



# INTERNATIONAL CONGRESS OF HYPERTHERMIC ONCOLOGY 2025

**PROGRAM BOOK**

**Sep.10(Wed) - 13(Sat), 2025**

Maria Hall, College of Medicine,  
The Catholic University of Korea



# 고주파온열암치료기 ALBA ON4000

New Generation  
Superficial Hyperthermia system

\* 유방암 및 두경부암 치료에 특성화 됨  
방사방식(Radiative) 표재성 고주파 온열암치료기  
[실시간 온도추적 및 고주파 출력조절]





# WITHUS MEDITECH

## TOTAL SOLUTION

**CQ MEDICAL™**  
Formerly CIVCO RT™ and Qfix®



Encompass SRS  
Fibreplast Mask



Breast Board

**LAP**



LUNA 3D (SGRT)



DORADOnova 5

**RAD** formation



AutoContour



EZFluence

**ScandiDos**

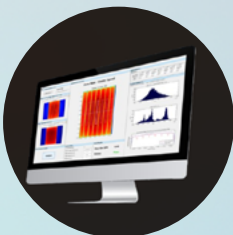


Delta4 Phantom+

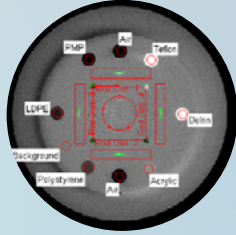


Delta4 Phantom+  
MR

**RIT**



Machine QA



Imaging QA

**STANDARD IMAGING**



DoseView 3D



QA BEAMCHECKER  
PLUS

info@withusmeditech.com  
0507-1480-6670



LinkedIn



YouTube

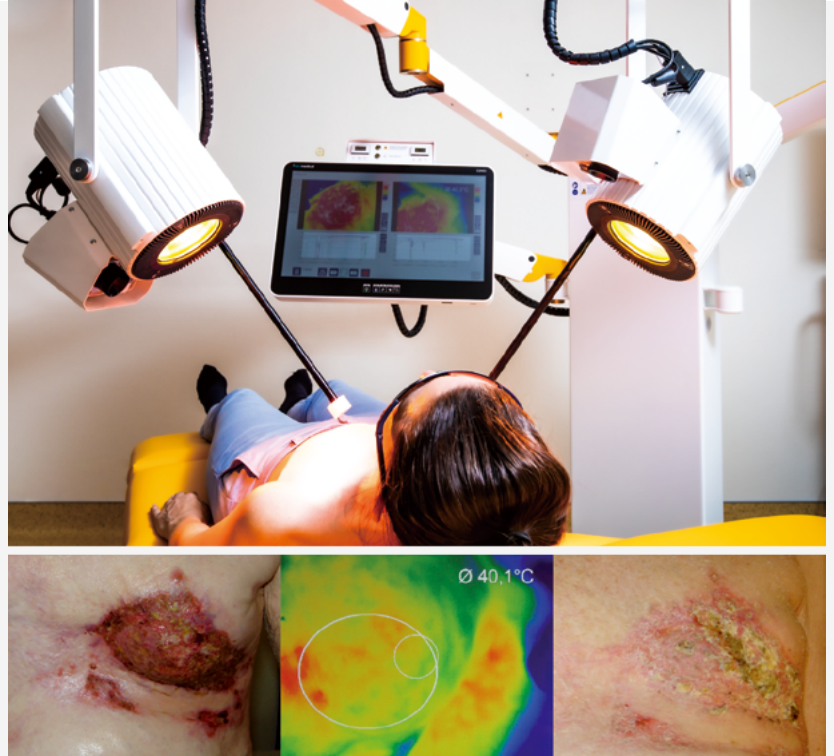


h y p e r t h e r m i e

**hydrosun® TWH**  
Thermography-controlled WIRA-Hyperthermia 1 5 0 0

### Thermography-controlled Water-filtered infrared-A superficial Hyperthermia

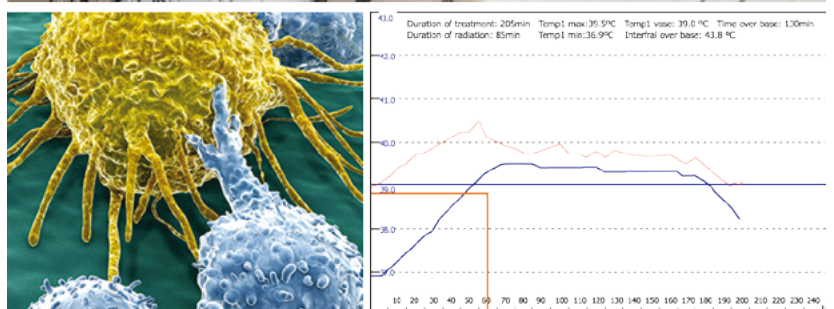
- Contact-free heating
- No risk of thermal skin damage
- Effective in combination with tolerable, reduced radiation doses even for large and heavily pretreated target areas



## heckel-HT3000

### Whole Body Hyperthermia with Water-filtered infrared-A Radiation

- Stimulation of antitumor immune response
- Enhancement of perfusion and drug delivery
- Fever-range and extreme WBH
- Oncological and non-oncological indications (e.g., chronic inflammation and infection, depression)



heckel medizintechnik gbmh Olgastasse 25, 73728 Esslingen / Germany, Fon ++49(0)711-12 89 89-0

info@heckel-hyperthermia.com

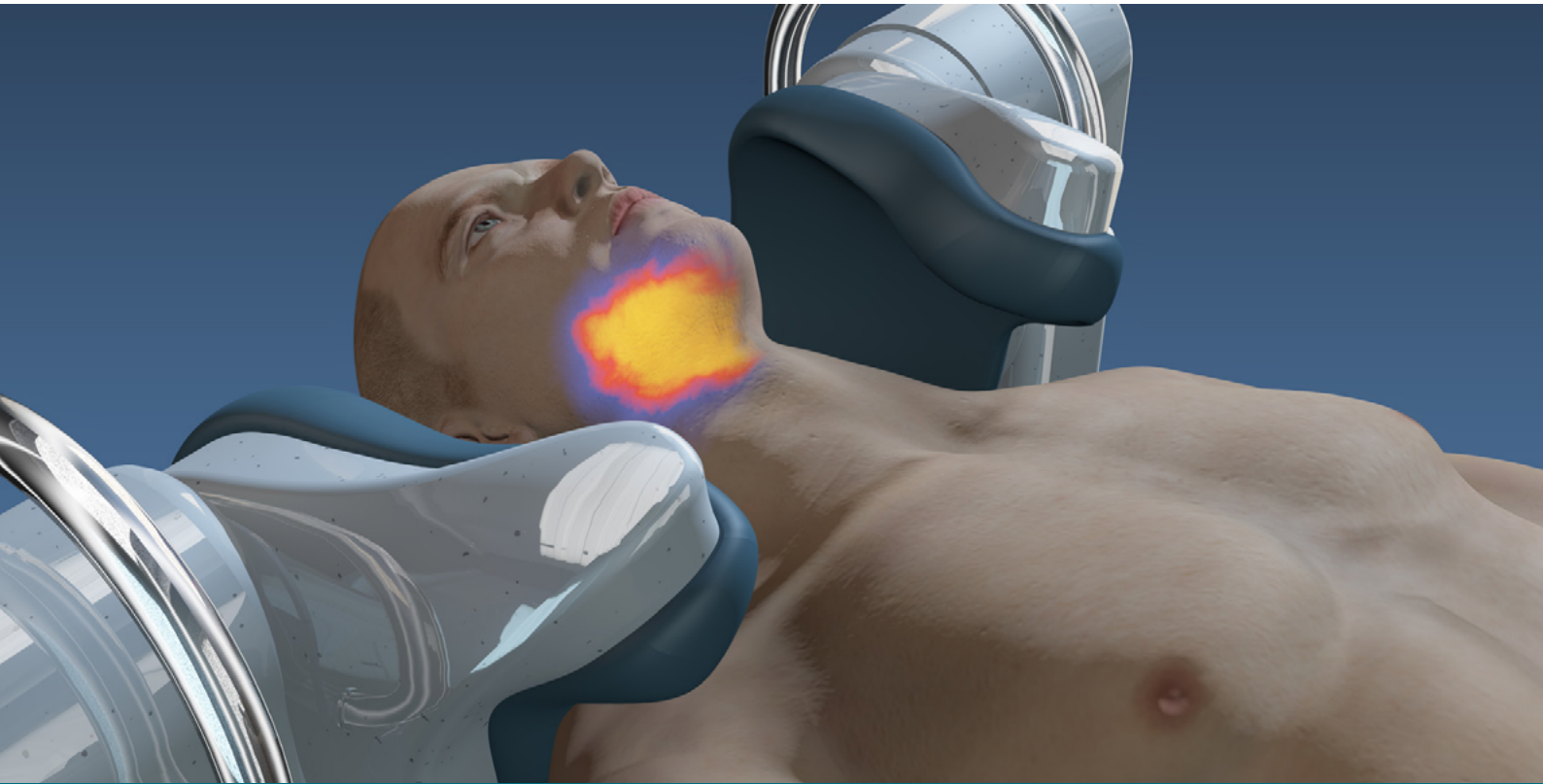
www.heckel-hyperthermia.com



# Sensius



balanced treatment



## BALANCING EFFICACY AND QUALITY OF LIFE

Fully integrated workflow



Innovative System for  
Advanced Deep oncological Hyperthermia

## HY-DEEP 600WM

HY-Deep 600WM is an innovative device developed by Andromedic Srl for deep capacitive oncological hyperthermia using radiofrequency. Designed to offer highly targeted and effective treatment, it represents a non-invasive and personalized solution for the management of deep-seated tumors.

By generating high-intensity electromagnetic pulses, HY-Deep 600WM increases the temperature within tumor tissues, enhancing the effectiveness of oncological therapies such as chemotherapy and radiotherapy, while improving the patient's biological response.



### Integrated Innovation

Thanks to the Thermal Modulation System (TMS) and advanced ASK modulation in OOK mode, the device:

Amplifies the biological response of treated tissues

Transmits specific therapeutic signals through bio-resonance frequencies

Increases the precision and selectivity of each session

### Smart and Safe Design

A temperature estimation system based on Kcal transfer

An indirect temperature monitoring algorithm for real-time control

An integrated cooling system to prevent burns and maximize comfort

### Andromedic Srl

is company in the field of advanced technological solutions for deep oncological hyperthermia therapy and is committed to placing technology and innovation at the service of health, improving patient's quality of life every day.



Via Casale di Malatesta, 10  
00049 Velletri (RM), Italy

+39 06 96 19 90 03  
[www.andromedic.it](http://www.andromedic.it)  
[info@andromedic.it](mailto:info@andromedic.it)



## 2 Cellytics® NK

### Hidden Immune Vulnerability NK Cells Know First

Activated NK cells eliminate cancer and virus-infected cells. NK cell activity testing objectively shows your immune status.

### Cellytics® NK is recommended for those who:

- need diagnosis or monitoring for cancer or immune-related conditions
- wish to evaluate the effects of anti-cancer or immune-boosting therapy
- experience stress or chronic fatigue with potential immune suppression
- want to regularly monitor their immune health

### Cellytics® NK Activity Test

Immune cell analysis available on the same-day!

**Speed** ✓ Minimal sample: Only 0.5 mL of blood  
✓ Fast: 1.5 hour turnaround

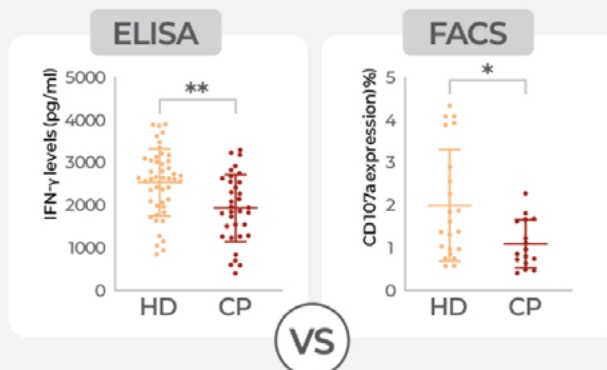
**Accuracy** ✓ NK cell isolation for unmatched precision  
✓ High-throughput imaging with single cell resolution  
✓ Dual insight: cell number and activity at once

**Simplicity** ✓ Minimal steps: No expertise required

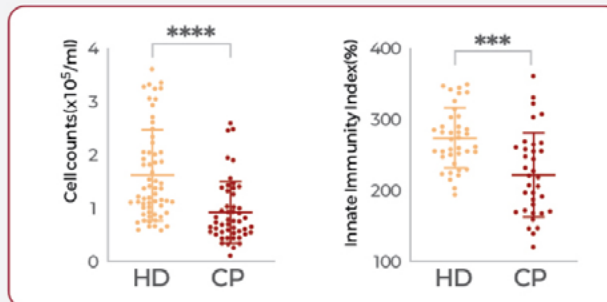
	ELISA	Cellytics® NK	FACS
Complexity	Moderate ★ ★ ★	Low ★ ★ ★	High ★ ★ ★
Analyte	IFN-γ	Unlabeled Cell	FL-labeled cell
Method	ELISA	DIH	FACS
TAT	2-3 days	<2 hours	>3 hours
Reliability	Moderate ★ ★ ★	High ★ ★ ★	High ★ ★ ★

### Proven Technology! Trusted Results!

Comparable to high-cost lab equipment in performance and precision



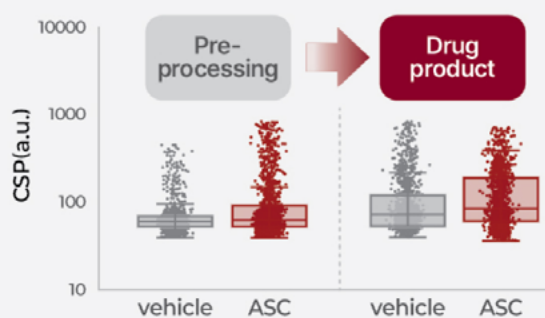
### Cellytics® NK NK Count + NK Activity



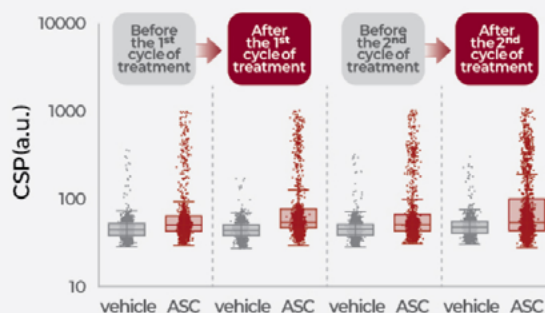
References: Bio sensors & Bio electronics 2024

NK cell therapy, covered from bench to bedside

### NK Tx potency QC



### NK monitoring in Clinical study

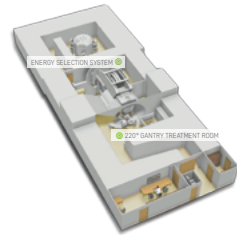


# PROTEUS<sup>®</sup>ONE

THINK BIG, SCALE SMART



- The only compact system with IMPT
- Efficiency in operation  
20% higher throughput
- Ergonomic design
- Imaging system
- Full access gantry



# PROTEUS<sup>®</sup>PLUS

CONFIGURED FOR EXCELLENCE



## ➤ Perfection in details

- Fast delivery & Room switching (<10s)
- Room matching (dose variation < 1%)
- Image-Guided PT
- Gantry rolling floor

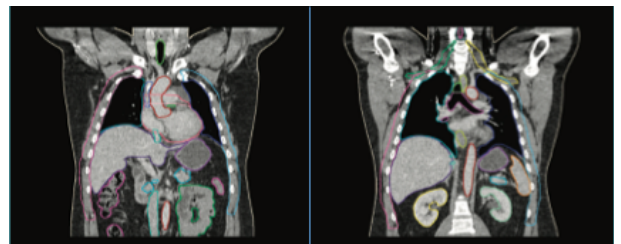
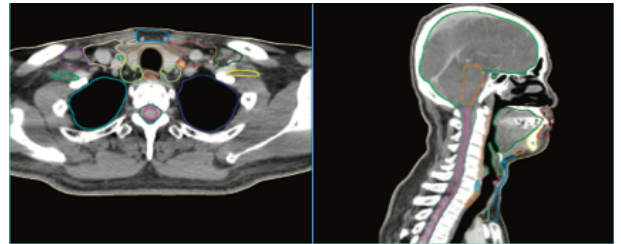
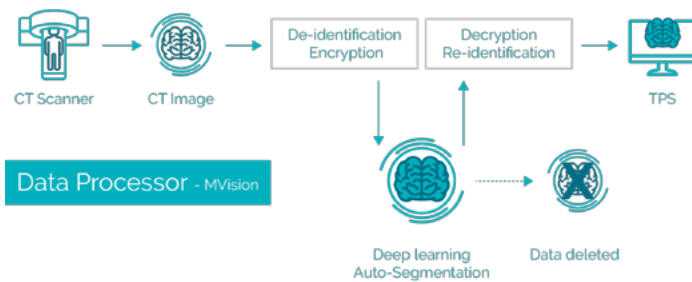


# MVISION

- AI for Precision Radiotherapy -

Automating target and organ-at-risk segmentation for radiotherapy

Data Controller - Clinic



## 국내유일 통합 서비스



CONSULTANT



SAFETY PERMISSION



MONTE CARLO



SHIELDING



DELIVERY



# A new standard for Hyperthermia treatment for cancer treatment. **celief**

## \* What is high-frequency hyperthermia treatment?

It is a treatment method that selectively applies heat energy of 42~43°C to tumor tissue using 13.56MHz high frequency to let the cells be necrotized without damaging normal cells.

## \* It utilizes the characteristics of cancer cells that are weaker to heat than normal cells.

### 8-way electrode movement

The arm's electrode can be moved in 8 directions, so it can be conveniently positioned anywhere and pressure can be minimized.

### Water bed - temperature controllable

Comfortable treatment is possible by adopting a water bed. (20°C~35°C)

### 10.4-inch LCD touch monitor

By adopting a 10.4-inch LCD monitor, all treatment can be performed nearby patients.

### Celief - Bed type CPB - 1200



100% developed with our own technology acquiring

Secured safety through experiments

All solid cancers treatable (except blood cancer)

IEC60601-1, 3.1 edition for the first time in Korea  
(ensured electromechanical stability)

Enhanced safety with cooling system, emergency button, and real-time display of operating status

Minimized installation space by incorporating high frequency generator into equipment

Maximized treatment effect with fully automatic impedance matching

### Celief - Mobile type CPB - 2100

Equipped with wheels, it can be moved freely for patients with limited mobility.

15.6-inch touch panel PC

Easy patient accessibility

6-way electrode movement

By adopting a 15.6-inch touch panel PC, all treatment can be performed nearby patients.

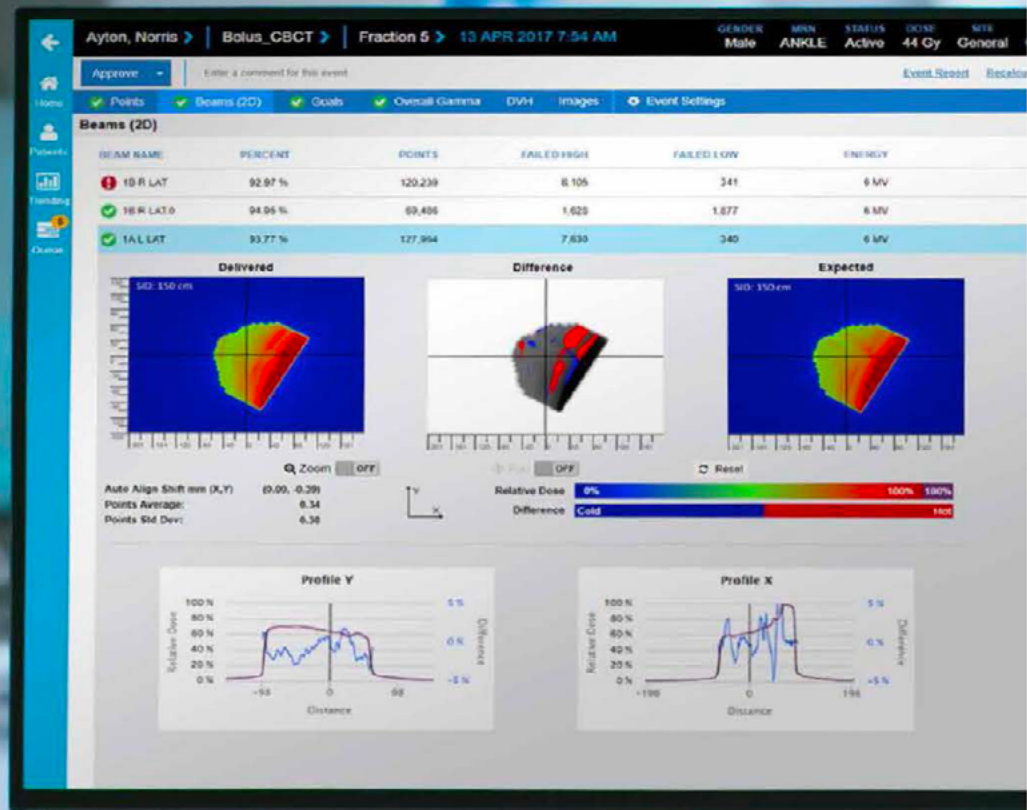
The arm's electrode can be moved in 6 directions, allowing convenient positioning in any area and minimizing pressure.



# SunCHECK™ Platform

Powering Quality Management  
in Radiation Therapy

**1,600+**  
Users Worldwide



## SNC Machine™

TG-142/VMAT Imaging and Mechanical QA



## SunSCAN™ 3D

The Next-Generation Cylindrical  
Water Scanning System





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## Venue

Maria Hall, College of Medicine, The Catholic University of Korea

Room 1002, Institute of Biomedical Industry, The Catholic University of Korea

## Hosting society

Korean Society for Thermal Medicine (KSTM)  
en.ksotm.com

## Congress Chair

Ihl Bohng Choi, M.D. Ph.D.  
Chair of Organizing Committee, KSTM

## Organizing Committee

### Chair of Organizing Committee

Ihl Bohng Choi, M.D. Ph.D.  
(KSTM, Clinical HT)

### Secretary General

Young Nam Kang, Ph.D.  
(KSTM, Physics & Engineering)

### Deputy Secretary General

Young Kyu Lee, Ph.D.  
(KSTM, Physics & Engineering)

## Congress Organization

Medicity Co., Ltd.

## Imprint

### Layout | Design & Editing

Medicity Co., Ltd.

### Print | Circulation

Seoul St. Mary's Hospital

### Editorial deadline

05 September 2025

## IDs

L = Lecture | P = Poster



**ICHO 2025**  
INTERNATIONAL CONGRESS OF HYPERTHERMIC ONCOLOGY 2025



# **WELCOME NOTE**

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Dear esteemed members of the International Congress of Hyperthermic Oncology (ICHO) 2025,

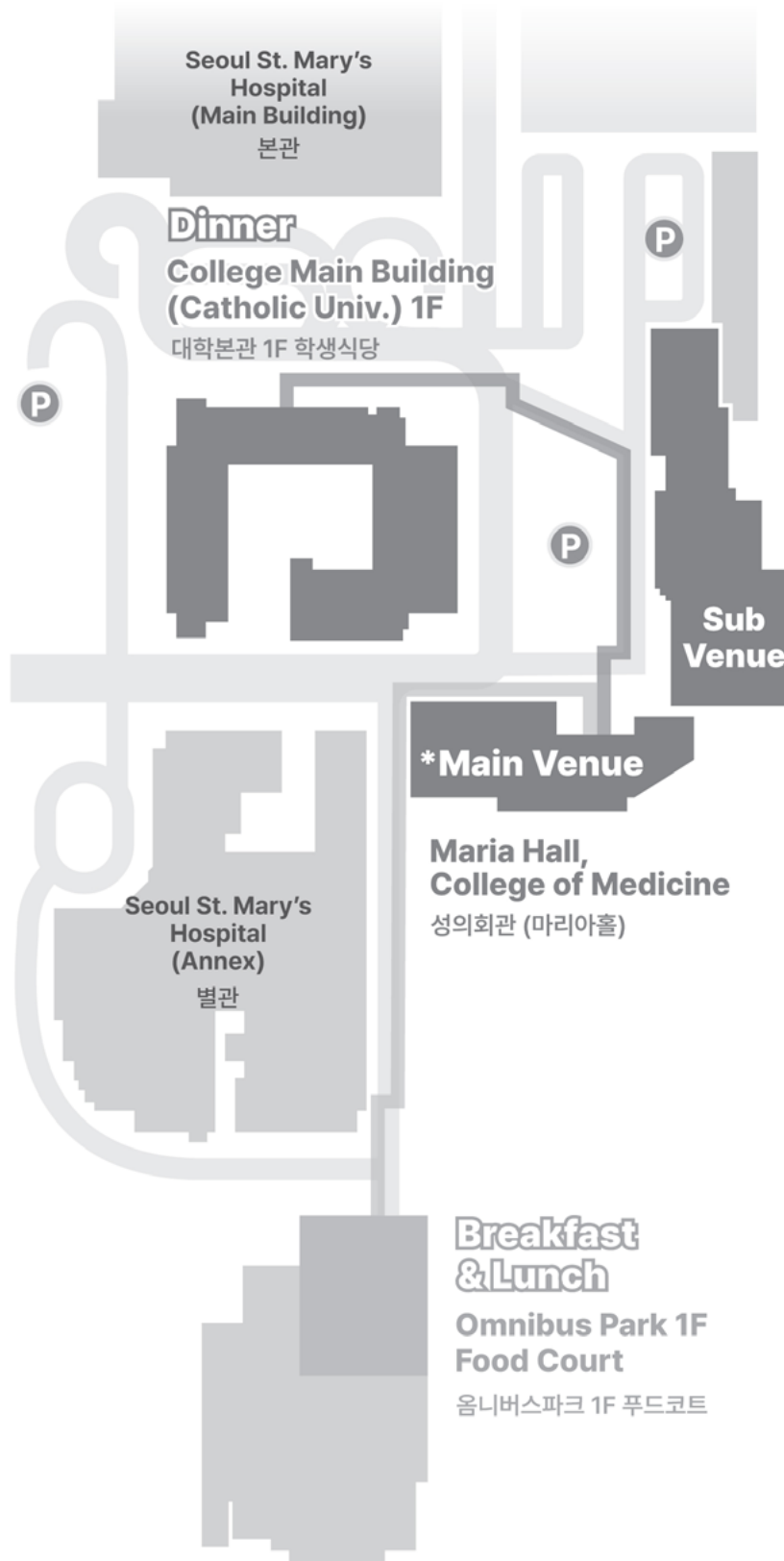
As chairman of the Organizing Committee, it is my pleasure to invite you all to international conference in South Korea, 2025. The conference will be held in our beautiful capital city Seoul, and we are honored to host such a prestigious event.

This conference will bring together professionals from all over the world to share their knowledge, experiences, and expertise regarding hyperthermia. I am confident that this conference will provide an excellent opportunity for participants to expand their knowledge, network with other professionals, and engage in discussions that will shape the future of our association. By attending ICHO 2025, we hope that it will be a forum where you can interact with experts in the field of hyperthermia and share the latest knowledge. The Organizing Committee has worked tirelessly to create a program that will be both informative and enjoyable. We have arranged various social events that will provide you with opportunities to interact with other participants and to experience our city's culture and hospitality as well. We hope that you will have a productive and memorable stay in Seoul. If there is anything we can do to assist you during your visit, please do not hesitate to reach out. On behalf of the Organizing Committee, I extend a warm welcome to all participants and wish you a successful conference.

**Prof.IHL BOHNG CHOI, M.D. Ph.D.**

A handwritten signature in dark ink, appearing to read 'I. Choi M.D.', written in a cursive style.

# FLOOR PLAN AND INDUSTRY EXHIBITION



**Scan for  
Campus Map**

캠퍼스 지도를 확인하려면  
QR 코드를 스캔하세요

**Room 1002,  
Institute of  
Biomedical Industry**

의생명산업연구원 1002호

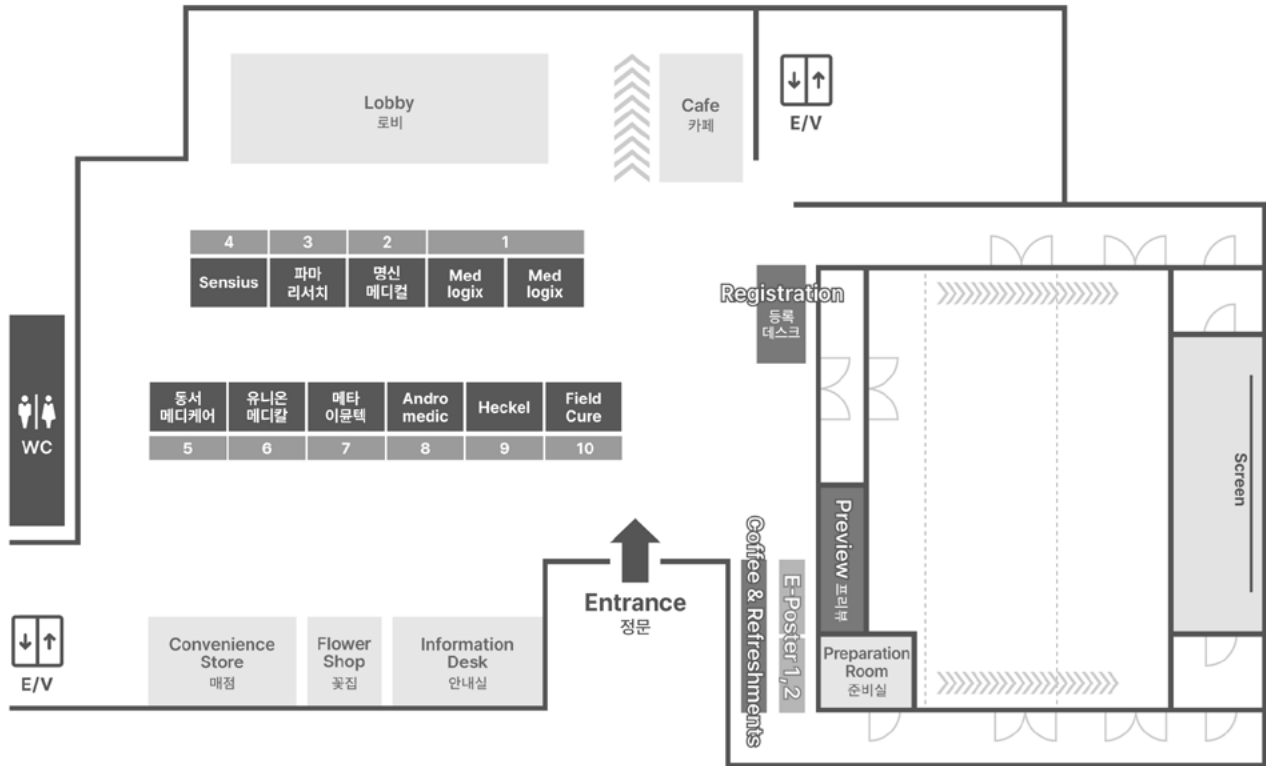
## Notice

All ICHO 2025 venues are located within the campus, within a 200m, 3-5 minute walking distance. Signage and staff will guide you on-site.

