoptotic effects
TME
ROS


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

Outline

- ✓ Strategy of mEHT – the immune activation
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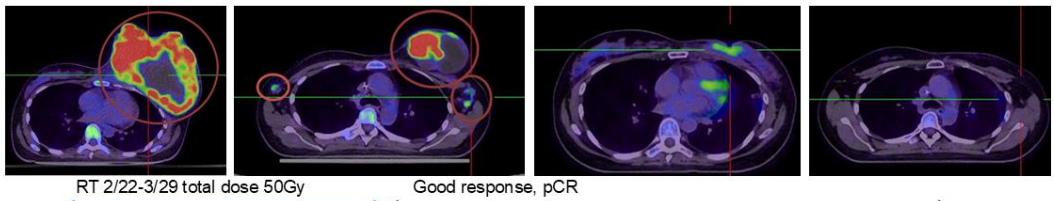
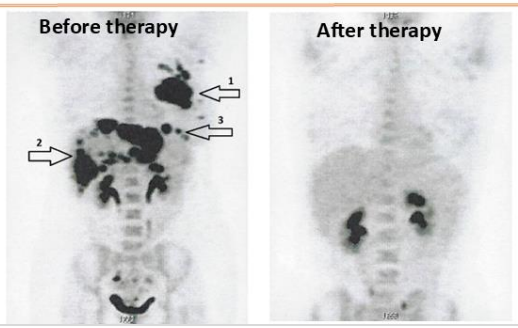
Marked local and distant response (immunogenic action)



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

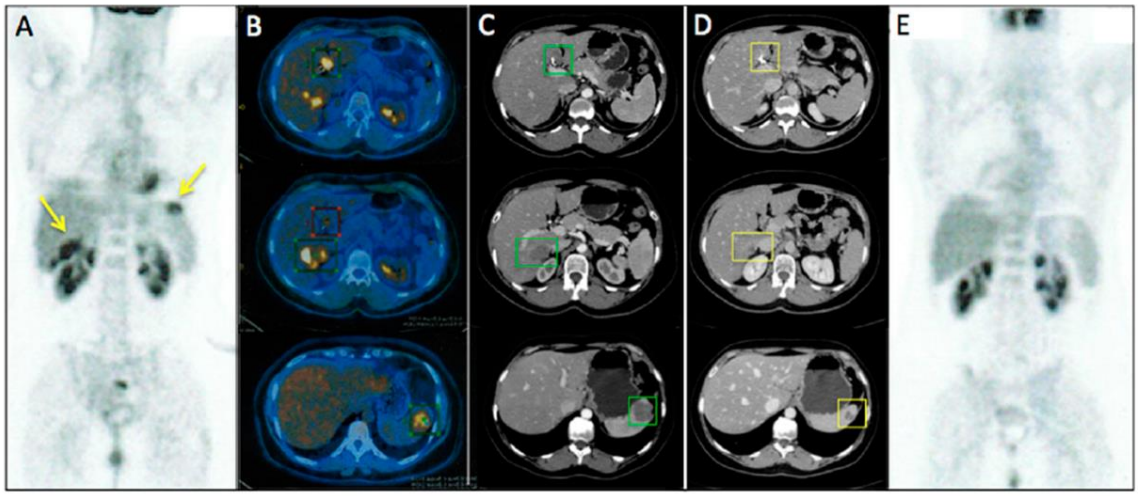
Stage IV Triple-Negative Breast Cancer



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

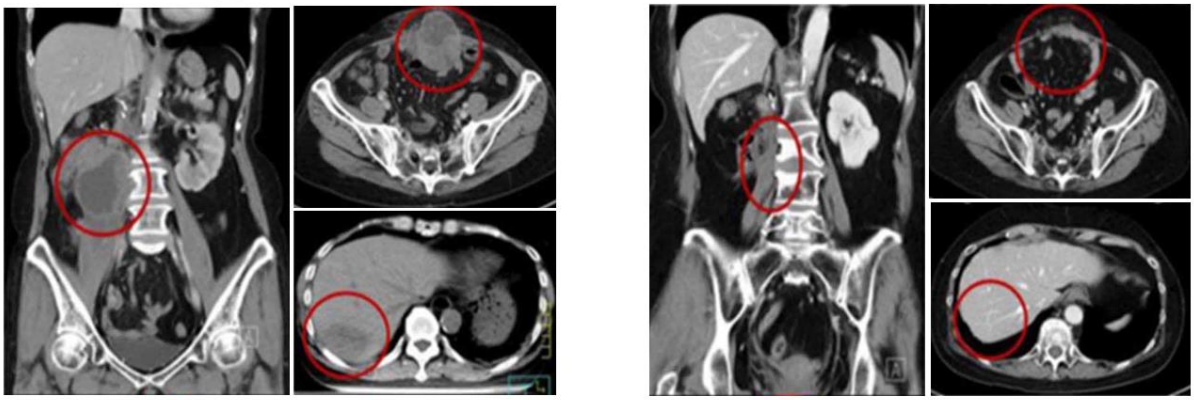


Metastatic urothelial carcinoma with abscopal tumor effect on liver metastases

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

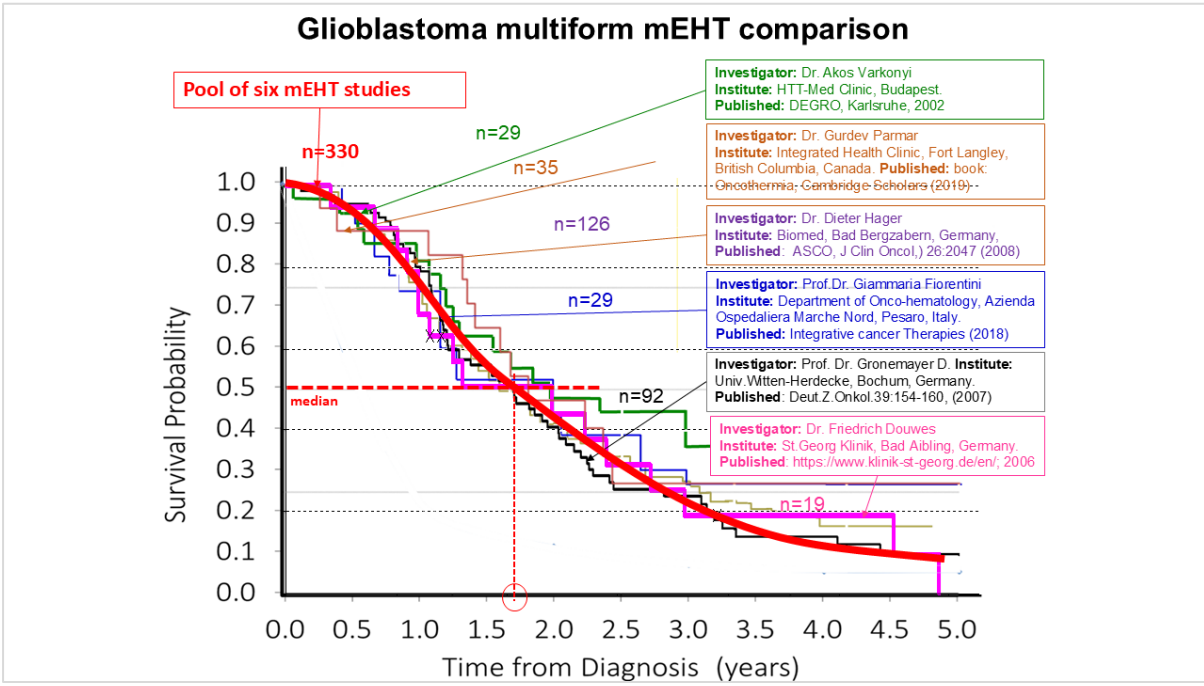
Before therapy

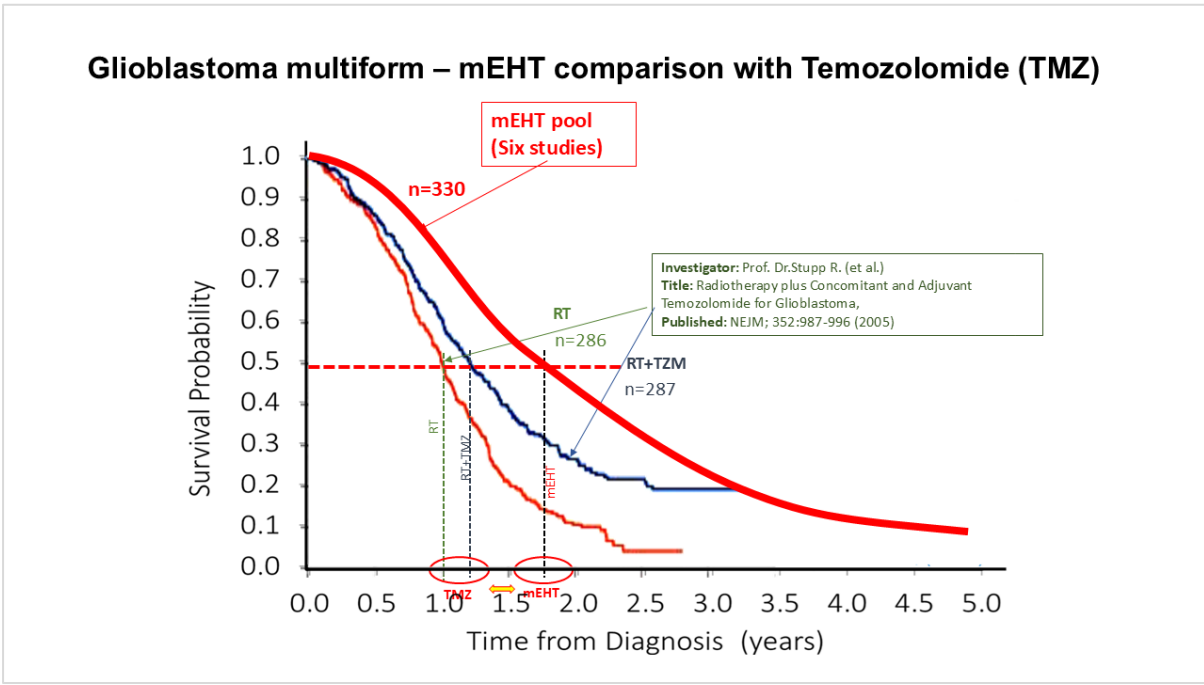
After therapy

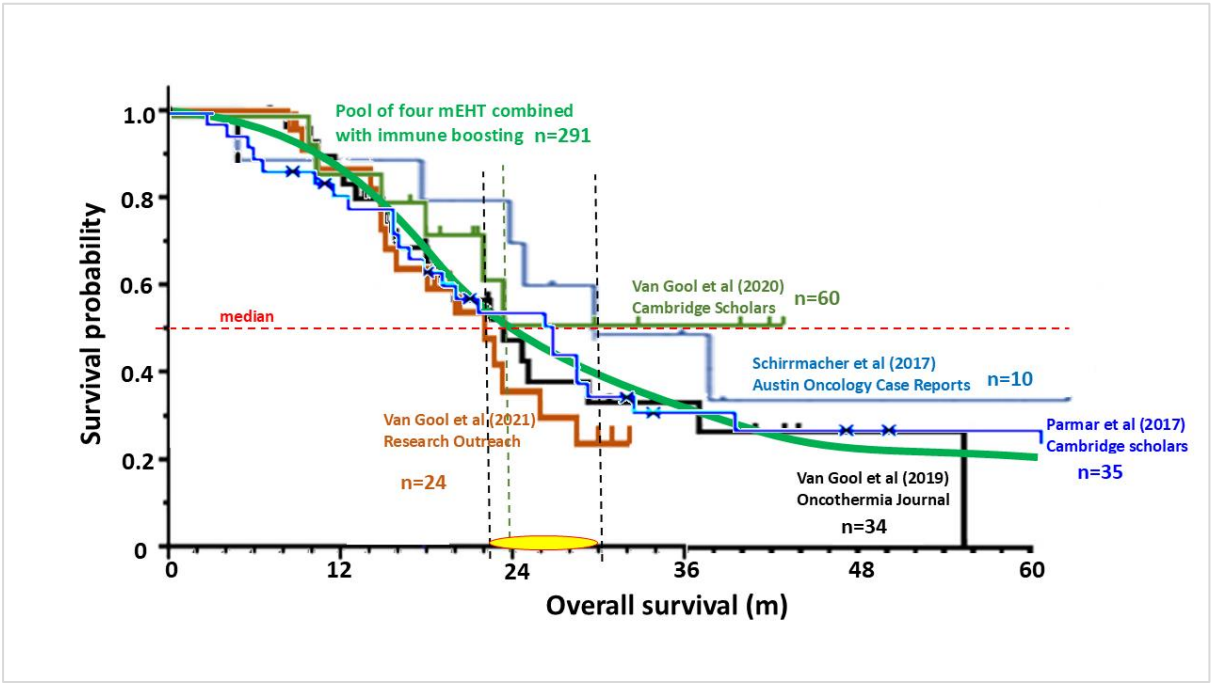


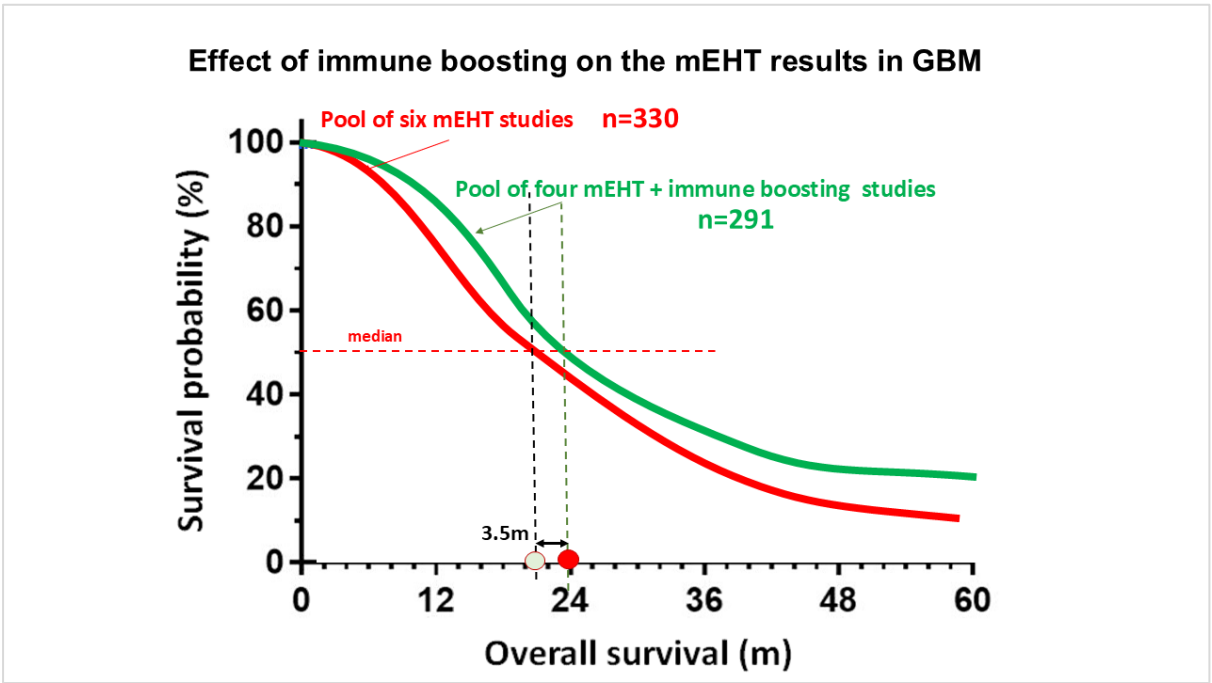
RT to abdomen mass 40Gy

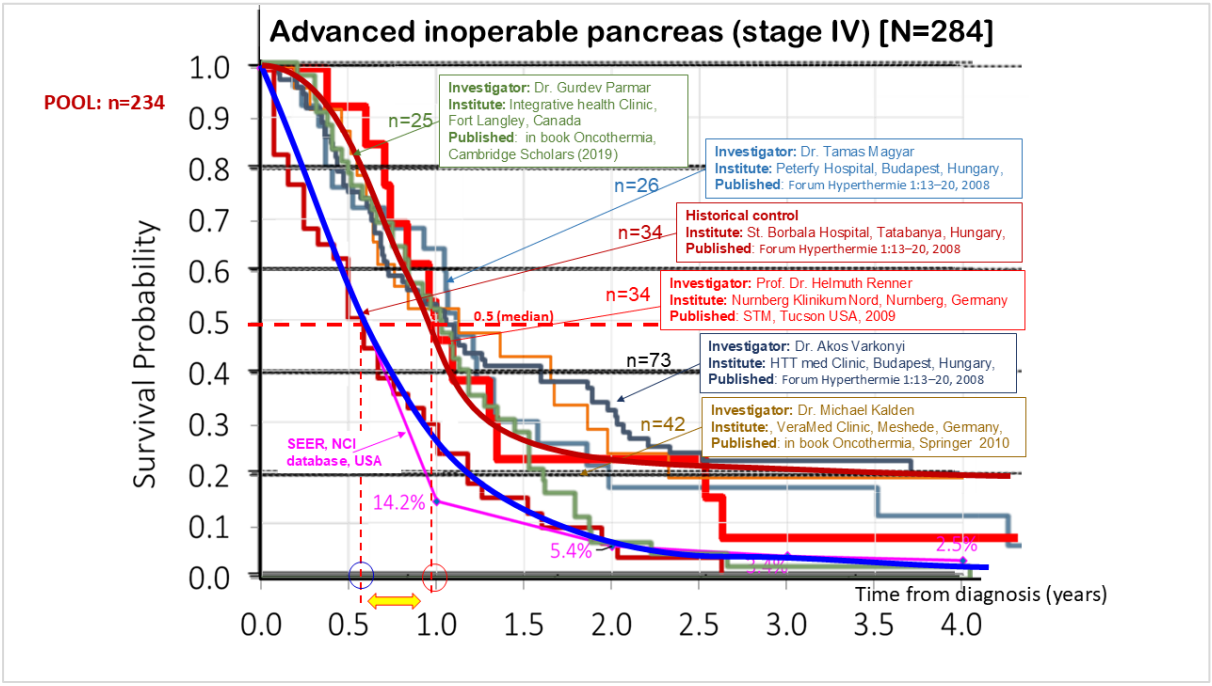
+ 6 x mEHT

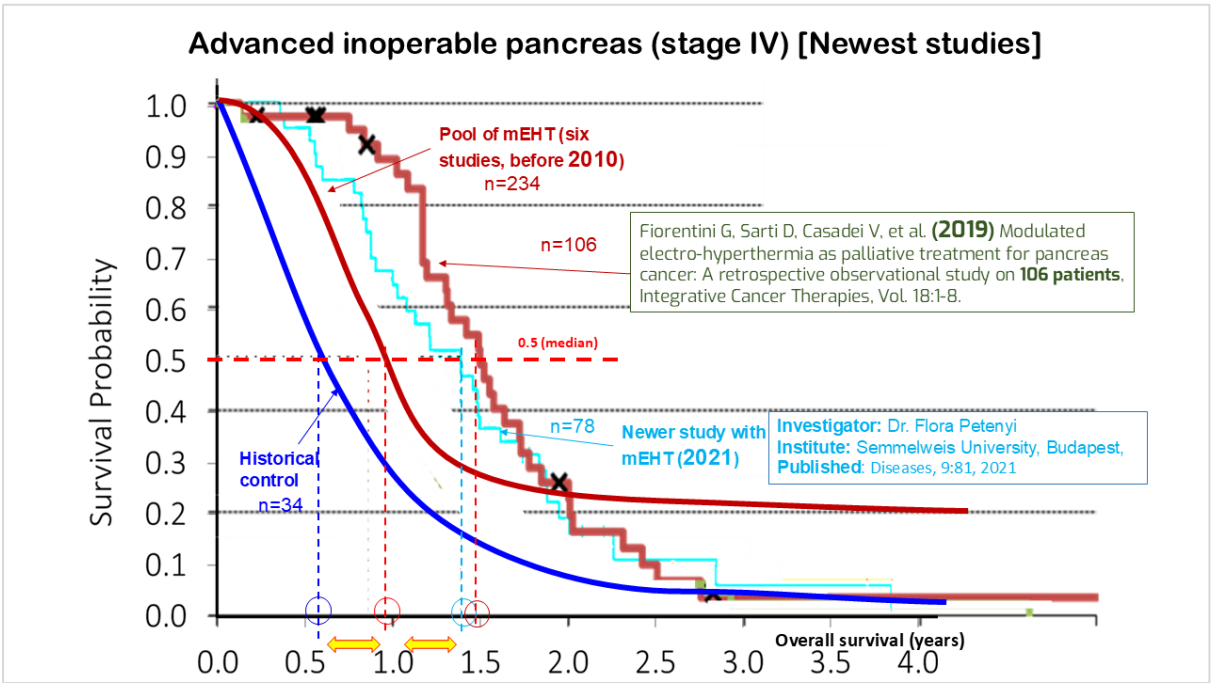

Glioblastoma multiform mEHT comparison
Pool of six mEHT studies
n=330
n=29
n=35
n=126
n=29
n=92
n=19
median
Investigator: Dr. Akos Varkonyi
Institute: HTT-Med Clinic, Budapest.
Published: DEGRO, Karlsruhe, 2002
Investigator: Dr. Gurdev Parmar
Institute: Integrated Health Clinic, Fort Langley, British 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
RT
n=286
RT+TZM
n=287
Investigator: Prof. Dr.Stupp R. (et al.)
Title: Radiotherapy plus Concomitant and Adjuvant Temozolomide for Glioblastoma,
Published: NEJM; 352:987-996 (2005)
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
1.0
0.8
0.6
0.4
0.2
0
0
12
24
36
48
60
Overall survival (m)

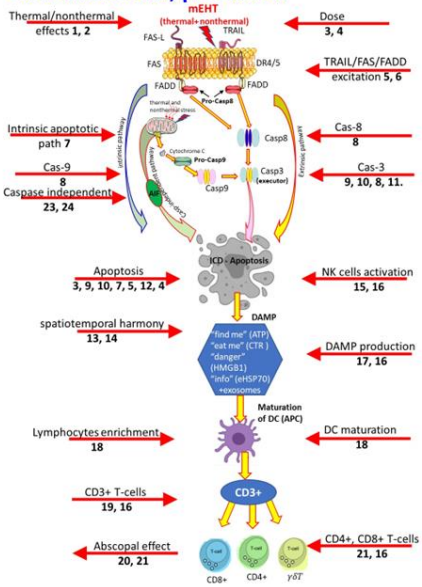

Effect of immune boosting on the mEHT results in GBM
Pool of six mEHT studies n=330
Pool of four mEHT + immune boosting studies
n=291
median
3.5m
Survival probability (%)
100
80
60
40
20
0
0
12
24
36
48
60
Overall survival (m)


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

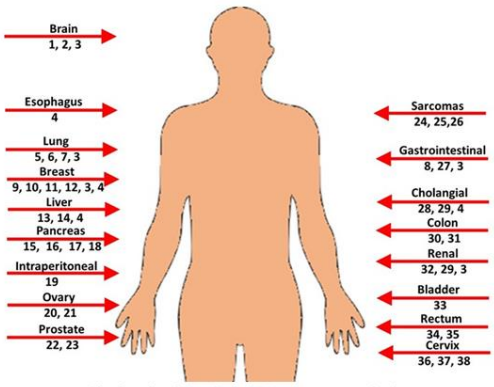
Publications

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],

Outline

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

Thank you for your attention

Prof.Szasz@gmail.com

15+ years of Oncothermia treatments in Italy

Presentation from "Oncotherm in Italy" conference 2025.04.02.

