EUROPEAN Society for Hyperthermic Oncology – 37th Annual Meeting

4–6 October 2026
Erlangen, Germany

ABSTRACTS

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Keynote Lectures

KL-001

Challenges of power deposition and Heat transfer in tissue: the requirements for effective hyperthermia in combination with innovative cancer therapies

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Therapeutic mild and moderate hyperthermia at 39-43°C is a clinically proven powerful sensitizer for radiotherapy and chemotherapy. At this moment novel combinations are arising, enabling promising innovative cancer therapies promising even better outcomes. Emerging new hyperthermia combinations include combination with spatially fractionated radiotherapy (SFRT), FLASH, immune therapy, heat-sensitive liposomal drug delivery. Optimal exploitation of these new combinations requires a thorough understanding of the heat dependency of biological synergistic and complementary actions, the fundamental characteristics and limitations to invasive and non-invasive heat deposition by internal and external heating applicators, the impact of heat transport in tissue on the ability to target, focus and steer heating, and the therapeutic temperature window of temperatures ensuring efficacy in the tumor, while avoiding side effects in normal tissues which may emerge at excessive temperature levels. Each existing and emerging multi-modality cancer treatment combination including hyperthermia has different requirements regarding heating level and heat distribution.

KL-004

A century of hyperthermic oncology in Europe – a family and personal experience

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It's 50+ years since I published my first hyperthermia paper in collaboration with my father who started his research into the topic almost 100 years ago, so I have a long and detailed history within the field. My father's introduction into hyperthermia was directly linked to the pivotal study by Westermark in 1898. Thus, I have a family interest and activity which span through 3 centuries.

The presentation will reflect the development of hyperthermia in Europe, not least the interaction with radiotherapy, and the biological, translational and technical attempt toward introducing this modality into clinical oncology in general.

I have been involved in the foundation of ESHO (president 1985-87); co-founding editor-in-chief of Int J Hyperthermia and initiator and principal investigator for the randomized protocols ESHO-1, ESHO-2 and ESHO-3 – thus I have been deeply involved in the rise and fall(?) of hyperthermic oncology from the excitement initiated at the international rebirth of hyperthermia at the Washington DC symposium in 1975 and the following 10-15 years, to the more humble search for a rationale and place in current cancer management.

Overall, the presentation aims to give a description and reflection of how hyperthermia and hyperthermic radiosensitization has developed in parallel to oncology in general, and the pitfalls associated with its (lack of) general implementation so far.

The future I will leave to you to handle wisely – I'm too old to part of it.

KL-005

Keeping Hyperthermia Relevant: Evidence, Visibility, and Integration in Modern Oncology

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Hyperthermia has a strong biological rationale and established clinical value in selected indications, yet its position in modern oncology is increasingly vulnerable. Rapid advances in systemic therapy, immunotherapy, radiotherapy, and surgery are redefining standards of care, while hyperthermia is often absent from the contemporary trials that shape guidelines and clinical practice.

This presentation will examine how hyperthermia can remain relevant, visible, and evidence-based. Key priorities include embedding hyperthermia in disease-specific multidisciplinary research, generating prospective comparative evidence against current standards of care, improving treatment standardization and quality assurance, and communicating beyond the traditional hyperthermia community. Greater engagement with radiation oncologists, medical oncologists, surgeons, trial groups, guideline committees, and patient organizations will be essential. The future of hyperthermia will depend not only on preserving existing expertise, but on repositioning it as a modern treatment enhancer that addresses relevant biological and clinical questions. Without stronger integration, visibility, and contemporary evidence, hyperthermia risks being phased out despite its potential value.

Oral Presentations

Challenges of Capacitive HT

OP-004

Impact of the variation in device parameters of commercial capacitive hyperthermia systems on heating effectiveness: the need for dedicated quality assurance

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Achieving optimal therapeutic temperatures is of utmost importance for good clinical results with hyperthermia, which requires high-quality heating equipment. Consequently, dedicated radiofrequency/microwave heating devices are commercially available for specific tumor locations. In addition, many vendors provide capacitive heating devices, which apply electrode pairs on the patient to treat superficial or deep-seated tumor sites with the same device, depending on the selected electrode sizes. Although the basic heating principle is the same for all capacitive devices, device parameters vary in commercial clinical systems. Important parameters include the electrode sizes, the water bolus medium, bolus temperature and output power. This work reviews the variation in device parameters and the impact on tumor heating and quality assurance (QA).