.....

ICHO 2025의 모든 행사 장소는 캠퍼스 내에 위치하며, 약 200m 거리로 도보 3-5분 이내입니다. 현장에서는 안내 표지판과 스태프가 길 안내를 도와드립니다.

## Main Venue



- 1 **PLATINUM MEDLOGIX** (주)마중솔루션
- 2 **BASIC MYUNG SHIN MEDICAL CO.,LTD** (주)명신메디칼
- 3 **BASIC PHARMARESEARCH** 파마리서치
- 4 **BRONZE SENSIOUS**
- 5 **BASIC DONGSEO MEDICARE** 동서메디케어
- 6 **BASIC UNION MEDICAL** (주)유니온메디칼
- 7 **BRONZE META IMMUNE TECH** (주)메타이문텍
- 8 **BRONZE ANDRO MEDIC**
- 9 **BRONZE HECKEL**
- 10 **BRONZE FIELD CURE**



# PROGRAM

## INTERNATIONAL CONGRESS OF HYPERTHERMIC ONCOLOGY 2025

**DAY 1** Wednesday, 10 September 2025

### Maria Hall

**13:00 - 13:30** Opening Welcome

**13:30 - 14:30** **Invited Symposium (Clinical HT& Biology & Chemistry)**

*(Chairperson: Robert Griffin)*

**Speaker:** 1. Ashish Ranjan 2. Emanuel Stutz

**Topic :** · Hyperthermia & Chemotherapy

· Hyperthermia + Radiation updates

**14:30 - 15:30** **Proffered paper Session: Technologies and Biological Optimization**

*(Chairperson: Chang Song, Ruud Dings)*

**14:30 – 14:45 (15')**

*First Clinical Experiences of the TANCA-I phase I clinical trial on Thermoradiotherapy for Locally Advanced Head and Neck Cancer*

**Speaker:** Tessa L. Coenraad

**14:45 – 15:00 (15')**

*Role of conventional hyperthermia in spatially fractionated radiotherapy bystander and immune checkpoint response*

**Speaker:** Robert J Griffin

**15:00 – 15:15 (15')**

*Optimization of the Fractionation Schedule of Radiotherapy plus Hyperthermia in Breast Cancer Cell Lines*

**Speaker:** Yihe Zhao

**15:15 – 15:30 (15')**

*Design and Evaluation of a Comfortable Breast Immobilization Platform for MR-Guided Thermo-Chemotherapy for Female Breast Cancer Patients*

**Speaker:** Linnea Verbeek

Coffee Break

**15:30 - 16:30  
(PL)**

**Keynote Session (Clinical HT)**

*(Chairperson: Ruediger Wessalowski)*

**Speaker:** Rolf Issels

**Topic :** Revisiting the EORTC 62961-

ESHO 95 randomized trial in Soft Tissue Sarcoma of Adults

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**16:30 - 17:45**

**Proffered paper Session: Clinical Applications of Hyperthermia 1**

*(Chairperson: Tae Hee Kim, Lars Lindner)*

**16:30 – 16:45 (15')**

*The impact of thermal dose on pathological complete response in locally advanced rectal cancer patients treated with deep regional hyperthermia combined with neoadjuvant chemoradiotherapy*

Speaker: Adela Ademaj

**16:45 – 17:00 (15')**

*Positive Impact of Hyperthermia on Cervical Cancer Brachytherapy*

Speaker: Yoshiaki Takagawa

**17:00 – 17:15 (15')**

*IMRT plus regional hyperthermia for high-risk prostate carcinoma: long-term results*

Speaker: Takayuki Ohguri

**17:15 – 17:30 (15')**

*Impact of thermal dose on recurrence-free survival in patients with recurrent non-muscle invasive bladder cancer undergoing MMC-based locoregional chemohyperthermia*

Speaker: C. Paola Tello Valverde

**17:30 – 17:45 (15')**

*Menadione as a Thermosensitizer in Bladder Cancer: Mechanistic and Functional Insights into Combination Treatments with Hyperthermia, Radiotherapy, and Chemotherapeutics*

Speaker: Jennate Elouach

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**18:00 - 20:30**

Welcome Reception

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**Room 1002**

**13:30 - 14:30**

**Invited Symposium (Clinical HT& Physics & Engineering)**

*(Chairperson: Nicholas Bachmann)*

Speaker: 1. Quentin Pankhurst 2. Takayuki Ohguri

Topic : · Hyperthermia & Chemotherapy  
· Hyperthermia + Radiation updates

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**14:30 - 15:30**

**Proffered paper Session: Technologies for Hyperthermia 1**

*(Chairperson: Kisoo Kim, Sergio Curto)*

**14:30 – 14:45 (15')**

*Tuning In: Frequency Selection for Deep Microwave Hyperthermia in Head & Neck and Brain Tumours*

Speaker: Robin Nilsson

**14:45 – 15:00 (15')**

*Towards Image Guided Breast Cancer Thermotherapy: Design and Validation of a Prototype Applicator for the intact breast*

Speaker: Alexandra de Boer

15:00 – 15:15 (15')

*Commissioning and Clinical Re-Release of the Hypercollar3D within European Medical Device Regulations*

Speaker: Patrick V. Granton

15:15 – 15:30 (15')

*Microwave hyperthermia for brain lesions: thermal coverage analysis in realistic clinical scenarios*

Speaker: Hana Dobšíček Trefná

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Coffee Break

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15:30 - 16:30  
(PL)

**Keynote Session (Clinical HT)**

*(Chairperson: Won Seok Choi)*

Speaker: Tae Hee Kim

Topic : HIFU for tumor ablation

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16:30 - 17:45

**Proffered paper Session: Modeling and Treatment Planning**

*(Chairperson: Petra Kok, Young nam Kang)*

16:30–16:45 (15')

*Optimization and evaluation of radiotherapy in combination with hyperthermia using a stochastic model for tissue-property uncertainties*

Speaker: Timoteo D. Herrera

16:45–17:00 (15')

*Mathematical Modeling of Chemotherapy Drug Delivery and Effectiveness: A Review*

Speaker: Luigi Rucher

17:00–17:15 (15')

*Influence of inter-patient variability in dielectric properties of lung nodules on computationally estimated microwave ablation zones*

Speaker: Anna Bottiglieri

17:15–17:30 (15')

*Reducing wideband dielectric tissue property uncertainties by ion assessment through multi-nuclear MRI*

Speaker: Laura Barendsz

17:30–17:45 (15')

*Favorable Effectiveness of Low-Dose Long-Duration Versus High-Dose Short-Duration Oxaliplatin-Based HIPEC Analyzed Using a Pharmacokinetic Model*

Speaker: Pouya Namakshenas

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## DAY 2 Thursday, 11 September 2025

### Maria Hall

**09:00 - 09:30  
(PL)**

#### **Keynote Session (Clinical HT)**

*(Chairperson: Chang W Song)*

**Speaker: Sun Ha Paek**

**Topic :** Magnetic Hyperthermia for Glioblastoma

**09:30 - 10:00  
(PL)**

#### **Keynote Session (Clinical HT)**

*(Chairperson: Chang W Song)*

**Speaker: Hong-seok Jang**

**Topic :** Role of Hyperthermia in Clinical Oncology

Coffee Break

**10:00 - 11:00**

#### **Invited Symposium (Clinical HT)**

*(Chairperson: Jin ho Song)*

**Speaker: 1. Lars Lindner 2. Emanuel Stutz**

**Topic :** Clinical results new technology

**11:00 - 11:45**

#### **Proffered paper Session: Clinical Applications of Hyperthermia 2**

*(Chairperson: Mark Hurwitz, Wonjoong Cheon)*

**11:00 – 11:15 (15')**

***Phase II Clinical Trials Combining Radiotherapy and Capacitive Hyperthermia at the Catalan Institute of Oncology: Results from the Superficial Hyperthermia Cohort in breast recurrences***

**Speaker: Marina Arangüena Peñacoba**

**11:15 – 11:30 (15')**

***3-Year Patterns of Care Analysis After Implementation of Superficial Hyperthermia at a Swiss University Radiation Oncology Center: Insights for Future Clinical Adoption***

**Speaker: Nicolas Bachmann**

**11:30 – 11:45 (15')**

***Development of a consensus lexicon for thermal medicine***

**Speaker: Dario Rodrigues**

**11:45 - 12:00**

#### **Proffered paper Session: Flash-Oral**

*(Chairperson: Mark Hurwitz, Wonjoong Cheon)*

**11:45 – 11:50 (5')**

***Proton CCRT With Deep Hyperthermia Achieves Complete Response in Cervical Cancer***

**Speaker: JENG-YOU WU**

**11:50 – 11:55 (5')**

***SAHARA Trial – Combining Hyperthermia and Radiotherapy for Non melanoma Skin Cancer: A multicenter, two-arm, open-label, randomized controlled phase II non-inferiority trial***

**Speaker: Maximilian Sturz**

11:55 – 12:00 (5')

*Comparing capabilities of three large language models DeepSeek-v1, Llama-3.3 and GPT-4o on answering specific questions about oncological hyperthermia treatment*

Speaker: Emanuel Stutz

12:00 - 13:00

Lunch

13:00 - 14:00

**Proffered paper Session: Technologies for Hyperthermia 2**

*(Chairperson: Quentin Pankhurst, Jason Molitoris)*

13:00 – 13:15 (15')

*Design of sparse array focused ultrasound transducer for targeted brain hyperthermia*

Speaker: Geunho Shim

13:15 – 13:30 (15')

*Sonothermogenetic Control of CAR T-Cell Immunotherapy for Brain Tumors using Closed-Loop Focused Ultrasound Hyperthermia*

Speaker: Chulyong Kim

13:30 – 13:45 (15')

*Feasibility study of Real-Time Temperature Monitoring Based on Electrical Impedance Tomography Using a Water Phantom Experiment*

Speaker: Jinyoung Hong

13:45 – 14:00 (15')

*DSRCT as a Hyperthermia-Driven Sequential Therapy Model for Curative-Intent Control in Pediatric Peritoneal Malignancies*

Speaker: Rüdiger Wessalowski

14:00 - 15:00

**Invited Symposium (Physics & Engineering)**

*(Chairperson: Myonggeun Yoon)*

Speaker: 1. Hana Dobsicek Trefna 2. Dario Rodrigues

Topic : Clinical safety / regulatory

-----  
Coffee Break

15:00 - 15:40

Industry Session(Medlogix, ALBA)

15:40 - 16:30

Exhibition Booth Tour

16:30 - 17:30

**Proffered paper Session: Integrated Biological in Hyperthermia**

*(Chairperson: Robert Griffin, Ashish Ranjan)*

16:30–16:45 (15')

*The role of hyperthermia in HIPEC*

Speaker: Arlene Oei

16:45–17:00 (15')

*Revealing the relevance of BRCA2 status for the efficacy of cisplatin-based hyperthermia intraperitoneal chemotherapy (HIPEC) in ovarian cancer: evidence from in vitro models*

Speaker: Fan Yang

17:00–17:15 (15')

*HPV Viral Load: Prognostic Clues for Personalizing Treatment in Locally Advanced Cervical Cancer*

Speaker: Seth-Frerich Fobian

17:15–17:30 (15')

*Quantitative Estimation of Radiobiological Parameters Using LeGO-Based High-Throughput Clonogenic Survival Assay in 12 Human Cancer Cell Lines Under Radiotherapy and Hyperthermia Conditions*

Speaker: Fernando Lobo Cerna

18:00

Speakers' Night

## Room 1002

09:00 - 10:00  
(PL)

### Keynote Session (Physics & Engineering)

(Chairperson: Mark Hurwitz)

Speaker: Kisoo Kim

Topic : Advances In Focused Ultrasound Technologies for Targeted Drug Delivery

Coffee Break

10:00 - 11:00

### Invited Symposium (Physics & Engineering)

(Chairperson: Anna Bottiglieri)

Speaker: 1. Petra Kok 2. Myonggeun Yoon

Topic : Standardization and Planning in Clinical Hyperthermia

11:00 - 12:00

### Proffered paper Session: Hyperthermia with Immune therapy

(Chairperson: Arlene Oei, Young-kyu Lee)

11:00 – 11:15 (15')

*CellyticsNK: A Novel Tool for Monitoring Immune Function Modulated by Hyperthermia in Cancer Patients*

Speaker: Sungkyu Seo

11:15 – 11:30 (15')

*Induction of Immunogenic Cell Death by Hyperthermia and Radiotherapy in a 3D Luminal A Breast Cancer Model*

Speaker: Khairunadwa Jemon

11:30 – 11:45 (15')

*Early Report of a Pilot Study of Chemoimmunotherapy Combined with Hyperthermia and Spatially-fractionated Radiotherapy in Biliary Tract and Hepatocellular Cancers*

Speaker: Jason Molitoris



11:45 – 12:00 (15')

*T-Cell Dynamics in Breast Cancer Patients Undergoing Combined wIRA-Hyperthermia and Radiotherapy*

Speaker: Anne-Marie Luechtenborg

12:00 - 13:00

Lunch

13:00 - 14:00

**Proffered paper Session: Clinical Applications of Hyperthermia 3**

*(Chairperson: Kisoo Kim, Rolf Issel)*

13:00 – 13:15 (15')

*Contact-free wIRA-hyperthermia combined with hypofractionated radiotherapy of non-melanoma skin cancers*

Speaker: Markus Notter

13:15 – 13:30 (15')

*Clinical Data confirm Galenic Principle and Demonstrate Therapeutic Potential of THE001 (DPPG2-TSL-DOX) plus Regional Hyperthermia in Soft Tissue Sarcoma*

Speaker: Lars Lindner

13:30 – 13:45 (15')

*Final report of the H2020 HYPERBOOST consortium: Hyperthermia boosting the effect of Radiotherapy*

Speaker: Hans Crezee

13:45 – 14:00 (15')

*Progress report on the CARES consortium: Development of personalized MR-guided thermo-chemotherapy for breast conserving surgery*

Speaker: Sergio Curto

14:00 - 15:00

Coffee Break

16:00 - 17:00

ESHO board meeting

18:00

Speakers' Night

## DAY 3 Friday, 12 September 2025

### Maria Hall

**09:00 - 10:00  
(PL)**

#### **Keynote Session (Biology & Chemistry)**

*(Chairperson: Rolf Issels)*

**Speaker: Robert Griffin**

Topic : The technology for thermal medicine is here- now to fully exploit biological mechanisms for each modality

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Coffee Break

**10:00 - 12:00**

#### **Panel discussion future directions**

*(Chairperson: Hans Crezee)*

**(Clinical HT, Biology & Chemistry, Physics & Engineering)**

**1. Sergio Curto (Physics & Engineering)**

**2. Ruud Dings (Biology & Chemistry)**

**3. Lars Lindner (Clinical HT)**

Topic : From Precision Delivery to Immune Modulation in Thermal Medicine

**12:00 - 13:00**

Lunch

**13:00 - 14:00**

#### **Proffered paper Session: Quality assurance and system verification**

*(Chairperson: Youngkyu Lee, Hana Trefna)*

**13:00 – 13:15 (15')**

***Evaluation of thermal mapping accuracy in clinical hyperthermia using quality assurance phantoms***

**Speaker: Mattia De Lazzari**

**13:15 – 13:30 (15')**

***Procedure for quality assurance dosimetry for hyperthermia applicators based on SAR characterization***

**Speaker: Remko Zweije**

**13:30 – 13:45 (15')**

***Compressed sensing for fast quality assurance of hyperthermia applicators by robotic electromagnetic field measurements***

**Speaker: Deovrat Phal**

**13:45 – 14:00 (15')**

***Experimental validation on agarose phantom of a capacitive hyperthermia device***

**Speaker: Gabriele Adabbo**

**14:00 - 15:00**

#### **Keynote Session (Biology & Chemistry/Clinical HT)**

*(Chairperson: Ihl Bohng Choi)*

**Speaker: Chang W Song**

Topic : Effect of hyperthermia on intratumor environment and anti-tumor immunity

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Coffee Break

**15:00 - 16:00**

Panel discussion with audience

<b>16:00 - 17:00</b>	Closing Ceremony & Award Session
<b>18:00 - 20:00</b>	Gala Dinner

## Room 1002

<b>09:00 - 10:00</b>	Coffee Break
<b>12:00 - 13:00</b>	Lunch

**13:00 - 14:15**

### **Proffered paper Session: Hyperthermia Technologies and Biological Mechanisms**

*(Chairperson: Markus Notter, Wonjoong Cheon)*

**13:00 – 13:15 (15')**

*The 1.66 GHz ALBA micro8 system: a novel device for focused locoregional heating in pre-clinical hyperthermia research*

Speaker: Petra Kok

**13:15 – 13:30 (15')**

*A preclinical microwave system for hyperthermia treatment of small animal superficial tumors*

Speaker: Hemanth Kumar Dontiboina

**13:30 – 13:45 (15')**

*Magnetic Nanoplatforms for Clinical Translation: Synergistic Hyperthermia, ChemoDynamics, Immune Activation in Cancer Treatment*

Speaker: Deepika Sharma

**13:45 – 14:00 (15')**

*Unravelling Thermotolerance in Adrenocortical Carcinoma: Implications for Hyperthermia-Based Therapies*

Speaker: Solene Fiachetti

**14:00 – 14:15 (15')**

*Global Trends in Hyperthermia Research: A Bibliometric Analysis of Publications in the International Journal of Hyperthermia*

Speaker: Fabio Dennstädt

<b>14:00 - 15:00</b>	Coffee Break
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# INVITED SPEAKER

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**DAY 1** Wednesday, 10 September 2025

**Invited Speaker**

## **Hyperthermia & Chemotherapy Hyperthermia & Radiation updates**

*Maria Hall / 13:30 - 14:00*



### **Ashish Ranjan**

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UT Southwestern  
USA

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Dr. Ashish Ranjan is an Endowed Professor and Vice Chair of Comparative Oncology & Research Innovations, and Director of the Veterinary Research & Oncology Center (VROC) within the Department of Radiation Oncology at UT Southwestern Medical Center. Prior to joining UTSW, he held the Kerr Foundation Endowed Chair at the College of Veterinary Medicine, Oklahoma State University, where he also directed the INTERACT program.

Dr. Ranjan's laboratory is internationally recognized for advancing device–drug combination strategies in comparative oncology, with translational studies spanning murine models and companion animals with naturally occurring cancers. At UTSW, he is leading the development of a cross-species clinical trial platform that embodies the One Medicine/One Health paradigm.

His research portfolio focuses on integrating focused ultrasound with nanomedicine to reprogram the tumor microenvironment in treatment-resistant cancers such as melanoma, soft tissue sarcoma, and metastatic disease. His lab is supported by federal, state, and private foundation funding and maintains active collaborations with both academic and industry partners.

A veterinarian by training with deep expertise in translational oncology, Dr. Ranjan is committed to bridging animal and human health through innovative cancer therapies. He is the recipient of numerous honors, including the NIH MERIT Award, and serves on advisory boards for several research foundations.

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## Hyperthermia & Chemotherapy Hyperthermia & Radiation updates

*Maria Hall / 14:00 - 14:30*



### Emanuel Stutz

Inselspital Bern, University Hospital  
Switzerland

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Dr. Emanuel Stutz is Head of the Hyperthermia Unit and Consultant in the Department of Radiation Oncology at the University Hospital Inselspital Bern, Switzerland. He established the hospital's superficial and deep hyperthermia program, which has treated approximately 250 patients—each in combination with radiotherapy—since its clinical launch three years ago.

Actively engaged in both patient care and the clinical application of superficial and deep hyperthermia, Dr. Stutz is also the principal investigator of a national, multicenter Phase II trial funded by the Swiss National Science Foundation. This study evaluates a multimodal, total neoadjuvant treatment for Sarculator-defined high-risk soft tissue sarcoma, combining chemotherapy and hyperthermia, followed by radiotherapy and surgery.

His clinical and research interests focus on sarcomas, bulky tumors, and the identification of predictive factors for hyperthermia response. He serves on the boards of the Swiss Hyperthermia Network (SHN) and the European Society of Hyperthermic Oncology (ESHO), and is a member of the Hyperthermia Focus Group within the European Society for Radiotherapy and Oncology (ESTRO).

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## Hyperthermia & Chemotherapy Hyperthermia & Radiation updates

Room 1002 / 13:30 - 14:00



### Quentin Pankhurst

University College London, Healthcare Biomagnetics Lab  
UK

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Quentin Pankhurst (QP) is Professor of Physics and Director of Healthcare Biomagnetics Laboratory at University College London – one of the top universities in the UK, and consistently rated one of the top 20 higher education institutions in the world.

QP has published more than 250 papers in peer-refereed international journals, with 21,500+ citations to date and an h-index of 52.

QP is a co-founder of three spinout companies: Endomagnetics Ltd in 2007; Resonant Circuits Limited in 2009; and MediSieve Ltd in 2014.

- Endomagnetics received a Queen's Award for Enterprise in 2018; a Queen's Award for International Trade in 2021, and a King's Award for International Trade in 2024; has ca. 150 employees; and has brought cancer treatment interventions to more than 800,000 patients to date. In 2024 it was acquired by Hologic Therapeutics Inc. for ca. \$310M.

- Resonant Circuits Limited has just completed a clinical trial in Barcelona, evaluating magnetic thermotherapy as an adjunctive intervention alongside standard-of-care chemotherapy to the treatment of pancreatic cancer patients with non-resectable locally-advanced tumours.

- In 2020 MediSieve received a £2.2M UK Government grant to adapt its cytokine-cleansing haemofiltration technology to the battle against Covid-19 and successfully completed initial clinical investigations on healthy volunteers in 2022. To date his companies have generated 200+ FTE new jobs in the UK, Europe, and the USA.

QP was born and raised in New Zealand and has lived in England since 1983. He is married and has two daughters.

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# Hyperthermia & Chemotherapy

## Hyperthermia & Radiation updates

Room 1002 / 14:00 - 14:30



### Takayuki Ohguri

University Hospital, Kitakyushu  
Japan

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#### Professional Experiences

2023-	Clinical Professor, Department Chair of Therapeutic Radiology, University Hospital of Occupational and Environmental Health.
2017-2022	Associate Professor, Department Chair of Therapeutic Radiology, University Hospital of Occupational and Environmental Health, Kitakyushu.
2016	Department of Radiology, University Hospital of Occupational and Environmental Health.
1997-1999	Resident, University Hospital of Occupational and Environmental Health

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#### Education

2003	Graduate school at University of Occupational and Environmental Health, Department of Pathology and Oncology
1991	Medical school, University of Occupational and Environmental Health

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#### Memberships

Editorial board of International Journal of Hyperthermia  
Member of the Japanese Society for Thermal Medicine  
Member of the Japanese Society of Radiation Oncology

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#### Honors And Awards

Japanese Society for Thermal Medicine (JSTM), Society Award 2020  
Int. J. Hyperthermia, Informa-Yamamoto Editorial Award 2011

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#### Major Research Interests

Hyperthermic Oncology, especially for deep regional hyperthermia, and Radiation Oncology especially for Re-irradiation, IMRT, Stereotactic Radiotherapy and Oligometastases.

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## Keynote Speaker

### Revisiting the EORTC 62961-ESHO 95 randomized trial in Soft Tissue Sarcoma of Adults

Maria Hall / 15:30 - 16:30(PL)



## Rolf Issels

Ludwig-Maximilians-Universität, Munich  
Germany

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### Scientific CV

<b>2013 – present</b>	Clinical Research Senior Consultant / Medical Oncology, Medizinische Klinik III – Ludwig-Maximilians-University Munich
<b>2011 – 2017</b>	Head of SarkUM (Sarcoma Center University of Munich)
<b>1999 – 2013</b>	Head of the Clinical Cooperation Group at the Helmholtz Center Munich – German Research Center for Environmental Health
<b>1982 – 1983</b>	Harvard Medical School Research Fellow, Department of Radiotherapy, Massachusetts General Hospital Boston (Prof. Suit), USA

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### Society memberships

<b>ASCO</b>	American Society of Clinical Oncology
<b>CTOS</b>	Connective Tissue Oncology Society
<b>ESHO</b>	European Society for Hyperthermic Oncology / Chairman: Head of Clinical Committee
<b>ESMO</b>	European Society of Medical Oncology
<b>EORTC-STBSG</b>	European Organization for the Research and Treatment of Cancer: Soft Tissue and Bone Sarcoma Group
<b>IAH</b>	Interdisciplinary Working Group Hyperthermia of the German Cancer Society: Chairman
<b>STM</b>	Society of Thermal Medicine

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### Publications

Prof. Issels published more than 150 papers within his scientific areas in peer-reviewed journals

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## **HIFU for tumor ablation**

*Room 1002 / 15:30 - 16:30(PL)*



### **Taehee Kim**

Seoul Hicare clinic

*Korea*

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#### **Scientific CV**

- |                    |   |
|--------------------|---|
| <b>2003 – 2007</b> | Chung-ang university hospital department of surgery |
| <b>2008 – 2010</b> | Tae-an public health center department of emergency |
| <b>2011 – 2013</b> | Gang-nam St. Peter's hospital HIFU center           |
| <b>2014 – 2016</b> | Chung-dam GY & GS clinic                            |
| <b>2016 – 2025</b> | Seoul Hicare clinic                                 |

Korean NECA member

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**Keynote Speaker**

**Magnetic Hyperthermia for Glioblastoma**

*Maria Hall / 09:00 - 09:30(PL)*



**Sun Ha Paek**

Seoul National University Hospital  
*Korea*

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**Sun Ha Paek, M.D. Ph.D.**

Professor  
Department of Neurosurgery  
Seoul National University Hospital  
Seoul National University College of Medicine

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**Subspecialty**

Stereotactic functional neurosurgery, Neurooncology,  
Gamma knife radiosurgery

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**Training & Academic Carrier**

<b>2009 -</b>	Professor
<b>2004 - 2008</b>	Associate professor
<b>2003 - 2004</b>	Research fellow (postDoc) Department of Neurosurgery , Thomas Jefferson University, Philadelphia
<b>2002 - 2003</b>	Research fellow (postDoc), Department of Neurology, Cornell University Weill Medical College, NY
<b>1999 - 2004</b>	Assistant professor, Department of Neurosurgery, Seoul National University College of Medicine, Seoul, Korea
<b>1996 - 1999</b>	Instructor, Department of Neurosurgery Gyeongsang University College of Medicine, Jinju, Korea
<b>1995 - 1996</b>	Fellowship, Department of Neurosurgery Seoul National University College of Medicine, Seoul, Korea

<b>1992 - 1995</b>	Military service (Captain), Department of Neurosurgery Jeju Medical Center, Jeju island, Korea
<b>1988 - 1992</b>	Residency, Department of Neurosurgery Seoul National University Hospital, Seoul, Korea
<b>1987 - 1988</b>	Internship Seoul National University Hospital

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## Education

<b>Feb 1999</b>	Ph.D. in Neurosurgery Seoul Nat'l University College of Medicine
<b>Feb 1992</b>	M.S. in Neurosurgery Seoul Nat'l University College of Medicine
<b>Feb 1987</b>	M.D. Seoul Nat'l University College of Medicine

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## Membership

The Congress of Neurological Surgeons (Active International member)  
The Korean Neurosurgical Society  
The Korean Brain Tumor Society  
The Korean Skull Base Society  
The Korean Society of Stereotactic and Functional Neurosurgery

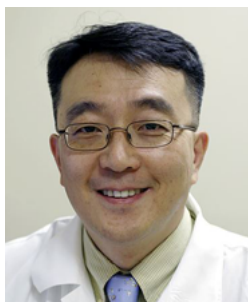
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**SCI(E) Publications : total 373 publications as of July, 2025**  
**SCI citation number: 14377, H-index: 56**

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# Role of Hyperthermia in Clinical Oncology

Maria Hall / 09:30 - 10:00(PL)



## Hong seok Jang

Seoul St. Mary's Hospital  
Korea

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### Prof. Jang Hong-seok

Department of Radiation Oncology, Seoul St. Mary's Hospital

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### Society Activities

<b>2006 - Present</b>	Professor, Department of Radiation Oncology, Seoul St. Mary's Hospital, School of Medicine, The Catholic University of Korea
<b>2015 - 2023</b>	Director of research institute, Advanced Institute for Radiation Fusion Medical Technology
<b>2006 - 2013</b>	Chairman, Department of Radiation Oncology, The Catholic University of Korea
<b>2014 - 2015</b>	President, Korean Radiosurgery Society
<b>2013 - 2014</b>	Vice President, Korean Radiosurgery Society
<b>2011 - 2016</b>	Member of Committee, Korean Board of Radiology
<b>2012 - 2016</b>	Director, Korean Cancer Association
<b>2013 - 2015</b>	Director, Public Relations Committee in Korean Society for Therapeutic Radiology Oncology
<b>2007 - 2013</b>	Director, Insurance Committee in Korean Society for Therapeutic Radiology Oncology
<b>2004 - 2007</b>	Director, Information & Communication Committee in KOSTRO
<b>2001 - 2004</b>	Director, General Affairs Committee in Korean Society for Therapeutic Radiology Oncology
<b>1999 - 2000</b>	Visiting Professor, Dr. Jirtle's Laboratory, Department of Radiation Oncology, Duke University Medical Center, Chapel Hill NC USA

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# Advances In Focused Ultrasound Technologies for Targeted Drug Delivery

Room 1002 / 09:30 - 10:00(PL)



## Kisoo Kim

Kyung Hee Univ  
Korea

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### Education

10/2016-11/2019	Ph.D. in Biotechnology at University of Strasbourg, France Thesis title: "Interventional MR Elastography for the monitoring of thermal ablations"
03/2014-02/2016	M.Sc. In Biomedical Engineering at Kyung Hee University, South Korea
03/2008-02/2014	BS in Biomedical Engineering at Kyung Hee University, South Korea Compulsory Military Service in South Korea 2010-2012

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### Experience

09/2024-CURRENT	Assistant Professor in Department of Biomedical Engineering, Kyung Hee University, South Korea
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### Key Publications