Prof. Giammaria Fiorentini

Società Italiana Ipertermia Oncologica (SIIO) – Via Casale Malatesta 10, 00049 Velletri, Roma, Italy;
segreteria@siio.it

Citation

Fiorentini, G. (2025) 15+ years of Oncothermia treatment results in Italy – Oncotherm in Italy, 2025.04.02.
https://www.youtube.com/watch?v=oph8_i84BBU&list=PLEaAiXVgvMsGMMHSufONT8E7zYBSSDNO4

Oncothermia Journal 37, September 2025., 24-45.
https://oncotherm.com/FiorentiniG_2025_Oncotherm_in_Italy_20250402

EMBASSY OF HUNGARY IN ROME
2ND APRIL 2025

15+ YEARS OF ONCOTHERMIA TREATMENT RESULTS IN ITALY

(STUDI CLINICI E ATTIVITA' DELLA SOCIETA' ITALIANA IPERTERMIA ONCOLOGICA-SIIO)

Prof. Giammaria Fiorentini

Società Italiana Ipertermia Oncologica (SIIO)

Via Casale Malatesta 10, 00049 Velletri, Roma

segreteria@siio.it

AGENDA

- ONCOTHERM DEVELOPMENT IN ITALY
- LIMITATIONS TO THE DEVELOPMENT OF HYPERTHEMRIA IN EUROPE AND ITALY
- FOUNDATION OF A NEW SCIENTIFIC SOCIETY DEDICATED TO HYPERTHERMIA
- LATEST NEWS

Development of Oncothermia in Italy (2004-2025)

2003 Prof Andras Szasz visiting professor at San Giuseppe Hospital, Empoli, Florence

2004 April, first Oncotherm 2000 device activated at Empoli-Florence, Italy

2005 May, second Oncotherm 2000 device activated at Massa Carrara Hospital, Italy

ONCOTHERM 2000 DEVICES IN ITALY (2005-2025)

1. San Giuseppe Hospital, Empoli, Florence (oncotherm 2000, active since 2004)
2. Apuane Regional Hospital, Massa Carrara (oncotherm 2000, active since 2005)
3. Istituto Tumori "Giovanni Paolo II" I.R.C.C.S. Bari (since 2007), actually with 2 devices: 2000 plus and new 2030
4. Casa di Cura Salaria , dott Carlo Pastore, Roma (oncotherm 3010 ML, active since 2012-22, ceased)
5. Centro Aktis, Napoli (oncotherm 2000, active since 2008)
6. Casa Di Cura M. Tommasini , Dott Astara, Jerzu, Sardegna, (oncotherm 2000, active from 2004 to 2008, ceased)
7. Clinica Demetra then Clinica Bellessere, dott Ballerini, Terni (oncotherm 2000, active since 2011)
8. ARTOI , Roma , prof Bonucci (oncotherm 2000, active since 2019) *
9. Department of Oncology, San Salvatore Hospital, Pesaro (oncotherm2000 plus active from 2016 to 2024, ceased) #
10. Integrative Oncology, IHF Out-patient Clinic, Bologna (oncotherm2000, active from 2021 to 2024, ceased)
11. Oncologia, Spedali Civili di Brescia (oncotherm 2000, active from 2008 to 2019, actually suspended) ,
12. Ospedale Poliambulanza , Brescia (oncotherm 2000, active from 2006 to 2012, ceased) #
13. Servizi Medici Avanzati, Republic of San Marino (active from 2012 to 2017,ceased) *

INTERNATIONAL CLINICAL HYPERTHERMIA SOCIETY – ITALIAN NETWORK

International Clinical Hyperthermia Society

Italian Network

(ICHS-IT)

About us

ICHS-IT is a working group dedicated to the use and development of modulated Electro Hypertermia (mEHT).

Our Protocols and Projects

ICHS-IT programs are oriented to treat any type of tumor with mEHT alone or in association with Chemo and/or radiotherapy

ICHS-IT is planning to activate several studies on mEHT for the treatment of brain, ovary, pancreatic, lung and kidney cancer and melanoma, in order to improve patients' care.

34th ANNUAL CONFERENCE OF THE INTERNATIONAL CLINICAL HYPERTHERMIA SOCIETY

International Training Workshop on
- Clinical Application of Local Hyperthermia
- Moderate and Extreme Whole Body Hyperthermia

4th International Oncotherm congress

September 22nd 2016

It has been requeted the patronage of

Programme: 34th ANNUAL CONFERENCE OF THE INTERNATIONAL CLINICAL HYPERTHERMIA SOCIETY (ICHS)

Thursday 22nd September 2016

Session 1

Topic: Biological basics, experimental and technical studies of hyperthermia

Chairman: S. Roussakow, G. Fiorentini

8.00 Technique of Whole-Body Hyperthermia and Fibromyalgia Syndrome
A. Von Ardenne

8.20 Critical Issues in the use of double antennas in superficial hyperthermia treatment. A. Di Dia

8.40 Local hyperthermia in combination with traditional chinese medicine C. Pang

9.00 Place and role of clinical hyperthermia in the system of thermotherapy in oncology: let' s define what we are doing
Sergey Roussakow

Session 2

Topic: Clinical evidences of increasing survival adopting hyperthermia alone or in combination with anti-cancer methods

Chairman: C. Pang, M. Hussein

9.30 Hypertermia combined with conventional and complementary anticancer treatment
J. Brenner

9.50 Colorectal cancer and the effect of the

10.50 Quo vadis oncological Hyperthermia:Update 2016 A. Szasz

11.10-11.20 coffee break

Session 3

Topic: Results and perspective of hyperthermia associated with radiotherapy and chemotherapy

Chairman: S. Dall'Oglio, F. Bunkeila

11.20 Hypertermia combined with radiation in cervical cancer C. Minnaar-Strauss

11.40 World-wide status of Hyperthermia
S. Maluta

12.00 Combination of hyperthermia and radiotherapy in pancreatic cancer
P. Gabriele

12.20 Prostate cancer: integration of radiotherapy and hyperthermia S. Dall'Oglio

12.40 Superficial Hyperthermia in association with Radiotherapy: toxicity and outcome in metastatic lesions. G. Cattari

1.00-1.30 pm LUNCH

Session 4

Topic: Workshop section

Chairman: P. Gabriele, S. Maluta

3.00 p.m. Extreme hyperthermia in lung lesions C. Gadaleta

3.20 p. m. Microwave ablation of large HCC by multiple synchronous antenne: technique, results and long term follow-up
L. Tarantino

Session 6

Topic: Peritoneal surface malignancies treated with Cytoreductive Surgery (CRS) and hyperthermic intraperitoneal chemotherapy(HIPEC) –PART I

Chairman: M. Deraco, S.Guadagni

3.40 p.m. HIPEC: state of the art
S. Kusamura

4.00 p.m. Ovarian Cancer I M. De Simone

4.20 p.m. Ovarian cancer II P. Sammartino

4.40 p.m. Use of C-Parp inhibitors in ovarian cancer F. Graziano

Session 7

Topic: Peritoneal surface malignancies treated with Cytoreductive Surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) -PART II

Chairman: C. Milandri. G. De Manzoni

TRATTAMENTI DI ONCOTHERMIA ESEGUITI IN ITALIA

Centro	Città	periodo	pz trattati	sedute ese	H pubblicc
INT Bari	Bari	gen-set 24	75	766	si
		2018-23	625	9997	si
H Carrara	MS	3/23-6/24	90	627	si
H Pesaro	Pesaro	2016-19	560	6720	si
H Pesaro	Pesaro	1/20-8/24	420	3870	si
IHF Bologn	Bologna	1/22-5/24	145	1312	no
H Empoli	Empoli	2004-2011	560	6000	si
			Totale 2475	29.292	

Villa Salaria, Roma, 2012-2022, dr Pastore,Oncotherm 3010 ML
5000 patients treated, 60.000 sessions delivered

ONCOTHERMIA IN THE TREATMENT OF PANCREATIC CANCER AND GLIOMA:RECENTE ARTICLES

- **Fiorentini G**, et Al. Modulated electro-hyperthermia in stage III and IV pancreatic cancer: Results of an observational study on 158 patients. World J Clin Oncol. **2021 Nov** 24;12(11):1064-1071. doi: 10.5306/wjco.v12.i11.1064. PMID: 34909400; PMCID: PMC8641006. **(IF 2.7)**

- Fiorentini C, Sarti D, Guadagni S, **Fiorentini G**. Immune response and locoregional treatments for peritoneal carcinomatosis. Int Rev Cell Mol Biol. 2022;371:97-116. doi: 10.1016/bs.ircmb. Epub 2022 Jul 8. **(IF 6.4)**

- **Fiorentini G**, et Al. Hyperthermia combined with chemotherapy *vs* chemotherapy in patients with advanced pancreatic cancer: A multicenter retrospective observational comparative study. World J Clin Oncol. **2023 Jun** 24;14(6):215-226. doi: 10.5306/wjco.v14.i6.215. PMID: 37398545; PMCID: PMC10311475. **(IF 2.7)**

ONCOTHERMIA IN THE TREATMENT OF PANCREATIC CANCER AND GLIOMA:RECENTE ARTICLES

- **Fiorentini G**, et Al. Modulated Electrohyperthermia in Integrative Cancer Treatment for Relapsed Malignant Glioblastoma and Astrocytoma: Retrospective Multicenter Controlled Study. Integr Cancer Ther. 2019 Jan-Dec;18:1534735418812691. doi: 10.1177/1534735418812691. Epub **2018 Dec 22**. PMID: 30580645; **(IF 3)**

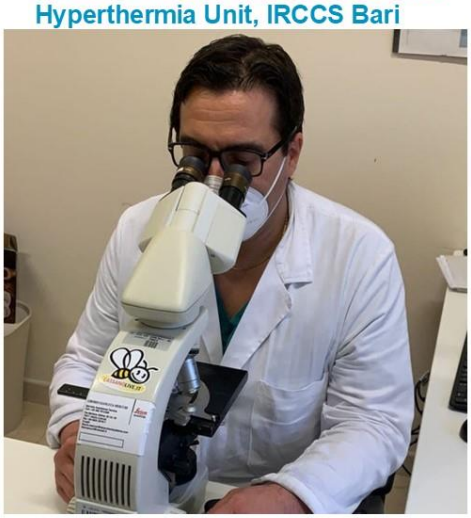
- **Fiorentini G** et Al. Modulated Electro-Hyperthermia as Palliative Treatment for Pancreatic Cancer: A Retrospective Observational Study on 106 Patients. Integr Cancer Ther. **2019 Jan-Dec**;18:1534735419878505. doi: 10.1177/1534735419878505. PMID: 31561722; PMCID: PMC6767725. **(IF 3)**

- **Fiorentini G** et Al. A Narrative Review of Regional Hyperthermia: Updates From 2010 to 2019. Integr Cancer Ther. **2020 Jan-Dec**;19:1534735420932648. doi: 10.1177/1534735420932648. PMID: 33054425 **(IF 3)**

- Lee SY, **Fiorentini G,** Szasz AM, Szigeti G, Szasz A, Minnaar CA. Quo Vadis Oncological Hyperthermia (2020)? Front Oncol. 2020 Sep 4;10:1690. doi: 10.3389/fonc.2020.01690. PMID: 33014841; PMCID: PMC7499808. **(IF 6.24)**

Today the Top Player is…..

Dr Girolamo Ranieri and his group Director Integrative Oncology and Hyperthermia Unit, IRCCS Bari



2018-2025 820 Pazienti , 11000 sedute ipertermia
ISTITUTO NAZIONALE TUMORI

Papers by Integrated Oncology Unit,Dr G. Ranieri, IRCCS Giovanni Paolo II Bari

- Gadaleta-Caldarola G, Infusino S, Galise I, **Ranieri G, et Al.**Sorafenib and locoregional deep electro-hyperthermia in advanced hepatocellular carcinoma: A phase II study. Oncol Lett. 2014 Oct;8(4):1783-1787. doi: 10.3892/ol.2014.2376. Epub 2014 Jul 24. PMID: 25202410; PMCID: PMC4156230. **(IF 2)**

- **Ranieri G, et Al**. Bevacizumab-Based Chemotherapy Combined with Regional Deep Capacitive Hyperthermia in Metastatic Cancer Patients: A Pilot Study. Int J Mol Sci. 2017 Jul 6;18(7):1458. doi: 10.3390/ijms18071458. PMID: 28684680; PMCID: PMC5535949. **(IF 5)**

- **Ranieri G**,et Al. Bevacizumab Plus FOLFOX-4 Combined With Deep Electro-Hyperthermia as First-line Therapy in Metastatic Colon Cancer: A Pilot Study. Front Oncol. 2020 Nov 3;10:590707. doi: 10.3389/fonc.2020.590707. Erratum in: Front Oncol. 2021 Feb 05;10:637880. doi: 10.3389/fonc.2020.637880. PMID: 33224885; PMCID: PMC7670056. **(IF 5.7)**

AGENDA

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- LATEST NEWS

MAJOR OBSTACLES TO THE SPREAD OF HYPERTHERMIA IN ITALY and EUROPE - 2025

In the studies reported in this last decade, HT confirms a general trend of improvement in clinical outcomes as can be observed in similar previous studies and reviews. Experts, who use HT daily, believe that the reasons for the low acceptance by doctors and diffusion between patients are not the poor efficacy of the method, but

1) the limited diffusion of qualified hyperthermia centers in Europe and Italy
2) the lack of guidelines to maintain temperature monitoring and poor quality of treatment schedules.
4) the hyperthermic centers don't have network and adopt heterogeneous practices and not easily reproducible everywhere
5) the lack of government funding and nothing from the non-interested pharmaceutical industry.
6) many hyperthermic centers have outdated technologies and devices that induce poor tolerance of patients

MAJOR OBSTACLES TO THE SPREAD OF HYPERTHERMIA IN ITALY and EUROPE - 2025

7) The lack of clear info given by Public Institutions and media that limits information access for patients, their families and doctors

8) the paucity of university teaching and training courses, specially in Italy

9)the competition with radiotherapy devices and the wrong idea that it is wasted time warming up a patient

In future the research should focus more on new devices and detecting these parameters: patients' acceptability, increased quality of life, tumor response, local control rates, time to progression, overall survival when HT is adjunct to classical therapies. Standardized equipments and treatments needed

AGENDA

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WHY SIIO IS NECESSARY IN ITALY AND EUROPE ?

Since 2018 randomized studies, with increased OS and PFS, have been published in Local Advanced Cancer of the Cervix (LACC), cancer of rectum and anus, soft tissues sarcoma, breast chest recurrences, prostatic cancer, gliomas and cancer of head and neck.

In 2022 AIRO and AIOM have accepted the ESTRO and ESMO guidelines, including hyperthermia in the thoracic recurrences from breast cancer and in not operable or borderline operable soft tissue sarcomas, both after major evidence from large randomized studies.

It seems essential to develop an official network of hyperthermia in Italy where patients can be treated with competence in the context of shared decisions in multidisciplinary groups

Lorem Ipsum sit doler amet

HYPERTHERMIC TREATMENTS IN ITALY: NUMBER OF PATIENTS

More than **3000 patients** were treated with hyperthermia every year in Italy, **86% in private clinics and 14% in public Hospitals**, all patients are in the metastatic phase relapsing after chemotherapy and radiotherapy with a life expectancy ranging from 3 months to 24 months. It is estimated by default that at least **28,000 sessions of hyperthermia are administered every year in Italy.**

Lorem Ipsum sit doler amet

HYPERTHERMIC TREATMENTS IN ITALY:

No patients are currently enrolled in research phase III studies. All patients are treated in a palliative way following experience and personalized protocols present in each individual centre and dictated by the experience of the physicians, expert in hyperthermia. Each patient received eleven hyperthermia sessions (range 3-28). The median duration of hyperthermia session was 55 minutes (range 50 -110), 2-3 weekly sessions were administered on alternate days,

Lorem Ipsum sit doler amet

HYPERTHERMIC TREATMENTS IN ITALY

The patients treated with hyperthermia concurrently received single chemotherapy at personalized doses and 90% of them received integrative and supportive therapies.

Consideration and attention in SIIO centres were given to evaluate the improvement in patients' quality of life and compliance using the ESAS scale, ECOG performance status scale and electronic self-report assessment .

Different brands of hyperthermia devices are currently adopted in Italy: Andromedic, Alba, BSD, Celsius, Oncotherm, Syncrotherm.

Lorem Ipsum sit doler amet

FOUNDATION of SIIO

- The Italian Society of Oncological Hyperthermia (Società Italiana di Ipertermia Oncologica - SIIO) was founded in September 2023 and became operative in January 2024 with the election of president, treasurer, secretary and councilors
- to promote oncological hyperthermia in Italy
- to better cure and serve cancer patients
- to give correct data to the Italian Ministry of Health and Regional Health Departments
- to reintroduce hyperthermia into the care services of the National Health System, cancelled on 31 December 2024

Lorem Ipsum sit doler amet

CENTRI SIIO

SOCIETA' ITALIANA DI IPERTERMIA ONCOLOGICA MOTTO

In the past, present and future...

…clinical experience and multidisciplinary together

RATIONALE and PURPOSES of SIIO

1. **To encourage** the advancement of hyperthermia in all areas of medical sciences.
2. **To organize a national database** regarding tumours treated with hyperthermia: defining histology, genetics, stage, line of therapy, therapeutic results, calculation of the duration of OS and response, and toxicities.

Lorem Ipsum sit doler amet

RATIONALE and PURPOSES of SIIO

3. **To define new phase II and III protocols** of chemo-hyperthermia, radio-hyperthermia, immuno-hyperthermia, magnetic hyperthermia, palliative medicine-hyperthermia.

4. **To develop Health Technology Assessment** (HTA) in hyperthermia as a multidisciplinary evaluation process that aims to determine the economic value of hyperthermia technologies and interventions to inform decision-making to promote an equitable, efficient and high-quality in NHS.

5. **To introduce the HYPERTHERMIA** medical service provided Italian NHS for oncological patients (free for oncological patients).

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CONCLUSIONS

SIIO wants to expand hyperthermia following the national and international guidelines through the increase the number of centres and the training of doctors, medical engineers, medical physics, nurses and technicians. SIIO is open to the participation of groups of patients and their families and to all interested professionals and stakeholders.

SIIO intends to collaborate constantly with the Agency for Regional Healthcare Services (AGENAS), chapter of Italian Ministry of Health, with all medical associations to provide truthful and real information on the use of hyperthermia to obtain the best results, lower costs for HS and facilitate the access of patients to hyperthermic treatments in Italy.

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EDUCATIONAL EVENTS

Società Italiana di Ipertermia Oncologica

Data: Aprile – Giugno 2025

Master Universitario II Livello " Oncologia Integrata Prevenzione, Terapie Tradizionali, Innovative e di precisione " VII Edizione. Corso Universitario di Alta Formazione : " Ipertermia applicazioni specialistiche" Education provider: Consorzio Inter-Universitario Humanitas, Roma

European Thermotherapy School 2025

Date: Monday, April 14-16, 2025

Education provider: Erasmus MC Cancer Institute, Amsterdam.