Most effective deep heating is achieved when the electrode diameters are larger than the body diameter. The larger the difference between the electrode diameters, the more superficial the heat deposition. Optimal flexibility in heating depth thus requires a large range and number of electrode sizes. Some vendors provide up to 6 different electrode sizes (ranging 7–30cm diameter), but devices typically come with only two or three different electrode sizes, ranging 15–30cm diameter.

Most devices use a water bolus for skin cooling and to reduce surface hot spots around the electrodes. To effectively mitigate the edge effects, the water bolus is preferably somewhat larger than the electrode. Most boluses contain de-ionized water, similar to radiative devices. However, a saline bolus improves the ratio of the central SAR with respect to the superficial SAR. Additional (electrolyte-filled) overlay boluses could further improve this ratio and reduce high temperatures caused by preferential heating of the subcutaneous fat. These devices provide a much higher output power to compensate for the power loss in the bolus. The maximum continuous net output power of commercial devices also varies significantly (120–1500W).

For some devices, bolus cooling depends on the room temperature, thereby reducing controllability of superficial temperatures. However, most devices provide a flowing exchange of bolus water at a controlled temperature for deep and superficial applications (i.e., range ~10–40°C).

Sparse phantom characterizations in the literature indicate that therapeutic heating is at least possible for superficial tumors and tumors at intermediate depth. However, the differences in device parameters indicate that the heating efficacy may vary per device. This underlines the importance of dedicated QA for capacitive devices, clearly defining conditions for good quality hyperthermia and identifying clinical conditions where a capacitive device can or cannot effectively heat the intended target region. Appropriate QA and patient selection are important to ensure effective and responsible use of capacitive devices.

OP-005

Waveform-Optimized Magnetic Hyperthermia Produces Glioblastoma Regression in Mice Using Trapezoidal Pulsed Fields

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Methodology. We compared conventional sinusoidal versus trapezoidal pulsed alternating magnetic fields (AMF) for magnetic nanoparticle–mediated hyperthermia in vivo at identical settings (200 kHz, 4.29 mT). Superparamagnetic iron-oxide nanoparticles (10.6 ± 0.2 nm) were synthesized and injected intratumorally into heterotopic CT2A glioma tumors established in C57BL/6 mice. Animals (n=10/group) were randomized into six groups combining presence or absence of nanoparticles and AMF, including treatment arms receiving nanoparticles plus sinusoidal AMF or nanoparticles plus trapezoidal pulsed AMF. Treatments were delivered under anesthesia for three consecutive days (1 h/day), with repeated intratumoral nanoparticle dosing over the first three days; tumor dimensions were measured by calipers through day 4, tumors were excised and weighed on day 5, and thermal imaging monitored body temperature during exposure.

Results. AMF exposure alone did not change tumor growth versus untreated controls, and nanoparticles alone did not inhibit progression. Combining AMF with nanoparticles reduced tumor burden with a marked waveform dependence: sinusoidal AMF produced growth delay (final normalized size ~1.42 versus ~1.77–1.99 in controls) with statistical significance only at the last measurement, whereas trapezoidal pulsed AMF produced regression (final normalized size ~0.82, i.e., ~18–20% below baseline). Final normalized tumor weight followed the same pattern, with the trapezoidal pulsed arm showing the largest reduction (~2.4 mg/mm² versus ~4.1–4.4 mg/mm² in controls and ~3.72 mg/mm² with sinusoidal AMF). Immunofluorescence showed stronger HSP70 and activated caspase-3 labeling in treated tumors, most prominently with trapezoidal pulsed AMF, consistent with heightened stress responses and apoptosis in regions containing nanoparticle deposits.

Conclusions. Trapezoidal pulsed AMF substantially improved the therapeutic efficacy of magnetic hyperthermia in a murine glioblastoma model compared with a conventional sinusoid under the same low-intensity field conditions, achieving tumor regression and a pronounced reduction in tumor weight. These findings support waveform optimization as a practical lever to enhance magnetic hyperthermia performance while remaining compatible with conservative safety constraints, and they motivate further mechanistic and translational studies.

References.

[1] Rodríguez García MR, Martínez Montero S, Serrano-Olmedo JJ, Ramos-Gómez M. Trapezoidal Pulsed Magnetic Fields Enhance the Therapeutic Efficacy of Magnetic Hyperthermia in a Glioblastoma Mouse Model. Manuscript under review.