1. K. Kim, P. Gupta, K. Narsinh, C. Diederich, E. Ozhinsky. Volumetric hyperthermia delivery using the ExAblate body MRgFUS system. International Journal of Hyperthermia 2024;41(1). <https://doi.org/10.1080/02656736.2024.2349080>
2. K. Kim, K. Narsinh, E. Ozhinsky. Technical advances in motion-robust magnetic resonance thermometry: a review. Magnetic Resonance in Medicine 2024 doi: 10.1002/mrm.30057
3. K. Kim, C. Diederich, K. Narsinh, E. Ozhinsky. Motion-robust, multi-slice, real-time MR Thermometry for MR-guided thermal therapy in abdominal organs. International Journal of Hyperthermia 2023;40(1):2151649. <https://doi.org/10.1080/02656736.2022.2151649>
4. K. Kim, M. Zubair, M. Adams, C. Diederich, E. Ozhinsky. Sonication strategies toward volumetric ultrasound hyperthermia treatment using the ExAblate body MRgFUS system. International Journal of Hyperthermia 2021;38(1):1590-1600 <https://doi.org/10.1080/02656736.2021.1998658>
5. K. Kim, E. Breton, A. Gangi, J. Vappou. Simultaneous fat-referenced proton resonance frequency shift thermometry and MR elastography for the monitoring of thermal ablations. Magnetic Resonance in Medicine 2019;00:1-9. doi.org/10.1002/mrm.28130

## Honors

1. 2023: Bruce Hasegawa Award from the 20th Annual Imaging Research Symposium, University of California, San Francisco, USA
  2. 2020: Best poster Award from the 17th Annual Imaging Research Symposium, University of California, San Francisco, USA
  3. 2020: Young investigator Award from 7th International Symposium on Focused Ultrasound by FUS foundation
  4. 2019: Magna Cum Laude Merit Award from ISMRM 27th Annual Meeting, Montréal, Canada
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## Academic Activites

1. 2024-Current: **Academic Editor**, PloS One
  2. 2024: **Co-Chair Moderator**, Focused Ultrasound Session, Society of Thermal Medicine (STM) 2024, Houston
  3. 2024-2025: **Trainee Representative**, the Interventional MR Study Group of the International Society of Magnetic Resonance in Medicine
  4. 2024-Current: **Active Reviewer**, Magnetic Resonance in Medicine
  5. 2022-Current: **Active Reviewer**, International Journal of Hyperthermia
  6. 2023-Current: **Active Reviewer**, Quantitative Imaging in Medicine and Surgery, Print ISSN 2223-4292; Online ISSN 2223-4306;
  7. 2023-2024: **Guest Editor**, Methods Collection "Magnetic Resonance Imaging Monitoring of Focused Ultrasound Treatments: Advancements and Techniques", Journal of Visualized Experiments, ISSN: 1940-087X
  8. 2023: Invited SpeakerL, MR Engineering study section, 11th International Congresson MRI, Seoul
  9. 2022: Invited Speaker, The Korean Society of medical sonographers, Virtual
  10. 2022: Invited Speaker, MR Engineering study section, 10th International Congresson MRI, Seoul
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## Invited Speaker

### Clinical results new technology

*Maria Hall / 10:00 - 10:30*



## Lars H. Lindner

LMU Munich

*Germany*

### Relevant Job Experience

Dates	Company/Institute, Location	Position held
Dec 2019 - ongoing	Medical Clinic III, LMU Klinikum, Munich	Full professor for Sarcoma Therapy, Head Sarcoma Medical Oncology
Since 2013	Medical Clinic III, LMU Klinikum, Munich	Senior physician, Head Hyperthermia Unit
2000 - 2012	Medical Clinic III, LMU Klinikum, Munich	Assistant physician

### Educational Background

(Graduation) Dates	Company/University/Institute incl. Faculty/Dept., Location	Educational level achieved + Discipline
2019	Medical Clinic III, LMU Klinikum, Munich	Appointment as Full Professor for Sarcoma Treatment
2011 - 2012	EORTC STBSG	Young Oncologist
2011	Medical Clinic III, LMU Klinikum, Munich	Board Certification for Hematology and Oncology
2010	LMU Klinikum, Munich	Habilitation for Internal Medicine
2010	LMU Klinikum, Munich	Board Certification for Hemostaseology
2008 - 2009	Laboratory for Experimental Surgical Oncology, Erasmus Medical Center, Rotterdam, Netherlands. Director: Prof. Dr. A. Eggermont, MD, PhD	Postdoctoral Fellowship
2008	LMU Klinikum, Munich	Board Certification for Palliative Care
2007	LMU Klinikum, Munich	Board Certification for Internal

<b>2001</b>	LMU Klinikum, Munich	Licence to practice medicine (Approbation 01.12.2001)
<b>1999</b>	Final year of Medical School at Cornell Medical Center, Memorial Sloan Kettering Cancer Center and Mount Sinai Medical College, New York, USA; Stadtspital Triemli, Zurich, Switzerland	Graduation from Medical School, LMU Munich, Germany
<b>1996 and 1998</b>	Frankfurt, Germany	United States Medical Licensing Examination (USMLE), Step 1 and 2
<b>1992 to 1998</b>	Georg-August-University, Goettingen, Germany	Medical School
<b>1985 to 1992</b>	Geretsried, Germany	Secondary School with High School Diploma

## Doctorate

Area	Description	Dates
Max-Planck-Institute for Biophysical Chemistry, Goettingen, Germany	„Liposomes Derived from Novel Cationic Lipids: Their Influence on Cellular Uptake and Biological Activity of Antisense-Oligodeoxynucleotides“, Summa Cum Laude Doctorate	1996-2000

## Scholarships & Awards

<b>2019</b>	ESHO Pyrexar Award
<b>2008</b>	Scholarship of the Dr. Mildred-Scheel-Stiftung, German Cancer Society
<b>2006</b>	Award of the „Wolfgang Wilmanns Foundation“
<b>2006</b>	2nd place, Munich Business Plan Competition with „LipoTherm“

## Membership

Soft Tissue and Bone Sarcoma Group of the European Organisation for Research and Treatment of Cancer (EORTC)

American Society of Clinical Oncology (ASCO)

European Society for Hyperthermic Oncology (ESHO)

Deutsche Gesellschaft für Innere Medizin, Gesellschaft für Thrombose- und Hämostaseforschung

<b>2021</b>	Deputy Head of the Certification Commission for Soft Tissue Sarcoma
<b>Since 2020</b>	Head of the study group Sarcoma of the AIO
<b>Since 2021</b>	Speaker of EURACAN Sarcoma domain for the CCC Munich
<b>Since 2013</b>	Head of the Soft Tissue Sarcoma Project Group of Munich (TzM)



## Clinical results new technology

*Maria Hall / 10:30 - 11:00*



### Emanuel Stutz

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Inselspital Bern, University Hospital  
Switzerland

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Dr. Emanuel Stutz is Head of the Hyperthermia Unit and Consultant in the Department of Radiation Oncology at the University Hospital Inselspital Bern, Switzerland. He established the hospital's superficial and deep hyperthermia program, which has treated approximately 250 patients—each in combination with radiotherapy—since its clinical launch three years ago.

Actively engaged in both patient care and the clinical application of superficial and deep hyperthermia, Dr. Stutz is also the principal investigator of a national, multicenter Phase II trial funded by the Swiss National Science Foundation. This study evaluates a multimodal, total neoadjuvant treatment for Sarculator-defined high-risk soft tissue sarcoma, combining chemotherapy and hyperthermia, followed by radiotherapy and surgery.

His clinical and research interests focus on sarcomas, bulky tumors, and the identification of predictive factors for hyperthermia response. He serves on the boards of the Swiss Hyperthermia Network (SHN) and the European Society of Hyperthermic Oncology (ESHO), and is a member of the Hyperthermia Focus Group within the European Society for Radiotherapy and Oncology (ESTRO).

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# Standardization and Planning in Clinical Hyperthermia

Room 1002 / 10:00 - 10:30



## Petra Kok

Amsterdam UMC

Netherlands

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Petra Kok received her MSc in Computational Science from Utrecht University in 2002. She started her professional career as a PhD student at the department of Radiation Oncology of the Academic Medical Center in Amsterdam (AMC; currently Amsterdam UMC) and received her PhD degree in 2007 (PhD thesis "Treatment planning for locoregional and intraluminal hyperthermia").

After that, she continued her research in the field of hyperthermia as a postdoc and she is presently a principal investigator and appointed as an associate professor at Amsterdam UMC. She leads several multidisciplinary research projects and has a main focus on hyperthermia treatment planning for various heating techniques, including loco-regional, superficial, capacitive heating and HIPEC for clinical application, as well as small scale phased-array heating for preclinical research. Another important research topic is biological modeling to translate radiosensitization by hyperthermia into an equivalent radiation dose.

The versatile and flexible hyperthermia treatment planning software developed, Plan2Heat, has been commercialized by Med-Logix Srl, Rome, Italy. Biological modeling research has led to a collaboration with RaySearch Laboratories, and a recently implemented framework for combined treatment optimization in a research version of RayStation.

She has more than 100 peer reviewed publications in PubMed.

H-index google scholar; July 2025: 41.

H-index web of science; July 2025: 33.

Full list of publications: <https://scholar.google.com/citations?user=Cu5bAJ8AAAAJ&hl=nl>

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# Standardization and Planning in Clinical Hyperthermia

Room 1002 / 10:30 - 11:00



## Myonggeun Yoon

School of Biomedical Engineering, Korea University  
Korea

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### Education

Dates	Colleges and Universities	Department	Specialized Field	Degree
08/1996 - 12/2001	Pennsylvania State University	Physics	Solid State Physics	Ph.D
08/1994 - 06/1996	University of Massachusetts	Physics	Digital Signal Processing	M.S
03/1988 - 08/1992	Korea University	Physics	N/A	B.S

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### Board Certification

Therapeutic Radiological Physics by The American Board of Radiology, June 2010

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### Professional Experience

Dates	Institution and Address	Position
03/2012 ~	Department of Biomedical Engineering, Korea University	Professor
03/2011 ~ 02/2012	Department of Radiological Science, Yonsei University	Associate Professor
03/2005 ~ 02/2011	Proton Therapy Center, National Cancer Center, Korea	Medical Physicist
10/2002 ~ 02/2005	Korea Basic Science Institute, Korea	Senior Scientist
01/2002 ~ 10/2002	System LSI, Samsung Electronics, Suwon, Korea	Principle Investigator

## Honors and Awards

Recognition Details	Dates	Remarks
Young Investigator Award	2007. 09. 14	Korean Society of Medical Physicists
Best Paper of the Year	2006. 08. 31	Korean Society of Medical Physicists
Fellowship for Foreign Study	1994. 07. 23	Korean Government

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Associations	Dates
American Association of Physicists in Medicine	Regular Member (2005 ~ )
American Association for Cancer Research	Regular Member (2015 ~ )
The European Society for Radiotherapy and Oncology	Regular Member (2005 ~ )
Korean Society of Medical Physics	Regular Member (2005 ~ )
The Korean Physical Society	Regular Member (2001 ~ )

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## Clinical safety/regulatory

*Maria Hall / 14:00 - 14:30*



### **Hana Dobsicek Trefna**

Chalmers University of Technology  
*Sweden*

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#### **Biography**

Professor in Biomedical Engineering with a focus on biomedical applications of electromagnetic fields. My research is dedicated to the engineering and development of microwave hyperthermia systems, including technology for focalized heating of tumours in difficult-to-treat regions such as the brain and head and neck, as well as the application of microwaves in medical diagnostics and treatment. I currently serve as Chair of the Technical Committee of the European Society for Hyperthermic Oncology, where I lead the development of standards for hyperthermia devices, including their testing protocols and clinical implementation.

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## Clinical safety/regulatory

*Maria Hall / 14:30 - 15:00*



### Dario Rodrigues

University of Maryland, Baltimore  
USA

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Dr. Dario Rodrigues is an Assistant Professor of Radiation Oncology, Lead Hyperthermia Physicist, and Director of the Hyperthermia Therapy Practice School at the University of Maryland School of Medicine (Maryland, USA).

He earned his Ph.D. in Biomedical Engineering through a joint program between NOVA University Lisbon (Portugal) and Duke University (Durham NC, USA), and completed a 4-year residency in clinical hyperthermia physics at Thomas Jefferson University (Philadelphia PA, USA).

As a medical physicist, Dr. Rodrigues specializes in delivering adjuvant hyperthermia therapy in combination with radiotherapy and chemotherapy for cancer patients. He oversees treatment planning, thermal dosimetry, and quality assurance of clinical microwave and radiofrequency (MW/RF) hyperthermia systems.

His research involves the development of novel MW/RF and magnetic nanoparticle-based applicators, hyperthermia treatment planning strategies, and the standardization of scientific, technical, and clinical use of hyperthermia. This includes theoretical modeling, engineering development, and performance evaluation with phantom, animal, and human subjects.

He serves as Councilor for Engineering/Physical Sciences at the Society for Thermal Medicine (STM), Chair of the Thermal Medicine Standards Committee (ASME), and a member of the Technical Committee of the European Society for Hyperthermic Oncology (ESHO).

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**Keynote Speaker**

**The technology for thermal medicine is here- now to fully exploit biological mechanisms for each modality**

*Maria Hall / 09:00 - 10:00(PL)*



**Robert Griffin**

University of Arkansas for Medical Sciences  
USA

Robert J. Griffin, PhD is a professor of Radiation Biology in the Department of Radiation Oncology at the University of Arkansas for Medical Sciences (UAMS). In a career now spanning over 30 years, a large part of his research has involved characterizing the effects of thermal therapy at mild or ablative levels on the solid tumor microenvironment and how to exploit these effects to improve tumor control with various therapeutic modalities. He trained with Chang W. Song at the University of Minnesota, obtaining his PhD in 1998 and became assistant professor there in 2000. After 15 years at the University of Minnesota, he moved to UAMS in 2006 as associate professor, and became full professor in 2016. He has been a proud member of the Society for Thermal Medicine since around 1995 and has published over 180 peer reviewed papers. He has also published several book reviews and chapters and given over 130 invited presentations on his research. Most recently, he has been working as vice president for small business development and faculty affairs in the technology transfer office at UAMS (Bioventures) since 2022.

Investigations using nanomaterials (e.g., nanoliposomes and various nanomedicines) for targeted delivery to the tumor vasculature to improve responses to radiation, thermal treatment, or chemotherapy have been a growing focus of his research group now for nearly 20 years. Most recently he worked with the startup company Rejuvenics Technologies, LLC to develop a radiation-triggered liposome for tumor selective drug release with the support of an SBIR contract award from the US National Cancer Institute. A number of publications have explored tumor-selective gold-based nanoparticles to deliver photothermal therapy. Earlier, his laboratory published a series of papers on anti-angiogenic/vascular targeting agents against myeloma and breast cancer models and the development of labeled compounds for PET imaging. These projects have been supported by continuous funding from the NIH or NSF since 2004. In 2023-2024, Dr. Griffin was fortunate to receive a fellowship from the Curie Institute and the University of Paris-Saclay to support a sabbatical research project in Paris on spatially fractionated radiation and immunotherapy. He is a past President and program chair for the Society for Thermal Medicine and has served on various committees for STM, the American Society for Radiation Oncology (ASTRO) and the Radiation Research Society. Current editorial posts include Seminars in Radiation Oncology, associate senior editor for radiotherapy for Technology in Cancer Research and Treatment, Radiation Research and section editor for biology for the International Journal of Hyperthermia.

## From Precision Delivery to Immune Modulation in Thermal Medicine

*Maria Hall / 10:00 - 12:00*



### Sergio Curto

Erasmus MC, Rotterdam  
Netherlands

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#### Background

I am an Assistant Professor and Group leader Hyperthermia Research at the Radiotherapy Department of the Erasmus MC (Rotterdam, The Netherlands). I am involved in patient treatment activities, which include treatment preparation and assessment, establishment of magnetic resonance (MR)-guided deep hyperthermia procedures and hyperthermia systems quality assurance. My research focuses on novel technology for improved cancer treatment using electromagnetic energy, which spans various research phases, from early innovations, development, validation to clinical implementation. My areas of research include magnetic resonance (MR)-guided hyperthermia, quality assurance, treatment planning and enhanced thermo-sensitive drug delivery.

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#### Current affiliation

Radiotherapy Department of the Erasmus MC, Rotterdam, The Netherlands.

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#### Publications

Pure Erasmus MC (<https://pure.eur.nl/en/persons/sergio-curto-ramos>)

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#### Professional experience

Position	Period	Institution
Assistant Professor and Group leader Hyperthermia therapy research	01/07/2021 to present	Hyperthermia therapy research
Radiotherapy, Erasmus MC Cancer Institute, University Medical Center Rotterdam, Rotterdam, NL	2006. 08. 31	Korean Society of Medical Physicists

Marie Skłodowska-Curie Action Individual Fellow	01/07/2019 to 30/06/2021	Radiotherapy, Erasmus MC Cancer Institute, University Medical Center Rotterdam, Rotterdam, NL
Senior Scientific Researcher	16/07/2016 to 30/06/2019	Radiotherapy, Erasmus MC Cancer Institute, University Medical Center Rotterdam, Rotterdam, NL
Post-doc	01/03/2014 to 30/06/2016	Electrical and Computer Engineering Department, Kansas State University, Manhattan, Kansas, USA
Electrical Radiofrequency Engineer	01/09/2010 to 28/02/2014	TRYO Aerospace, Arganda del Rey, Madrid, Spain
PhD candidate	01/09/2006 to 01/06/2010	TU Dublin, Dublin, Ireland

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## Education

- 2010**     PhD: Antenna development for radio frequency hyperthermia applications, Technological University Dublin (TU Dublin), Dublin, Ireland
- 2005**     Bachelor of Engineering in Computer Engineering, TU Dublin, Dublin, Ireland, First class honours degree
- 2005**     Degree in Technical Telecommunications Engineering, University of Alcalá, Alcalá de Henares, Madrid, Spain

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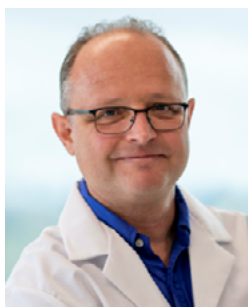
## Other Positions

Chair of the Hyperthermia Focus Group within the European Society of Radiation Oncology (ESTRO)

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## Selected grants

- 2024**     Thermoradiotherapy for locally Advanced head and Neck Cancer patients- a phase I dose finding study (TANCA-I).
  - 2023**     Development of personalized MR-guided thermo-chemotherapy for breast conserving surgery (CARES)
  - 2023**     Electromagnetic sensing, video control and metamodelling in thermotherapy of advanced H&N cancers (SENS-THERM)
  - 2023**     Postoperative Re-irradiation with or without Hyperthermia: Toxicity, quality of life and survival in patients with locoregional recurrent breast cancer (RT-HYPE)
  - 2023**     Electromagnetic sensing, video control and metamodelling in thermotherapy of advanced H&N cancers (SENS-THERM)
  - 2022**     Multi-coil magnetic resonance guided hyperthermia for precision treatment of advanced head and neck carcinoma
  - 2021**     Hyperthermia boosting the effect of Radiotherapy (HYPERBOOST)
  - 2020**     Learning-based Control in MR-guided Hyperthermia for 3D Adaptive Cancer Therapy (Learn-2-Act)
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## Ruud Dings

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University of Arkansas  
USA

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### Biography

Ruud P.M. Dings is an Associate Professor in the Department of Radiation Oncology at the University of Arkansas for Medical Sciences in Little Rock, Arkansas. He graduated from Maastricht University in The Netherlands with a M.Sc. degree in Biological Health Sciences and a Ph.D. degree specializing in tumor vascular immunology. His postdoctoral studies at the University of Minnesota centered on drug discovery and development targeting the tumor stroma, resulting in one of the lead compounds entering human clinical trials. His major research interest is overcoming the immune suppressive nature of the tumor microenvironment with treatment modalities such as radiotherapy, -hyperthermia and experimental therapeutics to improve immunotherapy.

He received the 2012 Informa-Yamamoto editorial award for Biology regarding his publication in the International Journal of Hyperthermia describing the involvement of vessel normalization during tumor thermotolerance, 2 awards from the American Association for Cancer Research (AACR), and has been senior editorial board member for the journal Angiogenesis for over 10 years. He has been an active member of STM since 2014.

Overall, Dr. Dings is an inventor on several patents and has an H-index of 40 resulting from more than 70 publications. His research has been funded by the US National Cancer Institute (NCI), National Institute of General Medical Sciences (NIGMS), and the Department of Defense (DoD).

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## Lars H. Lindner

LMU Munich  
Germany

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### Relevant Job Experience

Dates	Company/Institute, Location	Position held
Dec 2019 - ongoing	Medical Clinic III, LMU Klinikum, Munich	Full professor for Sarcoma Therapy, Head Sarcoma Medical Oncology
Since 2013	Medical Clinic III, LMU Klinikum, Munich	Senior physician, Head Hyperthermia Unit
2000 - 2012	Medical Clinic III, LMU Klinikum, Munich	Assistant physician

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### Educational Background

(Graduation) Dates	Company/University/Institute incl. Faculty/Dept., Location	Educational level achieved + Discipline
2019	Medical Clinic III, LMU Klinikum, Munich	Appointment as Full Professor for Sarcoma Treatment
2011 - 2012	EORTC STBSG	Young Oncologist
2011	Medical Clinic III, LMU Klinikum, Munich	Board Certification for Hematology and Oncology
2010	LMU Klinikum, Munich	Habilitation for Internal Medicine
2010	LMU Klinikum, Munich	Board Certification for Hemostaseology
2008 – 2009	Laboratory for Experimental Surgical Oncology, Erasmus Medical Center, Rotterdam, Netherlands. Director: Prof. Dr. A. Eggermont, MD, PhD	Postdoctoral Fellowship
2008	LMU Klinikum, Munich	Board Certification for Palliative Care
2007	LMU Klinikum, Munich	Board Certification for Internal
2001	LMU Klinikum, Munich	Licence to practice medicine (Approbation 01.12.2001)
1999	Final year of Medical School at Cornell Medical Center, Memorial Sloan Kettering Cancer Center and Mount Sinai Medical College, New York, USA; Stadtspital Triemli, Zurich, Switzerland	Graduation from Medical School, LMU Munich, Germany

<b>1996 and 1998</b>	Frankfurt, Germany	United States Medical Licensing Examination (USMLE), Step 1 and 2
<b>1992 to 1998</b>	Georg-August-University, Goettingen, Germany	Medical School
<b>1985 to 1992</b>	Geretsried, Germany	Secondary School with High School Diploma

## Doctorate

Area	Description	Dates
Max-Planck-Institute for Biophysical Chemistry, Goettingen, Germany	„Liposomes Derived from Novel Cationic Lipids: Their Influence on Cellular Uptake and Biological Activity of Antisense-Oligodeoxynucleotides“, Summa Cum Laude Doctorate	1996-2000

## Scholarships & Awards

<b>2019</b>	ESHO Pyrexar Award
<b>2008</b>	Scholarship of the Dr. Mildred-Scheel-Stiftung, German Cancer Society
<b>2006</b>	Award of the „Wolfgang Wilmanns Foundation“
<b>2006</b>	2nd place, Munich Business Plan Competition with „LipoTherm“

## Membership

Soft Tissue and Bone Sarcoma Group of the European Organisation for Research and Treatment of Cancer (EORTC)

American Society of Clinical Oncology (ASCO)

European Society for Hyperthermic Oncology (ESHO)

Deutsche Gesellschaft für Innere Medizin, Gesellschaft für Thrombose- und Hämostaseforschung

<b>2021</b>	Deputy Head of the Certification Commission for Soft Tissue Sarcoma
<b>Since 2020</b>	Head of the study group Sarcoma of the AIO
<b>Since 2021</b>	Speaker of EURACAN Sarcoma domain for the CCC Munich
<b>Since 2013</b>	Head of the Soft Tissue Sarcoma Project Group of Munich (TzM)

## Keynote Speaker

### Effect of hyperthermia on intratumor environment and anti-tumor immunity

*Maria Hall / 14:00 - 15:00*



## Chang W Song

Univ of Minnesota  
*Korea*

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### Education

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|------|--|
| 1957 | B.S. Seoul National University, Seoul, Korea. Chemistry        |
| 1959 | M.S. Korea University, Seoul, Korea. Biochemistry              |
| 1964 | Ph.D. University of Iowa, Iowa City of Iowa, USA. Radiobiology |

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### Professional Positions

- |             |   |
|-------------|---|
| 1964 - 1969 | Scientist. Albert Einstein Medical Center, Philadelphia, Pennsylvania   |
| 1969 - 1970 | Assistant Professor of Radiation Biology, Department of Radiology. Medical College of Virginia, Richmond, Virginia      |
| 1970 - 1974 | Assistant Professor of Radiation Biology, Department of Therapeutic Radiology, University of Minnesota, Minneapolis, MN |
| 1974 - 1978 | Associate Professor of Radiation Biology, Department of Therapeutic Radiology, University of Minnesota, Minneapolis, MN |
| 1978 - 2006 | Professor of Radiobiology, Dept. of Therapeutic Radiology, University of Minnesota, Minneapolis, MN                     |
| 2006 -      | Professor Emeritus. University of Minnesota   |

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### Awards

- |      |  |
|------|--|
| 1986 | Merit Award, NIH, USA  |
| 1998 | Outstanding Research and Teaching Service Award, University of Minnesota |
| 2000 | Eugene Robinson Award, North American Hyperthermia Society               |
| 2009 | T. Sugahara Award, International Society of Hyperthermic Oncology        |

## Research Interests

Effects of radiation on the vascular functions in normal tissues and tumors

Effects of hyperthermia on the vascular functions in normal tissues and tumors

Implication of intratumor microenvironment in tumor treatments

Role of HIF-1 in the immune response of tumors to radiotherapy, hyperthermia and chemotherapy

Radiobiology of high-dose hypo-fractionated radiotherapy (SABR, FLASH-RT, SART)

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# ABSTRACT

**DAY 1** Wednesday, 10 September 2025

Session 1: Technologies and Biological Optimization

## First Clinical Experiences of the TANCA-I phase I clinical trial on Thermoradiotherapy for Locally Advanced Head and Neck Cancer.

Tessa L. Coenraad<sup>1</sup>, Joris B.W. Elbers<sup>1</sup>, Patrick Granton<sup>1</sup>, Martine Franckena<sup>1</sup>, Lisa Tans<sup>1</sup>, Gerda Verduijn<sup>1</sup>, Esther Meerten, van<sup>2</sup>, Harmke A. Polinder-Bos<sup>3</sup>, Jose A.U. Hardillo<sup>4</sup>, Aniel Sewnaik<sup>4</sup>, Brend Jonker<sup>5</sup>, Anton Rink<sup>1</sup>, Erik D. Werkhoven, van<sup>1</sup>, Gerard C. Rhoo, van<sup>1</sup>, Margarethus M. Paulides<sup>1,6</sup>, Remi A. Nout<sup>1</sup>, Sergio Curto<sup>1</sup>, Michiel Kroesen<sup>1</sup>

<sup>1</sup>Department of Radiotherapy, Erasmus MC Cancer Institute, University Medical Center Rotterdam, The Netherlands,

<sup>2</sup>Department of Medical Oncology, Erasmus MC Cancer Institute, University Medical Center Rotterdam, The Netherlands,

<sup>3</sup>Department of Internal Medicine/Geriatrics, Erasmus MC Cancer Institute, University Medical Center Rotterdam, The Netherlands, <sup>4</sup>Department of Otorhinolaryngology Head and Neck Surgery, Erasmus MC Cancer Institute, University Medical Center Rotterdam, The Netherlands, <sup>5</sup>Department of Oral and Maxillofacial surgery, Erasmus MC Cancer Institute, University Medical Center Rotterdam, The Netherlands, <sup>6</sup>Department Electrical Engineering, Eindhoven University of Technology, The Netherlands

**Objective:** There is clinical need for hyperthermia (HT) as radiosensitiser for locally advanced head and neck cancer (LAHNC) patients. Currently, there is no commercially available HT applicator able to deliver controlled radiofrequency HT to deep head and neck (HN) tumours. To achieve this, we developed the HyperCollar3D (HC3D). The TANCA-I trial initiated in April 2025, investigates tolerability and safety of thermoradiotherapy administered with the HC3D. The primary end goal is the recommended phase II dose, defined as the highest feasible dose without increased acute or late toxicity compared to radiotherapy alone.

**Methods:** Within TANCA-I, LAHNC patients (max. 30) receive HT in addition to standard-of-care curative intent radiotherapy. Specific Absorption Rate (SAR) in healthy tissue in the pre-treatment planning is used to guide dose escalation by assessing toxicity. Five SAR dose levels are defined based on prior clinical data with the HC3D (40, 75, 100, 125, and 150 W/kg). We use a Time-to-Event Bayesian Optimal Interval (TiTE-BOIN) design to accelerate patient inclusion, including predefined escalation and de-escalation rules. HT is applied weekly within two hours post-radiotherapy, throughout the radiotherapy course. During the 6-month follow-up, toxicities are closely monitored, with special attention to trismus.

**Status of the trial:** The full clinical workflow is finalized within our centre. This includes a patient-specific fixation device designed to ensure reproducible positioning without compromising patient comfort. As of submission, the first patient is included in the trial. We expect to have enrolled three patients by September 2025.

**Conclusion:** Initial real-world experiences will be presented at ICHO, providing key insights into clinical feasibility and safety of thermotherapy in locally advanced head and neck cancer patients. We will focus on clinical challenges, early toxicity signs and provide a visual insight into the clinical workflow and patient journey for thermoradiotherapy in the head and neck region.



## Role of conventional hyperthermia in spatially fractionated radiotherapy bystander and immune checkpoint response

Robert J Griffin<sup>1</sup>, Azemat Jamshidi-Parsian, Amie A Brint,  
Hailey Campbell, Ruud PM Dings, Samir V Jenkins

<sup>1</sup> University of Arkansas for Medical Sciences, Department of Radiation Oncology

**Introduction:** Hyperthermia has been shown to increase radiation-induced cell killing and to be an immune adjuvant. Spatially fractionated radiation therapy (heterogeneous high and low doses across a tumor volume) has also been demonstrated to induce local and remote bystander effects in the form of cytotoxicity and immune/abscopal actions. We thus hypothesized that combined hyperthermia and radiation might significantly increase the response to immune checkpoint inhibiting antibodies.

**Methods:** Murine head and neck tumors (SCCVII) were implanted in immunocompetent (C3H) mice and treated with combinations of spatially fractionated radiation, immune checkpoint inhibitors, and mild hyperthermia. Spatial fractionation was applied in a honeycomb pattern with peak dose of 20 Gy and a valley dose of 3 Gy. Peak fields were 2 mm in diameter spaced 3 mm apart edge to edge.

**Results:** GRID alone did not significantly affect tumor growth relative to untreated controls. Addition of anti-PD1 and anti-CTLA-4 injected i.p. at 3, 5 and 7 days after GRID, specifically, led to tumor remission in more than 60% of tumors. Interestingly, hyperthermia at 42.5 °C for 60 min immediately following GRID radiation and immunotherapy resulted in less tumor growth delay and a lower percentage of remission. However, hyperthermia immediately prior to GRID radiation resulted in a similar growth delay as GRID and ICI alone, but an overall increase in the percentage of tumor remission.