This 3-day European thermotherapy school aims to teach radiation oncologists, (clinical) physicists, radiation therapists, other medical specialists, and researchers the knowledge to perform high quality hyperthermia treatments.

Lorem Ipsum sit doler amet

European Thermotherapy School 2025

The European thermotherapy school aims to provide knowledge about the fundamentals of thermoradiotherapy and how to perform high quality treatments by experts from the thermotherapy field.

ASSOCIATIONS OF CANCER PATIENTS SUSTAINIG SIIO

- Volto della Speranza, Massa Carrara,Toscana
- ASTRO, Empoli-Firenze,Toscana
- Il Giornale di Mirella Morigia, Roma
- ANVOLT, Regione Trentino - Alto Adige
- Salute Donna, Siracusa, Sicilia

REINTRODUCTION OF HYPERTHERMIA IN THE ESSENTIAL LEVEL OF CARE

To make hyperthermia present in the services of the National Health Service, free of charge to cancer patients, SIIO submitted an application to the Ministry of Health in March and November 2024 and had three meetings at the highest level with the most important Italian Authorities

PER SOSTENERE INTRODUZIONE DI IPERTERMIA NEI LEA
29/9/24 INCONTRO CON DOTT. MANTOAN, DIRETTORE AGENAS

18/11/24 INCONTRO CON PROF. AMERICO CICCHETTI (DIRETTORE GENERALE DELLA PROGRAMMAZIONE SANITARIA) PER INTRODUZIONE NEI LEA DI IPERTERMIA E VALURAZIONE HTA NEL PROGETTO NAZIONALE IPERTERMIA ONCOLOGICA

AGENDA

- ONCOTHERM DEVELOPMENT IN ITALY
- LIMITATIONS TO THE DEVELOPMENT OF HYPERTHEMRIA IN EUROPE AND ITALY
- FOUNDATION OF A NEW SCIENTIFIC SOCIETY DEDICATED TO HYPERTHERMIA
- LATEST NEWS

27/3/25 INCONTRO CON IL VICE-MINISTRO DEL MINISTERO DELLA SALUTE DOTT MARCELLO GEMMATO DI Dr. GIROLAMO RANIERI E Ing. DILETTA TRALDI

LATEST NEWS……

Yesterday 1st April 2025, the Spanish Ministry of Health has accepted the request of the SEOR (Sociedad Española de Oncología Radioterápica) and has included hyperthermia in the national handbook of therapeutic services for cancer patients. Each hyperthermia session will be paid to the hospital that provides it 270 Euros.

……but also in Italy something is changing..

Please Ing Diletta Traldi tell us your story

BUT… SOMETHING HAPPENED

MY EXPERIENCE WITH HYPERTHERMIA

My father has a metastatic colon cancer.

That led me to:

- **Get close to HT**
- **See its deep efficacy**

One year after surgery and adjuvant therapy metastases at lungs, liver and peritoneum, here particularly widespread

→ Dad had to start with chemotherapy (1st line Folfox+Bevacizumab)

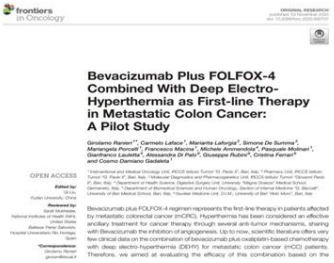
→ I started to look for some additional therapy to boost chemotherapy and after reading several papers I found HT

→ Dad started also with HT with Dr Ranieri at Istituto Tumori "Giovanni Paolo II" I.R.C.C.S. Bari

MY EXPERIENCE WITH HYPERTHERMIA

6 months later

complete response in abdominal area treated with HT and results at 1 year perfectly fit in a Pilot study led by Dr. Ranieri:



frontiers in Oncology

ORIGINAL RESEARCH

Bevacizumab Plus FOLFOX-4 Combined With Deep Electro-Hyperthermia as First-line Therapy in Metastatic Colon Cancer: A Pilot Study

OPEN ACCESS

PFS in patients treated with Folfox+bevacizumab+HT was 2.7 months longer (median 12.1 months) than patients only treated with same 1st line without HT

Dr Ranieri told me about SIIO and I was more than convinced to support. Dr Fiorentini accepted me as PRP (Public Relations Person)

My will is to assist SIIO in:

- **Encouraging use of HT through conferences and events**
- **Making cancer patients aware HT exists and is effective without any relevant side effect**
- **HT back in LEA soon (covered by NHS) as since January 1st it has been excluded**

DOUBLE ACTION: REGIONAL AND NATIONAL LEVEL

Since January 1st 2025 HT is not in LEA anymore, it meant interruption of care with NHS in Italy

1. We worked with Puglia administrators to the resumption of HT in Bari (hub also for patients coming from outside the region)

Nicola Paladino 18.03.2025 14:24:21 GMT+02:00

Michele Emiliano 18.03.2025 16:59:33 GMT+02:00

Provvedimento adottato in aggiunta agli argomenti iscritti all'o.d.g.: ai sensi dell'art.10, comma 3, del Regolamento interno.

REGIONE PUGLIA

Deliberazione della Giunta Regionale

N. 319 del 17/03/2025 del Registro delle Deliberazioni

Codice CIFRA: SGO/DEL/2025/00038

OGGETTO: Approvazione pacchetti di day-service. Modifica tariffario regionale ex D.G.R. n. 1863 23/12/2024.

L'anno 2025 addì 17 del mese di Marzo, si è tenuta la Giunta Regionale, previo regolare invito nelle persone dei Signori:

Sono presenti:	Nessuno assente.
Presidente Michele Emiliano	

PAC/DAY SERVICE TERAPEUTICO CHEMIO/IMMUNOTERAPIA PER NEOPLASIE MALIGNE IN COMBINAZIONE CON IPERTERMIA LOCOREGIONALE ESTERNA

Il Day Service chemioterapeutico - infusionale può comprendere diversi accessi a seconda del programma assistenziale specifico per il singolo paziente. Il numero di accessi massimo per ciclo è di n. 30 sedute/anno per singolo Day Service chemioterapeutico. Il costo del farmaco chemioterapico/antitumorale é rimborsato attraverso le procedure del File F.

Descrizione Diagnosi e Procedure per SDA	ICD9-CM		tariffa (€)
TARIFFA DAY SERVICE PER SINGOLO ACCESSO (Chemioterapia + Ipertermia)			189,00 €

DELIBERA

1. di approvare i pacchetti di day-service valutati positivamente nella riunione del Tavolo tecnico regionale "day-service" nella riunione del 12 marzo 2025, dettagliati nell'Allegato A, parte integrante e sostanziale del presente provvedimento, di seguito elencati :
   - CHEMIO/IMMUNOTERAPIA PER NEOPLASIE MALIGNE ED ONCOEMATOLOGICHE;
   - CHEMIO/IMMUNOTERAPIA PER NEOPLASIE MALIGNE ED ONCOEMATOLOGICHE IN COMBINAZIONE CON TRASFUSIONE;
   - CHEMIO/IMMUNOTERAPIA PER NEOPLASIE MALIGNE IN COMBINAZIONE CON IPERTERMIA LOCOREGIONALE ESTERNA;

DOUBLE ACTION: REGIONAL AND NATIONAL LEVEL

Since January 1st 2025 HT is not in LEA anymore, it meant interruption of care with NHS in Italy

2. We are working at the national level to push forward the formal request already submitted by SIIO represented by Dr Fiorentini

LEA1091 - Richiesta di aggiornamento LEA

Alla
Commissione nazionale per l'aggiornamento dei LEA e la promozione dell'appropriatezza nel Servizio sanitario nazionale
Direzione Programmazione sanitaria - Ufficio 5
Ministero della salute

Oggetto: LEA1091 - Richiesta di aggiornamento LEA

Sezione 1 - Questa sezione deve essere compilata se la richiesta riguarda una specifica prestazione o un servizio

1.1 - Prestazione o servizio:
Ipertermia Oncologica

2.1 - Indicazione clinica o condizione/patologia/forma o stadio clinico per cui la prestazione è necessaria e appropriata:
da studi fase III nei sarcomi e nelle recidive toraciche da cancro mammella da studi di fase II nei tumori del cervello, pancreas, retto, polmoni, carcinosi peritoneali , metastasi epatiche, metastasi ossee e

3.1 - Tecnologia utilizzata e rilevante per l'esecuzione della prestazione:
ipertermia capacitiva esterna, ipertermia radiativa

4.1 - Si propone che questa prestazione/servizio sia:
Inclusa

we met Deputy Minister of Health (Dr Marcello Gemmato) to highlight the current discrepancy: HT can be requested in an inpatient setting (as outlined in ICD-9) but cannot be provided in an outpatient setting


Thank you

Final 5 year results from the randomised controlled trial on modulated electro-hyperthermia added to chemotherapy for the management of locally advanced cervical cancer

Presentation from "Oncotherm in Italy" conference 2025.04.02.

Dr. Carrie Anne Minnaar

University of Witwatersrand, South Africa

Citation

Minnaar, C.A. (2025) Final 5 year results from the randomised controlled trial on modulated electro-hyperthermia added to chemotherapy for the management of locally advanced cervical cancer – Oncotherm in Italy, 2025.04.02.
https://www.youtube.com/watch?v=Br4kmGCCJQU&list=PLEaAiXVgvMsGMMHSufONT8E7zYBSSDNO4

Oncothermia Journal 37, September 2025., 46-58.
https://oncotherm.com/MinnaarCA_2025_Oncotherm_in_Italy_20250402

Final 5 year results from the randomised controlled trial on modulated electro-hyperthermia added to chemoradiotherapy for the management of locally advanced cervical cancer

Carrie Anne Minnaar[1]

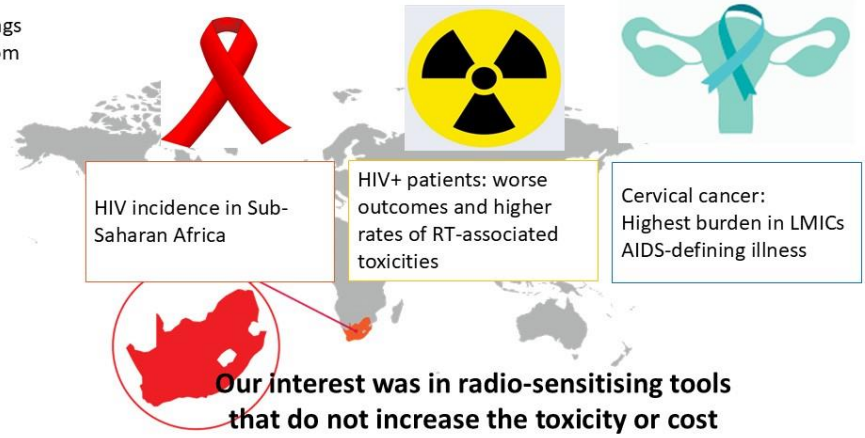
[1] University of Witwatersrand, South Africa

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG 100 1922 2022

Background

Resource constrained settings report poorer outcomes from cancer treatment:

- Inadequate access to treatment
- Sub-optimal treatment
- Co-morbidities
- Poverty



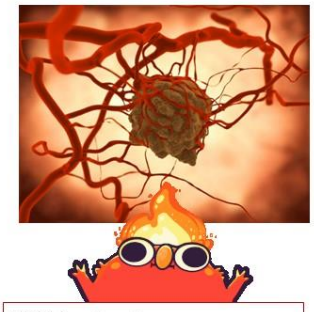
HIV incidence in Sub-Saharan Africa

HIV+ patients: worse outcomes and higher rates of RT-associated toxicities

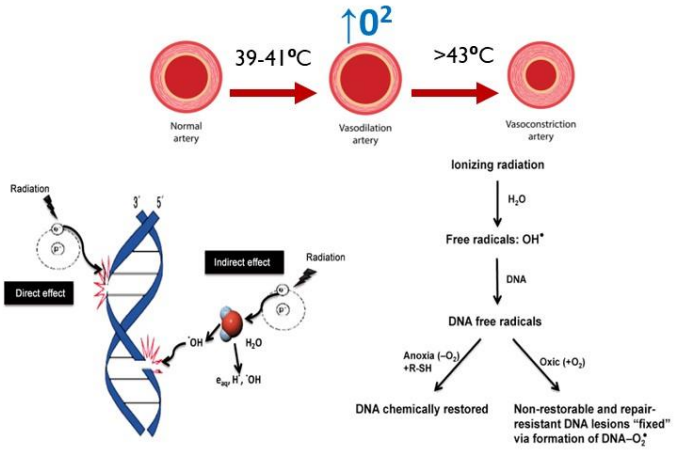
Cervical cancer:
Highest burden in LMICs
AIDS-defining illness

Our interest was in radio-sensitising tools that do not increase the toxicity or cost profile in resource constrained settings

Background



Mild heating increases oxygen perfusion, enhancing the damage done by ROS and inhibiting the repair processes



Methodology

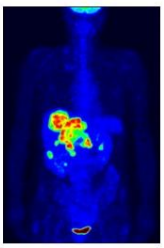
Sample:
Stage IIB-IIIB
Staged clinically: exam, chest x-ray; abdominal/pelvic ultrasound.

Control Group
50Gy EBRT
3x8Gy HDR
BT, 80mg/m²
cisplatin

Randomised using an online tool (RedCap)
Stratum: HIV status

Intervention Group
50Gy EBRT
3x8Gy HDR
BT, 80mg/m²
cisplatin
+ mEHT

HIV-positive participants were included provided their CD4 count was >200cells/mm³ /they had been on ART for >6m.



LDC:
PET/CT pre-treatment & 6m post-treatment.

Survival:
Last known disease status used for LTFU

QoL:
EORTC CX24 forms

Statistics:
Kaplan-Meier charts; Log rank tests; frequency tables; Markov model

Clinicians conducting follow ups were blinded to the group

Methodology:

mEHT

- 2 x per week
- Immediately before external beam RT
- Max 30 minutes between HT and RT
- Treated for 60 minutes and
- Aimed for at least 130W

Results

PLOS ONE

IJH INTERNATIONAL JOURNAL OF HYPERTHERMIA and thermal therapies

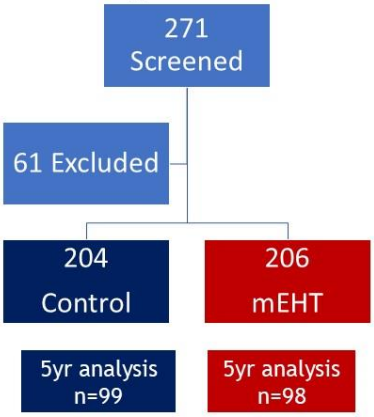
frontiers in Medicine

cancers

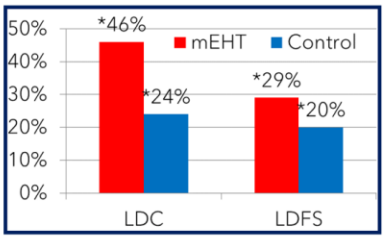
ICHS 38.
38th Conference of the International Clinical Hyperthermia Society

ESTRO 2021

Phase III RCT 2014-2023
HR Ethics Committee : M1704133
ClincialTrials.gov ID: NCT03332069



Results: Local Disease Control



210 Randomised Participants	Control		mEHT		Chi Squared
	n	%	n	%	
LDC achieved at 6 months	20	24.1%	40	45.5%	*p = 0.003*
LDFS at six months	20	19.8%	39	38.6%	*p = 0.003*

PLOS ONE

ESTRO 2024

Results: Safety

6 months post treatment

- No dose-limiting toxicities
- High Compliance (97% completed ≥8 treatments)
- No significant differences in CRT-related toxicity between treatment groups
- Toxicity:
  - grade 1–2 adipose burns: 9.5%
  - grade 1 surface burns: 2%
  - pain during mEHT: 8.6%

INTERNATIONAL JOURNAL OF HYPERTHERMIA and thermal therapies

Late Toxicity

At three years still no difference in late toxicities between the groups

cancers

No effect on late toxicity at 5 years

ESTRO 2024

Results: Local Disease Contr

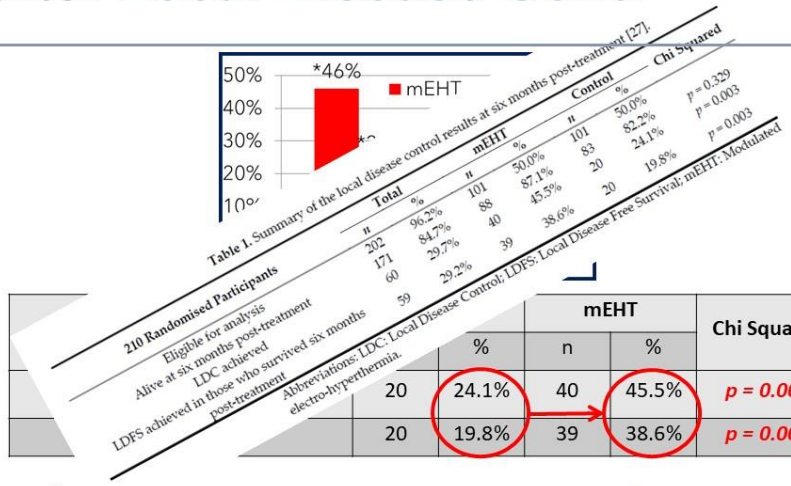


Table 1. Summary of the local disease control results at six months post-treatment [27].

	Total		mEHT		Control		Chi Squared
	n	%	n	%	n	%	
210 Randomised Participants							
Eligible for analysis	202	96.2%	101	50.0%	101	50.0%	$p = 0.329$
Alive at six months post-treatment	171	84.7%	88	87.1%	83	82.2%	$p = 0.003$
LDC achieved	60	29.7%	40	45.5%	20	24.1%	$p = 0.003$
LDFS achieved in those who survived six months post-treatment	59	29.2%	39	38.6%	20	19.8%	

Abbreviations: LDC: Local Disease Control; LDFS: Local Disease Free Survival; mEHT: Modulated electro-hyperthermia.

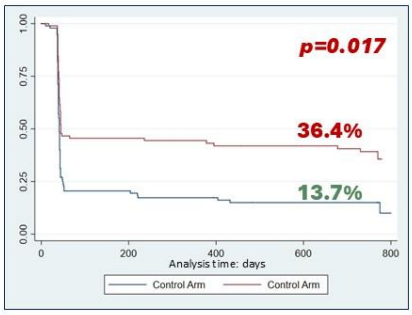
		mEHT		Chi Squared
	%	n	%	
20	24.1%	40	45.5%	*p = 0.003*
20	19.8%	39	38.6%	*p = 0.003*

PLOS ONE

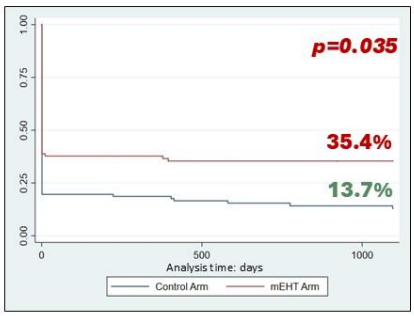
ESTRO 2024

Results: 3 year Disease Free Survival

2 Year Disease Free



3 Year Disease Free



	OR	p=value	[95%CI]
2 year	3.59	*0.001*	1.79-7.21
3 year	3.4	*0.001*	1.71-6.91

cancers

Results: Quality of Life

Table 9. Mean change in scores from baseline to 24 months in the mEHT and Control Group.

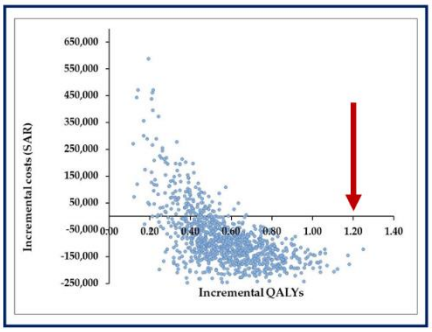
	mEHT				Control			
	Mean	SD	95%CI	*p*-Value	Mean	SD	95%CI	*p*-Value
Visual Analogue	25.1	21.5	16.6 to 33.6	$p < 0.0001$	15.6	31.9	2.9 to 28.2	$p = 0.0176$
Global Health	23.2	31.7	11.7 to 35.6	$p = 0.0002$	17.3	29.1	6.0 to 28.6	$p = 0.0041$
Financial Burden	−26.1	60.9	−48.0 to 4.1	$p = 0.0216$	−16.7	46.7	−34.8 to 1.4	$p = 0.0698$
Symptom Scales								
Pain Reduction	−34.4	32.8	−46.2 to −22.6	$p = 0.0001$	−15.5	35.7	−29.3 to −16	$p = 0.0298$
Nausea/Vomiting	−13.0	27.7	−23.0 to −3.0	$p = 0.0122$	−1.2	18.7	−8.4 to 6.1	$p = 0.7383$
Fatigue reduction	−18.4	27.9	−28.5 to −8.4	$p = 0.0008$	−10.7	34.0	−23.9 to 2.4	$p = 0.1071$
Functional Scales								
Social	12.0	31.2	0.7 to 23.2	$p = 0.0375$	17.3	41.7	1.1 to 33.4	$p = 0.0373$
Cognitive	19.8	33.2	7.8 to 31.6	$p = 0.0020$	−4.2	28.9	−15.4 to 7.0	$p = 0.4523$
Emotional	27.3	30.3	16.4 to 38.3	$p < 0.0001$	17.9	34.2	4.6 to 31.1	$p = 0.0101$
Role Function	9.4	35.1	−3.3 to 22.1	$p = 0.1415$	7.1	35.0	6.4 to 20.7	$p = 0.2893$
Physical	11.7	21.2	4.0 to `9.3	$p = 0.0040$	2.6	27.2	−7.9 to 13.2	$p = 0.6150$

Abbreviations: FIGO: CI: Confidence Interval; mEHT: Modulated Electro-Hyperthermia; SD: Standard Deviation.