OP-006

A Configurable RF Exposure Platform for Reproducible *In Vitro* Investigation of Thermal and Non-Thermal Electromagnetic Field Effects

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Introduction and Goal. Whether cellular responses to radiofrequency (RF) electromagnetic fields arise from heating or from non-thermal mechanisms remains a central and unresolved question in bioelectromagnetics. Investigating such effects requires exposure systems that independently control temperature and field parameters such as frequency, modulation, field strength, field direction while facilitating reproducible experiments. We present an early prototype of a purpose-built RF applicator designed to expose cells in 35 mm Petri dishes to electromagnetic fields simultaneously in triplicates, enabling direct on-plate comparison under matched conditions.

Methods. The system (Fig. 1) comprises an RF source capable of continuous-wave or amplitude-modulated output (tonal or noise modulation), followed by a Hubert A1020-25-250 power amplifier (Dr. Hubert GmbH, Bochum, Germany) with 40 dB of gain and 20 W maximum output. A Bruene-bridge directional coupler equipped with two AD8310 logarithmic detectors (Analog Devices Inc., Wilmington, U.S.) continuously monitors incident and reflected power, enabling real-time impedance characterization. A tunable matchbox, constructed from high-Q components for low-loss operation, achieves resonant matching at the target frequency. The system has been validated at 6.825 MHz and 13.65 MHz.

The applicator (Fig. 2) is a temperature-controlled waterbath housing a 3D-printed holder for three 35 mm dishes. The RF field is coupled via two copper electrodes (150 mm x 25 mm each). A closed water-circulation loop and a feedback control loop, informed by a four-channel Luxtron M330 fiber-optic thermometer (Advanced Energy, Denver, U.S.), maintains the intradish temperature at a user-defined setpoint. Three probes are introduced through 0.8 mm ports in the dish lids; their non-metallic construction eliminates RF detuning. The fourth probe measures the temperature of the surrounding water. The system is controlled via a web interface on a Raspberry Pi 4B (or any compact single-board computer), which acquires power and temperature data, executes the thermal control loop, and logs all measurements downloadable as CSV files.

Results. Simulations in CST Studio (Dassault Systèmes, Rhode Island, U.S.) revealed excellent field homogeneity in the Petri dish region. Validation was performed using 3 ml agar phantoms in 35 mm dishes, matching typical cell-culture medium volumes. Without forced water circulation, the system elevated phantom temperature up to 5 °C above the bath, covering the physiologically relevant range from 37 °C to 42 °C, adequate for both hyperthermic and normothermic exposure conditions. To probe directional non-thermal effects, dishes can be manually rotated within the applicator.

Summary. This platform provides a reproducible and flexible tool for systematic *in vitro* bioelectromagnetics research under controlled thermal and non-thermal conditions.