**Conclusions:** The addition of hyperthermia to spatial fractionation appears to have potential for designing therapy with curative intent. We are currently assessing the effect of hyperthermia and GRID on hypoxic cell bystander and direct effects, adhesion molecule expression and immune cell recruitment.

## Optimization of the Fractionation Schedule of Radiotherapy plus Hyperthermia in Breast Cancer Cell Lines

Yihe Zhao<sup>1,2</sup>, Timo L.M. ten Hagen<sup>2</sup>, Johannes Crezee<sup>1</sup>, Lukas J.A. Stalpers<sup>1</sup>, Arlene L. Oei<sup>1</sup>

<sup>1</sup> Amsterdam UMC, University of Amsterdam, The Netherlands,

<sup>2</sup> Erasmus MC, Erasmus University, Rotterdam, The Netherlands

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**Purpose:** Radiotherapy (RT) is a fundamental component of cancer treatment, administered to approximately 50% of patients. Since the 1920s, fractionated RT—delivering multiple small doses instead of a single large dose—has been the standard approach to improve tumor control while limiting damage to normal tissues. Hyperthermia (HT), which raises tumor temperature to 40–42°C for about one hour, is a well-known radiosensitizer. Recently, hypofractionation of radiotherapy, involving fewer fractions with higher doses per fraction, has become more common, especially in adjuvant breast cancer therapy. However, the biological effects of traditional radiotherapy schemes and hypofractionated radiotherapy on tumor cells have not been thoroughly investigated, especially when combined with HT.

**Methods:** We examined the radiobiological effects of three fractionation schedules with equal biological effective dose (BED) on four breast cancer cell lines:  $3 \times 5.4$  Gy,  $9 \times 2.67$  Gy, and  $13 \times 2$  Gy. Treatments were delivered with or without HT (one to three sessions of 60 or 90 minutes at 42°C). Surviving cells were cultured over several weeks to assess radiosensitivity, proliferation, DNA damage repair, and migration capacity.

**Results:** All irradiated cells showed changes in morphology and slower growth. A higher dose per fraction resulted in faster DNA repair and reduced radiosensitivity compared to those receiving lower doses per fraction, despite similar BED. Adding HT to RT improved tumor cell killing and prolonged cell cycle arrest without inducing increased radioresistance.

**Conclusions:** Our results indicate that fractionation schedules with equivalent BED can produce distinct cellular responses. Furthermore, HT may help overcome radioresistance and reduce tumor aggressiveness, especially in cells exposed to higher dose fractions. These findings warrant further investigation into the mechanisms and potential clinical benefits of combining HT with hypofractionated RT.

## Design and Evaluation of a Comfortable Breast Immobilization Platform for MR-Guided Thermo-Chemotherapy for Female Breast Cancer Patients

Linnea Verbeek<sup>1,2</sup>, Alexandra de Boer<sup>1</sup>, Jenny Dankelman<sup>2</sup>, Nick van de Berg<sup>1,2</sup>, Sergio Curto<sup>2</sup>

<sup>1</sup>Department of Radiotherapy, Erasmus MC Cancer Institute, University Medical Center Rotterdam, Rotterdam, the Netherlands,

<sup>2</sup>Department of BioMechanical Engineering, Delft University of Technology, Delft, the Netherlands

**Introduction:** While developing a breast thermotherapy device, it is crucial to ensure immobilization of the breast for accurate treatment delivery, as well as, to consider comfort to enable procedure endurance by patients and more consistent positioning throughout the procedure.

**Methods:** To quantify these aspects, a design evaluation was conducted (METC approved, N-WMO, MEC-2024-0767). Ten healthy female participants were evaluated in the prone position using a clinically established breast MR imaging platform (Figure 1A). This provided baseline data and a framework for designing a thermotherapy specific platform (Figure 1B), which was subsequently assessed using the same approach and healthy volunteers. The breast was submerged in water and its immobilization was monitored with Electromagnetic Tracking (EMT) sensors (Figure 2), for a duration of 90 minutes. Afterwards, participants were asked to assess discomfort (0-10: 0=no discomfort, 10=extreme discomfort) by completing a questionnaire.

**Results:** Eight out of the ten participants completed the evaluation for the full duration of 90 minutes on the MR imaging platform, reporting a median discomfort score of 5.0 (IQR 4.0-6.0). The head, sternum and shoulders were the most frequently mentioned areas of discomfort. The new immobilization platform made it feasible to hold the prone position for 90 minutes for all ten participants, with a median discomfort score of 4.5 (IQR 2.3-5.0). Immobilization results with the new immobilization platform showed nipple displacements within a margin of 8 mm, while the nipple displacements with the MR imaging platform were reported within a margin of 9 mm (Figure 3).

**Conclusions:** The new immobilization platform improved comfort and facilitated that all the volunteers endured the 90 minutes evaluation. However, a reduction in breast displacement was not found. Further studies with a larger number of samples are needed to support generalizable findings.

## The impact of thermal dose on pathological complete response in locally advanced rectal cancer patients treated with deep regional hyperthermia combined with neoadjuvant chemoradiotherapy

Adela Ademaj<sup>1</sup>, Oliver J. Ott<sup>2</sup>, Cihan Gani<sup>3</sup>, Olav Dahl<sup>4,5</sup>, Emsad Puric<sup>1</sup>, Benjamin Frey<sup>2</sup>, Manfred Schmidt<sup>2</sup>, Dietmar Marder<sup>1</sup>, Hans Crezee<sup>6</sup>, Torbjørn Frøystein<sup>4</sup>, Rainer Fietkau<sup>2</sup>, Oliver Riesterer<sup>1</sup>

<sup>1</sup>Centre for Radiation Oncology, Cantonal Hospital Aarau, <sup>2</sup>Department of Radiation Oncology, Universitätsklinikum Erlangen, <sup>3</sup>Department of Radiation Oncology, Universitätsklinikum Tübingen, <sup>4</sup>Department of Oncology and Medical Physics, Haukeland University Hospital, <sup>5</sup>Medical Faculty, Institute of Clinical Science, University of Bergen, <sup>6</sup>Department of Radiation Oncology, Amsterdam UMC, University of Amsterdam, Cancer Center Amsterdam

**Purpose:** To investigate the impact of thermal dose expressed as cumulative equivalent minutes at 43°C (CEM43) on clinical outcomes in locally advanced rectal cancer patients (LARC) treated with neoadjuvant chemoradiotherapy (CRT) and deep regional hyperthermia (HT).

**Methods:** In this multinational retrospective study, 257 LARC patients treated at four clinical centers between April 2003-March 2020 were included. All patients were treated with neoadjuvant CRT (total radiation dose of 45-56Gy and 54% chemotherapy with 5-FU only) and a median of 7 HT sessions. Patients were subdivided into "low" CEM43 and "high" CEM43 groups by the HT session with highest median CEM43 <3.5 min and ≥ 3.5 min, respectively. The primary outcome was pathological complete response (pCR), secondary outcomes were disease free survival (DFS), local progression free survival (LPFS) and overall survival (OS). The outcomes were compared between "low" and "high" CEM43 groups by applying propensity scores using full- and nearest neighbor- matching methods. Propensity-matched groups were evaluated for covariate balance with absolute standardized differences ≤0.1 deemed acceptable.

**Results:** The median follow-up of patients was 57 months [95CI:54-60]. The pCR rate was significantly higher in patients treated with "high" CEM43 compared to "low" CEM43 in the full-matched cohort (11%[95%CI:7-19] vs 28%[95%CI:19-39], p=0.01) and in the nearest-neighbor-matched cohort (11%[95%CI:6-20] vs 27%[95%CI:18-38], p=0.04). The uni- and multi-variable logistic regression analyses in full-matched cohort showed that pCR was significantly associated with "high" CEM43 (odd ratio (OR):1.2 [95%CI:1.1-1.3]), lymph node involvement status (OR:1.3 [95%CI:1.1-1.6]) and moderately or poorly differentiation grade of the tumor (OR:0.7 [95%CI:0.5-0.9]). Similar results were obtained in the nearest-neighbor-matched cohort. No significant difference was observed between "low" and "high" CEM43 groups for 5-year LPFS, DFS and OS.

**Conclusions:** The CEM43≥ 3.5 min was associated with high pCR rate for LARC patients treated with neoadjuvant CRT+HT.

## Positive Impact of Hyperthermia on Cervical Cancer Brachytherapy.

Yoshiaki Takagawa<sup>1,2</sup>, Masanori Machida<sup>2</sup>, Hiroki Sato<sup>2</sup>, Shinya Komori<sup>2</sup>, Masato Kato<sup>2</sup>, Saki Sato<sup>2</sup>,  
Narie Sato<sup>2</sup>, Chika Watanabe<sup>2</sup>, Asuka Sato<sup>2</sup>

<sup>1</sup>Department of Minimally Invasive Surgical and Medical Oncology, Fukushima Medical University,

<sup>2</sup>Department of Radiation Oncology, Southern TOHOKU General Hospital

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**Purpose:** This study aimed to analyze the impact of hyperthermia (HT) on cervical cancer brachytherapy (BT).

**Methods:** We enrolled cervical cancer patients treated by curative chemoradiotherapy (CRT) or radiotherapy (RT) followed by BT in our hospital between January 2020 and March 2025. HT was used weekly during external beam RT with/without chemotherapy. BT technique was intracavitary BT (ICBT), interstitial BT (ISBT), and intracavitary/interstitial BT (IC/ISBT). We calculated the reduction rate (RR) of gross tumor volume (GTV) using pretreatment and pre-BT MRI images. Statistically analyzed the factors that influence the RR.

**Results:** Seventy patients were enrolled in this study. The median age was 65 years old. T stage was as follows: 1/2/3/4 were 5/41/19/5. CRT had 52 patients, and RT had 18 patients. HT was used in 35 patients (50%). The BT technique was as follows: ICBT was 41, ISBT was 1, and IC/ISBT was 27. Only one patient did not receive brachytherapy due to private reasons. HT use, larger pretreatment GTV ( $70\text{cm}^3 \leq$ ), and without center shield technique had a significantly higher RR ( $p < 0.01$ , each). HT use also showed significantly higher RR in both the CRT and RT groups ( $p = 0.02$ , each). The larger pretreatment GTV was only statistically significant in multivariate analysis ( $p = 0.04$ ). In the patients with larger pretreatment GTV ( $n = 34$ ), HT (+) with ICBT, HT (-) with ICBT, HT (+) with IC/ISBT, and HT (-) with IC/ISBT were 10 (29.4%), 6 (17.6%), 15 (44.1%), and 3 (8.8%) patients, respectively. The median number of interstitial needles was 3 in the HT (+) with the IC/ISBT group and 5 in the HT (-) with the IC/ISBT group.

**Conclusions:** The use of HT during CRT or RT for cervical cancer showed statistical significance in RR before BT. This higher RR due to HT has the potential to contribute to less invasive brachytherapy for cervical cancer.

## IMRT plus regional hyperthermia for high-risk prostate carcinoma: long-term results

Takayuki Ohguri<sup>1</sup>, Tatsuya Nakaya<sup>1</sup>, Yasuhisa Matsuura<sup>1</sup>, Subaru Tani<sup>1</sup>

<sup>1</sup>Dept. of Therapeutic Radiology, University of Occupational and Environmental Health

**Purpose:** This study aimed to evaluate the long-term efficacy and toxicity of adding regional hyperthermia to intensity-modulated radiotherapy (IMRT) combined with neoadjuvant androgen deprivation therapy (ADT) for high-risk localized prostate carcinoma.

**Methods:** We retrospectively analyzed data from 121 consecutive high-risk prostate carcinoma patients, defined according to NCCN guidelines, who received definitive IMRT at our institution between March 2011 and December 2018. All patients were prescribed a total IMRT dose of 76 Gy in 38 fractions. Of these, 70 patients also received hyperthermia. Intra-rectal temperatures at the prostate level were measured to evaluate the thermal dose.

**Results:** The median number of heating sessions was five, and the median total thermal dose (CEM43T90) was 7.5 minutes. The median follow-up duration was 89 months. The addition of hyperthermia to IMRT was a predictor of better clinical relapse-free survival. A higher thermal dose (CEM43T90 > 7 minutes) tended to predict improved biochemical disease-free survival. There was no significant difference in the occurrence of acute and delayed toxicity of Grade  $\geq 2$  between patients who received hyperthermia and those who did not.

**Conclusion:** In this study, the addition of regional hyperthermia to IMRT plus neoadjuvant ADT significantly improved clinical relapse-free survival in patients with high-risk localized prostate carcinoma, without increasing treatment-related toxicity. Our findings suggest that hyperthermia, particularly with a higher thermal dose, plays a crucial role in enhancing treatment efficacy for this patient population.



## Impact of thermal dose on recurrence-free survival in patients with recurrent non-muscle invasive bladder cancer undergoing MMC-based locoregional chemohyperthermia

C. Paola Tello Valverde<sup>1,2,3</sup>, Konstantinos Pateras<sup>4</sup>, Elisabeth D. Geijssen<sup>1</sup>, Theo M. de Reijke<sup>5</sup>, Ben J. Slotman<sup>2</sup>, Jorg R. Oddens<sup>3,5</sup>, Hans Crezee<sup>1,3</sup>

<sup>1</sup> Department of Radiation Oncology, Amsterdam UMC, University of Amsterdam, <sup>2</sup> Department of Radiation Oncology, Amsterdam UMC, Vrije Universiteit Amsterdam, <sup>3</sup> Cancer Treatment and Quality of Life, Cancer Center Amsterdam, <sup>4</sup> University of Thessaly, Faculty of Public and One Health, Laboratory of Epidemiology & Artificial Intelligence, <sup>5</sup> Department of Urology, Amsterdam UMC, University of Amsterdam

**Purpose:** We aimed to investigate the continuous thermal dose (TD)-effect relationship for estimating the probability of 5-year recurrence-free survival (RFS) in patients with non-muscle invasive bladder cancer (NMIBC) treated with locoregional chemohyperthermia.

**Methods:** In this cohort follow-up study (2009-2020), patients with recurrent intermediate- or high-risk NMIBC received six weekly sessions of locoregional chemohyperthermia with mitomycin C (MMC), followed by four maintenance sessions. Intravesical and perivesical temperatures (urethra, rectum, and, if applicable, vagina) were recorded. The continuous log-transformed Average CEM43T50 (median cumulative equivalent minutes at 43°C), was selected based on Weibull univariate and stepwise regression analyses, adjusted for recurrence rate, multifocality, and WHO 2004/2016 grade classification. Additionally, the effect of continuous log-transformed Average CEM43T50 on 5-year recurrence risk was evaluated using Fine and Gray competing risks analysis.

**Results:** Sixty patients with ≤5 years of follow-up were included in the final analysis, of whom 83% (n=50) were classified as high-risk and 17% (n=10) as intermediate-risk according to EAU guidelines. Overall, 30 patients experienced a recurrence after locoregional CHT, with a median time to recurrence of 2.1 years (IQR 0.8-6.5 years). Median Average CEM43T50 was 2.5 minutes ranging between 0.09-15.2 minutes. Continuous TD parameter analysis showed that a higher TD was significantly associated with an increasing RFS ( $P < .001$ ). Both univariate and multivariate Weibull regression analyses showed that a twofold increase of TD was associated with 31% (95%CI 14%-45%;  $P < .001$ ) and 30% (95%CI 11%-46%;  $P = .003$ ) decrease in the hazard of recurrence, respectively. Fine and Gray analysis confirmed that increasing Average CEM43T50 TD was significantly associated with a reduced risk of recurrence (unadjusted  $P = .006$ ; adjusted  $P = .007$ ).

**Conclusion:** A twofold increase in hyperthermia TD was significantly associated with improved RFS across the continuous TD range in patients with NMIBC treated with MMC-based locoregional chemohyperthermia. Results confirm the importance of adequate TD for achieving high RFS.

## Menadione as a Thermosensitizer in Bladder Cancer: Mechanistic and Functional Insights into Combination Treatments with Hyperthermia, Radiotherapy, and Chemotherapeutics

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**Purpose:** Hyperthermia (HT), the controlled heating of tumors between 39–43°C, enhances the efficacy of conventional therapies like radiotherapy and chemotherapy by disrupting DNA repair, redox balance, and protein homeostasis. In bladder cancer, HT is clinically applied in protocols such as Hyperthermic Intravesical Chemotherapy (HIVEC), but its effectiveness remains limited in certain cases. Menadione (vitamin K3), a redox-active compound, induces oxidative stress, mitochondrial damage, and apoptosis in cancer cells and may serve as a promising thermosensitizer. This study investigates Menadione's thermosensitizing potential in bladder cancer and its combinatorial effects with HT, radiotherapy, and HIVEC-relevant chemotherapeutics.

**Methods:** Bladder cancer cell lines RT112, T24, and J82 were treated with Menadione followed by HT at 42°C for 1 hour. Cell viability was measured 72 hours later to calculate Thermal Enhancement Ratios (TERs). Mechanistic studies included  $\gamma$ H2AX immunostaining for DNA damage, cell cycle analysis, Western blotting for heat shock proteins (HSP70/90), and cell growth tracking. In silico analysis explored affected pathways in redox metabolism, mitochondrial function, and proteostasis. Combinations with Mitomycin C, Cisplatin, Epirubicin, and radiotherapy were assessed for synergistic effects.

**Results:** Menadione significantly increased HT-induced cytotoxicity (TER > 1.5) across all cell lines. Combined treatment caused sustained DNA damage, G2/M arrest, and strong induction of heat shock proteins. Menadione and HT disrupted ROS balance, ATP production, and protein folding, leading to enhanced cell death. Triple combinations with chemotherapy or radiotherapy showed synergistic cytotoxicity.

**Conclusion:** Menadione acts as a potent thermosensitizer in bladder cancer, enhancing the impact of HT and improving the response to chemo- and radiotherapy. Ongoing validation in 3D bladder organoid models will support clinical translation for optimized HIVEC and radiotherapy protocols.

## Tuning In: Frequency Selection for Deep Microwave Hyperthermia in Head & Neck and Brain Tumours

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**Introduction:** The operating frequency in deep hyperthermia critically influences the thermal dose delivery to the target volume. Yet, consensus of optimal operating frequency for head and neck (H&N), and brain has yet been established, but considered to range between 400 – 600MHz [\*], while 434MHz is used in clinical settings for practical reasons. This study assess the choice of operating frequency by means of numerical simulation for a variety of H&N and brain tumours as well as applicators.

**Method:** SAR-based treatment planning using iterative-Time Reversal [\*\*] was performed in the frequency range of 250 – 800 MHz. EM fields and thermal distributions were simulated using COMSOL Multiphysics using a twelve-antenna applicator with various configurations. Initially, a healthy model (Billie; IT'IS foundation) with synthetic brain tumours of varied size, position, shape, were sequentially constructed to isolate geometrical and tissue property effects on the frequency choice. The findings were further examined and validated using real patient models, including both paediatric brain cancer patients and head and neck (H&N) patients from the ESHO Grand Challenge[\*\*]. Temperature-based metrics—particularly T90—were employed as validation indicators.

**Results:** Results indicate that regardless of tumour geometry, tissue properties or applicator arrangement, lower frequencies in range of 250 – 350 MHz consistently yield higher T90 values. On average, simulations show a 4.9% improvement over the corresponding 400–800 MHz range, ranging from 2.6% to 8.6%. Slight additional gains may also be achieved with multi-frequency use, particularly in H&N cases where a combination of 350 and 600 MHz yielded 0.2oC higher than any single frequency.

[\*] Paulides et al 2005, IJROBP.

[\*\*] Zanolli et al 2021, PMB.

[\*\*\*] Paulides et al 2021, IJH.

## Towards Image Guided Breast Cancer Thermotherapy: Design and Validation of a Prototype Applicator for the intact breast

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**Purpose:** The CARES consortium aims to revolutionize breast cancer treatment by developing a personalized magnetic resonance (MR)-guided local thermochemotherapy, striving for efficacy while minimizing toxicity. The overarching goal is to enhance the therapeutic window of neoadjuvant chemotherapy to ultimately enable breast conservative surgery.

This work focuses on the design and validation of an MR-compatible thermotherapy prototype device to treat tumors in the intact breast and describes a framework for device validation.

**Methods:** A prototype design consisting of 12 heating antennas is chosen after extensive simulations of different antenna configurations' heating capabilities with the electromagnetics (EM) and thermal solver Sim4Life (ZMT, Zurich, Switzerland). The EM performance of the device is evaluated by reflection and cross-coupling measurements. Heating capabilities of the full 12-antenna device was validated with a breast tissue-mimicking split phantom for a central target location using infrared (IR) imaging. To confirm the device's MR compatibility and MR thermometry (MRT) performance, a 6-antenna heating experiment was performed in the MR.

**Results:** The measured antenna reflection and cross-coupling coefficients of the device were within acceptable limits ( $< -15$  dB)(Fig.1). A temperature increase of at least 9°C after 3 minutes of heating with 200W input power was obtained for a centrally located target using all antennas and its simulated thermal focal spot location is in good agreement with the obtained experimental result (Fig.2). Using six antennas and approximately 180 W of total power, both MRT and IR imaging detected a temperature increase of 15 °C after 15 minutes of heating in the MRI scanner (Fig.3).

**Conclusion:** An MR-compatible thermotherapy device was designed and constructed for breast cancer treatment. Initial results from validation experiments shows that the device performs according to guidelines and is MR compatible. Further quantification of simulation and experimental correspondence is ongoing and will be presented.

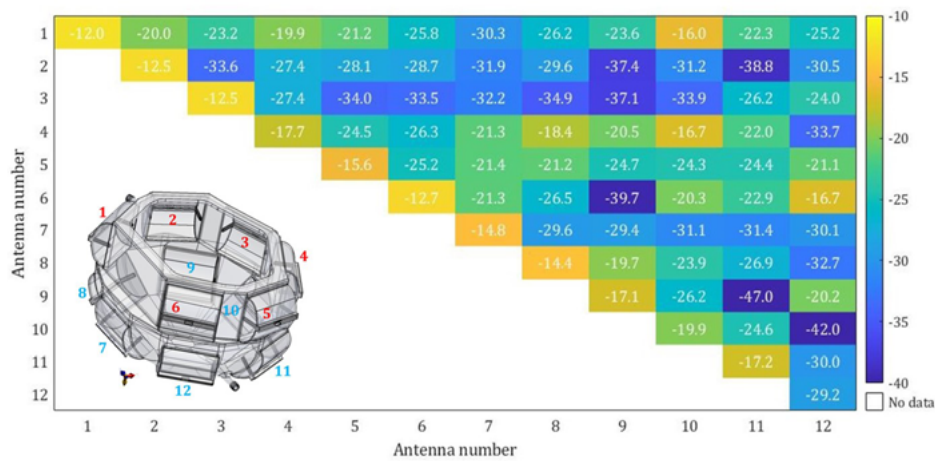


Fig. 1: Scattering matrix showing both reflection coefficients ( $S_{ii}$ ) and cross-coupling ( $S_{ij}$ ) measurements in decibels (dB). In the left corner is an overview of the applicator and its antenna locations, i.e., red being the antennas in the upper ring and blue the lower.

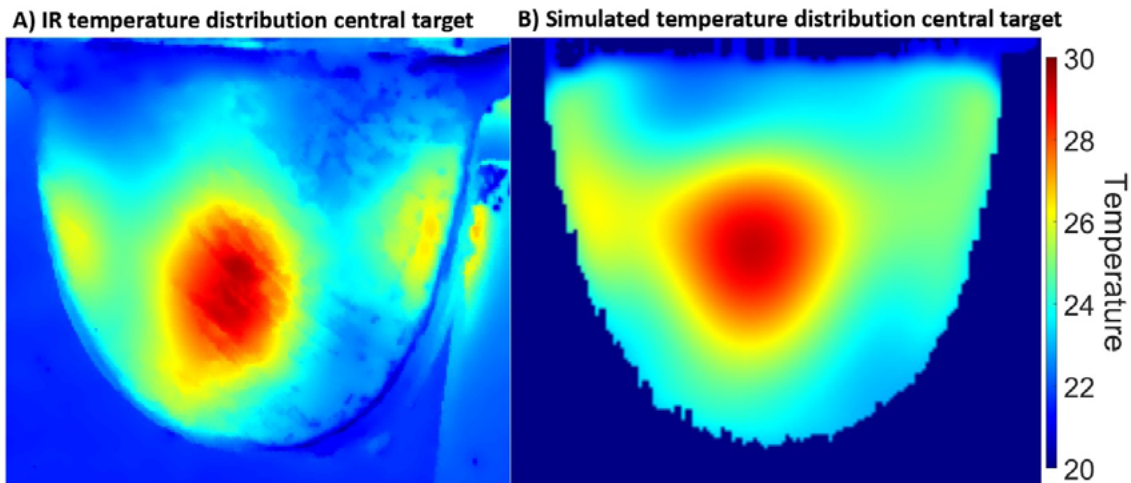


Fig. 2: A) IR image of temperature profile before and after heating a breast phantom for 3 min at 200W for a central target location, B) Corresponding simulated thermal distribution for this experimental setup.

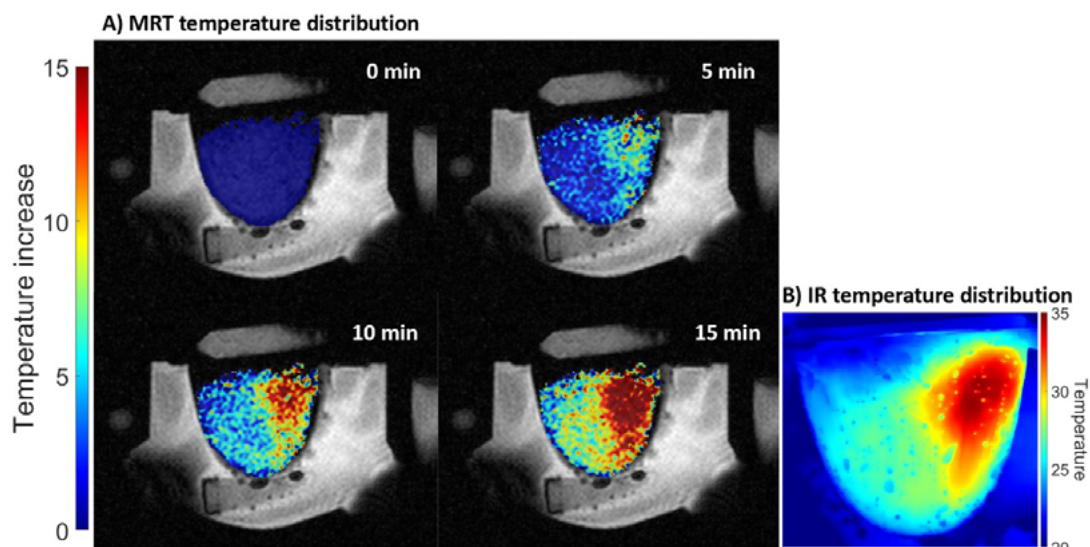


Fig. 3: A) MRT images of temperature profile in breast phantom before and during 5, 10 and 15 minutes of heating, B) IR image of temperature profile after 15 min of experimental heating in the MR scanner

## Commissioning and Clinical Re-Release of the Hypercollar3D within European Medical Device Regulations

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**Purpose:** Mild hyperthermia therapy (HT) in combination with radiotherapy and/or chemotherapy is a proven sensitizer for a number of cancer indications with a low toxicity profile, for example: HT could benefit head and neck squamous cell carcinoma (HNSCC) patients who do not receive chemotherapy due to age. Since 2005, our department has treated head and neck cancer patients with HT using our in-house designed Hypercollar3D. However the Hypercollar3D has been out-of-service since 2018. The purpose of this study is to report on the clinical re-release of the Hypercollar3D in-line with the current European Medical Device Regulation (MDR EU 2017/745).

**Methods:** This work began end 2022 with a market consultation and resulted in a decision to invest time into the clinical re-release of the Hypercollar3D but within compliance to MDR art. 5.5 (In-house manufacturing) supported by the Medtech Innovation Support Office (Depart. Medical Technology, Erasmusmc).

**Results:** The Hypercollar3D was approved for use as an internal investigational device by the Expertise Centrum (Depart. Medical Technology, Erasmusmc ) in October, 2024. Clinical re-release of the device was granted on May 1st, 2025 by the associated medical physicist within study (TANCA-1, MEC-2024-0784). The result of the MDR Annex I compliance process contributed to additional electrical safety measures, patch antenna adjustment, improved water bolus circulation, patient fixation and water bolus fabrication.

Re-commissioning revealed that routine calibration of the amplifiers (< 1 month) is required to achieve less than 5%/5° power and phase deviations. Consistency checks of three nominal plans (cranial, central, and caudal) reported a 2-D gamma evaluation having a 10 mm distance-to-agreement and 10% deviation criteria resulting in 82, 77, and 92% passing pixels, respectively.

**Conclusions:** Ensuring MDR Annex I compliance cost time, but helps to generate strict product requirements useful for routine quality assurance and performance metrics.



## Microwave hyperthermia for brain lesions: thermal coverage analysis in realistic clinical scenarios

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**Introduction:** Microwave hyperthermia (MW-HT) is effective for various cancers but remains underexplored for brain tumors due to challenges in achieving therapeutic temperatures. This study investigates the feasibility of MW-HT for treating brain lesions through computational modeling of clinically realistic scenarios, incorporating variations in tumor size, location, and tissue properties. A tailored ultra-wideband (UWB) helmet applicator, optimized for focused intracranial heating, is integrated with SAR-based treatment planning. Simulations are conducted on three representative clinical cases.

**Materials and methods:** Three 3D patient models were segmented from CT scans (1×1×1 mm resolution) into 18 tissue types using combined automatic and manual methods. The models included one adult with recurrent frontal meningioma and two pediatric cases: ependymoma in the parietal lobe and medulloblastoma in the dorsal brain region. Dielectric and thermal property variability was considered. EM and thermal simulations were performed in COMSOL Multiphysics using a hemispherical helmet applicator based on self-grounded bow-tie antennas, optimized for 250–500 MHz arranged into array to maximize tumor energy deposition. Treatment plans were determined using iterative time-reversal, with particle swarm optimization as the benchmark. The plans were assessed by index temperatures T90 and T50 calculated from steady-state temperature distributions.

**Results:** Peak temperatures of 42 °C were consistently achieved at the tumor center in all three cases, while a strict upper limit of 42 °C was maintained in surrounding healthy tissues. Tumor coverage varied with lesion size and geometry, yielding average T50 and T90 values of 40.6 °C and ~40.0 °C, respectively. Iterative time-reversal optimization significantly improved thermal coverage, increasing T90 by approximately 1 °C compared to the PSO-based benchmark.