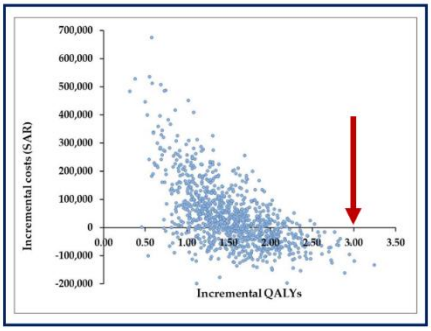
Overall significant improvement in 10 out of 11 scores in the mEHT group at 2 years

Results: Cost Effectiveness Analysis

Government model
82.2% probability



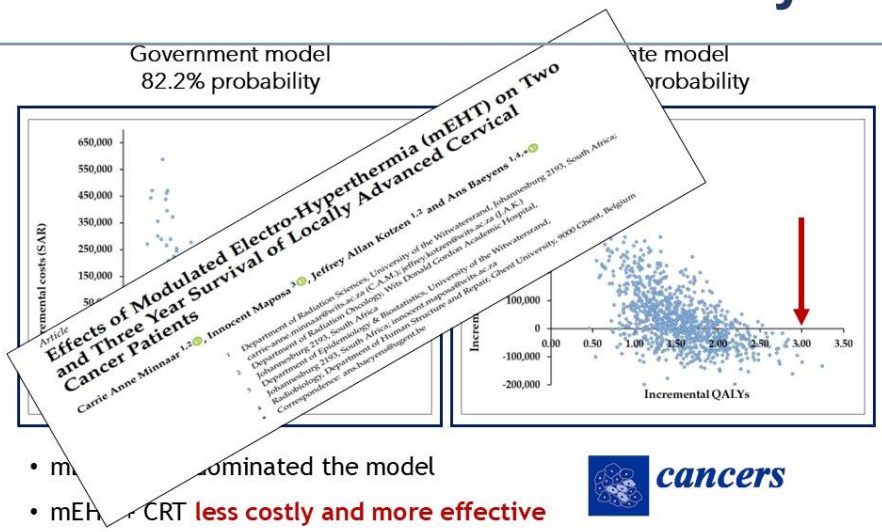
Private model
77.7% probability



- mEHT + CRT dominated the model
- mEHT + CRT **less costly and more effective**

Results: Cost Effectiveness Analysis

Government model
82.2% probability



Article
Effects of Modulated Electro-Hyperthermia (mEHT) on Two and Three Year Survival of Locally Advanced Cervical Cancer Patients
Carrie Anne Minnaar 1,2, Innocent Maposa 3, Jeffrey Allan Kotzen 1,2 and Ans Baeyens 1,4,*
1 Department of Radiation Sciences, University of the Witwatersrand, Johannesburg 2193, South Africa; carrie-anne.minnaar@wits.ac.za (C.A.M.); jeffrey.kotzen@wits.ac.za (J.A.K.)
2 Department of Radiation Oncology, Wits Donald Gordon Academic Hospital, Johannesburg 2193, South Africa
3 Department of Epidemiology & Biostatistics, University of the Witwatersrand, Johannesburg 2193, South Africa; innocent.maposa@wits.ac.za
4 Radiobiology, Department of Human Structure and Repair, Ghent University, 9000 Ghent, Belgium
* Correspondence: ans.baeyens@ugent.be

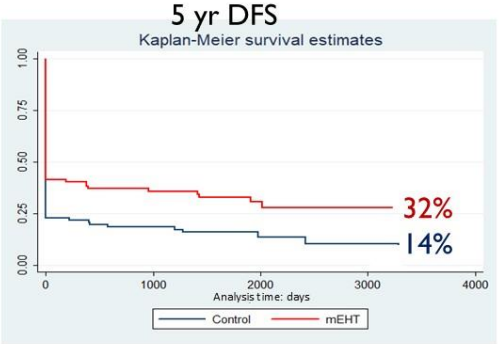
- m… …ominated the model
- mEH… CRT **less costly and more effective**

cancers

Results: 5 year Disease Free Survival

5yr OS	mEHT	Control	
All	33% [33/99]	26% [25/98]	HR:0.74; 95%CI:0.53-1.03; p=0.083
Stage III	**34% [21/61]**	**23% [15/65]**	HR:0.65; 95%CI:0.43-0.99; p=0.046

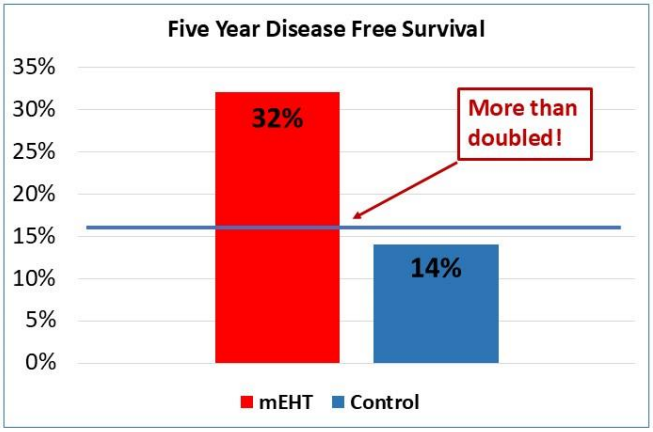
5 yr DFS



OR:3.00; 95%CI:1.49-6.07; ***p=0.002;***
HR:0.73; 95%CI:0.53-1.00; ***p=0.049;***
Chi2: ***p=0.002***

ESTRO 2024

Results: 5 year Disease Free Survival



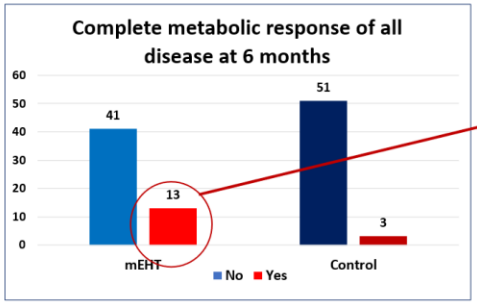
32%[32/99] of hyperthermia participants

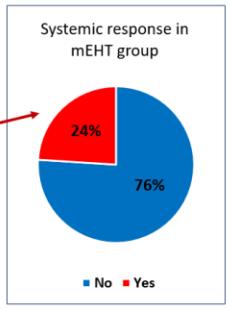
14%[14/102] of control participants

Achieved 5 years DFS

Odds were increased by 3x!

Results: Abscopal Response





In a multivariate analysis:
- Age,
- Number of cisplatin doses,
- Total RT dose,
- Days between last RT and PET/CT,

were not associated with an abscopal effect

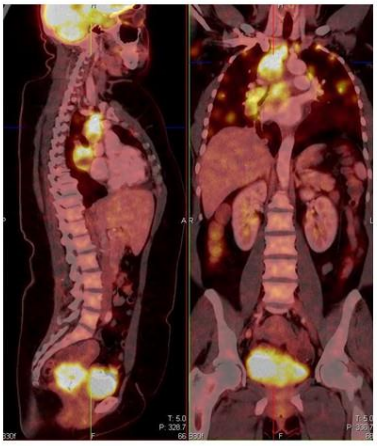
In a univariate analysis, CD4 count was also not predictive of an abscopal effect

Results: Abscopal Response

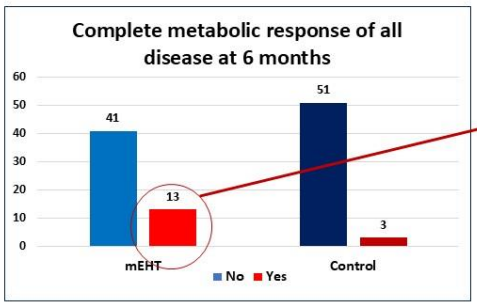
Pre-treatment PET/CT studies showed:

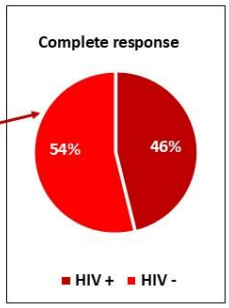
- **108 Participants had extra pelvic disease**
- **54 participants in each group**

!!!!!



Results: Abscopal Response





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- Age,
- Number of cisplatin doses,
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- Days between last RT and PET/CT,

were not associated with an abscopal effect

In a univariate analysis, CD4 count was also not predictive of an abscopal effect

Potentiation of the abscopal response by mEHT?!

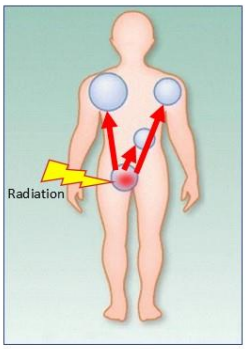
frontiers in Medicine

Results: Abscopal Response

SUSTAINED SYSTEMIC RESPONSE

- Participants with stage IVB disease outside the pelvis,
- who showed an abscopal response at 6 months,
- remained disease free at 5 years
- With the exception of 2 participants who died of non-cancer related causes

24 % of participants with stage IV disease outside the pelvis achieved 5yr disease free survival with addition of mEHT to RT



ESTRO 2024

Abscopal Response

mEHT damages cell membranes

Promotes ICD and DAMP

= apoptosis and release of apoptotic bodies

= release of mHSPs into the extra cellular matrix

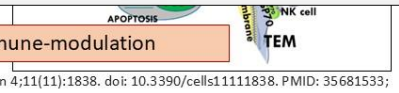
→ transport intracellular antigenic peptides to DCs

= maturation of DCs into APCs

→ produce antigen-specific cytotoxic T-lymphocytes and activated NK cells

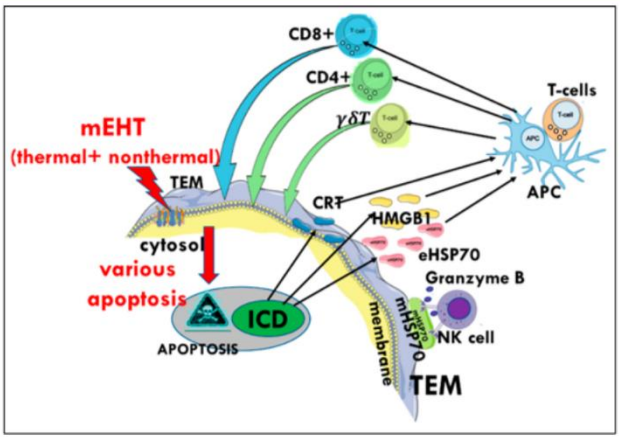
Potentially = adaptive immune response

Immunogenic Hyperthermia = mild heat + immune-modulation



Minnaar CA, Szasz A. Forcing the Antitumor Effects of HSPs Using a Modulated Electric Field. Cells. 2022 Jun 4;11(11):1838. doi: 10.3390/cells11111838. PMID: 35681533;

Abscopal Response



mEHT damages cell membranes

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→ transport intracellular antigenic peptides to DCs

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Minnaar CA, Szasz A. Forcing the Antitumor Effects of HSPs Using a Modulated Electric Field. Cells. 2022 Jun 4;11(11):1838. doi: 10.3390/cells11111838. PMID: 35681533;

Conclusion:

Modulated electro-hyperthermia added to CRT for the management of cervical cancer:

- ✓ **Significantly increases local disease control**
- ✓ **Significantly increased 5y DFS rates,**
- ✓ **Does not alter the toxicity profile**
- ✓ **Has potential to lower treatment costs**
- ✓ **Improves Quality of Life.**

- ✓ **Promotes a sustained long-term, immune-mediated, systemic response to the disease.**

Acknowledgements

Supervisors:
Dr Jeffrey Kotzen (Co-PI) and Prof Ans Baeyens

Department of Radiation Oncology
Department of Nuclear Medicine

Support and administrative staff

Our deepest thanks and appreciation go to all the participants who showed bravery and grace throughout their treatment and follow up

Thank you

Dr. Carrie Anne Minnaar (MSc PhD)
carrie@onc-hyperthermia.co.za
Johannesburg, South Africa

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG 100 1922 2022

Modulated electro-hyperthermia: Experience along the years...

Presentation from "Oncotherm in Italy" conference 2025.04.02.

Prof. Dr. Elisabeth Arrojo

Radiation Oncologist
Director of hyperthermia's department at University Hospital Marqués of Valdecilla in Santander, Sapin;
Medical Director and Founder of the Medical Institute of advanced Oncology (INMOA) and CNPC, Spain
Professor at Catholic University of Murcia (UCAM)

Citation

Arrojo, E. (2025) Modulated electro-hyperthermia: Experience along the years – Oncotherm in Italy, 2025.04.02.
https://www.youtube.com/watch?v=u92N727a_Nw&list=PLEaAiXVgvMsGMMHSufONT8E7zYBSSDNO4

Oncothermia Journal 37, September 2025., 59-92.
https://oncotherm.com/ArrojoE_2025_Oncotherm_in_Italy_20250402

Rome, April 2025

Modulated electrohyperthermia: Experience along the years...

Elisabeth Arrojo, MD, PhD

Radiation Oncologist

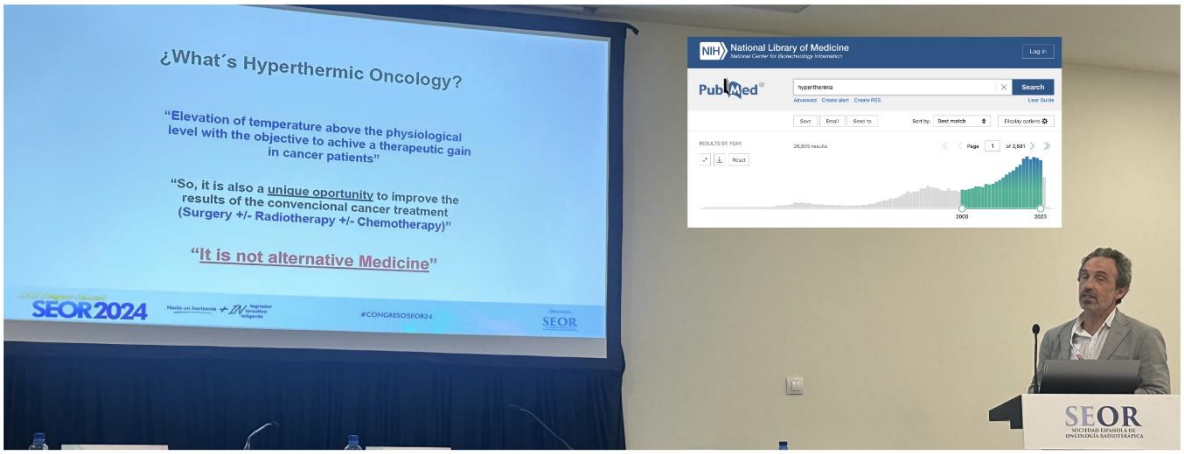
- Director of hyperthermia's department at University Hospital Marqués of Valdecilla in Santander, Spain.
- Medical Director and Founder of the Medical Institute of advanced Oncology (INMOA) and CNPC, Spain
- Professor at Catholic University of Murcia (UCAM)

Reial Acadèmia Europea de Doctors
Real Academia Europea de Doctores
Royal European Academy of Doctors
BARCELONA · 1914

Valdecilla · INMOA · UCAM Universidad Católica de Murcia · CNPC

- European award of medicine.
- "Person of extraordinary abilities on sciences" by USA.

Spanish Radiation Oncology Society meeting - SEOR 2024



CNC HACIA EL FUTURO 2022 DE LA MANO DEL PACIENTE

GOBIERNO DE ESPAÑA · MINISTERIO DE LA PRESIDENCIA, RELACIONES CON LAS CORTES Y MEMORIA DEMOCRÁTICA

Agencia Estatal Boletín Oficial del Estado

Castellano · Buscar · Mi BOE · Menú

Está Vd. en › Inicio › Buscar › Documento BOE-A-2006-17950

Orden SCO/3142/2006, de 20 de septiembre, por la que se aprueba y publica el programa formativo de la especialidad de Oncología Radioterápica.

DE LOS INMIGRANTES

MINISTERIO
DE SANIDAD Y CONSUMO

17950 *ORDEN SCO/3142/2006, de 20 de septiembre, por la que se aprueba y publica el programa formativo de la especialidad de Oncología Radioterápica.*

El artículo 21 de la Ley 44/2003, de 21 de noviembre, de ordenación de las profesiones sanitarias, establece el procedimiento para aprobar los programas formativos de las especialidades sanitarias en ciencias de la salud, previendo su publicación en el Boletín Oficial del Estado para general conocimiento.

La Comisión Nacional de la Especialidad de Oncología Radioterápica ha elaborado el programa formativo de dicha especialidad que ha sido

Disposición final.

Esta Orden entrará en vigor
«Boletín Oficial del Estado».

Madrid, 20 de septiembre de
Elena Salgado Méndez.

PROGRAMA OFICIAL DE L
RAD

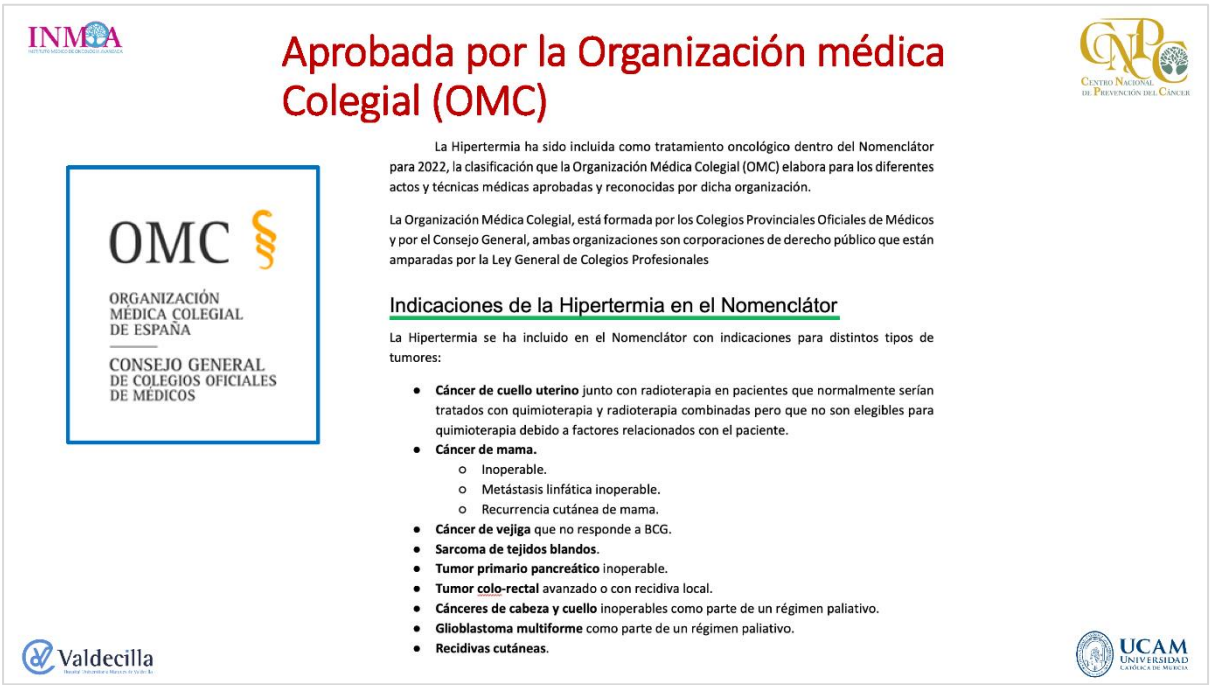
Denominación oficial de la especialidad y requisitos de titulación

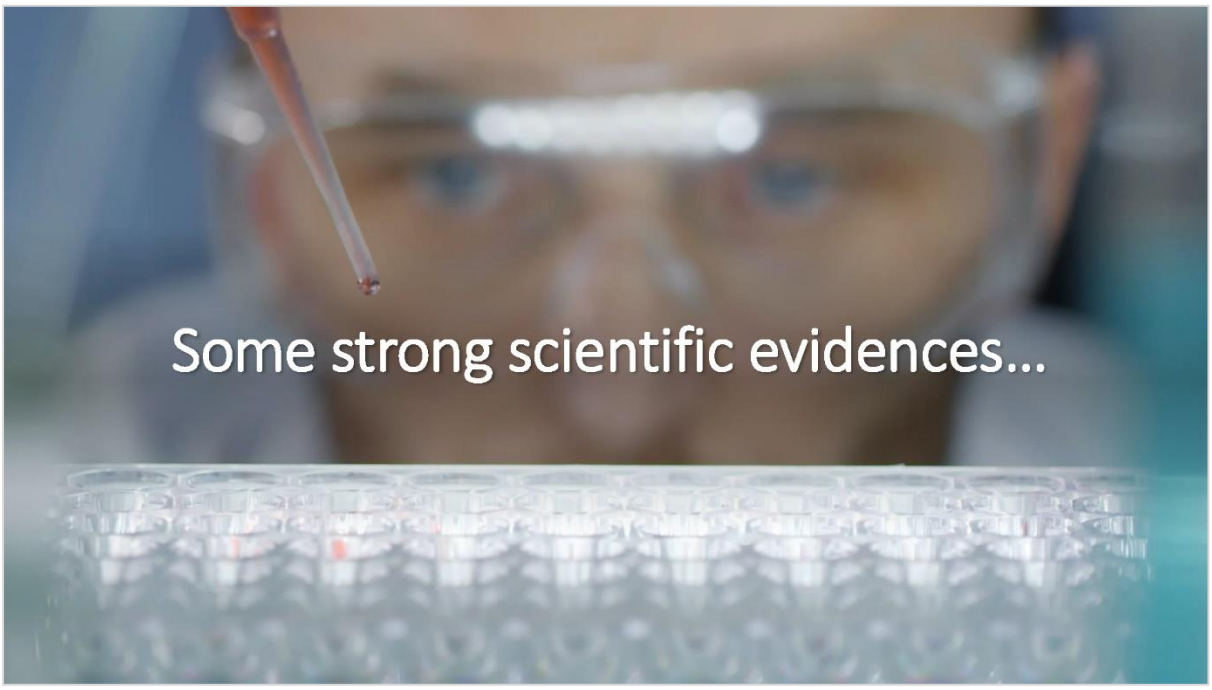
Oncología radioterápica.
Duración: 4 años.
Licenciatura previa: Medicina.