Fig 1: System block diagram

Fig 2: Photo of applicator

Fig. 1

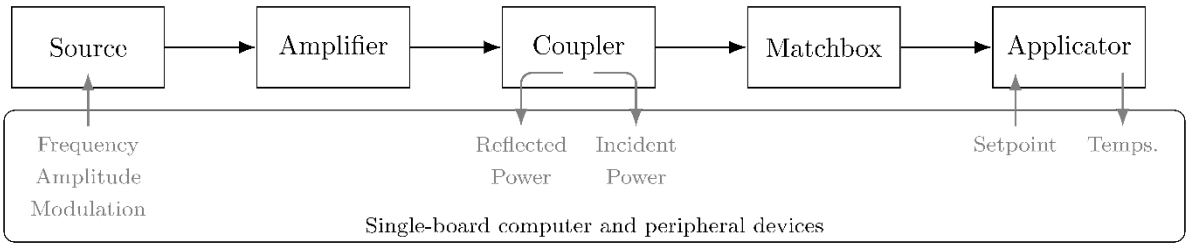
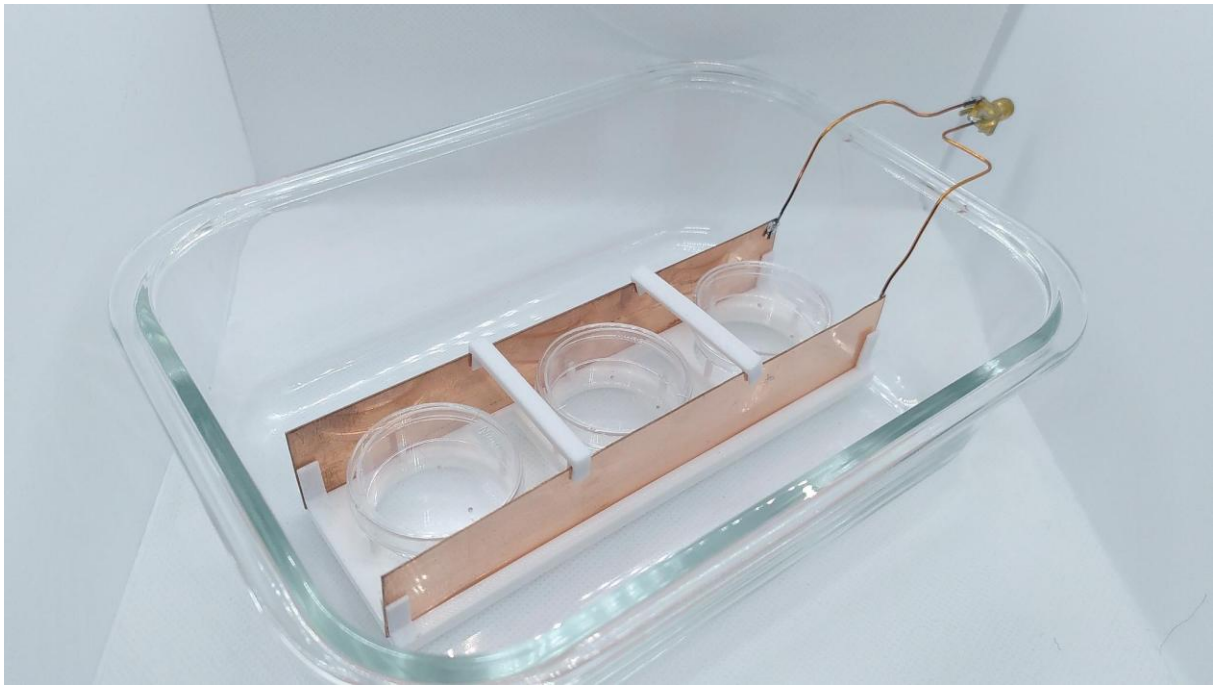

Source
Amplifier
Coupler
Matchbox
Applicator
Frequency
Amplitude
Modulation
Reflected
Power
Incident
Power
Setpoint
Temps.
Single-board computer and peripheral devices

Fig. 2



OP-007

International Survey on Clinical Practice Patterns of Capacitive Hyperthermia: An Initiative of the ESHO Capacitive Hyperthermia Working Group

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Question. Capacitive hyperthermia is widely utilized in combination with radiotherapy, chemotherapy, and emerging immunotherapy approaches; however, substantial heterogeneity exists in clinical protocols, treatment timing, thermometry practices, and technical parameters among institutions and countries. In contrast to radiative hyperthermia systems, international data regarding the real-world implementation of capacitive hyperthermia remain limited. To address this gap, the ESHO Capacitive Hyperthermia Working Group initiated an international survey to characterize current clinical practice patterns and technical approaches in capacitive hyperthermia.

Methods. An international questionnaire-based survey was developed by the ESHO Capacitive Hyperthermia Working Group to collect institution-level data regarding clinical and technical practices in capacitive hyperthermia. The survey targets centers using various capacitive hyperthermia platforms, including 8 MHz and 13.56 MHz systems, as well as emerging resistive-capacitive technologies. The survey assesses device utilization, treatment indications, integration with radiotherapy and systemic therapies, thermometry practices, treatment parameters, and reimbursement issues.

Participating institutions were asked to provide anonymized aggregate information only, without patient-level data.

The primary objective is to evaluate international variability in clinical implementation and technical protocols. Secondary objectives include assessment of thermometry utilization (and registered thermometric parameters), synchronization strategies with multimodal therapies, and perceived future roles of capacitive hyperthermia in combination with advanced radiotherapy and immunotherapy.

Results. Data collection from the survey is currently ongoing. Preliminary analyses will include descriptive statistics of institutional practices, device distribution, treatment timing relative to radiotherapy, thermometry implementation rates, and disease indications across participating countries and regions. Final analyses and updated results will be presented at the meeting.