Re-commissioning revealed that routine calibration of the amplifiers (< 1 month) is required to achieve less than 5%/5° power and phase deviations. Consistency checks of three nominal plans (cranial, central, and caudal) reported a 2-D gamma evaluation having a 10 mm distance-to-agreement and 10% deviation criteria resulting in 82, 77, and 92% passing pixels, respectively.

**Conclusions:** High intra-tumoral temperatures were reached, with very good coverage of the lesion volume. Hot spots at tumor borders limited the possibility of higher index temperatures. In general, these findings demonstrate the feasibility of MW-HT for brain lesions.

## Optimization and evaluation of radiotherapy in combination with hyperthermia using a stochastic model for tissue-property uncertainties

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**Purpose:** Uncertainties in thermal and dielectric tissue-properties affect temperature predictions of hyperthermia treatment planning. The chance of needing adjustments due to hotspots (normal tissue exceeding 45°C) can be reduced with robust optimization. For this study, we evaluated the impact of tissue-property variability, and of robust hyperthermia planning, in the combination with radiotherapy. We performed the analysis in terms of enhanced equivalent radiation dose (EQDRT).

**Methods:** Using Plan2Heat, we computed a conventional and robust hyperthermia plan for a cervical cancer case. We calculated temperature distributions for both plans, using 100 random samples from tissue-property distributions, excluding cases with hotspots. Temperature distributions with median tissue-property values for both hyperthermia plans were input for two EQDRT optimized radiotherapy plans (58 Gy EQDRT to tumor) in a research version of RayStation 12A. We also created a conventional radiotherapy plan prescribing 46 Gy. We calculated EQDRT distributions for non-hotspot samples for: conventional radiotherapy alone, conventional radiotherapy with conventional hyperthermia, EQDRT optimization with conventional hyperthermia, and EQDRT optimization with robust hyperthermia.

**Results:** Results are presented as value (range), where value corresponds to median tissue-property values, and range considers all non-hotspot samples. Tumor T90 was 39.8°C (38.8-40.2°C) for conventional hyperthermia, with 28 non-hotspot samples. Robust hyperthermia had T90 = 39.5°C (38.6-40.7°C), increasing non-hotspot samples to 41. Conventional radiotherapy alone had EQDRT95% = 45.8 Gy, increased to 50.0 (48.4-50.7) Gy with conventional hyperthermia. Adding EQDRT optimization to conventional hyperthermia raised EQDRT95% further to 56.7 (53.3-57.4) Gy. Robust hyperthermia improved the achieved range of EQDRT95% to 56.7 (54.6-59.3) Gy.

**Conclusion:** Adding hyperthermia to radiotherapy, as well as adding EQDRT optimization to conventional radiotherapy, have a clear benefit even when considering EQDRT variability due to tissue-property uncertainties. Robust hyperthermia plans enhance the achievable range of temperature levels, which reflects in an increased range of EQDRT levels when performing EQDRT optimization.

## MATHEMATICAL MODELING OF CHEMOTHERAPY DRUG DELIVERY AND EFFECTIVENESS: A REVIEW

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**Purpose:** Mathematical modeling integrating physical and biological laws with experimental data is useful for predicting tumor behavior and treatment outcomes. This review focuses on models assessing effects of specific approximations or parameter variations, with emphasis on thermosensitive liposomemediated drug delivery and hyperthermia modeling.

**Methods:** Pharmacokinetics (PK) models are used to simulate drug transport dynamics. These models solve hydrodynamic equations to estimate pressure and velocity fields within blood vessels and interstitial spaces, which are then used to predict drug transport across tissue compartments. Parameters used in these models are often derived from existing literature or experimental data. Pharmacodynamic (PD) models are then applied to predict biological effects, including therapeutic efficacy and systemic side effects.

**Results:** Current PKPD models show strong performance in *in vitro* and in animal studies, but their predictions often lack reliability in human clinical cases. A key limitation is the oversimplified or homogeneous representation of tumor microenvironments, which fails to capture the heterogeneity of human vasculature, reducing the accuracy of drug distribution and treatment response modeling. Clinical applicability is further constrained by generalized or nonpatientspecific parameters. In real tumors, vascular networks and temperature variations, critical in hyperthermiabased therapies, are difficult to model accurately due to sparse realtime data. Notably, temperaturedependent behavior significantly influences drug release: extracellular liposome concentration increases by a factor of 70 at temperatures exceeding 42°C.

All reviewed models indicate TSLmediated delivery as the best performing targeteddelivery method, achieving higher tumor drug concentration while minimizing healthy tissue exposure compared to free drug infusion.

**Conclusions:** Recent advances in medical imaging and data integration will permit adaptation of existing PKPD models to individual patient use. By reconstructing patientspecific parameter maps and incorporating temperature effects, these models can be made more predictive and clinically relevant. This personalized approach improves treatment planning precision and may accelerate translational research in oncology.

## Influence of inter-patient variability in dielectric properties of lung nodules on computationally estimated microwave ablation zones

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<sup>1</sup>The George Washington University

**Background:** The relatively high variability in treatment outcomes following microwave ablation procedures of localized lung nodules (< 3 cm) has revealed the need for computational models capable of providing reliable estimates of the ablation zone for treatment planning. Variability of the baseline values of lung tissue dielectric properties – relative permittivity and electrical conductivity – across patients and tissue state are hypothesized to considerably impact the microwave ablation zone.

**Methods:** A computational model of 2.45 GHz microwave ablation was implemented, coupling Maxwell's and bioheat transfer equations. High [ $\epsilon_r = 50.38$ ,  $\sigma = 1.88$  (S/m)] vs. low [ $\epsilon_r = 28.3$ ,  $\sigma = 1.00$  (S/m)] dielectric properties, measured in *ex vivo* human lung tissue reported in two published studies, are used as initial values in simulations, and integrated with established expressions for temperature-dependent dielectric properties. Computational models comprised homogeneous, perfused tissue with a 3 cm diameter target, within which a water-cooled microwave applicator is centrally placed. Models are solved for 5 minutes, with an input power of 60 W. The following clinically relevant metrics are identified to estimate the ablation zone based on the 60 °C isotherm extent: 1) length and diameter of the ablation zone; 2) fractional volume of the tumor that was ablated,  $TM_0$ ; 3) fractional volume of the tumor and a 10 mm circumferential tissue margin that was ablated,  $TM_{10}$ .

**Results:** Although the two modeled scenarios exhibit a contrast > 40 % in baseline dielectric properties, analysis of clinically relevant metrics from computational models revealed: 1) less than 2 mm difference in diameter and length of the ablation zone; 2) less than 5% difference in  $TM_0$ ; and 3) less than 1% in  $TM_{10}$ .

**Conclusions:** Computational models indicate baseline values of lung dielectric properties play a negligible role on microwave ablation profiles, potentially de-emphasizing the need for patient-specific estimates of these properties.

## Reducing wideband dielectric tissue property uncertainties by ion assessment through multi-nuclear MRI

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**Purpose:** Hyperthermia treatment planning aims to maximize targeted energy deposition in tissues. However, uncertainties in dielectric tissue properties (DPs) can lead to large standard deviations up to 3.5 °C [1], leading to sub-optimal treatment. Current DP data are primarily based on ex-vivo measurements, which do not account for physiological changes that affect tissue properties in-vivo. Previously, we showed that combining water and sodium information provides wideband dielectric properties, but inaccuracies in conductivity estimations were observed [2]. Since intracellular fluid becomes relevant above 1 MHz, we hypothesized that incorporating potassium, abundant within cells, would improve the accuracy of DP determination. To do so, we assessed non-invasively the ion content by quantitative multinuclear MRI.

**Methods:** Sodium, potassium and the water fraction were measured with a 7T MRI. The measurements were performed on six phantoms, with different compositions of proteins, and salt. Furthermore, the DPs in 6 healthy volunteers (3 male, 3 female, age  $32.6 \pm 7.4$  years, BMI  $23.9 \pm 3.4$ ) were estimated as verification of the method.

**Results:** The MRI images are shown in Fig. 1. Fig. 2 shows that the addition of potassium leads to a reduction in error from 89.5% to 4.3% for effective conductivity. Fig. 3 shows the in-vivo DPs. These now fall, at least partially, in the uncertainty range as reported in literature. There is a difference of 28% in effective conductivity between two volunteers. This emphasizes the need for an accurate method to determine the DPs.

**Conclusion:** Adding potassium to the method leads to significant better results as demonstrated with the ex-vivo measurements. Moreover, for the in-vivo case, the effective conductivity is in the same range as the literature values. While this method gives accurate results from 200 MHz onwards, future work should focus on improving the accuracy in the 50 – 200 MHz frequency range.

[1] Groen J, J. CMPB 2023

[2] Barendsz L, ESHO 2024

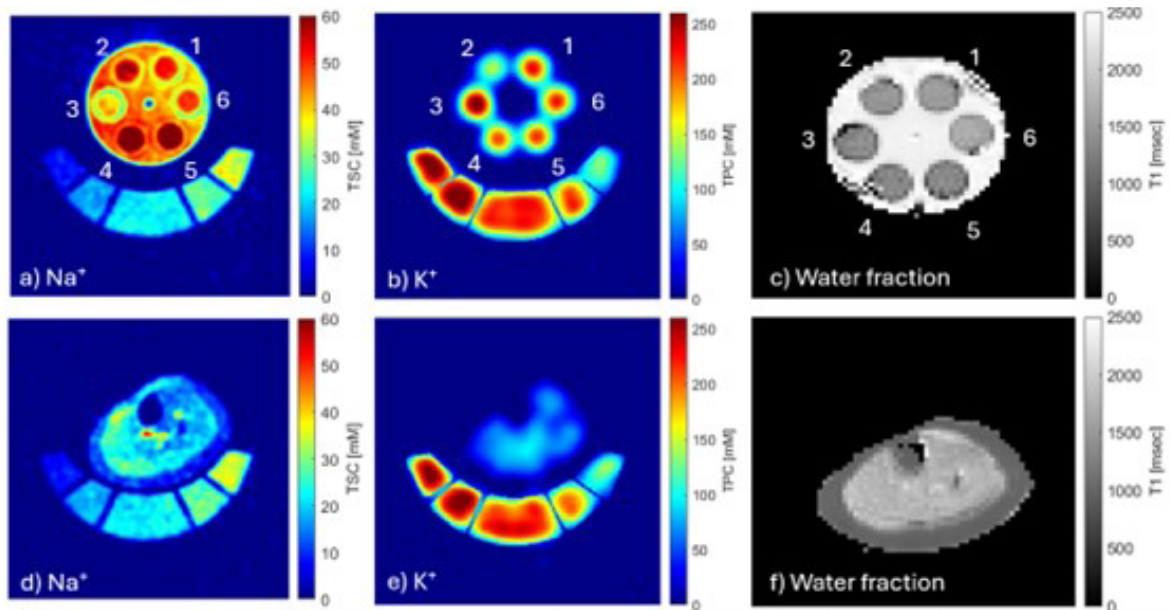


Fig. 1 MRI images of the muscle-mimicking phantoms (top-row) and one volunteer (bottom-row) for the  $\text{Na}^+$ ,  $\text{K}^+$ , and water fraction measurements. The phantoms are 1. "healthy", 2. "obese 1", 3. "obese 2", 4. "dehydrated 1", 5. "dehydrated 2", and 6. "less protein". The reference phantoms for calibration of the  $\text{Na}^+$  and  $\text{K}^+$  can also be seen in a), b), d), and e).

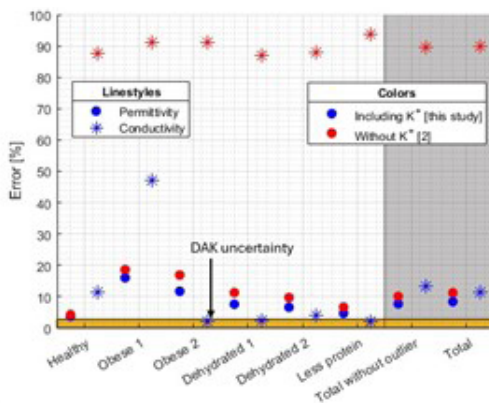


Fig. 2 Error of the DP estimation with and without  $\text{K}^+$  for the muscle-mimicking phantoms with different compositions, compared to dielectric assessment kit (DAK) measurements.

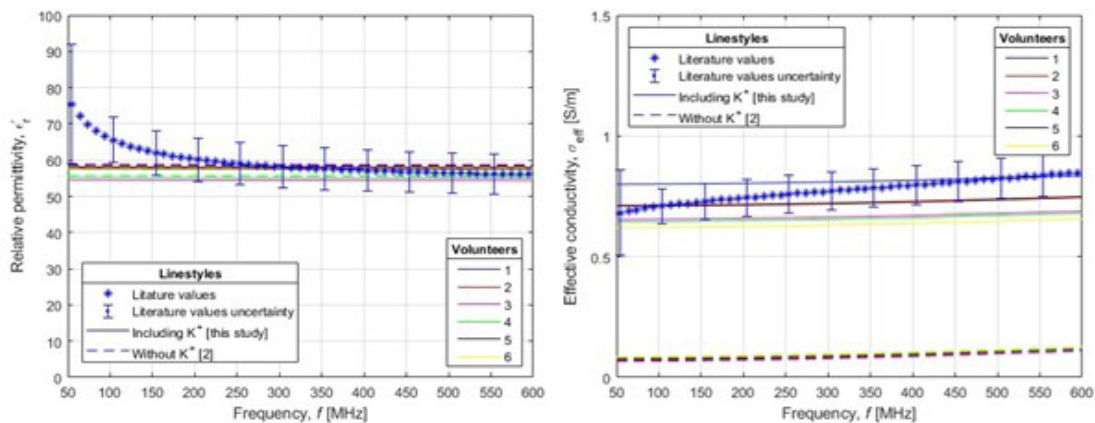


Fig. 3 Estimated DPs (with and without  $\text{K}^+$ ) in-vivo compared to literature values.



## Favorable Effectiveness of Low-Dose Long-Duration Versus High-Dose Short-Duration Oxaliplatin-Based HIPEC Analyzed Using a Pharmacokinetic Model

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Hyperthermic Intraperitoneal Chemotherapy (HIPEC) with oxaliplatin has emerged as a treatment strategy for peritoneal metastases from colorectal and other gastrointestinal malignancies. However, considerable variation exists in clinical practice regarding optimal drug dosing and treatment duration. In this study, we developed a pharmacokinetic model to compare two commonly used oxaliplatin-based HIPEC regimens: high-dose short-duration (460 mg/m<sup>2</sup>, 30 min, 2L/m<sup>2</sup> D5W, 41.5–43°C) versus low-dose long-duration (200 mg/m<sup>2</sup>, 120 min, 3L D5W solution, 40°C).

We developed a reaction-diffusion drug transport model in OpenFOAM, applying dynamic oxaliplatin concentration profiles in the peritoneal cavity as boundary conditions for virtual tumor nodules labelled with a diameter of 2.5 mm, representing CC-1 residual disease. The model was validated against platinum signal profiles from laser ablation–inductively coupled plasma–mass spectrometry (LA-ICP-MS) images reported in the literature, measured along multiple paths in tumor samples from patients. We used the tumor-to-plasma ratio of the Area Under the Curve (AUC) to evaluate HIPEC efficacy, as this indicates the relative drug concentration reaching the tumor compared to systemic circulation.

In both regimens, platinum concentration exhibited exponential decay with increasing distance from the tumor surface. Analysis of the two regimens over a 2-hour period revealed substantial differences in tumor-to-plasma AUC ratios: **2.2** for the high-dose, short-duration regimen (tumor AUC: 5.1 mM·min; plasma AUC: 2.3 mM·min) versus **5.6** for the low-dose, long-duration regimen (tumor AUC: 6.2 mM·min; plasma AUC: 1.1 mM·min).

These findings suggest that extending treatment duration at lower concentration may achieve superior drug delivery to tumor tissue compared to higher-dose shorter treatments, potentially with reduced systemic toxicity. The model may help guide clinical decisions and inform future trials by highlighting pharmacokinetic differences between HIPEC protocols.



## **Phase II Clinical Trials Combining Radiotherapy and Capacitive Hyperthermia at the Catalan Institute of Oncology: Results from the Superficial Hyperthermia Cohort in breast recurrences**

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Catalan Institute of Oncology (ICO)

**Purpose/Objectives:** Two prospective, single-arm phase II clinical trials are being conducted at the Catalan Institute of Oncology (ICO) to evaluate the combination of capacitive radiofrequency hyperthermia (HT) with radiotherapy (RT). The primary objective is to assess acute and late toxicity (CTCAE v5.0); secondary endpoints include local control, overall survival, and recurrence-free survival at 6 months. This report focuses on the completed superficial HT trial in recurrent breast cancer. The second trial, still open, investigates deep HT for pelvic tumors (locally advanced or recurrent) and bone metastases.

**Materials and Methods:** Thirty women with recurrent breast cancer—post-mastectomy or after a second conservative treatment—were treated with normofractionated RT and superficial HT using the Hy Deep 600 device. Patients previously irradiated received 46 Gy, while those without prior RT received 50 Gy. Lesions were superficial or deep; 73% had received prior RT. HT was applied twice weekly ( $\geq 72$ h apart) for 60 minutes, immediately after RT. Treatments were delivered with curative or palliative intent. Data were prospectively collected in REDCap.

**Results:** Treatment adherence was 90%. HT tolerance was excellent in 56.7%. Others reported transient burning (13.3%) or symptoms such as sweating, power intolerance, claustrophobia, or heat discomfort (30%). No  $\geq$  grade 3 HT-related toxicity occurred. Combined RT+HT acute toxicity was grade 1 in 16.7%, grade 2 in 46.7%, and grade 3 in 30%, mainly radiodermatitis and fibrosis. Bolus use (40%) may have influenced higher skin toxicity. At 6 months, overall survival was 95.6%, and recurrence-free survival was 87%.

**Conclusion:** This combined approach is safe, well tolerated, and shows promising early outcomes. While the lack of a control group is a limitation, toxicity rates align with those expected from RT alone. These findings support the integration of HT as an effective adjunct in recurrent breast cancer.

## 3-Year Patterns of Care Analysis After Implementation of Superficial Hyperthermia at a Swiss University Radiation Oncology Center: Insights for Future Clinical Adoption

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**Purpose:** Moderate hyperthermia in combination with radiotherapy (RT) is gaining increasing interest in Europe. We analyzed patterns-of-care 3 years after introducing superficial HT (sHT) at our university radiation oncology center, aiming to provide insights for institutions considering sHT implementation.

**Methods:** Baseline patient characteristics and sHT parameters were captured for 109 patients with 112 treatment sites treated with sHT+RT with the ALBA ON 4000D (MedLogix, Rome, Italy) device between May 2022 and May 2025.

**Results:** Median age was 69 years (range, 33-99) and 52.3% were female. ECOG performance status was 0 in 14.7%, 1 in 36.7%, 2 in 36.7%, and 3 in 11.9% of patients. Most common primary tumor types were breast cancer (26.6%), sarcoma (22.9%), and head and neck (H&N) tumors (22.9%). Median planned sHT sessions were 5 (IQR 4-6), with an overall adherence rate of 77.7%. sHT was discontinued in the remaining 22.3%, primarily due to worsening general condition (8.9%), inability to tolerate position required for treatment (6.3%) or side effects (5.4%). The beta (42.9%) and alpha (25.9%) applicators were most frequently used, and 10% of patients received additional radiative deep HT. Treatments were predominantly delivered with palliative intent (77.1%) targeting primary tumors (51.8%), distant metastases (25.9%) or lymph nodes (22.3%), mainly in the H&N region (33%), breast/chest wall (26.8%), and extremities (22.3%). sHT was applied in a re-irradiation setting in 27.7% of cases. 69% were in-house patients and 31% were referred for sHT+RT from external hospitals.

**Conclusion:** Within 3 years after implementation, 109 patients – approximately 2% of all patients treated at our RT center – underwent sHT. The majority of patients were treated with palliative intent. The most common treatment sites were the H&N region, breast/chest wall, and extremities, mainly targeting breast cancer, sarcoma, and H&N malignancies.

## Development of a consensus lexicon for thermal medicine

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**Introduction:** Thermal medicine encompasses diverse modalities, including hyperthermia, ablation, cryotherapy and thermometry, used for therapeutic, diagnostic, and monitoring purposes. As the field expands, inconsistent terminology and overlapping definitions pose challenges for research reproducibility, regulatory compliance, clinical translation, and device development. To address this, the American Society of Mechanical Engineers (ASME) and Society for Thermal Medicine (STM) initiated the development of a standardized Thermal Medicine Lexicon to unify the field's foundational language and harmonize definitions across engineering, clinical, and biological domains.

**Methods:** Interdisciplinary working groups were organized across eight thematic areas: hyperthermia, ablation, cryotherapy, thermometry & image guidance, thermal medicine physics, thermal biology & pathology, and tissue properties. Each group synthesized terms from peer-reviewed literature, clinical guidelines, and engineering standards. Draft definitions were reviewed in iterative consensus meetings involving domain experts from academia, clinical practice, industry, and regulatory bodies. Sources of confusion were explicitly captured, and illustrative examples were included to enhance clarity and practical relevance.

**Results:** The lexicon comprises over 100 rigorously vetted definitions, including foundational terms such as thermal dose, specific absorption rate (SAR), thermal bioeffects, and thermometry. Special attention was given to clarifying distinctions (e.g., between hyperthermia and ablation or between thermal damage and adverse effects) and reinforcing the importance of time-temperature dependence in thermal response. The lexicon also documents terminology gaps and frequent misuses encountered across modalities and platforms. Context-specific sources of confusion—such as unit inconsistencies and modality overlap—are documented to support proper application across preclinical, computational, and clinical settings.

**Conclusions:** This consensus lexicon establishes a foundational language for thermal medicine, enabling clearer interdisciplinary communication, improved reproducibility, and alignment with safety and efficacy standards. Continued collaboration among stakeholders will ensure the lexicon evolves in step with scientific advances, emerging technologies, and evolving clinical applications.

## Proton CCRT With Deep Hyperthermia Achieves Complete Response in Cervical Cancer

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**Purpose:** To evaluate the efficacy and safety of a multimodal treatment regimen involving concurrent chemoradiotherapy (CCRT) with proton intensity-modulated proton therapy (IMPT), weekly cisplatin, and deep hyperthermia, followed by high-dose-rate vaginal brachytherapy, in achieving tumor control and minimizing toxicity in a 73-year-old postmenopausal woman with stage IIa2 cervical squamous cell carcinoma (SCC).

**Methods:** In September 2024, a 73-year-old woman with postmenopausal bleeding was diagnosed with cervical SCC (cT2aN0M0) through comprehensive tumor staging, including biopsy, pelvic MRI, PET/CT, and ultrasound. Due to her advanced age, she received IMPT (5040 cGyE, including 4500 cGyE to pelvic lymphatics and 5040 cGyE to the cervical mass) with weekly cisplatin in December 2024. Concurrent deep hyperthermia using the Pyrexar BSD-2000 system was delivered weekly for six sessions, guided by intravaginal thermometry to maintain a therapeutic temperature ( $>40^{\circ}\text{C}$  for 60 minutes), with CEM43 values ranging from 4.55 to 7.72. Following external beam radiotherapy, she received high-dose-rate vaginal brachytherapy (3000 cGy in 5 fractions to the residual cervical tumor). Post-treatment, she underwent regular outpatient follow-up with imaging, blood tests, and pelvic examinations.

**Results:** The patient completed all treatments without interruption. Acute toxicities were limited to grade 1 fatigue and occasional loose stools, without clinical colitis or radiation dermatitis. Mild pubic symphysis soreness was alleviated with rest or NSAIDs. Pelvic MRI and examination in April 2025 confirmed complete remission with no residual tumor.

**Conclusions:** Proton-based CCRT combined with deep hyperthermia and vaginal brachytherapy was well-tolerated, achieving excellent local control with minimal toxicity in an elderly patient. This combination offers robust tumor control with negligible side effects, suggesting promise for similar populations and warranting further clinical evaluation.

## SAHARA Trial – Combining Hyperthermia and Radiotherapy for Non melanoma Skin Cancer: A multicenter, two-arm, open-label, randomized controlled phase II non-inferiority trial.

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**Background:** Non-melanoma skin cancer (NMSC) is the most common malignancy among elderly individuals of Caucasian descent, and its incidence is projected to rise with an aging population. While surgical excision is the standard treatment, it is often unsuitable for older patients due to tumor location or comorbidities. In such cases, radiotherapy (RT) remains the only curative approach. However, conventional RT can involve prolonged treatment durations and carry risks of acute and late toxicity as well as impaired cosmetic outcomes.

**Methods:** The SAHARA trial (ClinicalTrials.gov ID: NCT06384053) is a multicenter, open-label, randomized, controlled phase II non-inferiority study designed to enroll 100 patients aged  $\geq 65$  years with histologically confirmed, invasive basal or squamous cell carcinoma of the skin ( $\geq T2$ ,  $\leq 2$  cm depth, ECOG 0–2). Patients will be randomized in a 1:1 ratio into two treatment arms:

- **Arm A (intervention):** 6 fractions of 5 Gy RT (total 30 Gy) over 3 weeks (2×/week), combined with superficial water-filtered infrared-A (wIRA) hyperthermia applied for 45–60 minutes immediately before each RT session.
- **Arm B (control):** 12 fractions of 4 Gy RT (total 48 Gy) over 4 weeks (3×/week), without hyperthermia.

Efficacy will be assessed by local tumor control at two years. Secondary outcomes include safety (CTCAE v5.0) and quality of life (EORTC QLQ-ELD14), with assessments at baseline and scheduled follow-ups over 24 months. Tumor response will be documented clinically and photographically.

**Discussion:** This study addresses the need for effective and tolerable cancer therapy in older adults with NMSC. The combination of wIRA hyperthermia with reduced-dose RT may lessen treatment burden, minimize side effects, and maintain or improve functional and cosmetic outcomes. If non-inferiority is confirmed, this approach could become a preferred option for older patients with limited treatment tolerance, improving care while preserving efficacy. Recruitment began in January 2025 and will continue over two years, with study completion expected by the end of 2028.

## Comparing capabilities of three large language models DeepSeek-v1, Llama-3.3 and GPT-4o on answering specific questions about oncological hyperthermia treatment

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**Purpose:** Large language models (LLMs) are rapidly integrating into human society. Since hyperthermia (HT) is increasingly recognized as an additional oncological treatment modality, LLMs will also be consulted for hyperthermia-related questions. Integration of LLMs into clinical practice must be carefully evaluated to ensure accuracy, reliability and safety. Therefore, we conducted a validation study to compare the capabilities of three general LLM to answer questions about HT.

**Methods:** Forty open-ended questions (22 clinical and 18 physics) were given as prompts to the LLMs DeepSeek-v1, Llama-3.3-70B-instruct and GPT-4o. In a blinded review process, their responses were evaluated regarding overall quality by 20 international experts (12 HT physicians for clinical questions, 8 HT physicists for physics questions), using a 5-point Likert scale ranging from 1 to 5 ("very bad", "bad", "acceptable", "good", and "very good"). Additionally, the evaluators indicated whether answers were potentially harmful if used for decision-making.

**Results:** For the clinical questions the three LLMs achieved mean scores of 3.15 (DeepSeek-v1; variance 1.28), 3.14 (Llama-3.3-70B-Instruct; variance 1.16) and 3.07 (GPT-4o; variance 0.98) (Friedman Test;  $p=0.306$ ), with at least one rater indicating an answer was potentially harmful in 14 (63.6%), 14 (63.6%), and 13 (59.1%) of 22 cases. Slightly worse results were observed for the physics questions, with average scores of 2.80 (variance 1.14), 2.61 (variance 0.95), and 2.60 (variance 0.79) (Friedman Test;  $p=0.522$ ), and harmful responses flagged in 15 (83.3%), 18 (100%), and 16 (88.9%) of 18 cases, respectively. All models produced multiple factually incorrect statements.

**Conclusions:** While LLMs show promise in oncology and radiation therapy, their performance in the specialized domain of hyperthermia ranges from bad to acceptable. The high frequency of potentially harmful responses is alarming and can be attributed to limited availability of domain-specific training data. These findings are giving concerns, particularly given the growing reliance on LLMs in clinical practice.

## Design of sparse array focused ultrasound transducer for targeted brain hyperthermia

Geunho Shim , Kisoo Kim

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**Purpose:** Focused ultrasound (FUS) hyperthermia is emerging as a promising non-invasive approach for treating brain tumors and modulating neurological functions. However, efficient and safe heating in deep brain tissue through the skull requires precise transducer design. This study aims to develop a sparse array transducer optimized for focal energy delivery and thermal confinement in brain hyperthermia applications.

**Methods:** Sparse array configurations were designed and evaluated using simulations based on the Hybrid Angular Spectrum method. Two central frequencies—300 kHz (low) and 700 kHz (high)—were analyzed to assess frequency-dependent heating performance. Randomized nearest-neighbor distance (NND) distributions were employed to construct diverse sparse geometries. Key transducer parameters—aperture size, element diameter, and number of elements—were systematically varied. The acoustic field and corresponding thermal deposition were analyzed to assess focal sharpness, heat diffusion, and energy efficiency.

**Results:** Simulation results demonstrated that specific sparse configurations enhanced focal energy concentration and thermal confinement, while reducing off-target exposure.

Furthermore, results clearly highlight the trade-offs in thermal efficiency and spatial coverage between low and high frequency regimes. Optimal designs achieved well-confined heat volumes within the therapeutic range, indicating feasibility for safe brain hyperthermia.

**Conclusions:** The findings provide a quantitative design framework for sparse array FUS transducers tailored to brain hyperthermia. The identified configurations show potential for achieving targeted heating with minimal collateral exposure. Detailed thermal and acoustic performance metrics of the optimal design will be presented at the upcoming meeting.



## Sonothermogenetic Control of CAR T-Cell Immunotherapy for Brain Tumors using Closed-Loop Focused Ultrasound Hyperthermia

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Chimeric Antigen Receptor (CAR) T-cell therapies face significant challenges in treating solid brain tumors like glioblastoma (GBM) and breast cancer brain metastases (BCBM). Durable response is often limited by antigen heterogeneity, causing tumor escape, and an immunosuppressive tumor microenvironment (TME). We present a "sonothermogenetic" strategy using non-invasive, mild hyperthermia to precisely and remotely control CAR T-cell activity, addressing these critical barriers.

We employed primary human and mouse CAR T-cells with a genetically encoded thermal bioswitch that regulates expression of a T cell engager (TCE) targeting NKG2D stress ligands. Using a custom-built, closed-loop MRI-guided focused ultrasound (MRgFUS) system, we delivered localized, mild hyperthermia (~41.5°C) transcranially to activate these cells in murine models. In a heterogeneous BCBM model (HER2+/-), we evaluated if thermally-induced TCEs could eliminate antigen-negative cancer cells. In a syngeneic GBM model (SB28), we assessed if TCE production could remodel the TME by depleting myeloid-derived suppressor cells (MDSCs).