2.1.26.2 Hipertermia e irradiación:

Efectos biológicos de la hipertermia.
Termotolerancia.
Interacción radiación-hipertermia.
Indicaciones de la hipertermia en la radioterapia del cáncer.


Grupo Hipertermia SEOR
SEOR
Inicio
El Grupo
Hipertermia
Contacto
hipertermia@seor.es
Potenciando el tratamiento contra el cáncer
Hipertermia oncológica
El cuarto pilar en el tratamiento contra el cáncer
Uso
La hipertermia es un potenciador potente de tratamientos de radioterapia/quimioterapia
Inhibe la reparación del ADN
Potencia la expresión de antígenos
Reduce las zonas hipóxicas
Aumenta la permeabilidad de la membrana
Potencia el efecto abscopal
Y más beneficios Vea más >>
Evidencia científica
Patologías con nivel de evidencia IA y grado de recomendación A
Colorrectal avanzado
Mama locorregional avanzado/recidivante
Cérvix en tratamiento QT/RT
Sarcoma de partes blandas
Recidivas cutáneas
Cabeza y cuello avanzado Vea más >>
Valdecilla
UCAM


Aprobada por la Organización médica Colegial (OMC)
OMC
ORGANIZACIÓN MÉDICA COLEGIAL DE ESPAÑA
CONSEJO GENERAL DE COLEGIOS OFICIALES DE MÉDICOS
La Hipertermia ha sido incluida como tratamiento oncológico dentro del Nomenclátor para 2022, la clasificación que la Organización Médica Colegial (OMC) elabora para los diferentes actos y técnicas médicas aprobadas y reconocidas por dicha organización.
La Organización Médica Colegial, está formada por los Colegios Provinciales Oficiales de Médicos y por el Consejo General, ambas organizaciones son corporaciones de derecho público que están amparadas por la Ley General de Colegios Profesionales
Indicaciones de la Hipertermia en el Nomenclátor
La Hipertermia se ha incluido en el Nomenclátor con indicaciones para distintos tipos de tumores:
Cáncer de cuello uterino junto con radioterapia en pacientes que normalmente serían tratados con quimioterapia y radioterapia combinadas pero que no son elegibles para quimioterapia debido a factores relacionados con el paciente.
Cáncer de mama.
Inoperable.
Metástasis linfática inoperable.
Recurrencia cutánea de mama.
Cáncer de vejiga que no responde a BCG.
Sarcoma de tejidos blandos.
Tumor primario pancreático inoperable.
Tumor colo-rectal avanzado o con recidiva local.
Cánceres de cabeza y cuello inoperables como parte de un régimen paliativo.
Glioblastoma multiforme como parte de un régimen paliativo.
Recidivas cutáneas.
Valdecilla
UCAM



JAMA Oncol. 2018;4(4):483-492.
doi:10.1001/jamaoncol.2017.4996

JAMA Oncology | Original Investigation

Effect of Neoadjuvant Chemotherapy Plus Regional Hyperthermia on Long-term Outcomes Among Patients With Localized High-Risk Soft Tissue Sarcoma
The EORTC 62961-ESHO 95 Randomized Clinical Trial

- Phase 3 randomized clinical trial
- Germany (6), Norway (1), Austria (1), and the United States (1).
- Ages 18 - 70 years.
- Histologically proven **soft tissue sarcoma** with the following risk criteria:
  - Tumor diameter ≥ 5 cm or larger.
  - Grade 2 or 3.
  - Deep to the fascia.
  - No evidence of distant metastases.
- **Objectives:**
  - **Primary:** Local progression-free survival.
  - **Secondary:**
    - Tumor response to induction therapy.
    - Disease-free survival.
    - Survival.

9 HYPERTHERMIA CENTERS

EUROPE:
- University Hospital Munich-Grosshadern of the LMU
- Argirov Clinic Starnberger See
- Rotkreuz Krankenhaus Munich
- Essen University Hospital
- Düsseldorf University Hospital
- Charité – Universitätsmedizin Berlin
- University Hospital Graz
- Haukeland University Hospital, Bergen

USA:
- Duke University Hospital, Durham

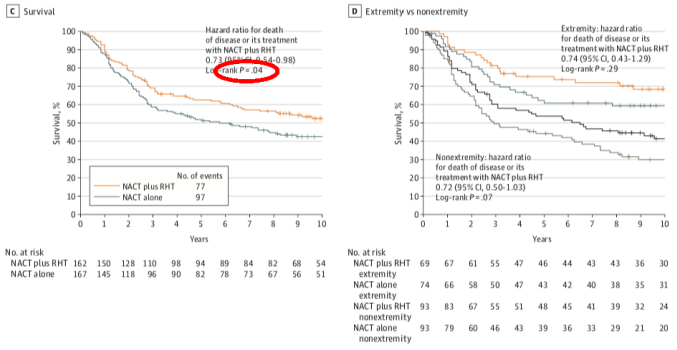
The median follow-up duration was 11.3 (9.2-14.7) years.

OS HT+CT vs CT:

- 5 years:
  62.7% vs 51.3%,
  (p = 0.04)

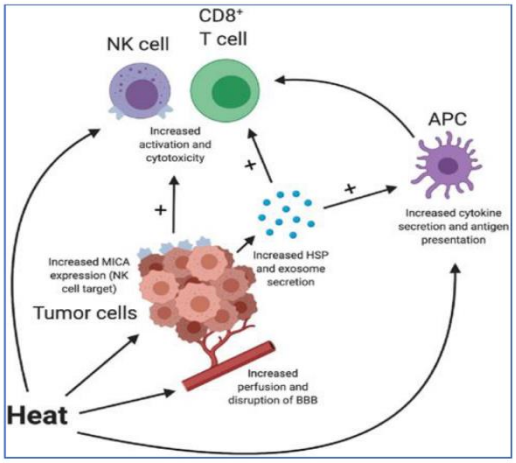
JAMA Oncology | Original Investigation

Effect of Neoadjuvant Chemotherapy Plus Regional Hyperthermia on Long-term Outcomes Among Patients With Localized High-Risk Soft Tissue Sarcoma
The EORTC 62961-ESHO 95 Randomized Clinical Trial



A, Median local progression free survival was 5.6 years (95% CI, 2.9-8.7) in the NACT plus RHT group compared with 2.4 years (95% CI, 1.7-4.2) in the NACT-alone group. B, Median disease-free survival was 2.8 years (95% CI, 2.0-4.9) in the NACT plus RHT group compared with 1.5 years (95% CI, 1.1-2.1) in the NACT-alone group. C, Median survival was 15.4 years (95% CI, 6.6 to >17.0 [the upper confidence limit cannot be estimated and represents the lower bound for the value to be expected]) in the NACT plus RHT group compared with 6.2 years (95% CI, 3.2-10.3) in the NACT-alone group. D, Extremity tumor-survival rates at 5 and 10 years were 75.2% and 68.3% in the NACT plus RHT group compared with 60.8% and 59.2% in the NACT-alone group. The absolute difference at 5 years was 14.4% (95% CI, 0%-29.5%) and was 9.1% (95% CI, 0%-24.7%) at 10 years. Nonextremity tumor-survival rates at 5 years and 10 years were 53.5% and 41.3% in the NACT plus RHT group compared with 44.0% and 29.9% in the NACT-alone group. The absolute difference at 5 years was 9.5% (95% CI, 0%-23.8%) and was 11.4% (95% CI, 0%-25.1%) at 10 years. NACT indicates neoadjuvant chemotherapy consisting of doxorubicin, ifosfamide, and etoposide; RHT, regional hyperthermia.

Hyperthermia estimulates immune system...



Srinivasan, et al. The intersection between immunotherapy and laser interstitial thermal therapy: a multipronged future of neuro-oncology. International Journal of Hyperthermia.

European Journal of Cancer 158 (2021) 123–132

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

Immune infiltrates in patients with localised high-risk soft tissue sarcoma treated with neoadjuvant chemotherapy without or with regional hyperthermia: A translational research program of the EORTC 62961-ESHO 95 randomised clinical trial

Rolf D. Issels [a,*,1], Elfriede Noessner [b,1], Lars H. Lindner [a], Michael Schmidt [c], Markus Albertsmeier [d], Jean-Yves Blay [e], Emanuel Stutz [f], Yujun Xu [g], Veit Buecklein [a], Annelore Altendorf-Hofmann [h], Sultan Abdel-Rahman [a], Ulrich Mansmann [g], Michael von Bergwelt-Baildon [i], Thomas Knoesel [j]

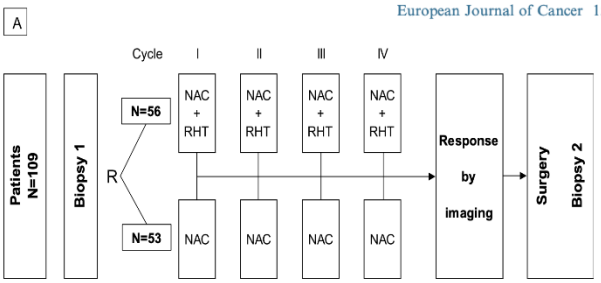
[a] Department of Medicine III, University Hospital, LMU, Marchioninistr.15, Munich, 81377, Germany
[b] Helmholtz Zentrum München, German Research Center for Environmental Health, Germany
[c] Munich Cancer Registry, Institute of Medical Information Processing, Biometry and Epidemiology, LMU, Munich, Germany
[d] Department of General, Visceral and Transplantation Surgery, LMU Munich, Munich, Germany
[e] Department of Medicine, Centre Leon Berard, 28 Rue Laennec1, Lyon, 69373, France
[f] Dept. of Radiation Oncology, Inselspital, Bern University Hospital, University of Bern, Bern Freiburgstr.18, Switzerland
[g] Institute of Medical Informatics, Biometry and Epidemiology (IBE), LMU Munich, Germany
[h] Department of General, Visceral and Vascular Surgery, University Hospital Jena, Germany
[i] Deutsches Konsortium für Translationale Krebsforschung, Bayrisches Zentrum für Krebsforschung, and Comprehensive Cancer Center LMU, Munich, Germany
[j] Institute of Pathology, LMU, Thalkirchner Str.36, Munich, 80337, Germany

Received 31 July 2021, received in revised form 6 September 2021, accepted 10 September 2021
Available online 16 October 2021

- The study protocol included an optional accompanying **translational program, to determine immune cells of tumour tissue.**

Immune infiltrates in patients with localised high-risk soft tissue sarcoma treated with neoadjuvant chemotherapy without or with regional hyperthermia: A translational research program of the EORTC 62961-ESHO 95 randomised clinical trial

European Journal of Cancer 158 (2021) 123–132



- **28 patients had paired samples** (only available for patients who had been biopsied and finally operated at the Munich Centre).
  - NAC-RHT: 13
  - NAC: 15

Immune infiltrates in patients with localised high-risk soft tissue sarcoma treated with neoadjuvant chemotherapy without or with regional hyperthermia: A translational research program of the EORTC 62961-ESHO 95 rando

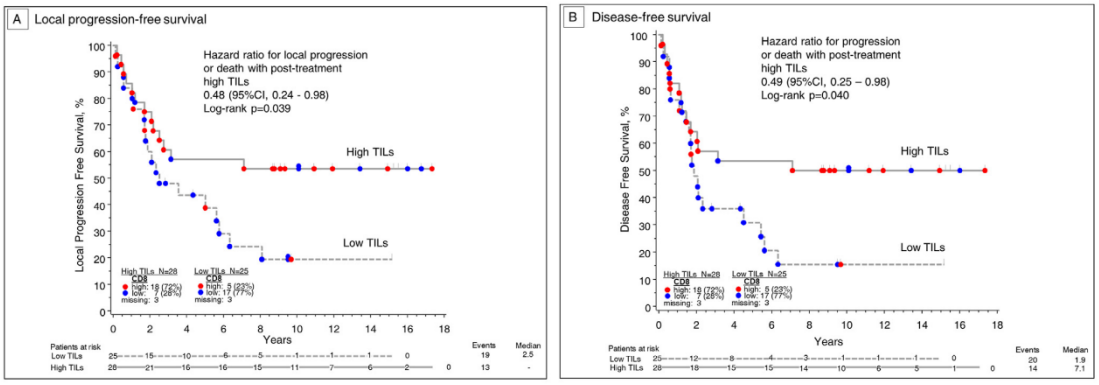
European Journal of Cancer 158 (2021) 123–132

- Examined for **TILs (Infiltrating tumor lymphocytes)** and immune biomarker expression, including **CD8, PD-1, PD-L1, and FOXP3.**
  - The TIL score was assigned as high (>5 cells per HPF) or low (5 cells per HPF).
  - The CD8 cell score was defined by anti-CD8 antibody immunoreactivity as high (>10 cells per HPF) or low (<10 cells per HPF)

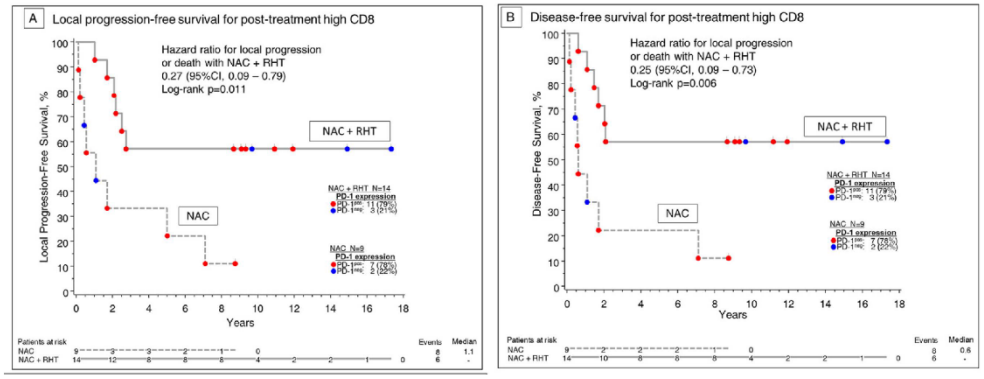
Immune infiltrates in patients with localised high-risk soft tissue sarcoma treated with neoadjuvant chemotherapy without or with regional hyperthermia: A translational research program of the EORTC 62961-ESHO 95 randomised clinical trial

European Journal of Cancer 158 (2021) 123–132

- In post-treatment samples (biopsy 2): **53%** (28/53) tumours **high TIL infiltrate** *vs* 47% (25/53) with low TIL infiltrate.
- **High TILs significantly associated with prolonged LPFS (p 0.039) and DFS (0.040)**



High CD8 by groups



Patients of the NAC-RHT group, whose tumours exhibited high CD8 counts, had significantly longer LPFS (p=0.011) and DFS (p =0.006) compared to the NAC group.

CONCLUSIONS

- **Preoperative chemotherapy +/- concomitant Hyperthermia turned the state of a cold, non-immunogenic sarcoma into a more immunogenic tumour** with high TILs, a decrease of immune-suppressive FOXP3 regulatory Tcells, and absence of PD-L1 expression.
- In patients with **high increase in CD8, the addition of hyperthermia significantly increased local progression free survival and disease free survival.**

Immune effect of hyperthermia

World Journal of Clinical Oncology

Submit a Manuscript: https://www.f6publishing.com

World J Clin Oncol 2021 November 24; 12(11): 1064-1071

DOI: 10.5306/wjco.v12.i11.1064

ISSN 2218-4333 (online)

ORIGINAL ARTICLE

Observational Study

Modulated electro-hyperthermia in stage III and IV pancreatic cancer: Results of an observational study on 158 patients

Giammaria Fiorentini, Donatella Sarti, Girolamo Ranieri, Cosmo Damiano Gadaleta, Caterina Milandri, Andrea Mambrini, Stefano Guadagni

INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY • BIOLOGY • PHYSICS ASTRO

CLINICAL INVESTIGATION | VOLUME 100, ISSUE 1, P78-87, JANUARY 01, 2018

Comparing the Effectiveness of Combined External Beam Radiation and Hyperthermia Versus External Beam Radiation Alone in Treating Patients With Painful Bony Metastases: A Phase 3 Prospective, Randomized, Controlled Trial

Mau-Shin Chi, MD • Kai-Lin Yang, MD • Yue-Cune Chang, PhD • ... Kuang-Wen Liao, PhD • Motoharu Kondo, MD, PhD • Kwan-Hwa Chi, MD • Show all authors

Purpose

To compare the response, duration of pain relief, and time to achieve complete pain relief after radiation therapy (RT) with o

for updates

Conclusions

The addition of HT to RT significantly increases the pain control rate and extends response duration compared with RT alone for painful bony metastases.

Results

The study was terminated early after an interim analysis of 57 patients, 3 years after the first enrollment (November 2013 to November 2016): 29 patients in the RT + HT group and 28 patients in the RT-alone group. The CR rate at 3 months after treatment was 37.9% in the RT + HT group versus 7.1% in the RT-alone group (P=.006). The accumulated CR rate within 3 months after treatment was 58.6% in the RT + HT group versus 32.1% in the RT-alone group (P=.045). Median time to pain progression was 55 days in patients with CR (n=9) in the RT-alone group, whereas the endpoint was not reached during the 24-week follow-up in the RT + HT group (P<.01).

Conclusions

The addition of HT to RT significantly increases the pain control rate and extends response duration compared with RT alone for painful bony metastases.

Radiotherapy and Oncology 138 (2019) 1–8

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

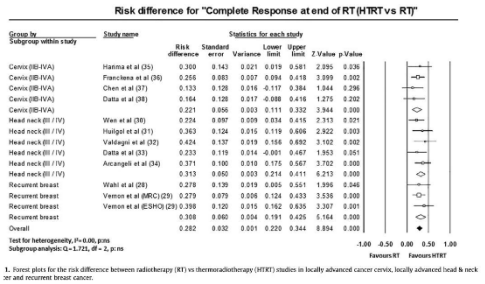
Original Article

Hyperthermia with radiotherapy reduces tumour alpha/beta: Insights from trials of thermoradiotherapy vs radiotherapy alone

Niloy R. Datta [a,*], Stephan Bodis [a,b]

[a] Centre for Radiation Oncology KSA-KSB, Kantonsspital Aarau; and [b] Department of Radiation Oncology, University Hospital Zurich, Switzerland

- Hyperthermia increase BED (biological equivalent dose in RT)
- Metaanalises randomized studies wtih radiotherapy vs radiotherapy + regional hyperthermia in:
  - Recurrent breast cancer
  - Locally advanced head and neck cancer
  - Locally advanced cervical cancer
- 12 stuides (show RT+HT significantly better in complete response than RT alone)
- Excluded those with different doses o dose fractionation



1. Forest plots for the risk difference between radiotherapy (RT) vs thermoradiotherapy (HTRT) studies in locally advanced cancer cervix, locally advanced head & neck cer and recurrent breast cancer.

Hyperthermia and BED

Table 1
Summary of the randomized studies of RT vs HTRT, complete responders in each arm, corresponding BED of the RT schedule and the estimated α/β with HTRT for each study.