Conclusions. This international survey represents one of the first collaborative efforts to systematically characterize real-world clinical practice patterns of capacitive hyperthermia across multiple countries and institutions. The findings may support future standardization efforts, optimization of evidence-based treatment protocols, and development of international consensus recommendations for capacitive hyperthermia.

Atzelsberger Circle

OP-016

Durable Local Control with Definitive Radiotherapy and Regional Hyperthermia in Unresectable Soft Tissue Sarcoma: A Retrospective Cohort Analysis

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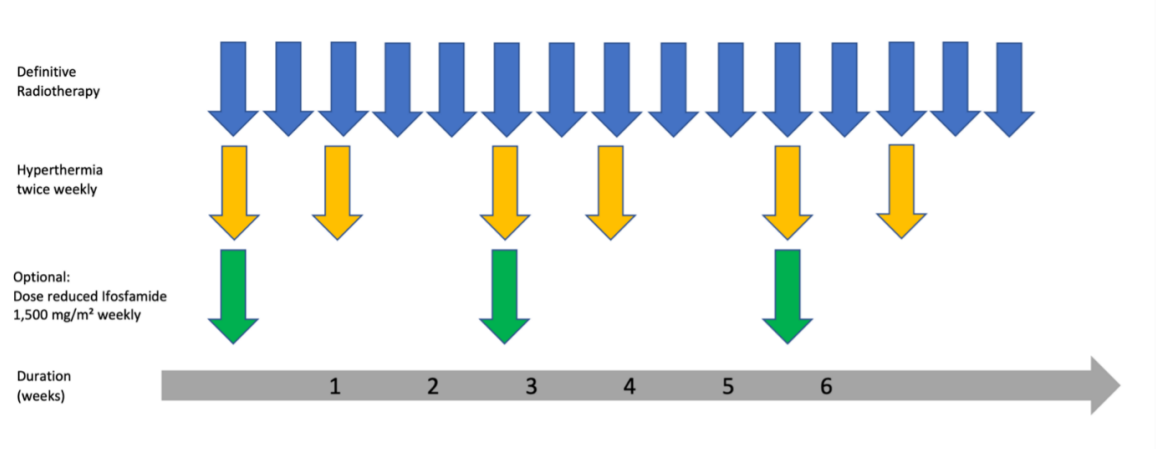
Background. Definitive radiotherapy (defRT) combined with regional hyperthermia (RHT) is a promising approach to improve local tumor control in unresectable soft tissue sarcoma (STS). Multimodal strategies incorporating defRT, RHT, and ifosfamide-based chemotherapy (CT) have shown encouraging results in small studies but lack validation in larger cohorts.

Methods. We retrospectively analyzed 42 patients with unresectable STS treated with defRT plus RHT, with or without concurrent dose-reduced ifosfamide CT as a radiosensitizer. Endpoints included feasibility, toxicity, and survival outcomes such as local progression-free survival (LPFS), distant metastasis-free survival (DMFS), and overall survival (OS). Treatment response (overall response rate [ORR], disease control rate [DCR]) was assessed according to RECIST v1.1. Prognostic factors were evaluated using multivariate and Lasso-penalized Cox regression models.

Results. Median RT dose was 60 Gy. RHT was administered twice weekly (median 8.3 sessions). Treatment feasibility was high: 93% of patients completed RT, and RHT was discontinued in 10%. Radiation-related toxicities ≥ grade 2 occurred in 14% of patients. Median LPFS, DMFS, and OS were 21.6, 13.2, and 31.2 months, respectively. ORR was 22%, while overall and local DCR were 75% and 79%. Metastatic disease at treatment initiation was an independent adverse factor for DMFS (HR 4.39, p=0.001) and OS (HR 10.09, p<0.001), while recurrent disease predicted worse LPFS (HR 4.28, p=0.036). Distant progression exceeded local failure over time. The addition of dose-reduced ifosfamide CT did not improve survival.

Conclusion. DefRT combined with RHT is a feasible treatment approach with durable local control and encouraging survival in unresectable STS. The addition of dose-reduced ifosfamide CT did not confer a survival benefit.