The closed-loop MRgFUS system achieved precise spatiotemporal temperature control, enabling transient and repeatable CAR T-cell activation within intracranial tumors without causing lasting adverse effects to healthy brain tissue. In the BCBM model, metronomic sonothermogenetic induction of TCEs overcame antigen escape, led to the eradication of HER2-negative tumor cells and significantly prolonged survival. In the GBM model, localized TCE production robustly depleted intratumoral MDSCs, mitigated immunosuppression and significantly reducing tumor burden compared to controls. In both models, therapeutic activity was confined to the heated tumor, demonstrating a high degree of spatial control and improved safety profile.

Overall, closed-loop sonothermogenetic provides a non-invasive, effective platform to dynamically control the location, timing, and intensity of immunotherapy in the brain. Using mild hyperthermia for local production of immunomodulatory molecules, this approach offers a promising strategy to enhance cell-based therapies for aggressive brain cancers.

## Feasibility study of Real-Time Temperature Monitoring Based on Electrical Impedance Tomography Using a Water Phantom Experiment

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**Purpose:** High-frequency electric field-based therapies generate heat within biological tissues by applying high-voltage currents through electrodes, typically leading to an increase in tissue electrical conductivity. This study aims to evaluate the feasibility of using Electrical Impedance Tomography (EIT) for real-time monitoring of internal temperature distributions based on conductivity changes induced by heating.

**Methods:** The simulation study and experimental study were separately used to evaluate EIT-based temperature monitoring. In the simulation study, FEM-based voltage data were generated by modeling temperature-dependent conductivity, and conductivity images were reconstructed in two model (with ROI and without ROI). In the experimental study, a gelatin phantom was placed in a water bath and heated, and EIT data were collected during temperature elevation.

**Results:** In the simulation study, the reconstruction error was low in both cases. Without ROI, the average error was 0.16%, and with ROI, it was 0.24%. Over 95% of mesh nodes showed error rates below 1% in both settings. In the experimental study, the reconstructed conductivity closely followed the temperature variation, demonstrating temperature-dependent behavior, with a normalized root mean square error of 0.0827.

**Conclusions:** This study demonstrates that EIT is capable of detecting temperature-induced conductivity changes, as evidenced by the clear increasing trend in reconstructed values with rising temperature. These results highlight the potential of EIT as a tool for real-time monitoring of internal temperature distributions during thermal therapies.

## DSRCT as a Hyperthermia-Driven Sequential Therapy Model for Curative-Intent Control in Pediatric Peritoneal Malignancies

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**Purpose:** Desmoplastic small round cell tumors (DSRCTs) are rare, aggressive soft tissue sarcomas predominantly affecting adolescents and young adults. Prognosis is particularly poor in cases with extensive peritoneal spread and hepatic involvement. We evaluated a novel sequential therapy combining platinum-based chemotherapy with deep regional hyperthermia (RHT), followed—when feasible—by cytoreductive surgery (CRC), hyperthermic intraperitoneal chemotherapy (HIPEC), and whole-abdomen radiotherapy (WART). This hyperthermia-driven approach aims to improve systemic and locoregional control and establish DSRCT as a model for multimodal therapy sensitized by hyperthermia.

**Methods:** In this single-arm prospective trial, patients under 25 years with histologically confirmed abdominal DSRCT received 2–4 cycles of PEI-chemotherapy (cisplatin or carboplatin, etoposide, ifosfamide) combined with RHT (41–43°C, days 1 and 4). Responders proceeded to maximal CRC followed by HIPEC (cisplatin ± doxorubicin; 41–42°C, 60–90 minutes). Postoperative consolidation included 2–4 additional PEI-RHT cycles. WART (20–24 Gy) was added in later patients with clinical remission and prior liver involvement to control residual microscopic disease. Primary endpoint: objective response (RECIST v1.1).

**Results:** Fourteen patients (11 male, 3 female; median age 17.5 years) were enrolled. All received salvage PEI-chemotherapy plus 127 RHT sessions. Nine underwent CRC (six R1, two R2 resections); eight subsequently received HIPEC. Eight patients showed objective responses, four had stable disease, and two progressed. Follow-up ranged from 5 to 53 months.

**Conclusions:** DSRCT illustrates the feasibility of a sequential, thermally enhanced treatment cascade: (1) RHT-chemotherapy enables cytoreduction, (2) CRC + HIPEC manage residual disease, (3) WART consolidates local control. This protocol offers effective disease control where standard regimens fail, suggesting DSRCT as a replicable model for hyperthermia-based multimodal therapy in pediatric peritoneal malignancies. Future strategies should incorporate targeted or immune therapies.

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## The role of hyperthermia in HIPEC

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**Introduction:** Peritoneal metastases frequently occur in colorectal and ovarian cancers, affecting up to 75% of ovarian cancer patients and 20-30% of colorectal cancer patients. For colorectal cancer, cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy (HIPEC) is currently the only curative-intent treatment. In ovarian cancer, systemic chemotherapy with carboplatin and paclitaxel plus cytoreductive surgery is standard, with HIPEC immediately after surgery showing potential benefits. However, HIPEC's role remains controversial due to mixed clinical trial results, high complexity, cost, and unclear biological mechanisms.

**Method:** To elucidate HIPEC's therapeutic mechanisms, we conducted in vitro and in vivo studies. Tumor cells from colorectal and ovarian cancers were treated with chemotherapy agents (oxaliplatin, mitomycin C, cisplatin) at temperatures of 37°C, 39°C, and 42°C for 30, 60, or 90 minutes. We assessed cell viability, clonogenic capacity, and DNA damage repair. In vivo, tumor cells were injected into rats' peritoneal cavity, with tumor growth monitored by ultrasound. HIPEC parameters (drug, temperature, duration) were varied, and effects on tumor response and immune infiltration were evaluated.

**Results:** Hyperthermia combined with chemotherapy significantly decreased cell viability and clonogenicity in ten tumor cell lines. Platinum drugs and mitomycin C induced G2 cell cycle arrest, but only platinum agents showed temperature-dependent synergy, increasing drug uptake and apoptosis at higher temperatures. In vivo, longer HIPEC duration and higher temperature improved drug uptake and tumor control. Shorter HIPEC treatments were less effective and linked to poorer survival. Immune profiling is ongoing to assess hyperthermia's impact on antitumor immunity.

**Conclusion:** Our findings highlight the importance of treatment duration and temperature for optimizing HIPEC efficacy. Extended exposure (90 minutes) at 42°C enhances tumor cell kill and may improve clinical outcomes.

## Revealing the relevance of BRCA2 status for the efficacy of cisplatin-based hyperthermia intraperitoneal chemotherapy (HIPEC) in ovarian cancer: evidence from in vitro models

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**Background:** The addition of HIPEC to cytoreductive surgery for peritoneal metastases has shown promising survival outcomes. Hyperthermia is a treatment that inhibits the DNA damage repair (DDR) homologous recombination (HR) pathway by inducing degradation of BRCA2. However, the impact of BRCA2 status for cisplatin-based HIPEC's efficacy remains unclear, also when combining HIPEC with systemic chemotherapy. This study aims to evaluate the efficacy of cisplatin-based HIPEC and assess the impact of BRCA2 status on HIPEC sensitivity, for both high grade serous and non-high grade serous ovarian tumor profiles.

**Methods:** High grade and non-high grade serous ovarian cancer cell lines were treated with different doses of standard-of-care systemically used drugs carboplatin and paclitaxel. In addition, cells were treated with cisplatin at clinically relevant hyperthermic temperatures, ranging from 37 - 43°C for 90 min, to mimic HIPEC treatment. Furthermore, the effectiveness of HIPEC in BRCA2 wild type and BRCA2 mutated cells was compared. The colony formation was detected by crystal violet assay, cell viability was measured by MTT assay, the apoptosis and cell cycle distribution were measured with flow cytometry, the formation of  $\gamma$ -H2AX foci was observed by immunofluorescence microscopy after treatment.

**Results:** All cell lines exhibited sensitivity to hyperthermia alone, with a more pronounced sensitivity of high grade serous ovarian cancer cell lines. Cisplatin demonstrated a temperature-dependent synergy with heat, resulting in increased DNA damage, apoptosis and G2-arrest. Both BRCA2 wild type and mutation show significant sensitivity to HIPEC. The benefit is even greater in BRCA mutated carriers, which increased 20% apoptosis level and reduced 30% survival rate.

**Conclusion:** Ninety minutes hyperthermic exposure to cisplatin effectively targets both high and non-high grade serous ovarian cancer cells, suggesting that cisplatin-based HIPEC could be clinically effective in both subtypes, also for BRCA2 mutated subtypes.

## HPV Viral Load: Prognostic Clues for Personalizing Treatment in Locally Advanced Cervical Cancer

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**Background:** Locally advanced cervical cancer (LACC) is usually treated with chemoradiotherapy, but radiotherapy combined with hyperthermia (thermoradiotherapy) is an option for patients who cannot receive chemotherapy. Despite treatment, five-year overall survival remains low at about 66%, necessitating better therapies. Because cervical cancer is caused by persistent infection with high-risk human papillomavirus (HPV), we investigated whether HPV viral load, which is the amount of HPV DNA in cervical tissue, could predict treatment response and guide treatment choice. Previous research showed that hyperthermia disrupts the interaction between the HPV E6 protein and tumor suppressor p53, restoring p53 function and possibly reducing tumor growth. This suggests that patients with high HPV viral load may benefit more from thermoradiotherapy than from chemoradiotherapy.

**Methods:** We measured HPV viral load in biopsies from 44 LACC patients treated at Amsterdam UMC. We then correlated viral load with clinical outcomes, proliferation markers, and immune status using multiplex immunostaining. At the same time, we conducted a systematic literature review of studies from EMBASE, PubMed, and Web of Science to assess the evidence for these associations.

**Results:** Most patients received chemoradiotherapy. Those with high HPV viral load showed lower overall and disease-free survival as well as fewer tumor-infiltrating lymphocytes, indicating immune suppression. These results matched most studies in the review, which found that higher viral load is linked to worse outcomes. Some conflicting reports exist, likely due to differences in how viral load was measured.

**Conclusion:** The review confirms that high HPV viral load is associated with poor prognosis and immune suppression in LACC. Standardized viral load measurement is needed. Our clinical data suggest that thermoradiotherapy may improve outcomes by turning immunologically 'cold' tumors into 'hot' ones, especially in patients with high HPV viral load. HPV viral load could be a useful biomarker to personalize treatment and improve prognosis.

## Quantitative Estimation of Radiobiological Parameters Using LeGO-Based High-Throughput Clonogenic Survival Assay in 12 Human Cancer Cell Lines Under Radiotherapy and Hyperthermia Conditions

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**Purpose:** Hyperthermia (HT) is a clinically validated radiosensitizer, capable of enhancing the effects of radiotherapy (RT) by impairing DNA repair, increasing blood flow, and altering tumor microenvironments. Despite its clinical potential, the quantitative characterization of HT's impact on radiobiological parameters, particularly the linear-quadratic  $\alpha$  and  $\beta$  coefficients, remains limited across tumor types due to technical challenges in conventional clonogenic assays.

We aimed to systematically evaluate how HT influences radiosensitivity by quantifying key radiobiological parameters such as  $\alpha$  (initial DNA damage),  $\beta$  (repairable damage), and thermal enhancement factors (TEF). To achieve this, we developed a high-throughput imaging-based clonogenic assay using fluorescent genetic barcoding (LeGO-CSA), enabling precise clonal tracking and quantification of small or overlapping colonies.

**Methods:** Twelve human cancer cell lines were lentivirally transduced with red (mCherry), green (Venus), and blue (Cerulean) fluorescent proteins. Nuclei were counterstained with DRAQ5 for segmentation and quantification. Cells were exposed to ionizing radiation (0–8 Gy), followed by a 1-hour HT treatment (37–43°C) applied at intervals of 15, 30, or 60 minutes post-RT. Clonal survival was quantified using automated imaging and deep-learning-based analysis. Survival curves were fitted to an extended linear-quadratic model accounting for both radiosensitization and direct thermal effects.

**Results:** HT significantly increased  $\alpha$  values in multiple cell lines, indicating enhanced DNA damage following combined RT+HT. The degree of radiosensitization was temperature- and timing-dependent, with earlier and higher-temperature HT yielding stronger effects.  $\beta$  values varied, reflecting heterogeneous repair responses. TEFs provided a quantifiable measure of HT's radiosensitizing efficiency.

**Conclusion:** Our study provides a robust framework to derive quantitative thermoradiobiological parameters, offering valuable insights for optimizing personalized RT+HT regimens and informing predictive treatment models.



## Cellytics NK: A Novel Tool for Monitoring Immune Function Modulated by Hyperthermia in Cancer Patients

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Natural killer (NK) cells play a pivotal role in innate immunity and cancer immunosurveillance. Monitoring NK cell function is essential for evaluating immune competence and treatment response in oncology. **Cellytics NK** is an innovative, label-free analytical platform that quantifies NK cell activity by detecting morphological changes in activated NK cells using lens-free shadow imaging and AI-driven analysis. This reagent-free, rapid approach enables high-throughput immune monitoring with minimal sample processing.

We highlight two clinical applications and its potential utility in hyperthermia-induced immune modulation:

### 1 Immune Monitoring in Immunocompromised Patients:

Patients with hematologic malignancies in sterile environments are at high risk for infections due to immune suppression. In a study of leukemia patients in sterile rooms (N=14), Cellytics NK revealed significantly reduced I3 values compared to healthy donors, reflecting diminished NK cell function and vulnerability to opportunistic infections.

### 2 Monitoring NK Cell-Based Immunotherapy:

As immunotherapies evolve, especially those involving NK cell expansion and immune checkpoint inhibitors, real-time immune monitoring becomes critical. In a cohort of small cell lung cancer (SCLC) patients (N=8) receiving autologous NK cell therapy and maintenance immunotherapy, increased post-treatment I3 values were observed, suggesting enhanced NK cell responsiveness.

Emerging evidence suggests that hyperthermia can enhance immune function by promoting NK cell activation. Leveraging its sensitivity to activation-induced morphological changes, Cellytics NK offers a practical and effective means of monitoring immune responses during hyperthermia-integrated cancer therapies.

In conclusion, Cellytics NK provides a rapid, scalable, and label-free platform for tracking NK cell dynamics, supporting its potential use in both cancer immunotherapy and hyperthermia-enhanced immune interventions.

## Induction of Immunogenic Cell Death by Hyperthermia and Radiotherapy in a 3D Luminal A Breast Cancer Model

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**Purpose:** Recurrence and immune evasion remain major challenges in breast cancer treatment, particularly in luminal A subtypes, which are the most common and often less immunogenic forms of the disease. Although standard therapies such as chemotherapy and radiotherapy induce tumour cell death, they frequently result in non-immunogenic forms, limiting activation of anti-tumour responses. Immunogenic cell death (ICD) is a regulated process characterized by the release of danger-associated molecular patterns (DAMPs) that promote immune recognition of dying tumour cells. This study aimed to investigate whether combining hyperthermia (HT) with radiotherapy (RT) could induce ICD features in a clinically relevant 3D luminal A breast cancer model.

**Methods:** T47D luminal A breast cancer cells were seeded into agarose microwells to generate uniform 3D spheroids. To simulate clinically relevant treatment conditions, spheroids were exposed to hyperthermia (1 hour at 42 °C), radiotherapy (7.5 Gy), or a combination of both (HT+RT). Untreated spheroids served as negative controls. Apoptosis was evaluated at 24 and 48 hours post-treatment. Key markers of immunogenic cell death, including extracellular ATP and surface calreticulin (CRT), were quantified using luminescence assays and flow cytometry.

**Results:** A time-dependent increase in apoptosis was observed, with the highest levels detected in the combined HT+RT group at 48 hours. Extracellular ATP levels peaked at 24 hours, indicating early DAMP release. Surface CRT expression was also significantly elevated in the HT+RT group.

**Conclusions:** These findings demonstrate that combined HT and RT induce key features of immunogenic cell death in a 3D luminal A breast cancer model. This approach may enhance tumour immunogenicity and support more effective therapeutic strategies targeting resistant breast cancer subtypes.

## Early Report of a Pilot Study of Chemoimmunotherapy Combined with Hyperthermia and Spatially-fractionated Radiotherapy in Biliary Tract and Hepatocellular Cancers

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**Purpose:** Advanced Biliary Tract and Hepatocellular Cancers (BTC/HCC) have a poor prognosis despite recent advances including the addition of checkpoint blockade. Novel techniques such as hyperthermia therapy (HT), and spatially fractionated radiotherapy (SFRT), can positively modulate the tumor immune microenvironment and potentially broaden the patient population who respond to frontline systemic therapy.

**Methods:** In this single-arm pilot study, we are enrolling up to 15 patients to assess the safety and feasibility of combining standard of care systemic therapy including checkpoint blockade with deep HT and SFRT in patients with locally advanced unresectable or metastatic BTC/HCC. Participants will receive HT and SFRT to 1 measurable lesion on day one of the second cycle prior to infusional systemic and HT alone will be delivered to the same lesion on day 1 of cycles 3 and 4. Feasibility is defined as the ability of participants to receive a minimum of 30 minutes of heating at the target temperature for at least 2 of the planned 3 deep HT treatments. Safety is defined by < 30% rate of grade 3 or higher non-hematologic adverse events.

**Results:** To date we have enrolled 2 patients, with tolerability of HT and SFRT and no adverse events. Radiographic response rates, oncological outcomes and immunological correlates will be presented for all patients enrolled.

**Conclusions:** We are currently enrolling patients and will present our early experience combining immunotherapy, HT and SFRT for advanced Biliary BTC and HCC.

## T-Cell Dynamics in Breast Cancer Patients Undergoing Combined wIRA-Hyperthermia and Radiotherapy

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**Introduction:** Combining hyperthermia (HT) with radiotherapy (RT) is an emerging strategy for treating recurrent or locally advanced breast cancer, enhancing tumor response and local control by sensitizing cancer cells to radiation. HT inhibits radiation-associated DNA repair, improves tumor oxygenation, and stimulates immune mechanisms, increasing CD4+ and CD8+ T-cell activity, as demonstrated in pre-clinical studies. HT+RT improves local control and outcome in breast cancer patients.

**Methods:** The HISTOTHERM study enrolled breast cancer patients with locoregional recurrence. Patients received hypofractionated, low-dose RT (4 Gy/week, total 20 Gy) immediately after 60 minutes of water-filtered infrared A (wIRA) hyperthermia (target tissue temperature 39–43°C). Punch biopsies were collected before the first treatment, during therapy, and at follow-up. Formalin-fixed paraffin-embedded tissues were stained for CD4 and CD8. Immune cells were quantified in 26 patients at one to three timepoints and correlated with clinical outcomes.

**Results:** In a first analysis of patient tissue, we have longitudinally investigated T-cells changes over time in the course of a HT+RT treatment with wIRA. Baseline densities of CD4 and CD8 lymphocytes and percentage of lymphocytes varied considerably among patients, ranging from 0% CD4 or CD8 positive cell to 27 % and 36 %, respectively. Across the cohort, changes in lymphocyte numbers over time were heterogeneous; in some individuals CD4 and CD8 cell densities increased, while in others, they decreased or remained stable. In follow-up biopsies, patients with low residual tumor had higher CD4 and CD8 cell population than those with greater tumor burden.

**Conclusions:** This study is the first to investigate lymphocyte alterations in breast cancer tissue during HT+RT. While the current sample size limits definitive conclusion, preliminary observations suggest there may be emerging trends between lymphocyte dynamics and clinical outcome. Ongoing analyses will further elucidate these potential relationships.

## Contact-free wIRA-hyperthermia combined with hypofractionated radiotherapy of non-melanoma skin cancers

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**Purpose:** Based on published clinical data, superficial hyperthermia (39-43°C for 60 min) immediately followed by low-dose radiation therapy has been accepted in Switzerland as standard, reimbursed treatment of irresectable, locally recurrent breast cancer (LRBC) in preirradiated areas and for malignant melanoma. Only few data are available on combined superficial hyperthermia followed by radiotherapy of non-melanoma skin cancers (NMSC).

Most patients presenting with irresectable squamous and basal cell carcinoma of the scalp and face are at an advanced age, and additionally suffer from age-related co-morbidities which significantly impair the tolerability of normofractionated radiotherapy protocols. Even in cases of primary/surgically treated skin cancer, further treatment might be contraindicated because of associated general burden and stress. Thus, there is an urgent need for patient-friendly treatment schedules for this increasing patient group.

**Methods:** Due to the heterogenous surface contours and high skin sensitivity of this area, the contact-free, thermography-controlled water-filtered infrared-A (wIRA) superficial hyperthermia is particularly suitable for this patient population. Hyperthermia sessions of 45-60 min in a comfortable body position without any mechanical fixation are immediately followed by radiotherapy using a hypo-fractionated schedule of 5-6 session of 4-5 Gy, 1x/week, up to a total dose of 20 – 30 Gy.

**Results:** 12 Patients with large NMSC (diameter > 5 cm) showed in 9/12 a complete remission, 3 patients a partial remission. In 2 patients with extended skin spread of a Merkel cell carcinoma (MCC) resistant to former treatments (surgery, systemic immuno-chemotherapy) a distinct partial remission was achieved.

**Conclusions:** Considering tumor extensions and difficult patient situations in NMSC and MCC, satisfying clinical results were obtained upon treatment using significantly decreased total doses and number of RT-sessions.

## CLINICAL DATA CONFIRM GALENIC PRINCIPLE AND DEMONSTRATE THERAPEUTIC POTENTIAL OF THE001 (DPPG2-TSL-DOX) PLUS REGIONAL HYPERTHERMIA IN SOFT TISSUE SARCOMA

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**Objective:** Despite limited efficacy, Doxorubicin (DOX) remains standard therapy for soft tissue sarcoma (STS). THE001 (DPPG2-TSL-DOX) is a thermosensitive liposomal DOX formulation designed for heat-triggered, intravascular release, enabling high local drug concentrations with systemic exposure comparable to conventional DOX. In preclinical models, THE001 + regional hyperthermia (RHT) achieved up to 15-fold higher intratumoral DOX correlating with enhanced tumor response.

**Methods:** Phase 1 dose-escalation trial [NCT05858710] in heavily (including DOX-) pretreated participants (pts) with advanced unresectable/metastatic STS. THE001 IV was administered q3w for up to 12 cycles. From cycle 2 onwards, RHT is applied. Primary objectives are safety and definition of Highest Tolerated Dose (HTD); responses are assessed per RECIST v1.1 and Choi. Pharmacokinetics (PK) evaluate heat-induced DOX release and systemic exposure of DOX and liposomal components.

**Results:** Seven pts were treated in DL1 (20mg/m<sup>2</sup>; n=4) and DL2 (40mg/m<sup>2</sup>; n=3). No dose-limiting toxicities occurred with low rate of grade  $\geq 3$  TRAEs for THE001 + RHT (3.4% of all AE), leading to determination of 40mg/m<sup>2</sup> as HTD for THE001 + RHT in this setting. In DL<sub>1</sub>, 3 pts achieved local tumor control in RHT-region with one stable disease (SD) per RECIST 1.1. In DL<sub>2</sub>, all pts achieved SD, with 2 of 3 meeting Choi response criteria. Two pts completed 12 cycles with one (epithelioid sarcoma) becoming eligible for resection with no vital tumor cells in resected target lesion. PK profiles showed near-complete DOX release upon heating. Systemic AUC<sub>inf</sub> was comparable to conventional DOX, while C<sub>max</sub> was substantially lower, suggesting reduced cardiotoxicity.

**Conclusions:** THE001 + RHT demonstrates clinical activity, proof of galenic principle, and a favorable safety profile in STS. Exploration in the neoadjuvant setting aims to enhance pathological responses (e.g., pCR rate) and immune induction. Orphan Drug Designation by EMA and FDA were granted for THE001 + RHT, validating the potential in STS.

## Final report of the H2020 HYPERBOOST consortium: Hyperthermia boosting the effect of Radiotherapy

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**Purpose:** Effective clinical application of hyperthermia requires well-designed clinical protocols and experienced staff. HYPERBOOST was created to bridge these gaps in a 4-year European Horizon 2020 Innovative Training Network (H2020-MSCA-ITN-2020-955625) with 11 beneficiaries and 7 partner organizations in 7 countries. The aim was to train hyperthermia experts and to develop an advanced personalized combined radiotherapy and hyperthermia treatment planning platform based on extensive (pre)clinical data.

**Methods:** HYPERBOOST ran from December 2020 to December 2024. Hyperboost integrated expertise from different disciplines, including physics, pre-clinical research and clinical studies, aiming to train dedicated staff for hyperthermia. Aims included:

- 1) preclinical hyperthermia research
- 2) development of personalized planning
- 3) clinical implementation, evaluation and quality assurance.

Fourteen PhD students were trained to become the next-generation of hyperthermia professionals with multidisciplinary skills and expertise to develop, apply and optimize advanced multi-modality cancer treatments through close interaction with academic and industrial consortium partners. Novel training methods were applied for hyperthermia, radiotherapy and translational skills.

**Results:** HYPERBOOST training courses included successful online courses and onsite training weeks. Secondments established fruitful research collaborations between beneficiaries and partners across different disciplines both within and outside HYPERBOOST, thus promoting more collaboration between European and American hyperthermia centers.

The final HYPERBOOST report summarized results and recommendations for the clinical hyperthermia field.



The EU evaluation was very positive about progress and scientific results achieved which promote high quality assurance standards for hyperthermia protocols and high-level treatment delivery standards with much attention for safeguarding and documenting therapeutically effective temperature levels.

**Conclusions:** HYPERBOOST contributed to high-level hyperthermia research and clinical practice by initiating, stimulating and facilitating multidisciplinary cross-pollination between the disciplines involved in hyperthermic oncology. This leads to the consolidation and expansion of the European industry and infrastructure for more effective clinical hyperthermia research and application.

## Progress report on the CARES consortium: Development of personalized MR-guided thermo-chemotherapy for breast conserving surgery

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**Purpose:** Breast cancer remains a leading cause of morbidity and mortality among women worldwide. While chemotherapy is widely used to shrink tumors and enable breast-conserving surgery, nearly half of patients still require more invasive procedures, including mastectomy. This may be attributed to low and heterogeneous intratumoral drug accumulation.

**Methods:** The CARES consortium was established to address this challenge by developing a personalized, MR-guided, temperature-mediated chemotherapy approach aimed at improving treatment efficacy and reducing the extent of surgery, thereby enhancing patients' quality of life. This multidisciplinary effort brings together five partner organizations. The project is supervised by multiple principal investigators and involves four PhD students and one postdoctoral researcher. It is structured into five synergistic work packages:

1. Development of a thermotherapy applicator with real-time, non-invasive MR monitoring capability
2. Optimization of MR sequences tailored for breast tissue
3. Advanced, breast-specific treatment planning using personalized models of dynamic temperature, perfusion, and drug distribution
4. Design of target-specific thermosensitive liposomes for intravascular drug release
5. Creation of a semi-automatic feedback control framework to optimize treatment delivery based on real-time MR data

**Results:** Launched in December 2023, the CARES project is progressing well. Collaboration among PhDs and the postdoc is central to its success, supported by close supervision from PIs and the NWO program director. Regular bimonthly PI meetings and monthly PhD meetings ensure strong coordination, complemented by annual consortium-wide gatherings to align short- and long-term objectives and maximize societal impact. Robust collaborations have been established both within and beyond the consortium, fostering a dynamic and innovative research environment.

**Conclusions:** The CARES project is laying the groundwork for a transformative approach to breast cancer treatment, with the potential to significantly improve therapeutic outcomes and reduce surgical invasiveness.

## Evaluation of thermal mapping accuracy in clinical hyperthermia using quality assurance phantoms

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**Introduction:** Real-time temperature monitoring is essential in clinical hyperthermia (HT) for both safety and efficacy, especially given the strong dose–effect relationship to achieve therapeutic temperatures in the target region while preserving surrounding healthy tissues. A widely used temperature monitoring method is thermal mapping, where temperature probes are mechanically retracted along catheters in fixed steps to measure spatial temperature distributions. The reliability of this system is essential for accurate treatment delivery. This study evaluates thermal mapping reliability by comparing measured temperature profiles with expected distributions in standardized quality assurance (QA) phantoms.

**Methods:** We analyzed two BSD 2000 deep HT systems at different institutions, each equipped with Sigma 60 applicators and thermal mapping devices. Probes were calibrated in a temperature-controlled water bath, ensuring a maximum uncertainty of  $\pm 0.2^\circ\text{C}$ . The probe position accuracy was assessed in a dry run using a transparent catheter with 1 cm steps over a 25 cm range, comparing expected and actual probe positions when using two, three, or four probes simultaneously. QA experiments were then performed with a standardized phantom, measuring the temperature distribution along its central z-axis. All non-mapping-related uncertainties were minimized. Parallel numerical simulations closely replicated the experimental setup, accounting for probe misplacements, and were compared with the measured temperature profiles.

**Results:** Position deviations increased with probe count:  $1.0 \pm 0.1$  cm (2 probes) vs.  $3.8 \pm 1.0$  cm (4 probes). Temperature profiles showed excellent agreement between measurements and simulations when using 2 probes (difference:  $0.2 \pm 0.1^\circ\text{C}$ ), but discrepancies grew with 4 probes (difference:  $0.7 \pm 0.5^\circ\text{C}$ ). The use of more than 2 probes required continuous visual inspection and manual adjustment to maintain probe tension and position.

**Conclusion:** Our findings demonstrate how thermal mapping consistency decreases with increasing number of mapping probes, reducing reproducibility and control during treatment and QA procedures. We recommend using no more than 2 probes simultaneously to ensure reliable temperature monitoring.

## Procedure for quality assurance dosimetry for hyperthermia applicators based on SAR characterization

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**Purpose:** The application of uniform and reproducible hyperthermia treatment delivery is essential to ensure consistent treatment quality. We propose an efficient and flexible automated quality assurance (QA) procedure for characterising hyperthermia applicators based on specific absorption rate (SAR) distributions following ESHO QA guidelines to use EFS and EPD as quality metrics. The presented procedure is similar to dosimetric characterization in radiotherapy. We demonstrated the proposed procedure using contact flexible microstrip applicators (CFMA) for superficial hyperthermia, operating at 434 MHz.