Author	Site	RT/HTRT		Hyperthermia				RT			HTRT			BED (RT) ($Gy_{\alpha/\beta}$)	$\%CR_{HTRT}/\%CR_{RT}$ (%)	BED_{HTRT} (Gy)	Estimated α/β for HTRT (Gy)
		Dose (Gy)	Dose/fr (Gy)	T (°C)	Time (mins)	Per week	Total sessions	Total	CR		Total	CR					
Wahl et al. [35]	RcBC	48.0	2.0	NA	NA	NA	NA	18	7	39	24	57.6	1.71	98.7	1.89		
Vernon et al. (MRC) [36]	RcBC	28.8	3.6	43.0	60.0	1	3	59	17	90	51	39.2	1.97	77.0	2.15		
Vernon et al. (ESHO) [36]	RcBC	32.0	4.0	43.0	60.0	2	8	29	11	27	21	44.8	2.05	91.9	2.14		
Wen et al. [37]	LAHNC	70.0	2.0	44.4	60.0	2	6	49	23	49	34	84.0	1.48	124.2	2.58		
Huilgol et al. [38]	LAHNC	70.0	2.0	42.3	30.0	1	7	26	11	28	22	84.0	1.86	156.0	1.63		
Valdagni et al. [39]	LAHNC	68.0	2.0	42.5	30.0	2	12	22	9	18	15	81.6	2.04	165.0	1.38		
Datta et al. [40]	LAHNC	64.0	2.0	42.5	50.0	2	12	32	10	33	18	76.8	1.75	134.1	1.83		
Arcangeli et al. [41]	LAHNC	60.0	1.5	42.5	45.0	3	7	43	18	38	30	69.0	1.89	130.1	1.28		
Harima et al. [42]	LACC	52.2	1.8	40.6	60.0	1	3	20	10	20	16	61.6	1.60	98.6	2.03		
Franckena et al. [43]	LACC	48.3	2.0	42.0	60.0	1	5	56	32	58	48	58.0	1.45	83.9	2.71		
Chen et al. [44]	LACC	40.0	2.0	42.0	45.0	2	8	30	14	30	18	48.0	1.29	61.7	3.68		
Datta et al. [45]	LACC	60.0	2.0	42.5	45.0	2	12	26	15	27	20	72.0	1.28	92.4	3.70		

Abbreviations: RT: Radiotherapy; HTRT: Thermoradiotherapy; T: Temperature; RcBC: Recurrent breast cancer; LAHNC: Locally advanced head and neck cancer; LACC: Locally advanced cancer cervix; BED: Biologically effective dose; RcBC: Recurrent breast cancer; LAHNC: Locally advanced head and neck cancer; LACC: Locally advanced cancer cervix; $\%CR_{HTRT}$: % complete response with HTRT; $\%CR_{RT}$: % complete response with RT.
BED_{HTRT} and α/β_{HTRT} are estimated as described in text.
[a] Average dose to RT group: 68 Gy whilst to HTRT 67.5 Gy.
[b] Only patients with neck nodes were considered, treated with 1.5 Gy–2 Gy per fraction, 3 fractions/day.
For all LACC studies, only external RT doses were considered.

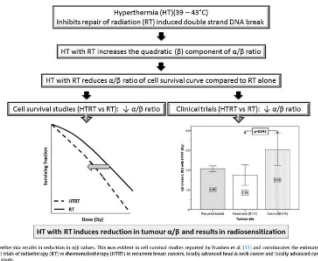
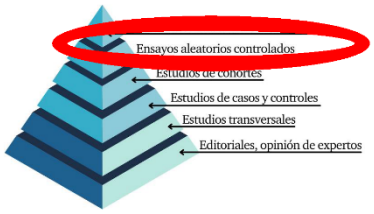


Fig. 4. Hyperther mia results in reduction in α/β values. This was evident in cell survival studies reported by Fyrodes et al. [9] and corroborates the estimated α/β values from clinical trials of radiotherapy (RT) vs thermoradiotherapy (HTRT) in recurrent breast cancers, locally advanced head & neck cancer and locally advanced cancer cervix in the present study.

BED

Tipo tumor	BED RT	BED RT + HT
Mama Recurrente	47.2Gy (39.2-57.6)	**89.2 Gy** (77.0-98.7)
HYN LA	79.1Gy (69-84)	**141.9Gy** (124.2–165.0)
Cérvix LA	59.9Gy (48-72)	**84.2Gy** (61.7–98.5)



Locally advanced rectal cancer

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2021, VOL. 38, NO. 1, 144-151
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Beneficial effects of modulated electro-hyperthermia during neoadjuvant treatment for locally advanced rectal cancer

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[a] Department of Radiation Oncology, Wonju Severance Christian Hospital, Yonsei University Wonju College of Medicine, Wonju, Korea [b] Department of Biostatistics, Yonsei University Wonju College of Medicine, Wonju, Korea

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MATERIALS AND METHODS Clinical data were analyzed for 120 patients who received neoadjuvant treatment for locally advanced rectal cancer (T3/4 or N+, M0) from May 2012 to December 2017. Capecitabine or 5-fluorouracil was administered along with radiotherapy. Patients were categorized into mEHT group (62 patients) and non-mEHT group (58 patients) depending on whether mEHT was added. Surgery was performed 6–8 weeks after the end of radiotherapy.

Table 1. Patient characteristics before neoadjuvant treatment. (Table view)

Characteristics	mEHT group ($n = 62$)	non-mEHT group ($n = 58$)	p value
Median age, yrs. (range)	59 (33–83)	57 (43–82)	.511
Sex, n			.300
Male	46 (74.2%)	38 (65.5%)	
Female	16 (25.8%)	20 (34.5%)	
Pathology, n			.160
Adenocarcinoma	59 (95.2%)	55 (94.8%)	
Mucinous adenocarcinoma	2 (3.2%)	3 (5.2%)	
Tubular adenocarcinoma	1 (1.6%)	0 (0.0%)	
Differentiation, n			.895
Well differentiated	10 (16.1%)	9 (15.5%)	
Moderate differentiated	48 (77.4%)	47 (81.0%)	
Poor differentiated	3 (4.8%)	1 (1.7%)	
Unknown	1 (1.6%)	1 (1.7%)	
Anal verge range, n			.379
<5cm	38 (61.3%)	41 (70.7%)	
≥5cm, <10cm	16 (25.8%)	9 (15.5%)	
≥10cm	8 (12.9%)	8 (13.8%)	
Initial clinical T stage, n			.887
cT2	2 (3.2%)	3 (5.2%)	
cT3	46 (74.2%)	43 (74.1%)	
cT4	14 (22.6%)	12 (20.7%)	
Initial clinical N stage, n			.052
cN0	0 (0%)	4 (6.9%)	
cN+	62 (100.0%)	54 (93.1%)	
Mean initial primary tumor volume, mL (± SD*)	62.6 (± 41.8)	61.9 (± 66.7)	.941

*SD: standard deviation.

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Table 2. Neoadjuvant treatment summary. (Table view)

Treatment	mEHT group ($n = 62$)	non-mERT group ($n = 58$)
Radiation dose, n (mEHT No. range)		
40 Gy	57 (8–9)	0
50.4 Gy	5* (1–12)	58
Chemotherapy regimen, *n*		
5-fluorouracil with leucovorin	6 (9.7%)	27 (46.6%)
Capecitabine	55 (88.7%)	31 (53.4%)
others	1 (1.6%)	0 (0%)
Type of resection, *n*		
Low anterior resection	53 (85.5%)	47 (81.0%)
Abdominoperineal resection	4 (6.5%)	9 (15.5%)
Others	5 (8.0%)	2 (3.5%)
Mean overall treatment time†, day (± SD‡)	80.2 (± 8.4)	90.9 (± 9.6)

*One of them had a radiation dose of 47.4 Gy, † Overall treatment time: Duration from first radiotherapy day to operation day. ‡SD: standard deviation.

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Table 3. Surgical pathology results. (Table view)

	mEHT group (n = 62)	non- mEHT group (n = 58)	*p* value
Pathologic T stage, *n*			.196
ypT0-is	13 (21.0%)	6 (10.4%)	
ypT1-2	21 (33.9%)	18 (31.0%)	
ypT3-4	28 (45.1%)	34 (58.6%)	
T-downstaging rate, n/all	41/62 (66.1%)	33/58 (56.9%)	.299
Pathologic N stage, *n*			.180
ypN0	50 (80.7%)	41 (70.7%)	
ypN+	12 (19.3%)	17 (29.3%)	
N-downstaging rate, n/all	56/62 (90.3%)	48/54† (88.9%)	.800
ypStage, n			.422
ypCR	11 (17.7%)	5 (8.6%)	
Stage 0 (ypTisN0)	1 (1.6%)	1 (1.7%)	
Stage I	18 (29.0%)	13 (22.4%)	
Stage II	20 (32.3%)	22 (38.0%)	
Stage III	12 (19.4%)	17 (29.3%)	
Downstaging rate, n/all	50/62 (80.7%)	39/58 (67.2%)	.094
Resection margin status, n/all (%)			.841
Negative	56 (90.3%)	53 (91.4%)	
Positive	6 (9.7%)	5 (8.6%)	
TRG*, *n*			.146
TRG1 (Minimal regression)	9 (14.5%)	8 (13.8%)	
TRG2 (Moderate regression)	31 (50.0%)	27 (46.6%)	
TRG3 (Near total regression)	10 (16.1%)	18 (31.0%)	
TRG4 (Total regression)	12 (19.4%)	5 (8.6%)	
Good TRG score, TRG 3 + 4/all	22/62 (35.5%)	23/58 (39.7%)	.637
Initial primary tumor volume <65 mL	16/43 (37.2%)	23/43 (53.5%)	.130
Initial primary tumor volume ≥65 mL	6/19 (31.6%)	0/15 (0%)	.024

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*TRG: Tumor regression grade. †Excluding 4 patients with icN0.

RESULTS

- The **median radiation dose was significantly less for mEHT group (40 Gy) than for non-mEHT group (50.4 Gy).**
  - In mEHT group, 80.7% showed down-staging compared with 67.2% in non-mEHT group.
  - For **large tumors of more than 65 cm³** (mean), **improved tumor regression was observed in 31.6% of mEHT group compared** with 0% of non-mEHT group **(*p* = .024).**
  - The **gastrointestinal toxicity rate of mEHT group was 64.5%,** which was found to be **statistically significantly less than 87.9% of non-mEHT group (*p* = .010).**
  - The 2-year disease-free survival was 96% for mEHT group and 79% for non-mEHT group (*p* = .054).

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CONCLUSIONS

- The **overall mEHT group had a comparable response and survival using less radiation dosing compared with standard care.**
- **The subgroup with large tumors showed significantly improved efficacy for tumor regression after mEHT.**
- **The mEHT group had significantly less GI toxicity.**

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cancers

MDPI

Systematic Review

Meta-Analysis of Modulated Electro-Hyperthermia and Tumor Treating Fields in the Treatment of Glioblastomas

Attila Marcell Szasz [1,*], Elisabeth Estefanía Arrojo Alvarez [2,3], Giammaria Fiorentini [4,5], Magdolna Herold [1,6], Zoltan Herold [1], Donatella Sarti [4] and Magdolna Dank [1]

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[4] Department of Oncology, Azienda Ospedaliera "Ospedali Riuniti Marche Nord", 61121 Pesaro, Italy
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Citation: Szasz, A.M.; Arrojo Alvarez E.E.; Fiorentini, G.; Herold, M.; Herold, Z.; Sarti, D.; Dank, M. Meta-Analysis of Modulated Electro-Hyperthermia and Tumor Treating Fields in the Treatment of Glioblastomas. *Cancers* **2023**, *15*, 880. https://doi.org/10.3390/cancers15030880

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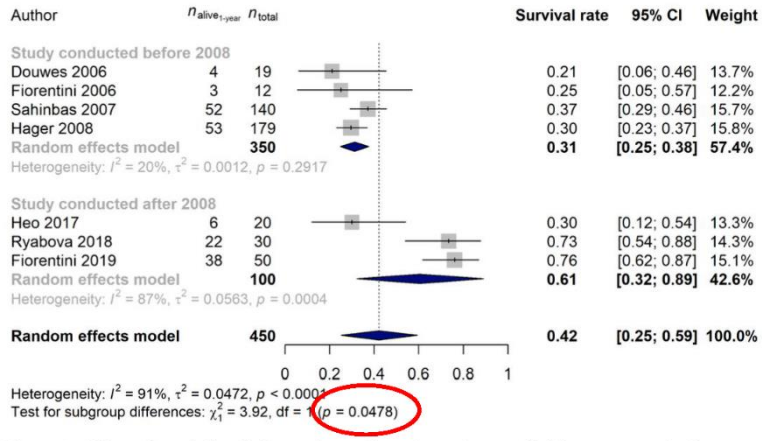

Figure 3. Effect of modulated electro-hyperthermia on 1-year glioblastoma survival rate, grouped by studies published before and after 2008 [43,46–51].

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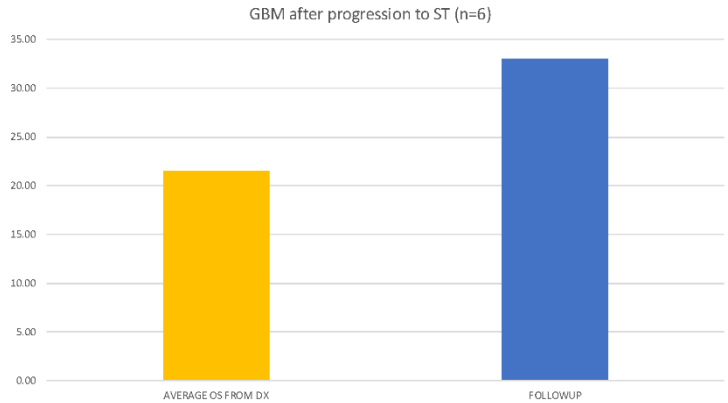
mEHT Glio Trial

Progression group: Analyzing the impact of adding mEHT to standard second line chemotherapy in patients with progression after ST for GBM.

- 6 patients were included (100% IDH negative).
- Average age was 54 years old (42-70).
- Second line chemotherapy was Fotemustine in 66.6%, Bevacizumab in 16.6% and Temozolamide in 16.6% of the cases.

Valdecilla UCAM Universidad Católica de Murcia INMOA Instituto Médico de Oncología Avanzada

mEHT Glio Trial



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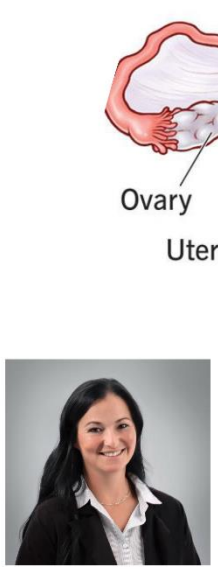
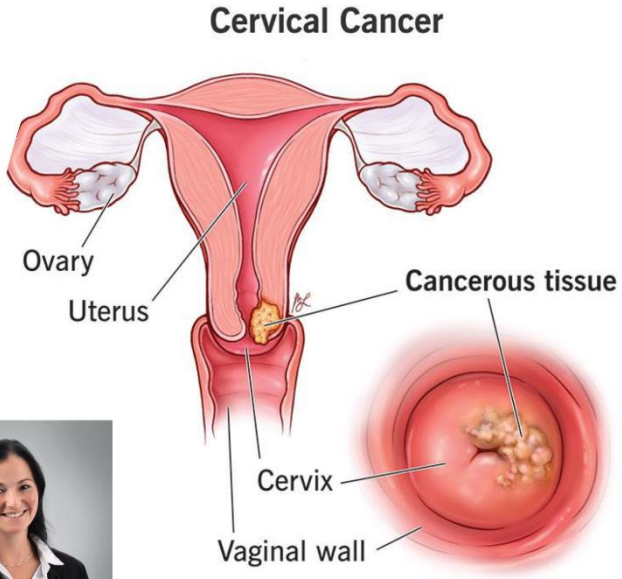
HT level I evidence (ESTRO)



Dr. Carrie Minnaar



9 months after finishing my residency program....

Fuente: EFE, 31 de enero. 2014 12:37

El Hospital Valdecilla, en Santander, aplica en una sesión la radioterapia para cáncer de mama

Pioneer technique for breast cancer RT: From 6-7 weeks lenght to only 1 treatment of about 15 min

El gerente del Hospital, César Pascual, ha presentado hoy esta nueva técnica junto al jefe del Servicio de Oncología Radioterápica, Pedro Prada, y a la **médico adjunto que está al frente del proyecto, Elisabeth Arrojo.**

Valdecilla INMA UCAM

Research coordinatior

400 clinics in USA

Michigan USA

Valdecilla INMA UCAM

My mum…

- **Brain surgery June 2018**
- Radiosurgery
- 4 different types of immunotherapy
  - Almost lethat side effect
  - 5 brain metastases → March 2019 no more options for treatmet

58 yo

MY HEALTH CAN'T WAIT

- **Create: Medical Institute of Advanced Oncology**

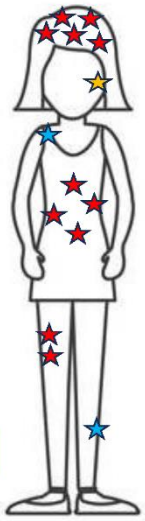
INMOA
INSTITUTO MÉDICO DE ONCOLOGÍA AVANZADA

My mum:

- Diagnosed in December 2015
- 1st brain metastases june 2018
- Every six months new lesions...
  - 5 brain metastases, 1 in bowel 7cm length, leg, thorax...

RT + mEHT for 2 years (2019 to 2021)

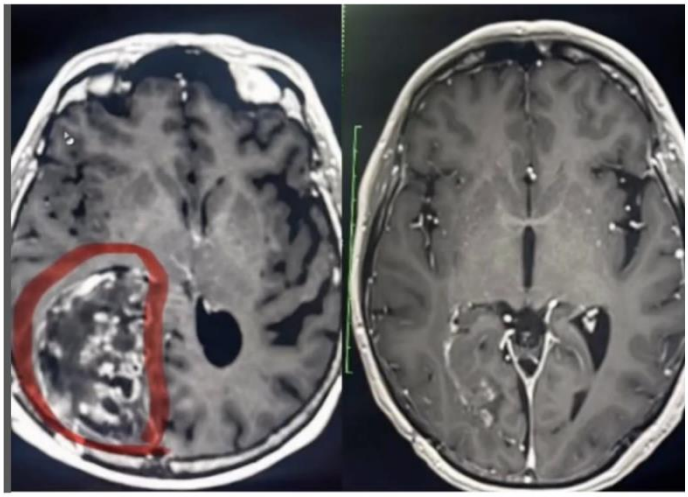
RT + mEHT + low dose IT since January 2022 ...



Metastases
Primary infiltrating melanoma
In situ melanoma

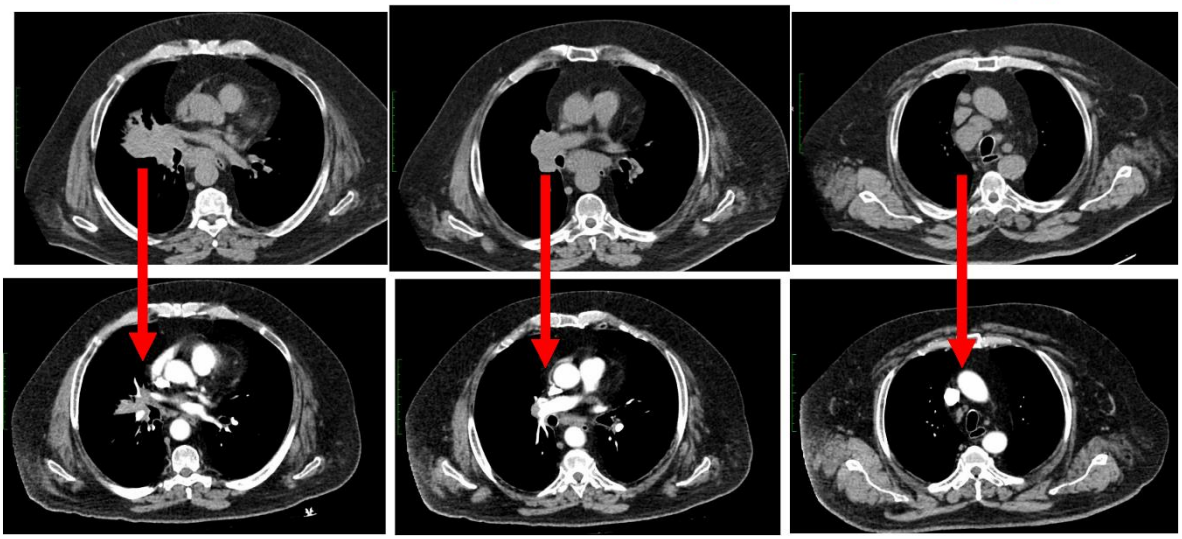
GBM treated with TMZ + mEHT
(18 treatments)

- Not candidate for surgery
- 10 months after treatment free of disease

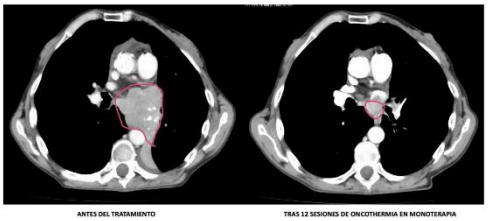


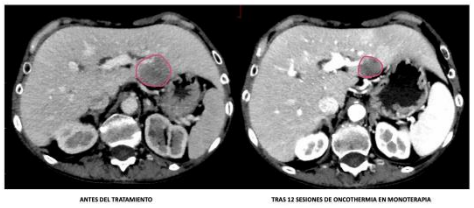
Microcitit lung cancer + Carboplatin-Etoposide
(12 mEHT treatments)