Fig. 1



OP-017

Clinical Experience in Treating Low-Seated Hyperthermia Target Volumes Near the Vulva with Hyperthermia and Radiotherapy

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Introduction. Patients with low-seated hyperthermia target volumes (HTVs) near the vulva pose treatment challenges, particularly in recurrent disease or when chemotherapy is contraindicated. Hyperthermia combined with radiotherapy is a potential alternative but is technically complex. This abstract reports our clinical experience, focusing on practical challenges and mitigation strategies.

Methods. Fourteen patients with low-seated HTVs near the vulva treated with hyperthermia and radiotherapy between 2023 and 2026 were included. Superficial hyperthermia was applied for tumors ≤4 cm, while deep hyperthermia was used for deeper lesions. Deep treatments used Sigma 60 or Sigma Eye applicators; superficial treatments used lucite cone applicators.

Treatment planning was CT-based and included tissue segmentation, patient contouring, and applicator simulation using Sim4Life, with VEDO used for energy optimization. Temperature monitoring included vaginal, rectal, and bladder probes (≤10 cm).

Results. Standard applicator positioning for pelvic targets frequently caused excessive heating in the labial region. Achieving optimal energy distribution required an adaptive planning approach. Cranial displacement and slight tilting (±5°) improved tumor coverage and reduced heat accumulation in the labial region.

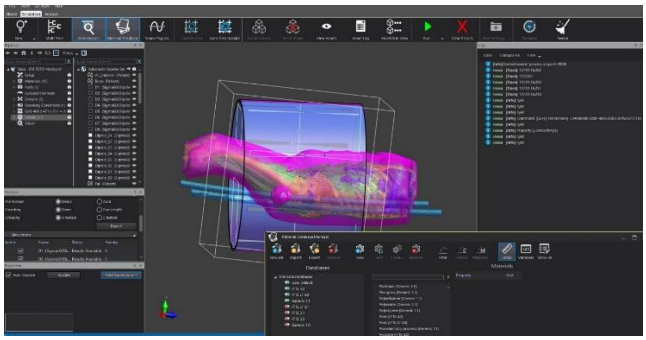
Patients with low-seated HTVs near the vulva were particularly prone to labial overheating. Limited thermometry due to patient-related factors, such as pain or bleeding, necessitated reliance on clinical judgment. The first two patients developed severe labial burns; no further cases occurred after preventive measures. Adding two surface probes in high-risk regions, alongside rectal, bladder, and vaginal probes, improved safety and treatment control.

For lesions <1 cm from the skin but extending deeper than 4 cm, a 39°C water bolus was applied during deep hyperthermia, ensuring therapeutic heating while protecting the skin.

Back pain was the most common complaint (10 patients); in eight cases, a 20 × 20 cm water bolus under the back provided relief. Pain and abdominal pressure were further managed with short treatment pauses, localized power reductions (50–100 W), and adjustments in water bolus filling. Less severe complaints in the hips, legs, and lower back were controlled using localized regions of reduced heating with adjustable size, intensity, and position. Elderly patients required slower power escalation to ensure tolerability.

Conclusion. Treatment of low-seated HTVs near the vulva with adjuvant hyperthermia is feasible but technically demanding. Effective delivery requires adaptive planning, strategic thermometry, and real-time adjustments. Additional water boluses during deep hyperthermia allow adequate heating while minimizing skin toxicity. Patients with low-seated HTVs near the vulva require particular attention to prevent labial overheating. Sharing practical experience is essential to optimize treatment safety and delivery.

Fig. 1



OP-018

Timing Matters: Regional Thermochemotherapy During Early Local Failure in High-Risk Pediatric Rhabdomyosarcoma

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Background. Failure of local tumor control remains one of the principal determinants of poor outcome in high-risk pediatric rhabdomyosarcoma (RMS). However, patients with inadequate response during frontline therapy are frequently analyzed together with patients experiencing established relapse, despite marked biological and clinical differences between these disease states. We explored whether intensified thermochemotherapy may be particularly effective during the transitional phase of early treatment resistance, before fully evolved relapse biology emerges and relapse-associated tumor biology becomes dominant.

Methods. Children and adolescents with localized refractory or recurrent RMS and RMS-like soft tissue sarcomas were prospectively treated within an institutional Hyper-PEI–based treatment strategy. Therapy combined multi-agent chemotherapy (etoposide/ifosfamide with cisplatin or doxorubicin, days 1–4) with locoregional microwave hyperthermia (41–43°C, days 1 and 4). Salvage radiotherapy was administered when clinically indicated. Radiographic response, secondary resectability, event-free survival (EFS), and overall survival (OS) were analyzed longitudinally.