**Methods:** A cartesian robot moves an E-field sensor in a 42×100×40 cm<sup>3</sup> PVC tank filled with saline solution (3 gr/L NaCl, electrical conductivity  $\sigma = 0.53 \text{ Sm}^{-1}$ , relative permittivity  $\epsilon_r = 78.7$ , @434MHz) to scan the volume underneath a CFMA. The data obtained from 2D and 3D measurements are used to analyse the effective field size (EFS), effective penetration depth (EPD) and the variation of the EPD across the applicator. The repeatability of the measurements is determined with measurements over several days. Parameters for evaluating accuracy of the scanning procedure are repeatability, selection of planes and resolution. Applicator setting variations serving as example for demonstrating the procedure included bolus thickness and applicator curvature.

**Results:** A spatial resolution between 1 and 2 cm provides enough information for routine QA. Standard deviation of EFS and EPD between days was below 5%. Planes passing through regions of high SAR (~80-90% of the maximum) can be used to evaluate the EPD from the measured distribution at 1 cm depth. Position uncertainty over repeated measurements was below 0.5 cm.

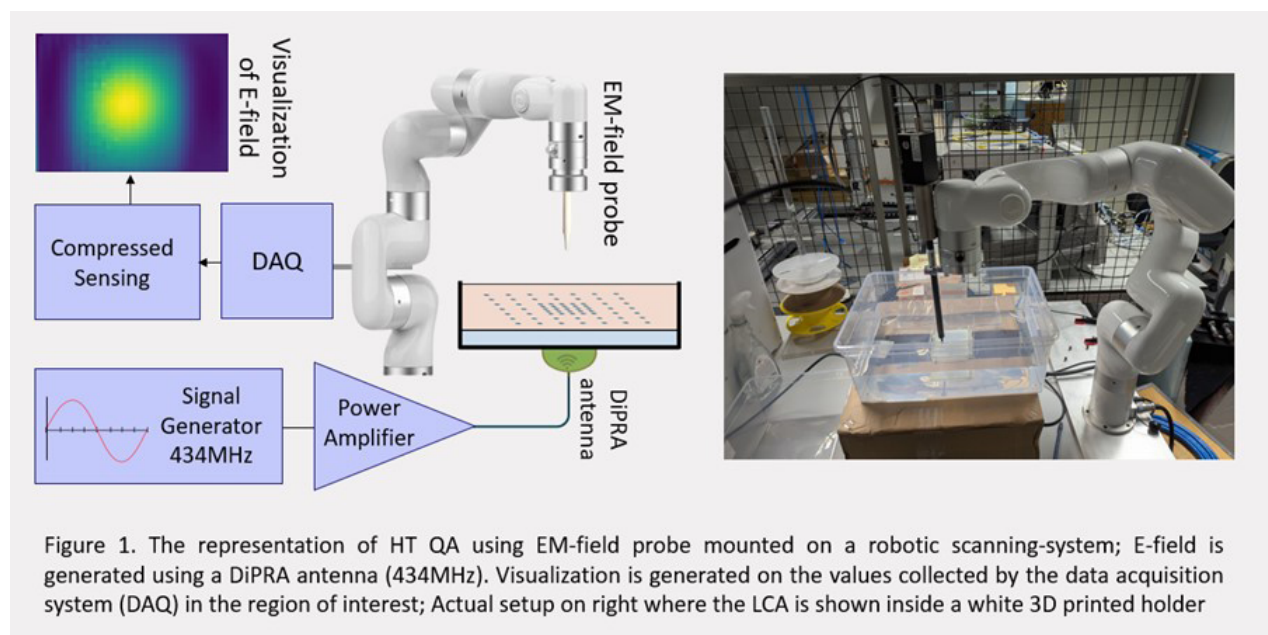
**Conclusions:** The proposed workflow proved fast (~40 min.), accurate and repeatable, making it suitable for hyperthermia applicator characterization and QA. The procedure was demonstrated for CFMAs and is also applicable for a diversity of hyperthermia systems.

# Compressed sensing for fast quality assurance of hyperthermia applicators by robotic electromagnetic field measurements

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**Purpose:** Hyperthermia(HT) therapy aims to elevate tissue temperatures to 40-44°, sensitizing radiotherapy and/or chemotherapy. Radiofrequency-phased-arrays focus heat by optimizing phase and amplitude of transmitted-signals, requiring rigorous quality-assurance(QA) to ensure precise energy-delivery. Existing HT-QA, predominantly based on temperature measurements (IR\_camera, Thermistor\_probes) require cooling-down and hence time-consuming and struggle to match radiotherapy's robust QA-standards. Electric(E)-field measurements are instantaneous and hence potentially accelerate HT-QA. However, dense E-field sampling using robotic-scanning-systems to assess whole region-of-interest still involves long total measurement-time. Our study explores whether compressed-sensing(CS) enables reconstructing E-field and specific-absorption-rate(SAR) by fewer measurement points.i.e.reducing scan-time, while maintaining highaccuracy assessment of metrics relevant in HT-QA.

**Methods:** CS-approach leverages sparsity of signals, where critical information is concentrated in few components and exploits randomly sampled measurements, projected onto2D-Discrete-Cosine-Transform\_(DCT) basis, and applying L1\_minimization for sparse-coefficients. In our application, E-field is generated using DiPRA\_antenna(434MHz). Quality of E-field-reconstruction is evaluated by common CS metrics: Structural-similarity-index\_(SSIM), Peak-signal-to-noise-ratio\_(PSNR), HT-QA-metric 50%\_iso\_field\_area. The E-field-probe on robotic-scanning-system collected 1564 E-field values in 90\_minutes, measured 2cm inside phantom 37×26×15cm( $\sigma_{eff}=0.94S/m$ ,  $\epsilon'=55.9$ ) separated by 2cm water-

bolus. We analysed quality of E-field reconstruction for sampling-points 1% (15\_measurement\_locations) to 50% (799\_locations), and determined projected QA-workflow efficiency by total data-acquisition time.

**Results:** Using only 8% of samples (127\_locations), reconstructed E-field retains high-accuracy(PSNR:27dB,SSIM:0.9) taking just 8\_minutes and reducing need for exhaustive QA-measurements. Our results also validate sampling beyond 13%(207-locations) provides minimal added benefits

**Conclusions:** CS potentially enables routine-use of robotic-QA-measurements: only 8% measurements suffice for determining 50%\_iso\_Field\_area with 2% error in less than 10\_minutes. Future work will address application of our approach to clinical HT-applicators

## Experimental validation on agarose phantom of a capacitive hyperthermia device

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Giuseppe Peter Vanoli<sup>1</sup>, Ciro Zaccagnini<sup>3</sup>

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**Purpose:** This study aims to develop and validate a comprehensive numerical and experimental framework for the HY-DEEP 600WM capacitive hyperthermia device. The goal is to support treatment planning and optimization by accurately simulating its electromagnetic and thermal behavior across diverse clinical scenarios.

**Methods:** A coupled multiphysics model was implemented in COMSOL Multiphysics, integrating electromagnetic and thermal phenomena by solving Maxwell's equations under the quasi-steady state assumption and Pennes' bioheat equation. The model incorporates detailed representations of the antenna geometry, material properties, and relevant boundary conditions. To verify simulation accuracy, experimental validation was performed using tissue phantoms and ex vivo biological samples. Temperature data collected during controlled exposures were compared with model predictions to assess spatial and temporal correspondence.

**Results:** Simulations demonstrated accurate reproduction of electric potential and temperature rise patterns within tissue-like media. Notably, localized electric field intensifications were observed near antenna edges, along with anisotropic thermal diffusion influenced by material characteristics and boundary convection. The simulated thermal dynamics closely matched experimental measurements, confirming the model's high predictive accuracy. These findings are consistent with existing literature, further validating the framework.

**Conclusions:** The validated framework enables a robust evaluation of the HY-DEEP 600WM device, allowing for systematic in silico testing under various conditions including different tissue types, applicator setups, and power inputs. It provides a valuable tool for optimizing therapeutic parameters to enhance efficacy while maintaining safety, thereby contributing to more effective and personalized hyperthermia treatment planning.



## The 1.66 GHz ALBA micro8 system: a novel device for focused locoregional heating in pre-clinical hyperthermia research

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Maarten Bijlsma<sup>3</sup>, Hans Crezee<sup>1</sup>

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**Background:** Pre-clinical research considering orthotopic tumour models is essential to further unravel hyperthermia mechanisms with optimal potential for clinical translation to patients. However, hyperthermia equipment for such research was not available, until recently. To address this need, Med-Logix Srl developed the ALBA micro8. This work applied measurements and numerical simulations to evaluate the ability of the ALBA micro8 to create and control a heating focus in phantoms and mouse anatomies.

**Methods:** The ALBA micro8 consists of eight individually-controlled miniature 1.66GHz waveguides in a ring with a 50mm diameter bore. E-field measurements were performed in a homogeneous phantom to determine focus size and power steering capabilities. Temperature rise measurements were performed in muscle-equivalent split phantoms, using an infra-red camera. A model of the ALBA micro8 was implemented into Plan2Heat and planning predictions were compared to the measurement results to validate this implementation. Next, numerical simulations were performed to evaluate the potential of focused heating in mice, using a digital mouse model, mimicking an orthotopic pancreatic tumour. Robustness of focused heating was evaluated considering the impact of positioning uncertainties and anatomical variations by respiratory motion and varying bowel/stomach filling on T90.

**Results:** E-field measurements showed confined, controllable, and predictable foci with an 8mm diameter. The measured temperature focus was 22×25mm. For both power and temperature, the measured and predicted focus size and location typically matched within 1mm. Simulations showed strong robustness of focused heating. Both respiratory motion and variations in intestine/stomach filling showed minor variation in tumour T90 ( $\leq 0.15^\circ\text{C}$ ). Positioning errors of  $\pm 5\text{mm}$  in cranial-caudal direction resulted in a T90 variation less than  $0.25^\circ\text{C}$ .

**Conclusions:** The ALBA micro8 enables robust, confined, controllable, and predictable heating of deep-seated targets. These features enable preclinical hyperthermia research using orthotopic tumour models to reveal clinically relevant biological and physiological effects and optimise combination treatments with hyperthermia.

## A preclinical microwave system for hyperthermia treatment of small animal superficial tumors

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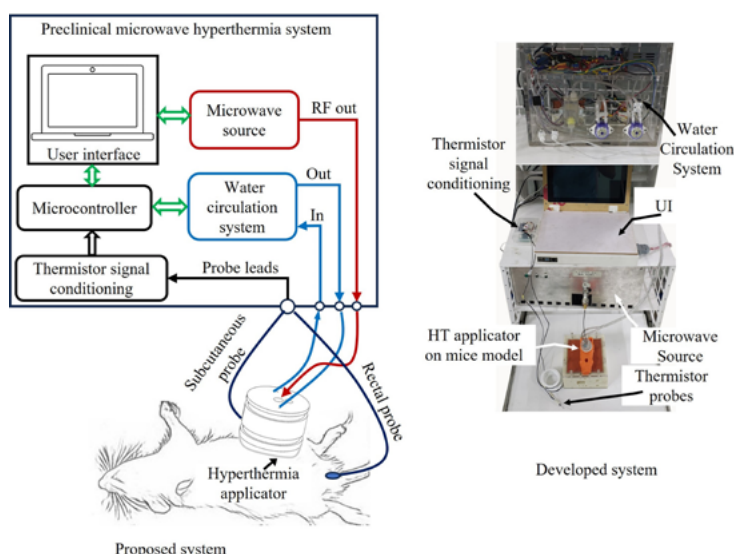
Normal 0 false false false EN-IN X-NONE TE Preclinical studies in cancer biology are vital for understanding disease mechanisms developing diagnostic therapeutic tools. They provide critical data on safety efficacy, forming the basis for regulatory approval of clinical trials. In this work, we introduce a preclinical microwave hyperthermia system designed for the targeted treatment of superficial tumor models in small animals (tumor volume < 1000 mm<sup>3</sup>), aiming to explore how radiative hyperthermia interacts with tumor tissues assess its potential to enhance therapeutic outcomes.

Our system includes a digitally controlled 2.45 GHz (1-30 W) microwave generator a 22 mm diameter microstrip antenna applicator, optimized for superficial tumor heating. It features a deionized (DI) water circulation module for temperature-controlled water in the water bolus, thermometry module to monitor core subcutaneous temperatures during treatment.

System performance was validated with homogeneous phantoms in line with ESHO guidelines. A preliminary in vivo study with five BALB/c mice bearing 4T1 tumors demonstrated safe localized tumor heating. Fractionated hyperthermia (45 minutes per session) was applied every two days for five sessions under anesthesia.

Phantom tests confirmed localized heating with 1356 mm<sup>3</sup> target coverage 8.6 mm treatment depth at 2.45 GHz - appropriate for superficial tumor studies. In vivo experiments showed stable system operation for 2-3 hours/day as hyperthermia treatment for this study lasted six days a week. Rectal skin temperatures were consistently maintained within a controlled range. Tissue pathology revealed at least 20 greater necrosis in hyperthermia-treated mice compared to controls.

These findings confirm the system's safety, stability, ability to induce localized thermal effects. The observed enhancement in necrotic damage supports the system's utility in preclinical hyperthermia research involving small animals.



The schematic illustration the developed system are shown below

## Magnetic Nanoplatforms for Clinical Translation: Synergistic Hyperthermia, ChemoDynamics, Immune Activation in Cancer Treatment

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<sup>1</sup>Institute of Nano Science and Technology

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**Title:** Magnetic Nanoplatforms for Clinical Translation: Synergistic Hyperthermia, Chemo-Dynamics, Immune Activation in Cancer Treatment

**Abstract:** Magnetic hyperthermia therapy (MHT), when combined with chemo-dynamic therapy (CDT), offers a synergistic approach to overcoming the limitations of conventional cancer treatments. This dual-modality strategy enhances reactive oxygen species (ROS)-mediated cytotoxicity, thereby improving therapeutic outcomes. In this study, we designed a Cu(II)Zn(II)Fe<sub>2</sub>O<sub>4</sub> magnetic nanoplatform integrated with vitamin K3 (Vk3) to amplify the combined effects of CDT MHT. The nanoplatform catalyzes Fenton-like reactions, converting endogenous hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) into highly toxic hydroxyl radicals ( $\cdot$ OH), while Vk3 promotes additional ROS production via activation of NAD(P)H quinone oxidoreductase-1 (NQO1). Localized heating induced by MHT further enhances radical formation, resulting in significant tumor growth inhibition with minimal off-target toxicity, as demonstrated through in vitro and in vivo experiments.

A major challenge in MHT is the induction of heat stress response (HSR), particularly the overexpression of heat shock proteins like HSP90, which can reduce treatment efficacy. We addressed this by co-administering 17-DMAG, a clinically relevant HSP90 inhibitor, alongside MHT. This combination significantly intensified oxidative stress, leading to enhanced glioma cell death. In a murine glioma model, the combinatorial treatment achieved primary secondary tumor inhibition rates of 65 53, respectively, with complete tumor regression observed within 20 days. Furthermore, systemic immune activation was evidenced by increased extracellular HSP90 release upregulation of interferon-gamma (IFN- $\gamma$ ), suggesting a broader immunotherapeutic effect.

Together, these results establish a clinically promising, dual-functional magnetic nanoplatform that leverages ROS amplification immune modulation to enhance cancer therapy. This work highlights the translational potential of combining hyperthermia with redox-based immune-targeted strategies for effective tumor eradication

## Unravelling Thermotolerance in Adrenocortical Carcinoma: Implications for Hyperthermia-Based Therapies

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**Introduction:** Adrenocortical carcinoma (ACC) is a rare, aggressive cancer with limited treatment options and frequent chemoresistance, highlighting the need for improved therapies. Hyperthermia is used to treat ACC metastases primarily through radiofrequency ablation to control disease burden. Incomplete tumour ablation risks exposure to sub-lethal hyperthermia in the transitional zone, potentially leading to thermotolerance development, where cells resist subsequent thermal stress after initial sublethal heat exposure.

We hypothesised that sublethal hyperthermia induces thermotolerance to subsequent exposure at 48°C or 50°C, mediated by the heat shock response and TMEM16F, a calcium-dependent scramblase involved in cellular repair.

**Methods:** ACC primary cell lines H295R and HAC15, and the metastatic line MUC-1 were pre-treated at 45°C, then rechallenged at 48°C or 50°C after 24 hours or 7 days. Rechallenge cells were compared to naïve (non-pretreated) cells. Cell death was assessed using Sytox Blue staining and flow cytometry. Protein expression of HSP70, HSP90, P-HSP27, and TMEM16F was analysed by Western Blot.

**Results:** Surviving ACC cells previously exposed to hyperthermia showed no evidence of thermotolerance. Viability at 48°C and 50°C was similar between pre-treated and naïve cells, though MUC-1 was more resistant at higher temperatures ( $\geq 48^\circ\text{C}$ ). While heat stress was evident following hyperthermia, no significant differences in HSP70 and HSP90 expression were observed between naïve and rechallenged cells. Additionally, P-HSP27 and TMEM16F expression was significantly decreased, in both naïve and rechallenge cells, at 48°C and 50°C, but reappeared 24 hours later at 48°C only.

**Conclusion:** Hyperthermia of 45°C did not confer thermotolerance in ACC cells. The transient but marked reduction in P-HSP27 and TMEM16F suggest a diminished and delayed heat shock response, insufficient to protect against subsequent thermal stress. These findings emphasise the complex ACC response to hyperthermia but suggest that thermotolerance may not develop in incompletely ablated cancers, whereby cells remain sensitive to further ablation challenges.

# Global Trends in Hyperthermia Research: A Bibliometric Analysis of Publications in the International Journal of Hyperthermia

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**Purpose:** Information creation accelerates rapidly, with 2-3.3 million research articles published annually and a 5% growth from 2017-2020. This volume presents both challenges and opportunities. Tools like iCite (NIH's bibliometric platform, which provides several bibliometric metrics) and PubMed (containing over 38 million biomedical citations) help researchers analyse trends and gain insights from the scientific literature.

**Methods:** On March 10, 2025, we downloaded the iCite and PubMed 2024 data of abstracts published in the International Journal of Hyperthermia and imported them into the analytical database. We manually inspected data quality, developed normalization strategies, and applied Natural language processing (NLP) techniques using a custom-made NLP pipeline and the Claude Large language model (LLM), along with custom rule-based scripts, to standardize affiliations into country, city, and organization fields according to ISO standards for countries and regions, as well as the Research Organization Registry (ROR) for research institutions' names. This process achieved 95% accuracy through iterative refinement and expert validation.

**Results:** Between 1985 and 2024, we analyzed 3'452 PubMed-indexed publications, involving a total of 26'550 authors. Using NLP, we successfully extracted geographical and institutional data from 98.5% of affiliations, identifying authors from 66 countries, 872 cities, and 1'862 institutions. Articles averaged 7.69 authors (median: 6) and 1.66 institutions per paper, with some outliers having exceptionally high counts (up to 154 authors and 22 institutions). The number of publications increased by 20.6% over the last 10 years, with a peak output in 2018 (236 publications). 60% of organizations have a declining trend in production, while 33% have increased their scientific output. The growth rate of production varies significantly, ranging from a 2300% increase to a 92% decline.

**Conclusion:** This 40-year bibliometric analysis successfully processed 3'452 articles and 26'550 authors. Using the International Journal of Hyperthermia as a case study, this research demonstrates how AI-powered tools can effectively analyze scientific literature to reveal patterns of publication and international research networks.

## Bioinformatics-based Screening and Analysis of Key Genes in EGFR TKI-Resistant Lung Cancer Cells

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**Purpose:** Epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs) serve as first-line therapeutic agents for patients with lung adenocarcinoma (LUAD) who harbor EGFR activating mutations. However, resistance to EGFR-TKIs presents a significant challenge to the efficacy of LUAD treatment. This study aims to utilize bioinformatics to explore the mechanisms underlying EGFR-TKI resistance and identify key genes involved in this process.

**Methods:** Data from GSE123066 and GSE83666 were extracted, functional enrichment analysis, gene set enrichment analysis (GSEA), and immune infiltration analysis were used to identify gefitinib resistance-related differentially expressed genes (GRRDEGs). Then constructed the GRRG\_score using least absolute shrinkage and selection operator (LASSO) and Cox regression analysis. The GRRG\_score was developed to evaluate its correlation with tumor microenvironment (TME) characteristics and tumor immune infiltration. Finally, the CTR-DB database was employed to validate the results of drug therapy predictions based on the identified genes.

**Results:** Totally 88 differentially expressed genes were identified. KEGG enrichment analysis indicated significant involvement in pathways related to JAK/STAT signaling, cytokine-cytokine receptor interactions, and sphingolipid metabolism. GO analysis revealed that biological processes strongly associated with gefitinib resistance included cell proliferation and immune-related pathways. The GRRG\_score was constructed based on the expression levels of eight genes, and subsequent screening and validation confirmed the predictive value of ID1 for prognosis and drug resistance.

**Conclusion:** Our study provided insights into the potential mechanisms underlying gefitinib resistance in LUAD. The findings of this research have significant implications for the development of more effective treatment strategies for patients with LUAD.

## **Combined inhibition of Wee1 and Checkpoint Kinases synergistically provokes mitotic entry and promotes cell death under heat stress**

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Hyperthermia, induced by heat stress (HS), inhibits cancer cell proliferation and induces cell death. We previously demonstrated that inhibition of checkpoint kinase 1/2 (Chk1/2) abrogated G2/M arrest and promoted cell death under HS conditions; however, the mechanisms underlying the regulations of cell cycle and cell survival under HS remains to be fully elucidated. Here, we investigated whether Wee1 inhibition promoted mitotic entry and cell death in cells exposed to HS in combination with a Chk1/2 inhibitor. MK-1775, a selective Wee1 inhibitor, promoted the HS-induced loss of cell viability and increased the SubG1 population in HeLa S3 cells, coinciding with the reduced accumulation of cells in the G2 phase observed under HS exposure. MK-1775 or AZD-7762, a Chk1/2 inhibitor, alone counteracted HS-induced G2 arrest, and their combination further promoted mitotic entry and loss of cell viability under HS, suggesting cooperative regulation of HS-induced G2 arrest by Wee1 and Chk1/2, which may contribute to cell survival. Moreover, the combination of MK-1775 and AZD-7762 abrogated G2 arrest and enhanced HS-induced cell death even in MG-63 and HSC-3 cells. These findings indicate that simultaneous inhibition of Wee1 and Chk1/2 could be a promising strategy for augmenting the therapeutic efficacy of hyperthermia.



## Enhanced Antitumor Effects of Combined Hyperthermia and Electric Field Therapy in NSCLC Cells

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<sup>1</sup> Korea University, <sup>2</sup> FieldCure Ltd, <sup>3</sup> Myonggeun Yoon

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This study investigates the synergistic anticancer effects of hyperthermia (HT) and electric field (EF) therapy in non-small cell lung cancer (NSCLC) cells. The combined treatment significantly increased  $\gamma$ -H2AX and cleaved PARP expression, indicating enhanced DNA double-strand breaks and apoptosis. It also led to the suppression of key DNA repair proteins including BRCA1 and PARP1. Furthermore, metastatic potential was inhibited via downregulation of vimentin, alongside reduced cell proliferation and colony formation. Compared to either monotherapy, the dual application of HT and EF exhibited superior efficacy in inhibiting cell viability, migration, and invasion. These findings suggest a synthetic lethality-like mechanism, wherein simultaneous induction of DNA damage and inhibition of repair pathways potentiates therapeutic effects. The combination strategy may provide a promising non-invasive alternative for improving NSCLC treatment outcomes with minimal systemic toxicity.

## Hyperthermia induces immunogenic modulation and reduces tumor immune escape in B16-F10 melanoma in vitro

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Recent progress in understanding and targeting immune checkpoint molecules has greatly advanced the development of immunotherapies. Despite these improvements, treatment efficacy remains limited. Immune checkpoint blockade (ICB) has shown success in inhibiting immune-suppressive pathways, thereby preventing tumor immune escape. Combining therapies can amplify the effects of each individual component, leading to enhanced tumor cell killing. However, the use of thermal ablation as a therapeutic adjuvant remains relatively unexplored.

To investigate the potential of hyperthermia, B16-F10 melanoma cells were cultured at either 37°C or 41°C. Culturing at 41°C led to a 70% reduction in cell migration within 24 hours. Cell proliferation was also significantly reduced—by 62% at 48 hours and 94% at 72 hours.

Protein expression analyses under elevated temperatures revealed substantial changes: pERK and ERK levels dropped by 86% and 50%, respectively, while Caspase-3 expression rose by 31%. Given that cellular stress can simultaneously trigger death pathways and the heat shock response, we examined the expression of inducible Hsp70. While Hsp70 was undetectable at 37°C, its expression increased by 188% at 41°C. Cytokine profiling of conditioned media indicated a shift toward a proinflammatory state, with increased TNF- $\alpha$  and decreased IL-4 levels at the higher temperature. These findings are consistent with literature reports linking hyperthermia to TNF- $\alpha$ -mediated apoptosis.

Programmed death-ligand 1 (PD-L1), a key molecule used by tumors to suppress immune activity and promote immune tolerance in the tumor microenvironment, was found to be downregulated by 35% in response to hyperthermia. This suggests that elevated temperatures may alter the tumor milieu in a way that enhances sensitivity to checkpoint inhibitors. Building on these promising in vitro results, we aim to investigate the therapeutic potential in vivo. B16-F10 melanoma cells will be implanted in C57BL/6 mice and treated with infrared radiation in combination with anti-PD-L1, anti-PD-1, or IL-15 therapy.

## **“A Storm Within Remission: Multisystem Complications of ATRA-ATO Therapy in Acute Promyelocytic Leukemia” - A case report**

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<sup>4</sup>International Training Fellow – Queen Elizabeth Hospital, Birmingham

**Background:** Acute promyelocytic leukemia (APML) is a hematologic emergency that has transformed into a highly curable disease with differentiation therapy using all-trans retinoic acid (ATRA) and arsenic trioxide (ATO). However, this regimen carries the risk of serious complications, particularly during induction.

**Case Presentation:** We report the case of a 22-year-old woman newly diagnosed with APML (PML-RARA positive), who developed a constellation of life-threatening complications within the first two weeks of induction therapy with ATRA and ATO. These included:

- **Electrolyte disturbances** (hypokalemia, hypomagnesemia)
- **QT interval prolongation**
- **Focal seizures**
- **Chest pain** with ECG changes suggestive of coronary vasospasm
- **Dural venous sinus thrombosis (DVST)** confirmed on imaging

Therapy was promptly paused, and a multidisciplinary team was engaged. After stabilization, treatment was resumed under close monitoring, and the patient completed induction with complete hematologic remission.

**Discussion:** This case illustrates the spectrum of ATRA-ATO-related toxicities. QT prolongation and electrolyte imbalance likely contributed to neurologic and cardiac events. The chest pain was consistent with ATO-induced coronary vasospasm—a rare but increasingly recognized phenomenon. DVST, although uncommon, has been described in APML, potentially exacerbated by coagulopathy and leukostasis.

**Conclusion:** Induction therapy for APML demands heightened clinical vigilance. This case reinforces the importance of:

- **Daily cardiac monitoring and electrolyte correction**
- **Rapid identification of neurologic or thrombotic events**
- **Multidisciplinary collaboration to ensure safe treatment continuation**

Timely intervention and individualized supportive care can prevent morbidity and ensure curative intent in APML is not compromised.

# Advances in Thermotherapy for Breast Cancer: A Systematic Review of Clinical and Technological Developments

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**Purpose:** Thermotherapy is an established adjunct to radiotherapy for treating recurrent and/or locally advanced breast cancer[1]. However, its clinical application for the intact breast remains limited, despite its proven potential. This systematic review presents the status quo of non-invasive thermotherapy applicators for tumors in the intact breast regarding clinical evidence, technology used, and quality assurance (QA) applied.

**Methods:** A systematic search was conducted by an information specialist using a tailored string across multiple databases, following PRISMA guidelines[2]. Two co-authors independently screened studies with blinded voting to reduce bias. Quality was assessed using QUIPS[3] for clinical papers and a custom method for technical ones.

**Results:** A total of 58 studies were included (Fig.1). Six clinical studies reported complete and partial responses. Five used commercially available superficial thermotherapy applicators and observed challenges in sufficiently heating deep-seated (>4 cm deep) tumors in the intact breast, limiting clinical adoption. The remaining 52 studies presented technical details of applicators, predominantly employing microwave technology, designed to heat tumors in the intact breast, in various technical development stages towards clinical implementation. One was successfully used in an included clinical study, which found pathological response rates significantly correlated with achieving sufficient thermal dose (CEM 43, T90). Reporting of treatment performance and QA parameters was inconsistent among all papers, complicating comparisons and highlighting a widespread lack of adherence to existing guidelines.

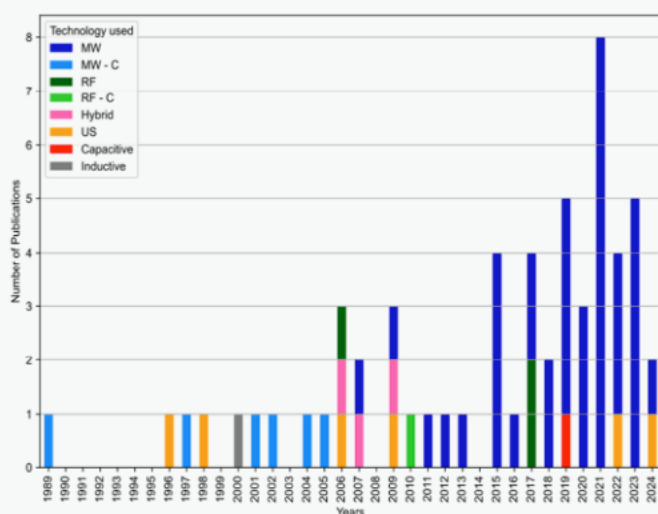


Fig.1: The number of publications over the years and corresponding technology used, after performing the literature search. RF: Radiofrequency system, MW: Microwave frequency system, US: Ultrasound system, RF-C: Clinically implemented RF system, MW-C: Clinically implemented microwave system.

**Conclusion:** This review found that clinical studies on thermotherapy involving the intact breast are extremely scarce, partly due to the lack of clinically available devices capable of sufficiently heating deep-seated tumors. Despite ongoing technical innovation, hardly any devices reach clinical use. Additionally, adherence to established QA guidelines and reporting standards[4] is essential to bridge the gap between development and clinical implementation – accelerating progress and improving outcomes for breast cancer patients.

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- 1.Bakker\_IntJHyp\_2019
- 2.Page\_BMJ\_2021
- 3.Hayden\_AnnInternMed\_2013
- 4.Paulides\_IntJHyp\_2021

## Feasibility Protocol for Phase II Clinical Trial of Capacitive Hyperthermia and Moderately Hypofractionated Radiotherapy in Breast Cancer Recurrences

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**Purpose/Objectives:** Following the encouraging results of our completed phase II trial combining capacitive hyperthermia (HT) with normofractionated radiotherapy (RT) in breast cancer recurrences, we propose a new prospective study to evaluate the feasibility of a shorter and more widely used RT regimen. In the previous trial, patients received 46 Gy (if reirradiated) or 50 Gy (if not), which extended overall treatment time. While some studies have explored hypofractionated RT with HT, none have assessed the 40.05 Gy in 15 fractions scheme—the most commonly applied in our clinical setting, including even in selected reirradiation cases with favorable tissue conditions. This trial aims to address that gap.