Male, 64 yo



Marina, Microcytic lung cancer with liver metastases

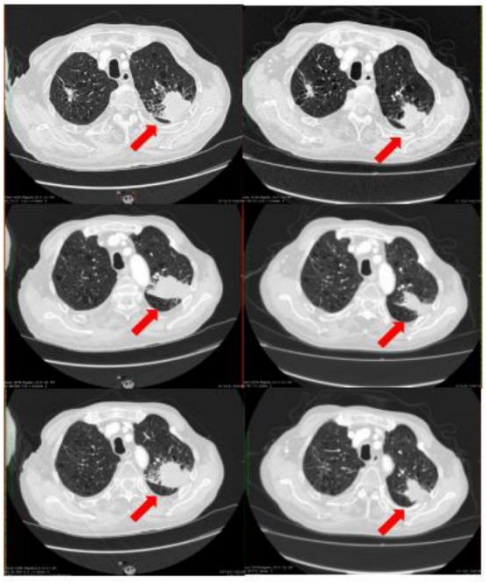




MONOTHERAPY

Not candidate for chemo/radiotherapy

BEFORE TREATMENT AFTER TREATMENT



EPIDERMOID LUNG CANCER

12 mEHT treatments

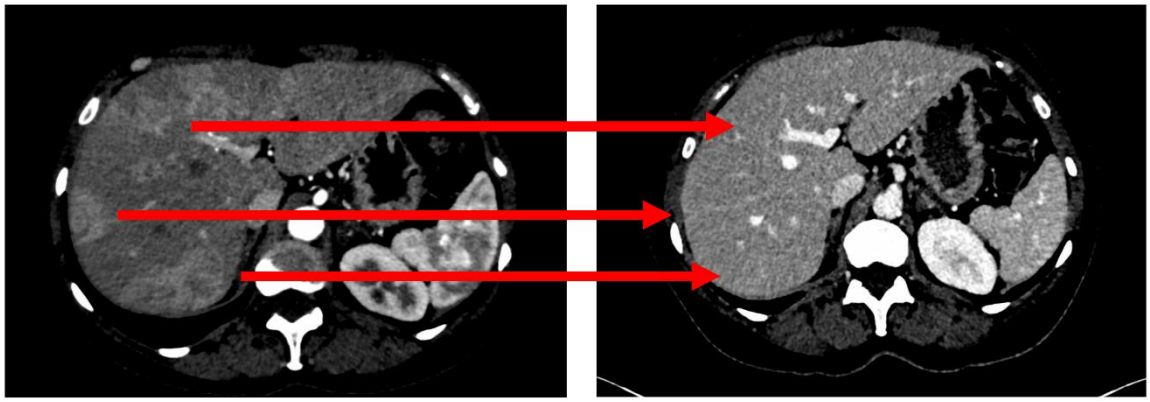
MONOTHERAPY

Female 53 yo, Renal cell cancer – stage IV (liver, lung, abdomen)

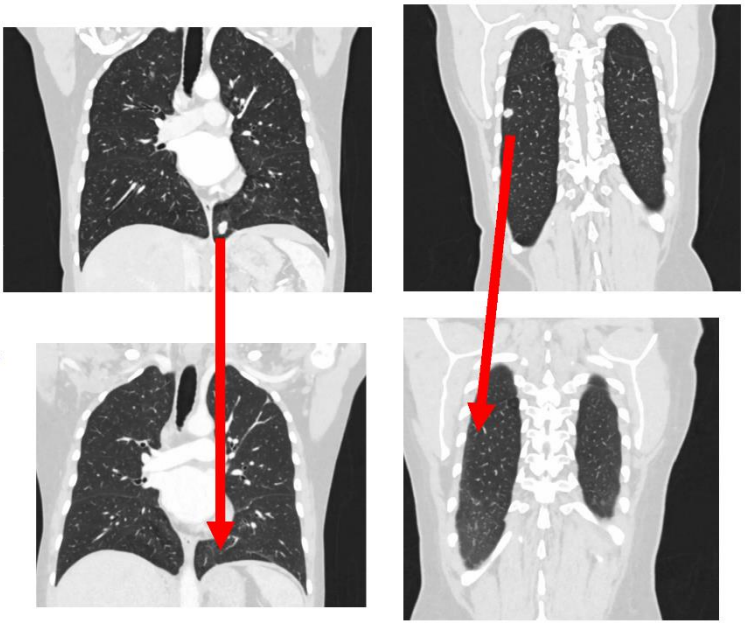
Cisplatin-Gemcitabine + mEHT (no tumor in 6 weeks)

Female 53 yo, Renal cell cancer – stage IV (liver, lung, abdomen)

Cisplatin-Gemcitabine + mEHT (no tumor in 6 weeks)



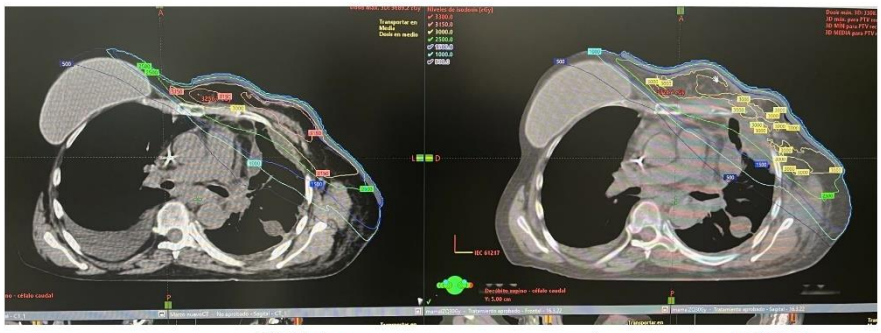
Female 53 yo, Renal cell cancer – stage IV (liver, lung, abdomen)
Cisplatin-Gemcitabine + mEHT (no tumor in 6 weeks)

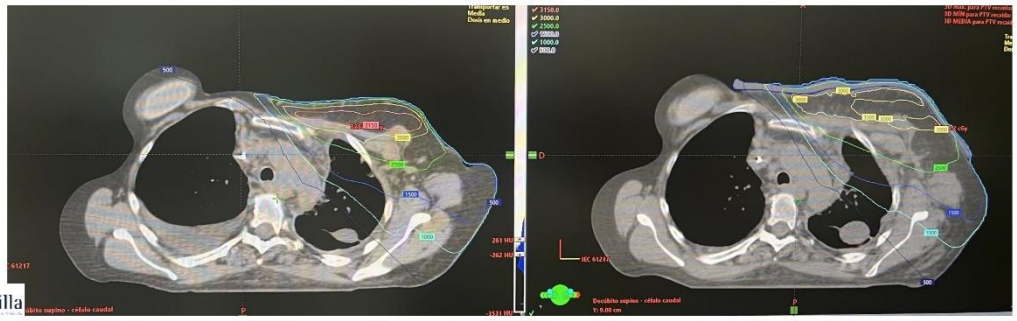


ABSCOPAL EFFECT

Breast Cancer

- No chemo
- 30 Gy





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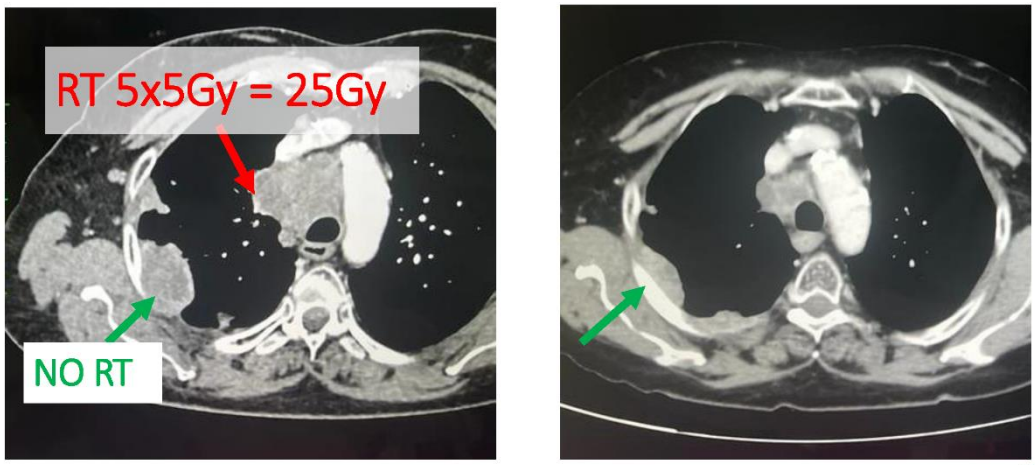
ABSCOPAL EFFECT - LUNG CANCER

Before treatment

2weeks after treatment

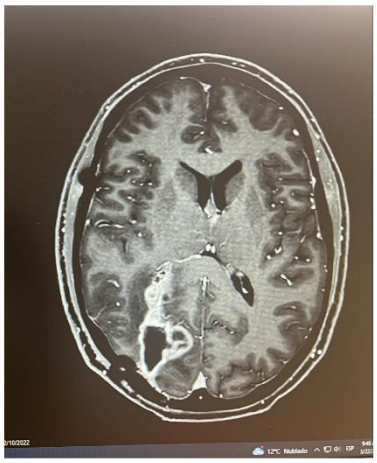


Thorax mEHT x 6

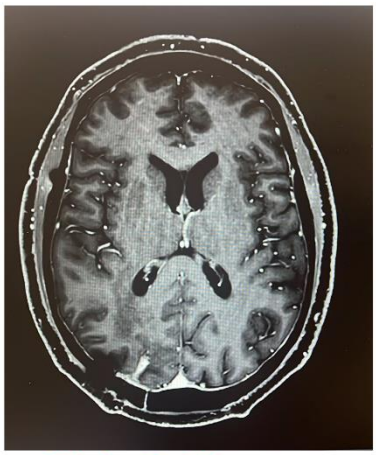
52 yo male, GBM IDH negative

Progressed 1 month after standard CT-RT

mEHT MONOTHERAPY

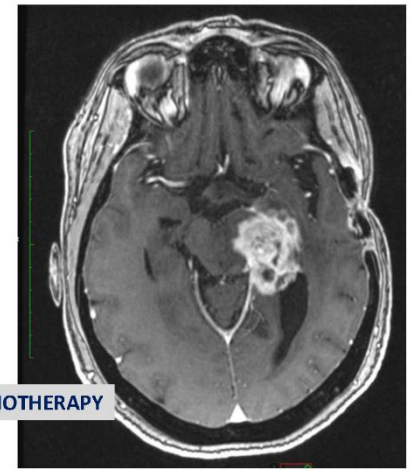


MRI after progression



MRI after 18 mEHT treatments

43 yo Female with "IDH –" GBM



mEHT MONOTHERAPY

MRI 1 month after mEHT treatment

5 years free of progression…

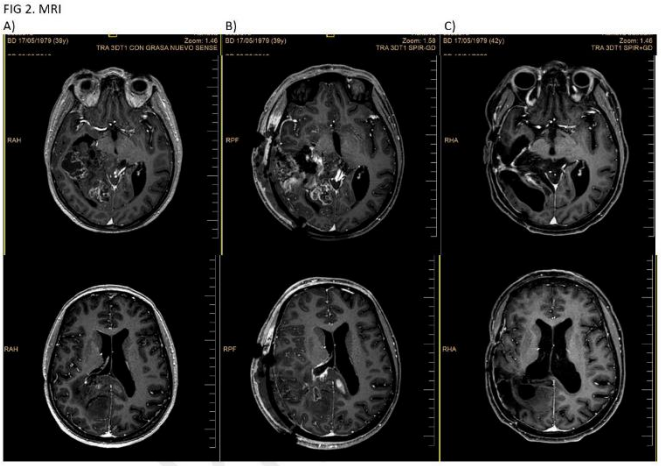
Grade II astrocitoma, female 37 yo. No complete surgery

RT 54Gy → Chemo PCV 6 months → **Progression after 3 months.**

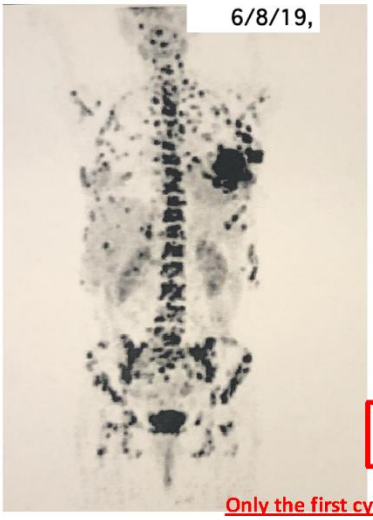
Partial surgery→ Not candidate chemo nor RT

mEHT MONOTHERAPY

FIG 2. MRI



A) MRI at progression after surgery, radiotherapy and chemotherapy; B) MRI after second surger… (after progression); C) Last MRI 44 months after last surgery. Only mEHT performed from that tim…



6/8/19,

28/10/19,

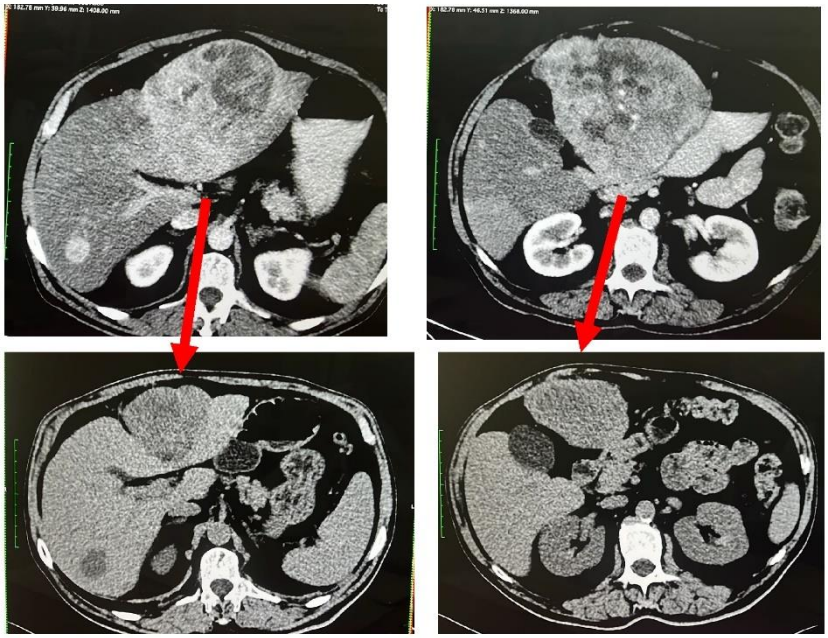
Breast cancer

4* CT cycles
29 mEHT treatments

2.5 months later
COMPLETE RESPONSE

Only the first cycle with paclitaxel + pertuzumab + trastuzumab.

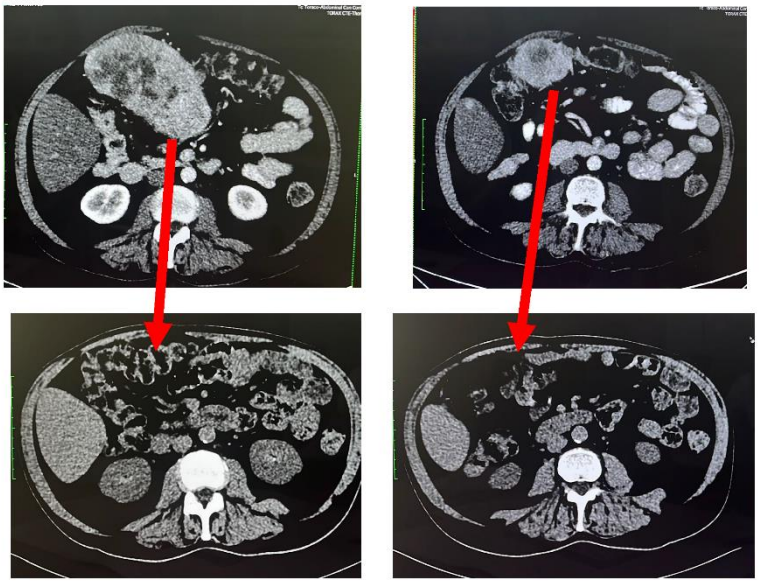
The other ones only pertuzumab + trastuzumab (patient desirees)