**Materials and Methods:** This phase II protocol will include patients with breast cancer recurrence, either postmastectomy or after a second conservative surgery, with or without previous RT. All will be treated with radical intent using adjuvant RT delivered to the breast or chest wall, with or without nodal areas, according to clinical indication. RT will follow a 40.05 Gy in 15 fractions schedule over three weeks. HT will be administered using the Hy Deep 600 capacitive radiofrequency device, twice weekly ( $\geq 72$ h apart), immediately after RT. Each session will last 60 minutes, totaling 6 superficial applications.

The study will evaluate acute and late toxicity, comparing outcomes between previously irradiated and non-irradiated patients. The Hy Deep 600 integrates real-time thermometry for continuous temperature monitoring and homogeneous heating. This system has recently been validated and will be presented at the 2025 International Hyperthermia Congress in Seoul.

**Conclusion:** We present the protocol for a new phase II trial combining capacitive HT with moderately hypofractionated adjuvant RT. It offers a more practical and evidence-aligned approach for breast cancer recurrences treated with curative intent.

# Pleural Mesothelioma Treated with Cytoreductive Surgery and Hyperthermic Intrathoracic Chemotherapy

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**Purpose:** Malignant pleural mesothelioma (MPM) is a rare, aggressive cancer associated with asbestos exposure, with poor prognosis and limited treatment options. This case report aims to present the first successful application of Hyperthermic Intrathoracic Chemotherapy (HITOC) combined with cytoreductive surgery for MPM in Kazakhstan, highlighting its safety, feasibility, and clinical outcomes.

**Methods:** A 35-year-old male patient diagnosed with Stage II epithelial MPM underwent six cycles of systemic chemotherapy (pemetrexed, carboplatin, bevacizumab) resulting in disease stabilization. Subsequently, he received cytoreductive surgery via open thoracotomy and pleurectomy followed by intraoperative HITOC with cisplatin at 42°C for 40 minutes. Postoperative assessments included clinical monitoring and imaging studies to evaluate disease status and complications.

**Results:** The patient tolerated the combined treatment well, with no significant intraoperative or postoperative complications such as nephrotoxicity or respiratory compromise. Early mobilization and pain management facilitated recovery. Follow-up CT scans at three months post-surgery revealed no evidence of disease progression or tumor recurrence. The combination of surgery and HITOC effectively controlled local disease, while systemic chemotherapy contributed to initial tumor stabilization.

**Conclusions:** This case demonstrates that HITOC, when combined with cytoreductive surgery, is a safe and feasible treatment option that may improve local control and potentially extend survival in patients with resectable MPM. The synergistic effects of hyperthermia and chemotherapy enhance drug penetration and cytotoxicity, targeting residual microscopic disease. Despite challenges such as lack of standardized protocols and the need for specialized expertise, this multimodal approach represents a promising addition to MPM management. Further studies are needed to optimize patient selection and standardize treatment parameters.

## Local hyperthermia using 8 MHz waves is feasible for pancreatic cancer patients with self-expandable metallic stents

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**Purpose:** To evaluate the safety and efficacy of hyperthermia (HT) in pancreatic cancer patients with self-expandable metallic stents (SEMS).

**Methods:** A retrospective analysis was conducted on patients who received HT for pancreatic cancer at our institution between 2022 and 2024. HT was delivered using the Thermotron-RF8, with 50-minute sessions administered concurrently with chemotherapy. For patients with SEMS, risks of HT-related adverse events were thoroughly explained, and treatment commenced at low power during the initial session. In the second session, intragastric temperature measured nasally via four-point sensor, with/without SEMS. A Cox proportional hazards model was used for survival analysis.

**Results:** Of 107 cases, 89 (SEMS: 33; no SEMS: 56) were analyzed, excluding postoperative patients. The SEMS group comprised exclusively pancreatic head tumors, with fewer stage I or resectable cases. Median cumulative HT sessions (6) and radiofrequency output (985 W) were comparable between groups. Maximum measured temperature (42.2°C) and mean CEM43T90 (2.8 minutes) showed no intergroup differences. Four cases (SEMS: 1) reached temperatures  $\geq 46^{\circ}\text{C}$  (biliary injury threshold), but no biliary bleeding or perforation occurred. Adverse events included thermal burns and fat induration (2 cases each).  $\geq$ Grade 3 myelosuppression (leukocytes: 20; neutrophils: 24; platelets: 3; anemia: 2) was observed; no treatment-related deaths.

One-year OS and PFS were 58.1% and 29.2%, respectively, with no survival difference based on SEMS status. Multivariate analysis revealed poorer OS in patients with elevated pre-treatment CA19-9 ( $p=0.02$ ) and unresectable disease ( $p=0.007$ ), while higher cumulative HT sessions correlated with better OS ( $p=0.004$ ). HT discontinuation within three sessions was more frequently due to patient refusal/communication issues (14 cases) than unavoidable circumstances (disease progression/chemotherapy completion; 5 cases).

**Conclusions:** HT appeared to be safely feasible even in patients with an inserted SEMS. Establishing a patient support system for continued HT is a future challenge.



# Preoperative chemoradiotherapy and deep regional hyperthermia in locally recurrent rectal cancer: a multicentre, retrospective analysis

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**Purpose:** To evaluate the effectiveness of combined preoperative chemoradiotherapy (CRT) and deep regional hyperthermia (HT) sessions in locally recurrent rectal cancer (LRRC) after previous multimodality treatment including CRT and surgery.

**Methods:** A multinational retrospective study was conducted among European clinical centers. As part of this study, 24 LRRC patients (22 male, 2 female), with median age of 60 years, treated between November 2003 and August 2021 at Erlangen University Hospital, LMU University Hospital, Haukeland University Hospital, and Kantonsspital Aarau with preoperative CRT (median radiotherapy dose: 50 Gy [range: 45–56 Gy]) combined with median HT (10 sessions [range: 3–10]) were included. For all patients, HT sessions aimed to maintain temperatures between 40–43°C for 60 minutes following a preheating phase. The clinical outcomes analyzed were 2- and 5-year local recurrence free survival (LRFS), distant metastases (DM), disease-free survival (DFS), and overall survival (OS). Survival analysis was performed using the Kaplan–Meier method in RStudio with the survival and survminer packages.

**Results:** The median follow-up was 40 months (range: 6–197). Ten patients died during follow-up, resulting in a 5-year OS rate of 55.95% (95% CI: 37.41–83.67). The 2- and 5-year LRFS rates were 74.05% (95CI:58.17–94.28) and 63.03% (95CI:45.34–87.63), and DM rates were 73.43%(95CI:57.21–94.27) and 61.19%(95CI:42.89–87.32), respectively. The 5-year DFS rate was 48.12% (95% CI: 30.37–76.27). Twelve patients underwent R0 resections, 5 had R1 resections, and 1 patient had an R2 resection. Regarding tumor regression, the Dworak grading system was used: 2 patients were classified as Dworak grade 0, 2 as grade 1, 4 as grade 2, 3 as grade 3, and 4 as grade 4.

**Conclusion:** Preoperative CRT+HT can be a promising treatment approach for LRRC patients. Collaborative efforts among clinical centers should be warranted to evaluate the effect of CRT+HT in the curative setting for LRRC patients.

# Real-world outcomes of hyperthermic intraperitoneal chemotherapy (HIPEC) in patients with peritoneal surface malignancy: a Malaysian tertiary centre experience

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**Purpose:** Peritoneal surface malignancies, whether primary or secondary, are associated with poor prognosis and limited response to systemic therapy due to inadequate peritoneal drug penetration. Median survival ranges from 11–17 months for primary and approximately 6 months for secondary peritoneal cancers. Cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemotherapy (HIPEC) has emerged as a promising treatment strategy by removing tumour burden and enhancing local drug efficacy. HIPEC was introduced at University Malaya Medical Centre (UMMC) in 2018 and remains available in only a few centres in Malaysia. Given that most available data are from Western populations, this study aims to assess the outcomes of CRS-HIPEC in a Malaysian tertiary hospital setting.

**Methods:** This is a single-centre, combined retrospective and prospective cohort study involving 56 patients with peritoneal malignancies who underwent CRS and HIPEC at UMMC between January 2018 and December 2024. Medical records were reviewed to collect demographic, clinical, and outcome data. The primary endpoint was overall survival (OS); secondary endpoints included progression-free survival (PFS), post-operative morbidity, and mortality.

**Results:** Among the patients, 69.6% were Chinese, 23.2% Malay, and 5.4% Indian. The most common tumour origins were appendix/caecum (39.3%), colorectal (26.8%), and ovary/fallopian tube (19.6%). The median peritoneal cancer index score was 11. Notably, 89.3% achieved complete cytoreduction (CC-0). One patient died within 30 days postoperatively. Grade  $\geq 3$  adverse events occurred in 55.4% of patients. At three years, the overall survival rate was 71.5%, and the median OS was not yet reached. Median PFS was 8 months (range: 5–11 months).

**Conclusions:** This study provides real-world evidence on the feasibility and effectiveness of CRS-HIPEC in Malaysian patients with peritoneal malignancy. Further analysis is ongoing to identify prognostic indicators for survival and predictors of high-grade complications.

# Clinical and pathological risk factors for pathological complete response in non-elderly patients with triple-negative breast cancer receiving neoadjuvant chemotherapy

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**Background:** Pathological complete response (pCR) to neoadjuvant chemotherapy has been previously shown to be associated with improved long-term outcomes in patients with breast cancer. The current study aimed to elucidate the clinical and pathological predictors of pCR in non-elderly patients with triple-negative breast cancer treated with neoadjuvant chemotherapy.

**Methods:** We retrospectively identified 142 non-elderly patients (age < 60 years) with triple-negative breast cancer treated with anthracyclines and paclitaxel-based neoadjuvant chemotherapy. pCR was defined as absence of any residual invasive cancer observed during pathological examination of the surgically resected specimen. Univariate and multivariate logistic regression analyses were performed to identify independent predictors of pCR.

**Results:** There were 51 patients with pCR and 91 with non-pCR included. Compared to the non-pCR group, the pCR group were associated with younger age, smaller tumor diameter, lower TNM stage, lower proportions of invasive carcinomas containing a ductal in situ component, higher proportions of concomitant special histologic subtypes, and higher Ki-67 percentages. The multivariate logistic regression analysis demonstrated that age < 40 years (OR= 1.43, 95% CI 1.32-1.59), lower TNM stage (I-II vs III, OR=3.21, 95%CI 2.12-4.02), Ki-67% > 50% (OR=1.69, 95%CI 1.34-2.05) and presence of special histologic subtypes (OR=2.83, 95%CI 2.42-3.41) were independently associated with a higher probability of pCR, whereas the presence of ductal in situ component (OR=0.69, 95%CI 0.53-0.86) was associated with a lower probability of pCR.

**Conclusion:** This study demonstrated that younger age, lower TNM stage, higher Ki-67, presence of special histologic subtypes, and absence of ductal in situ components were predictors of pCR in non-elderly patients with TNBC treated with neoadjuvant chemotherapy.

# Hyperthermia in Treating Patients with Painful Unresectable Abdominal or Pelvic Malignancy

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**Background:** Efforts have been raised to improve palliative treatment for patients with symptomatic advanced malignancies that negatively affect functional status and quality of life (QOL). There are growing evidences that hyperthermia used as an adjunct to standard oncological treatment provides improved symptom and tumour control. In Malaysia, the benefits of hyperthermia have not been fully explored. We evaluated the effectiveness of hyperthermia in terms of change in pain score and QOL.

**Methods:** This was a single-center, prospective study done on 30 patients with advanced unresectable or metastatic, abdominal or pelvic malignancies, with a baseline pain score of more than 3 in University of Malaya Medical Centre, Malaysia. Patients underwent hyperthermia for 2 hours, 3 times/week for a total of 4 weeks. Pain score and QOL were assessed every week for 8 weeks with the Edmonton Symptom Assessment System (ESAS): Numerical Scale and the European Organization for Research and Treatment of Cancer (EORTC) QOL questionnaire (QLQ-C30) respectively.

**Results:** The mean pain score at baseline was 6 with an improvement to 4 at week 8 compared to baseline. There were significant differences between the groups' pain scores over 8 weeks (p-value=0.004). The mean overall QOL score was 4. There were no significant differences in the overall QOL over 8 weeks.

**Conclusion:** The implementation of hyperthermia on top of standard oncological treatments proves to be beneficial in ameliorating pain and is recommended to enhance symptom control and the overall outcome of patients with advanced malignancies.

# The Swiss National Hyperthermia Registry: From concept to implementation

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**Purpose:** To present the design and system architecture of the Swiss National Hyperthermia registry, developed to electronically collect clinical data from cancer patients receiving radiotherapy (RT) in combination with superficial, deep regional, or water-filtered infrared-A hyperthermia (HT).

**Methods:** The registry is built on a secure, web-based REDCap database, enabling automated and standardized patient data entry across Swiss clinical centers. Seven electronic case report forms (eCRFs) were designed to capture prospective data at key time points, starting from the Swiss Hyperthermia Network (SHN) tumor board decision through clinical routine follow-up. Additionally, customized Python scripts were designed to process data files generated by hyperthermia devices to compute thermometric parameters (e.g.,  $T_{10}$ ,  $T_{90}$ ,  $T_{min}$ , CEM43T<sub>50</sub>), recorded in a dedicated eCRF. Additional fields in this eCRF capture the time interval between RT fractions and HT sessions, treatment-sequencing, probe specifications, and planning details. To support consistent implementation, a detailed training manual and streamlined workflows were prepared for study personnel.

**Inclusion Criteria:** Patients presented at the SHN tumor board, who have signed informed consent (in accordance with Swiss Ethics Committee guidelines), and are treated with RT+HT, with or without concurrent systemic therapy.

**Results:** The registry infrastructure was finalized and ready for pilot testing in a small cohort at Kantonsspital Aarau, aiming to assess the usability and workflow efficiency. Afterward, the registry will be accessible for use at other Swiss clinical centers. The registry will provide real-world data for future clinical studies, offering insights into short and long-term outcomes, side effects and the relationship between thermometric parameters and treatment efficacy.

**Conclusion:** By standardizing data collection nationally, the Swiss National Hyperthermia Registry improves the quality of patient data available for analysis, leading to stronger evidence-based decisions—benefiting hyperthermia specialists, healthcare providers, and ultimately, patients.

# Three cases of long-term follow-up after combined IMRT and hyperthermia treatment for prostate ductal adenocarcinoma

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**Objective:** Prostate ductal adenocarcinoma is a histological subtype of prostate cancer known for its aggressive clinical course. We report three cases where combined treatment with intensity-modulated radiation therapy (IMRT) and hyperthermia was performed, allowing for long-term follow-up.

**Cases:** Case 1 involved an 80-year-old man who presented with bladder tamponade six years prior. A tumor infiltrating the prostatic urethra was identified, leading to a diagnosis of prostate cancer (ductal adenocarcinoma, T3aN0M0, GS 4+4, PSA 6.7) via TUR-Bt. Case 2 involved a 70-year-old patient who presented with a papillary tumor protruding into the bladder nine years ago. He was diagnosed with prostate cancer (mixed ductal and papillary type, cT3aN0M0, GS 3+4, PSA 68.3). Both Case 1 and Case 2 received maximal androgen blockade (MAB) therapy followed by IMRT (76 Gy/38 fractions) and hyperthermia (Thermotron RF-8, 5 sessions). To date, neither patient has shown PSA recurrence, clinical recurrence, or late complications. Case 3 underwent radical prostatectomy 12 years ago and was diagnosed with prostate cancer (ductal adenocarcinoma, pT3aN0M0, GS 4+4). PSA recurrence occurred 3 years and 8 months postoperatively, leading to the administration of salvage IMRT (66 Gy/33 fractions) and hyperthermia (total of 5 sessions). Three years and three months later, PSA recurrence recurred, and LH-RH agonist therapy was administered for six months. Since then, there has been no further PSA elevation, clinical recurrence, or late complications, and the patient remains in good condition to date.

**Conclusion:** The long-term outcomes of these three cases of prostate ductal adenocarcinoma treated in our department were favorable. We report these findings, emphasizing the significance of hyperthermia as an adjunctive therapy.

# Bibliometric Analysis of Hyperthermia Research: Mapping Scientific Output and Translational Potential Using the Triangle of Biomedicine Framework

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**Purpose:** We evaluated scientific output in hyperthermia research by examining publications from the International Journal of Hyperthermia (IJH) from the time period from 1960 - January 1<sup>st</sup>, 2025 using iCite data. The study employs the Triangle of Biomedicine framework to categorize articles by research focus (human/clinical, animal, molecular/cellular). It uses the Approximate Potential to Translate (APT) metric to assess translational potential from basic science to clinical applications. We compared the publication form IJH with the overall PubMed body of work.

**Methods:** We employed a bootstrap resampling approach to compare the hyperthermia literature (n = 3'483) with general medical research (n = 38'545'491), due to the extreme sample size differences. The technique involved 1'000 bootstrap iterations, each creating equal-sized samples through random sampling with replacement. For each iteration, mean and median differences, as well as Mann-Whitney U statistics, were calculated across bibliometric metrics, including citation counts, field citation rates, relative citation ratios, and research focus indicators. Statistical significance was determined through 95% confidence intervals (using 2.5th-97.5th percentiles) and the proportion of significant tests across iterations, with differences considered robust if more than 95% of iterations showed  $p < 0.05$ .

**Results:** Hyperthermia research published in IJH exhibits better performance, with higher median citations per year (+3'873), relative citation ratio (+2'138), and NIH percentile rankings (+39'907) compared to the general medical literature. Additionally, hyperthermia research involves more animal studies (+733), fewer molecular and cellular studies (-550), and has a higher applied and translational focus (+814). Human studies showed modest increases (+323). The high proportion of significant results across bootstrap iterations (mostly 9'750-10,000 out of 10,000) indicates that these findings are highly robust.

**Conclusions:** Despite representing only 0.01% of biomedical literature, hyperthermia research occupies a unique and influential position with higher practical relevance and citation impact than typical medical research.



# Commissioning of a 12-Channel 434 MHz Amplifier System Designed for the HyperCollar 3D Applicator

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**Purpose:** This study presents user acceptance testing of the novel pinkRF amplifier system for integration into Head-and-Neck hyperthermia (HT) treatments using the HyperCollar 3D (HC3D) applicator.

**Background:** A novel, compact amplifier system was commissioned for development. To qualify for clinical use, the system must meet key performance criteria:

Power per channel:  $>120$  W

Power resolution:  $<5$  W

Relative power accuracy:  $<\pm 5\%$

Phase resolution:  $<1^\circ$

Phase accuracy:  $<\pm 5^\circ$

**System Overview:** The pinkRF system consists of twelve 434 MHz amplifiers distributed across three compact 4U-high, 19-inch rack units. Amplitude and phase are controlled via a Raspberry Pi using USB, and output is monitored internally. In coherent mode, one channel serves as a reference, allowing precise phase alignment across others.

**Methods:** Performance was evaluated using a spectrum analyzer and precision power/phase meters, focusing on RF spectral behavior, power and phase accuracy, and temporal stability.

**Results:** The system demonstrates low spurious emissions ( $< -65$  dBc) and high harmonic suppression ( $>37$  dB). Power accuracy remained within  $\pm 3\%$  over 60 days. During 60-minute tests, phase drift for all channels remained within the  $5^\circ$  limit, except for two channels which briefly exceeded it ( $<1^\circ$ ) for under 5 minutes. Each channel is capable of delivering a maximum output of at least 120 W. Power can be set with a resolution of 1 W. Long-term phase stability assessment is ongoing.

**Conclusions:** The pinkRF amplifier system, configured in a compact 3×4U 19-inch rack setup, meets the stability and accuracy requirements necessary for use in a phased-array applicator designed for hyperthermia Head-and-Neck and breast cancer treatments.

## Development of Hyperthermia Treatment Planning System

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**Purpose:** Effective hyperthermia therapy requires precise planning, but current hyperthermia treatment-planning systems remain at the research level or rely on complex interworking of various software, and the commercial system has limited implementation of advanced treatment strategies by supporting only static plans. This constrains the clinical use of advanced strategies that modulate energy delivery over time. We developed and validated "OncoField Lab," an integrated HTP software platform designed to support an end-to-end workflow, including time-sequential treatment planning.

**Methods:** OncoField Lab integrates medical image segmentation, 3D mesh generation, applicator modeling, finite-element electro-thermal solvers, and temperature-volume-histogram (TVH) analysis within a single graphical user interface. The platform facilitates the design and evaluation of time-sequential plans, enabling dynamic thermal dose shaping to protect organs at risk. Numerical accuracy was validated against a leading commercial software using benchmark phantoms. Clinical utility was assessed using a virtual patient with an abdominal tumor, comparing a conventional static plan against a time-sequential plan.

**Results:** The numerical validation demonstrated high fidelity, with a root-mean-square (RMS) temperature deviation of 0.15°C relative to the reference software. In the virtual patient simulation, a static plan achieved target tumor temperatures but caused significant overheating of adjacent normal tissues. In contrast, the time-sequential plan maintained comparable tumor coverage while reducing the volume of the stomach and skeletal muscle heated above 42°C by 96.7% and 37.9%, respectively.

**Conclusions:** OncoField Lab offers a consolidated platform that addresses the challenges posed by the workflow complexities of research instruments and the functional limitations of contemporary commercial systems. The implementation of this technology is expected to facilitate the creation of both static and sophisticated time-sequential plans, thereby serving as a pivotal instrument for the execution of more precise and secure patient-specific hyperthermia therapy within the clinical domain.

## Evaluating the DICOM standard for Specific Absorption Rate (SAR) data in hyperthermia therapy, a feasibility use case study

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Hyperthermia therapy (HT) is the controlled increase of temperature of tumor tissue to 40-44°C for 60 min. HT is a proven sensitizer of radiotherapy (RT) and chemotherapy and has demonstrated a strong therapeutic effect for a number of cancer indications with minimal added toxicity.

HT commercial devices that employ radiative technology provide the capabilities of focused target heating and make use of 2D or 3D electronic steering. Analogous to RT, HT can provide conformal deposition of electromagnetic energy quantified in terms of specific absorption rate (SAR) to heat target tissue. Optimizing the balance between target coverage and healthy tissues sparing requires treatment planning and, at a minimum for treatment evaluation, the registration of the applied 3D SAR energy distribution. Currently, there is no standardized file format for 3D SAR data, unlike in RT, where the digital imaging and communication in medicine (DICOM) dose standard already exists.

This research highlights the benefits of establishing a SAR DICOM standard for HT, including:

- permitting the exchange of SAR data between entities (e.g., device interoperability, hospitals);
- enhancing HT data integrity quality assurance (e.g., to meet credentialing requirements through queried through the Advanced Technology QA Center at Washington University Medical School);
- the ability to pool patient data between institutes for prospective or retrospective multi-center trials;
- enabling the safe storage and archiving within a Picture Archiving and Communication Systems (PACS);
- enhancing clinical workflows by enabling existing RT software platforms to make the current tools available for HT.

We will demonstrate use cases such as generating SAR volume histograms for analysis of target coverage or multimodality tumor control probability modeling (e.g., treatment strategy ranking).

Furthermore, we intend to identify the data groups and elements with well-defined attributes required to adequately characterize 3D SAR data within hyperthermia treatments.

# Exploring all hyperthermia-related scientific literature indexed in PubMed to date: A bibliometric and natural language processing approach and a proof-of-concept study

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**Purpose:** Expansion of scientific publications in hyperthermia (HT) provides us with an opportunity for data-driven discovery and knowledge synthesis. We aimed to identify all HT-related publications indexed in PubMed.

**Methods:** We designed an information technology framework to process data available from PubMed using natural language processing (NLP) technology based on SciBERT document embeddings, which represent the semantic meaning of published data. To extract HT-related publications, data specialists and HT domain experts systematically compiled specific terms related to therapeutic applications of HT in oncology, based on HT-associated MeSH terms. These terms were iteratively filtered, manually reviewed, and supplemented through expert evaluation and then classified into five principal HT categories: 1. ablative HT, 2. chemotherapy-based HT, 3. whole-body HT, 4. nanoparticle-based HT, and 5. radiotherapy-based, moderate HT (RT+HT).

**Results:** All PubMed abstracts published from 1950 to end of 2024 (38'921'932) were processed and categorized into the five principal categories using applied NLP. 60'322 (0.1%) abstracts focusing on one of these five HT categories were identified. Across the entire observed period, ablative HT was the predominant topic (n=35'245, 58.4%), followed by RT+HT (n=10'476, 17.4%), nanoparticle-based hyperthermia (n=7'593, 12.6%), chemotherapy-based hyperthermia (n=4'969, 8.2%), and whole-body hyperthermia (n=2'039, 3.4%). However, a significant shift has been observed in the last five years, with a 6.9-fold growth in nanoparticle-based hyperthermia compared to 10% decrease in RT+HT.

**Conclusion:** Using the relative number and trends of publications per HT category as a simple use case, we demonstrated that our method enables future in-depth comprehensive analyses of HT-related activities across all PubMed-indexed publications. This approach offers unprecedented opportunities to obtain a more systematic and comprehensive overview of the field. Close collaboration between data scientists and HT domain experts, particularly in the developing HT terminology, is fundamental to obtaining high-quality results.

# MR Thermometry of Water and Fat at 3T using proton resonance frequency for water and component-weighted T2 for fat

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**Introduction:** Noninvasive magnetic resonance (MR) thermometry using proton resonance frequency (PRF) shift has been used in clinical thermotherapies. This method exploits the temperature dependence of hydrogen bond strength, and thus cannot be applied to adipose tissue. For adipose tissue, usefulness of the transverse relaxation time  $T_2$  considering the differences in temperature coefficients between methylene and methyl protons has been demonstrated at 9.4T. However, separately measuring the  $T_2$ -values of these proton groups remains challenging at 3T. Therefore, in this study, we conducted quantitative thermometry of adipose tissue at 3T by voxel-wise  $T_2$ -values weighted according to the proton density ratio of the two proton groups. This technique was combined with PRF to visualize temperature distribution in water-fat mixed tissues.

**Methods:** A porcine specimen containing both muscle and fat tissues was heated to 35°C in a thermostatic bath, while the other was maintained at room temperature. A fiber-optic thermometer was inserted to each sample. Both samples were then scanned at 3T. For fat,  $T_2$ -mapping was performed by water-suppressed multiecho CPMG sequence (TR/TE = 1000/32ms), and temperature was estimated using a temperature coefficient weighted by methylene to methyl ratio. For muscle, temperature was estimated by PRF shift obtained with fat-suppressed SPGR (TR/TE = 35/15ms). The temperature distribution in the mixed tissue was then quantified by calculating a weighted sum of temperature changes in each tissue type, based on their respective proton density ratios. The same methodology was applied to a localized heating using a laser.

**Results:** The MR-measured temperature in the mixed tissues was showed excellent agreement with those obtained from the thermometer. The spatial distribution of laser-induced heating was also clearly captured.

**Conclusion:** The results demonstrate that the MR thermometry technique combining PRF-based and component-weighted  $T_2$ -based temperature estimation, is feasible at 3T. This method holds promise for clinical application.

# Thermal Field Simulation for RF Capacitive Hyperthermia Considering Temperature Dependence of Blood Perfusion Rate: Validation with Probe-measured Temperature in Prostate Cancer Cases

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**Introduction:** Numerical temperature estimation plays a crucial role in the planning and evaluation of capacitive RF hyperthermia. Accurate predictions require consideration of anatomical geometry, dynamic control of heating power, and temperature-dependent tissue properties—particularly blood perfusion rate. However, clinical validation of simulation accuracy through comparison with in vivo temperature measurements remains limited. This study aimed to assess the accuracy of temperature simulations by comparing simulated and measured rectal temperatures in prostate cancer cases, in order to identify key modeling parameters that yield clinically realistic predictions.

**Methods:** Simulations were performed on three prostate cancer patients for whom in vivo rectal temperatures were recorded during hyperthermia treatment. Patient-specific anatomical models were generated from X-ray CT images. Treatments were administered in the prone position using 30 cm diameter electrodes at 8 MHz. The overlay bolus boundary was set to 15°C, ambient room temperature to 25°C, and the initial internal body temperature to 37°C. Heating duration and initial power settings were customized per case. Temperature-dependent blood perfusion was modeled using three scenarios, and simulated rectal temperatures were compared with actual measurements. All simulations were conducted using Sim4Life (ZMT, Switzerland).

**Results:** Applying a two-step increase in voltage at the start of treatment and assuming an approximately eightfold increase in blood perfusion between 42°C and 45°C produced simulated rectal temperatures that closely matched clinical measurements. These results suggest early and significant enhancement of heat transfer via blood flow in periprostatic tissues, consistent with clinical experience.

**Conclusion:** Enhancing simulation fidelity requires patient-specific anatomical modeling, realistic temperature-dependent perfusion, and reproduction of actual heating protocols. Incorporating these factors yielded temperature predictions closely aligned with clinical data. Further validation across broader clinical cases is needed to generalize this approach for treatment planning.

# Design of a High-Power Terahertz Radiation Source Using a TWT for Hyperthermia Treatment of Gastrointestinal Cancer

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Our research team confirmed the potential of cancer treatment through mouse experiments using Terahertz (THz) wave irradiation in preliminary studies. Based on these experiments, we aim to develop a THz hyperthermia cancer treatment system as a next-generation cancer therapy technology. Especially, the THz hyperthermia cancer treatment system is being developed to treat the gastrointestinal cancer such as pancreatic cancer, stomach cancer, etc. This system requires high-power THz generation devices in the sub-THz frequency band to precisely raise the temperature of only the tumor area. To achieve this, we propose to implement a Traveling Wave Tube (TWT), which is one of the vacuum electronic devices (VEDs) suitable for high-power compact devices. We introduced a novel multi-step phase-velocity taper (MPT) slow-wave circuit to overcome the limitations of output power in conventional TWTs, and confirmed its successful performance through simulation. The results demonstrate a significant 38 % performance improvement in output power more than 20W at the center frequency of 122.5 GHz. The slow-wave circuit was fabricated using Nano-scale Computer Numerical Control (Nano-CNC) technology, achieving a machining tolerance within 2  $\mu\text{m}$  and an exceptionally low surface roughness of 40 nm. Finally, the transmission characteristics of the slow-wave circuit show very similar properties to the 3D simulation predictions. These results suggest the applicability of high-power compact vacuum electronic devices in the sub-THz band for THz hyperthermia cancer treatment systems.



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