Stage IV hepatocarcinoma

Atezolizumab + mEHT

Results 2 months after treatment

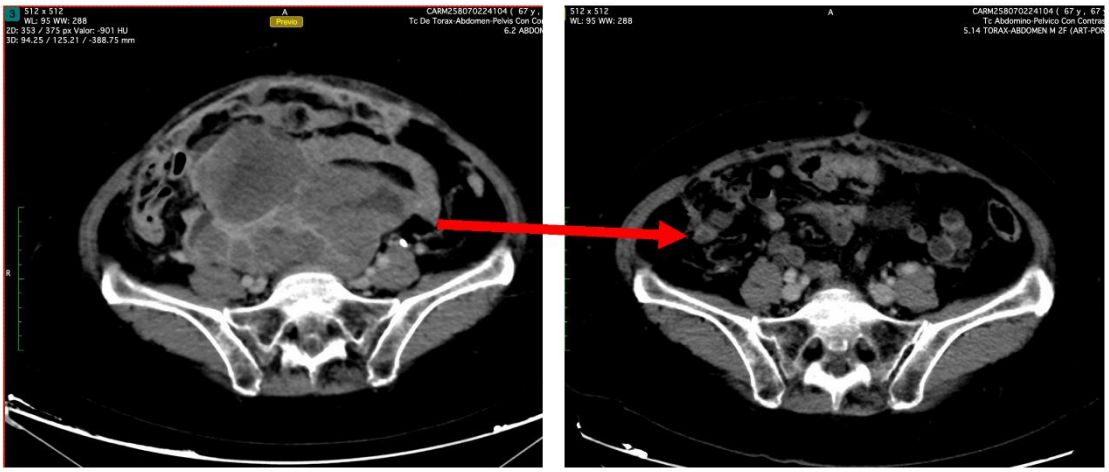


Stage IV
hepatocarcinoma

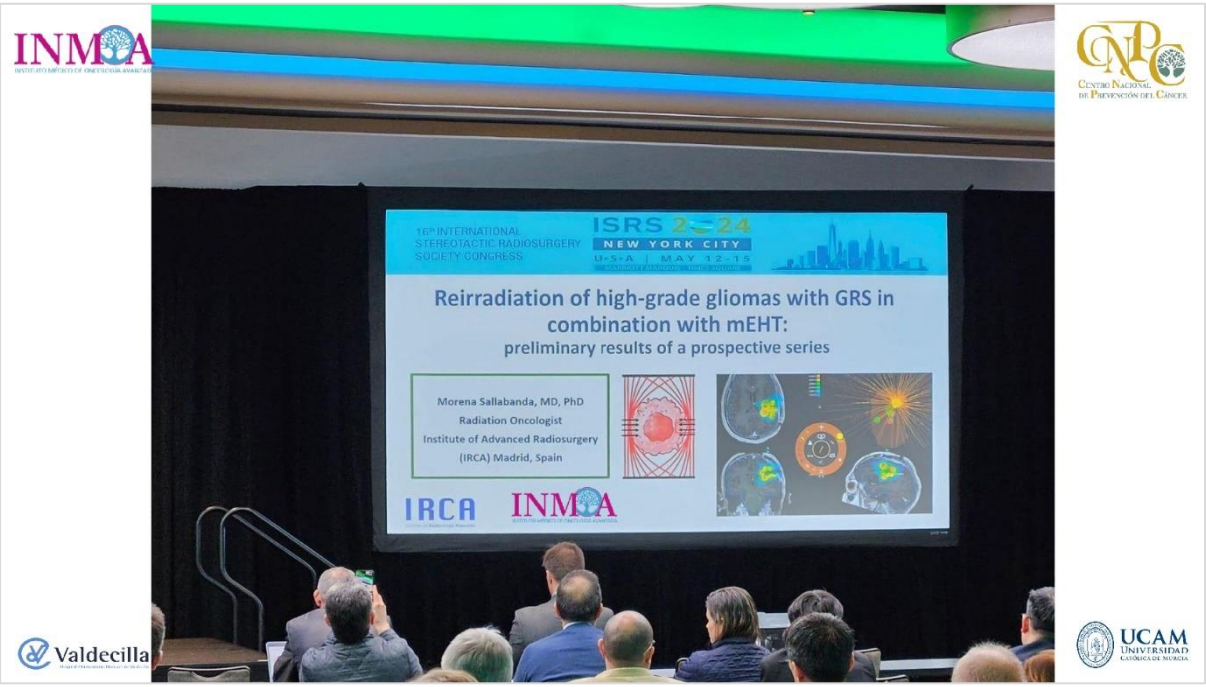
Atezolizumab + mEHT

Results 2 months after treatment

STAGE IV OVARIAN CANCER



3 CT CYCLES (CARBOPLATIN + TAXOL) + 15 mEHT treatments


INMOA
16th INTERNATIONAL STEREOTACTIC RADIOSURGERY SOCIETY CONGRESS
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Reirradiation of high-grade gliomas with GRS in combination with mEHT:
preliminary results of a prospective series
Morena Sallabanda, MD, PhD
Radiation Oncologist
Institute of Advanced Radiosurgery
(IRCA) Madrid, Spain
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A Round square with my name...
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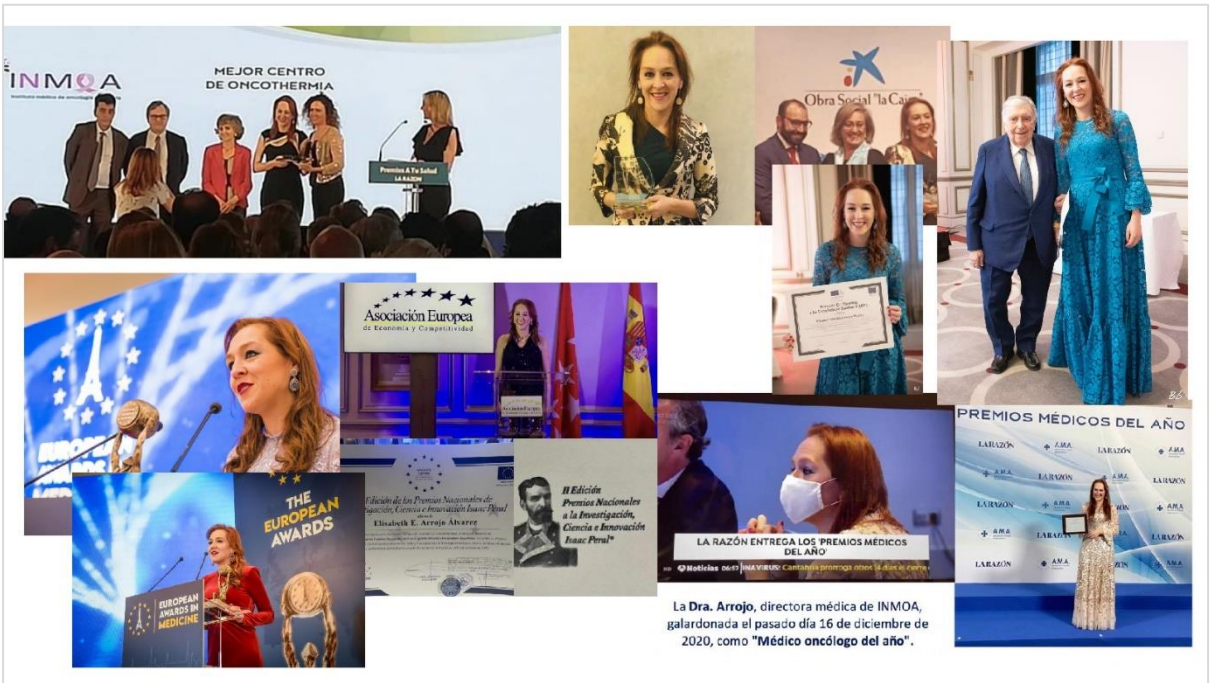
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LA RAZÓN ENTREGA LOS 'PREMIOS MÉDICOS
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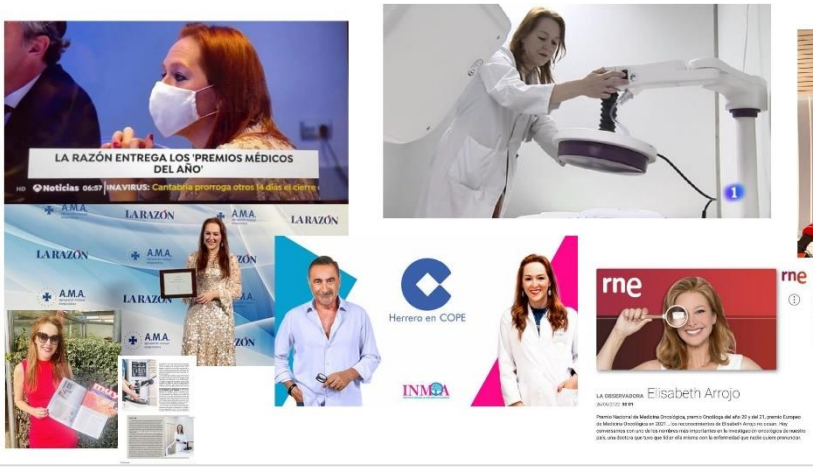
PREMIOS MÉDICOS DEL AÑO
La Dra. Arrojo, directora médica de INMOA,
galardonada el pasado día 16 de diciembre de
2020, como "Médico oncólogo del año".

INMOA in news...

News on TV...



A lot of interviews radio, newspapers, TV...

...

- INMOA, Madrid.
- INMOA, Vasque Country.

Murcia Catholic University


El Presidente y la Rectora de la
Universidad Católica San Antonio de Murcia

conforme a la propuesta formulada por el Excmo. Sr. Presidente de esta Universidad, y en virtud del acuerdo adoptado por su Consejo de Gobierno, en sesión celebrada el 20 de abril de 2022, se nombra a

Elisabeth Arroyo Álvarez

como

Catedrática Extraordinaria de Hipertermia Oncológica

y como prueba de ello, se expide el presente título acreditativo en Murcia, a 20 de abril de 2022.

El Presidente, La Rectora,

José Luis Mendoza Pérez — Josefina Gabriel Lozano

UCAM UNIVERSIDAD CATÓLICA DE MURCIA

First University Hyperthermia Professor

PRESENT/FUTURE...

cancers

MDPI

Review

Hyperthermia in Combination with Emerging Targeted and Immunotherapies as a New Approach in Cancer Treatment

Tine Logghe [1,†], Eke van Zwol [1,†], Benoît Immordino [2,3], Kris Van den Cruys [1], Marc Peeters [4], Elisa Giovannetti [2,5] and Johannes Bogers [1,6,*]

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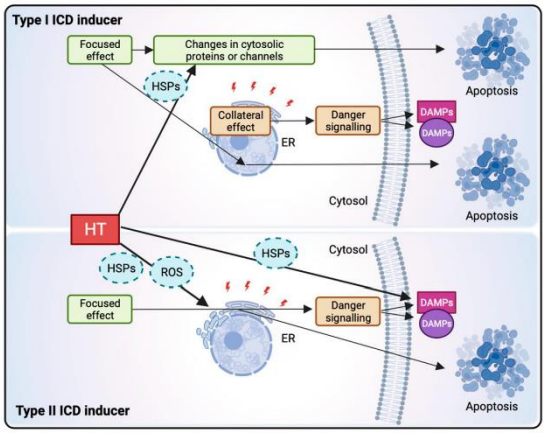
Cancers **2024**, *16*(3), 505; https://doi.org/10.3390/cancers16030505



PRESENT/FUTURE...

frontiers | Frontiers in Immunology

TYPE Review
PUBLISHED 12 August 2022
DOI 10.3389/fimmu.2022.969447

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SPECIALTY SECTION
This article was submitted to

Hyperthermia combined with immune checkpoint inhibitor therapy in the treatment of primary and metastatic tumors

Ximing Yang[1], Miaozhi Gao[1], Runshi Xu[1], Yangyang Tao[1], Wang Luo[1], Binya Wang[1], Wenliang Zhong[1,2], Lan He[3,4] and Yingchun He[1,2,3]*

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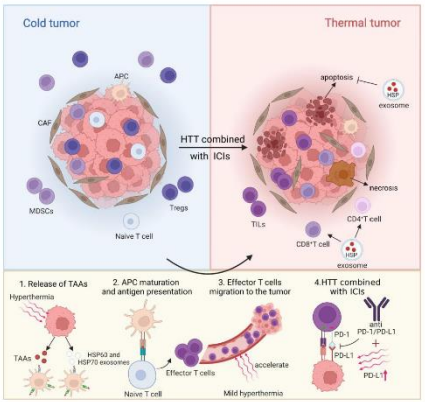

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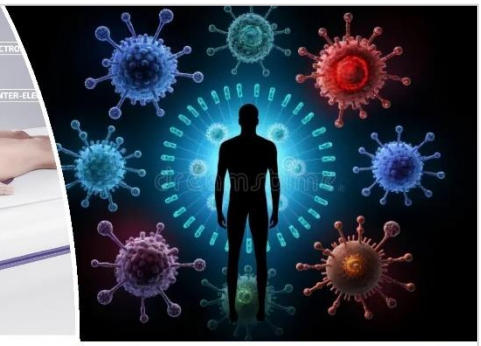
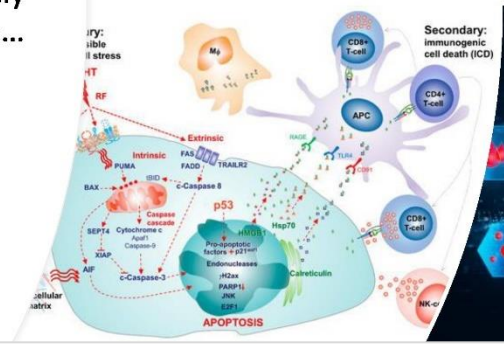
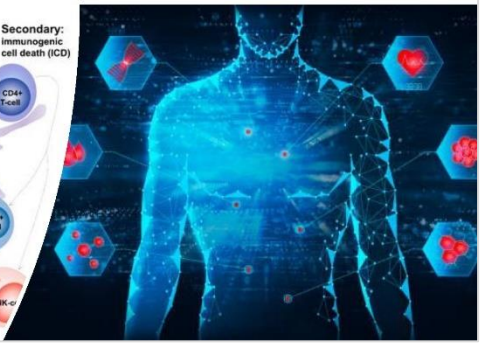
Modulated electrohyperthermia (mEHT)

More than only hyperthermia...







Conclusions

Scientifically Proven: Modulated electro-hyperthermia is supported by solid clinical and scientific evidence across various cancer types.

Treatment Amplifier: It significantly enhances the efficacy of both systemic therapies and radiotherapy, offering improved outcomes (From Good results to extraordinary...)

Standard of Care Potential: It deserves recognition and integration as a standard oncological treatment in multidisciplinary cancer care.

Immune system power: Its powerful immune-modulating effect opens a promising path for future research in cancer immunotherapy.

FOUNDATION AND FUTURE PROJECTS OF A NEW EUROPEAN HYPERTHERMIC SOCIETY: SOCIETÀ ITALIANA DI IPERTERMIA ONCOLOGICA (SIIO)

G. Fiorentini [1], M. Bonucci [2], S. Bonanno [3], G. Asero [4], G. Astara [5], M. Ballerini [6], S. Berardone [7], G. Berlino [8], G. Candiano [4], V. Cenaj [9], A. Ciabattoni [10], S. Conte [8], R. Consorti [10], G. Cipollini [11], F. Giaretta [11], A.M. Costa [12], S.R Curreri [13], P. Dentico [14], M. De Simone [15], V. Di Donna [16], F. Decian [17], G. Difede [18], G. Cristina [19], A. Gramaglia [13], S. Guadagni [20], R. Lo Dico [21], A. Mambrini [22], L. Ginocchi [22], S. Maluta [23], C. Milandri [24], R. Nani [25], M. Nicolucci [26], F. Panarisi [3], N. Pantano [27], E.M. Pasqual [28], E. Pontiggia [29], M. Porcelli [7], G. Ranieri [7], D. Sarti [1], T. Scipioni [30], I. Schito [31], P. Trecca [32], C. Zaccagnini [8], V. Cerreta [13], A. Barone [33], S. Bacchetti [28]

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Oncothermia Journal 37, September 2025., 93-98.
https://oncotherm.com/FiorentiniG_et_al_2025_Societa_Italiana_di_Ipertermia_Oncologica_SIIO

Abstract

The Italian Society of Oncological Hyperthermia (Società Italiana di Ipertermia Oncologica) was founded in September 2023 to promote oncological hyperthermia in Italy to better cure and serve cancer patients and give correct data to the Italian Ministry of Health and Regional Health Departments to develop a real Health Technology Assessment in oncological hyperthermia, currently not existing. SIIO intends to operate in all areas of medical, biological and physical research and promote all activities of support for patients, to organize data base, protocols of assistance, and new phase II and III trials. More than three thousand patients were treated with hyperthermia every year in Italy, 86% in private clinics and 14% in public Hospitals, all patients are in the metastatic phase relapsing after chemotherapy and radiotherapy. SIIO wants to expand the therapeutic paradigm of hyperthermia through the increase the number of Centres and the training of new doctors, nurses and technicians dedicated to hyperthermia.

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Key Words: regional hyperthermia, radiotherapy, chemotherapy, health technology assessment, solid tumours, integrative cancer therapy

Introduction

World Health Organization reported that the prevalence of cancer has increased worldwide in the last ten years (1,2). Hyperthermia is a generic term for different techniques using heat in cancer therapies. Temperatures of about 42° Celsius in combination with chemotherapy or radiotherapy may improve the effectiveness of those treatments.

Oncological hyperthermia is a well-known group of methods that overheat the malignant tissues locally or systematically. Nevertheless, hyperthermia is not widely accepted, primarily because although cancer cells are more sensitive to heat it has always been difficult to perform thermometry on deep tissue. Even if hyperthermia kills them, it should be theoretically possible that the temperature-triggered higher blood flow can increase both the useful arrival of chemotherapeutic drugs but also the nutrient supply to the tumour (3). Modulated electro-hyperthermia (mEHT) has been developed in the last two decades to overcome the risks of sustain cancer cells, it is a heating therapy that uses synergized thermal and nonthermal effects to heat and destroy malignant cells selectively without damaging healthy cells. The mEHT applies electromagnetic interactions to deliver energy to the cancer cells. This event is realized in the synergy of two effects. Thermal effects, as usual in hyperthermia, occur in the form of heat and temperature increase these are mostly unselective. The heat spreads all over the volume seeking thermal equilibrium. The temperature characterizes the homogeneous distribution as average energy of the heat-absorbers. Non thermal processes, mainly observed in mEHT, are electron excitations, generating chemical reactions. The non thermal impact may change the intercellular membrane, and intracellular processes select them by the dielectric and conductive heterogeneity of the target (5).The mEHT applies a precise, personalized theranostic selection and treatment of

malignancy, supporting natural homeostatic processes such as apoptosis, immune reactions, conditional effects, etc. (6).

Another deficiency is the lack of homogeneity of the hyperthermic treatments that the various public Hospitals and private centres adopt. Similarly, is the diversity of machines used and treatment protocols making it very difficult to compare the therapeutic results obtained (4).
Another important problem is who pays for hyperthermia. In some European countries such as Switzerland and the Netherlands, hyperthermia treatments for various cancers in well-defined stages are paid by the National Health Systems. In other countries there are insurances that cover the costs while in the United Kingdom the costs are paid by the citizens. Oncological hyperthermia had been present in Italy since 1991 and was removed from the National Health System's list of treatments paid by National Health System on December 31, 2024. To request a new inclusion in the services paid by the National Health System, the Italian Society of Oncological Hyperthermia (SIIO) was born. The President of SIIO, on behalf of the Society, went to the Ministry of Health in Rome in September and October 2024 to submit an official request for the reinstatement of the hyperthermia in the therapies offered by the National Health System.

In any case, there are different conditions in the various Italian Regions. In some Regions hyperthermia has been suspended while the Tuscany Region has maintained hyperthermia in the free services offered to cancer patients. On March 25, 2025, the Puglia Region resolved that at the John Paul II National Cancer Institute in Bari there is a package of services that includes hyperthermia in the care of cancer patients completely paid by the Puglia Region and without economic burden for patients.

To reintroduce hyperthermia into the National Health System and overcome these limits the Italian Society of Oncological Hyperthermia (Società Italiana di Ipertermia Oncologica - SIIO) was founded in September 2023 to promote oncological hyperthermia in Italy and develop it on the national territory to better cure and serve cancer patients and their families and give correct data to the Italian Ministry of Health and Regional Health Departments to develop a real Health Technology Assessment in hyperthermia, currently not existing. Currently the presence of a new medical society dedicated to hyperthermia as SIIO, appears to be significant in the fight against cancer in Italy because the two main medical societies dedicated to the treatment of cancer, the Italian Society of Radiotherapy (AIRO) and the Italian Society of Medical Oncology (AIOM) have accepted the European guidelines, based on greater evidence from randomized trials and included in their Guidelines the use of hyperthermia in thoracic recurrences from breast cancer and in not operable or borderline soft tissue sarcomas. This happened in 2022, and it seems essential to develop a network of hyperthermia centres in Italy where patients can be treated with competence in the context of shared decisions in multidisciplinary groups (7,8).

Material and Methods

The Italian Society of Oncological Hyperthermia (SIIO) was founded in September 2023 by fifty professionals belonging to 23 centres that administer hyperthermia to cancer patients. The first elective assembly took place in Rome on January 13, 2024. The President, the Vice-President, the Secretary and Treasurer and 4 members of the board were elected.

SIIO HAS AS STATUTORY PURPOSES THE FOLLOWING POINTS:

1. o promote oncological hyperthermia in Italy and develop it on the national territory to better cure and serve cancer patients (CP) and their families and give correct data to the Italian Ministry of Health and Regional Health Departments to develop a real Health Technology Assessment in hyperthermia, currently not existing (3).
2. To encourage the advancement of hyperthermia in all areas of medical sciences.
3. To organize a national database regarding tumours treated with hyperthermia: defining histology, genetics, stage, line of therapy, therapeutic results, calculation of the duration of OS and response, and toxicities.
4. To define new phase II and III protocols of chemo-hyperthermia, radio-hyperthermia, immuno-hyperthermia, magnetic hyperthermia, palliative medicine-hyperthermia.
5. To develop Health Technology Assessment (HTA) in hyperthermia as a multidisciplinary evaluation process that aims to determine the value of heath hyperthermia technologies and interventions to inform decision-making to promote an equitable, efficient and high-quality health system (9).

RESULTS

The collections of the preliminary data obtained are being processed. Approximately more than three thousand patients were treated with hyperthermia every year in Italy, 86% in private clinics and 14% in public Hospitals, all in the metastatic phase relapsing after chemotherapy and radiotherapy with a life expectancy ranging from 3 months to 24 months. It is estimated by default that at least 20,000 sessions of hyperthermia are administered every year in Italy.

No patients are currently enrolled in research phase III studies, the published papers have been significant retrospective comparative observational studies but never randomized. Actually, all patients are treated in a palliative way following experience and personalized protocols present in each individual centre and dictated by the experience of the physicians, expert in hyperthermia. Each patient received eleven hyperthermia sessions (range 3-28).

The median duration of hyperthermia session was 55 minutes (range 50 -110), 2-3 weekly sessions were administered on alternate days.

The patients treated with hyperthermia concurrently received single chemotherapy at personalized doses and 90% of them received integrative and supportive therapies Many treatments are based on papers recently published by Fiorentini G .and Szasz M. (11,12). Consideration and attention in SIIO centres were given to evaluate the improvement in patients' quality of life and compliance using the ESAS scale, ECOG performance status scale and electronic self-report assessment (10,11). Different brands of superficial and deep hyperthermia devices are currently adopted in Italy: Andromedic, Alba, BSD, Celsius, Oncotherm, Syncrotherm.

Conclusions

SIIO wants to expand the therapeutic paradigm of hyperthermia following the national and international guidelines and evidence more recognized (5-10) through the increase the number of centres and the training of new doctors, nurses and technicians dedicated to hyperthermia.

SIIO is open to the participation of groups of patients and their families and to all interested professionals and stakeholders. SIIO intends to collaborate with the Agency for Regional Healthcare Services (AGENAS), chapter of Italian Ministry of Health, with all Italian Regional Health Services (14) , with medical associations to provide truthful and real information on the use of hyperthermia to allow and obtain the best results by optimizing costs and facilitating the access of cancer patients to hyperthermic treatments on the Italian Territory.

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Author contribution

G.F, D.S, M.B, G.R, A.C, G.C, S.G, A.M, M.P conceived and designed the study. GF, DS, A. G, R. LD, and S.B drafting the manuscript. Critical revisions were performed by G.A, M.B, G.C, G.B, SB, CM, PD, PT,RC, and GL. Statistical analysis was performed by GF, DS, AM C, S.R. C, P.D, M.D,V.D, F.D.V.C, S.B. Administrative, technical, or material support were performed by DS, TS and SB. Supervision was carried out by GF, G.A,MB, GC, GR. V.C,S.C,G.C,F.G, F.D, L.G, S.M, C.M,R.N, M.N, F.P,N.P, EM. P, E.P, T.S, I.S, P.T, C.Z, A.B,
All authors read and approved the final manuscript.

Conflict of interest

The Authors have no conflicts of interest to report.

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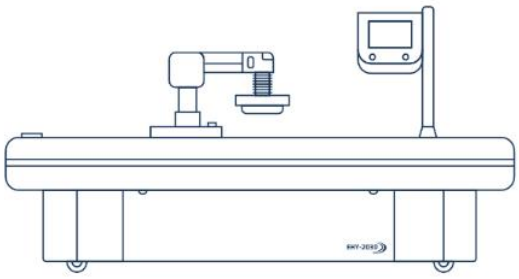
14. R E G I O N E P U G L I A - Deliberazione della Giunta Regionale N. 319 del 17/03/2025 del Registro delle Deliberazioni Codice CIFRA: SGO/DEL/2025/00038 OGGETTO: Approvazione pacchetti di day–service (chemioterapia-ipertermia). Modifica tariffario regionale ex D.G.R. n. 1863 23/12/2024.

EHY-2030

Loco-regional modulated electro-hyperthermia (mEHT) device

The EHY-2030 is Oncotherm's latest development for the loco-regional treatment of tumors. The newly designed device includes the Smart Electrode system and the integrated Patient Management System (PMS) and a user-friendly touch screen display with full system control. The new RF generator with impulse mode increased peak power has been developed with a new intelligently controlled step motor tuning system for rapid impedance matching to achieve shorter tuning-time.

The EHY-2030 device is a CE-marked medical device, and is intended for professional use.



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