Results. Fifty-four consecutive pediatric patients (median age 4.9 years) were treated within an institutional Hyper-PEI–based treatment strategy. Histologies included embryonal RMS (n=37), alveolar RMS (n=11), undifferentiated sarcoma (n=4), and synovial sarcoma (n=2). Objective responses were observed in approximately 43% of evaluable patients, while overall disease stabilization approached 90%. Secondary local control strategies became feasible in approximately 75% of patients, with R0/R1 resection achieved in over 80% of operated cases. A striking divergence emerged between patients treated during primary treatment resistance and those treated after overt recurrence. Patients receiving thermochemotherapy during early refractory disease demonstrated substantially superior long-term outcome, whereas patients treated after relapse frequently developed progressive metastatic dissemination despite initial local response. These findings suggest that timing of intervention may be biologically more relevant than treatment intensity alone.

Conclusions. Our data support a conceptual distinction between primary refractory RMS and recurrent RMS as biologically different therapeutic states. Early integration of regional thermochemotherapy during evolving treatment resistance may create a critical window for durable local control before metastatic escape mechanisms dominate disease progression. Rather than functioning solely as a late salvage modality, regional hyperthermia may represent a treatment-modifying strategy for biologically high-risk localized disease, particularly in the refractory setting before overt relapse biology becomes established.

Funding. Deutsche Krebshilfe e.V., Bonn, Germany; Elterninitiative Kinderkrebsklinik Düsseldorf e.V., Germany.

Quality assurance for treatment delivery

OP-019

Comparison of TFI and PDF for Susceptibility Correction in MR Thermometry during RF Hyperthermia of Soft Tissue Sarcomas

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Introduction. Mild radiofrequency hyperthermia (HT) combined with radio- and chemotherapy is an established treatment for soft tissue sarcoma. Proton resonance frequency shift (PRFS) MR thermometry enables non-invasive real-time temperature monitoring during treatment but is sensitive to magnetic field variations such as B_0 drift and motion-induced susceptibility changes. Background field removal methods from quantitative susceptibility mapping (QSM), including Projection onto Dipole Fields (PDF) and Total Field Inversion (TFI), may reduce susceptibility-induced artifacts during MR-guided hyperthermia.

Methods. Data from 30 patients with soft tissue sarcoma who underwent MR-guided HT at LMU Klinikum between April 2020 and January 2023 were retrospectively analyzed (16 lower extremities, 14 pelvis). Temperature maps were reconstructed from PRFS phase differences.

Three correction strategies were compared: (1) linear B_0 drift correction using oil reference tubes integrated into the applicator (clinical standard), (2) PDF-based background field removal, implemented using the MEDI toolbox [1,2], and (3) ℓ_1-regularized TFI, applied as described in [3,4].

Mean temperatures were evaluated within tumor, subcutaneous fat, and healthy muscle region of interests (ROI) for each treatment session. Fat and muscle ROIs served as references for residual temperature bias and correction performance, as no heating is expected in these tissues. Mean ROI temperature changes (ΔT) during HT were calculated after exclusion of the initial 30-minute warm-up phase. Correction methods were compared regarding residual temperature offsets, variability, and susceptibility-related artifacts in the reconstructed temperature maps.

Results. Mean ROI temperature changes (ΔT) during HT for all patients and correction methods are shown in fig. 1. Compared with uncorrected PRFS thermometry, all correction methods reduced residual temperature offsets in non-heated fat tissue. TFI maintained tumor temperature elevations comparable to linear drift correction, indicating effective susceptibility correction without evident attenuation of true heating. In contrast, PDF tended to overcorrect tumor heating, resulting in lower estimated temperature elevations across all ROIs. TFI showed the narrowest distribution of temperature values within tumor ROIs, consistent with the expected temperature increase during HT.

Both TFI and PDF reduced susceptibility-related artifacts in the temperature maps (example shown in fig. 2). The strongest improvements were observed in the pelvic region, where susceptibility-induced artifacts are most pronounced.

Conclusion. TFI-based susceptibility correction improves the robustness of PRFS MR thermometry compared with conventional drift correction and PDF, particularly in the susceptibility-prone pelvic region.

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[2] Wu, MRM 2020
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[4] Boehm, MRM 2022

Fig. 1

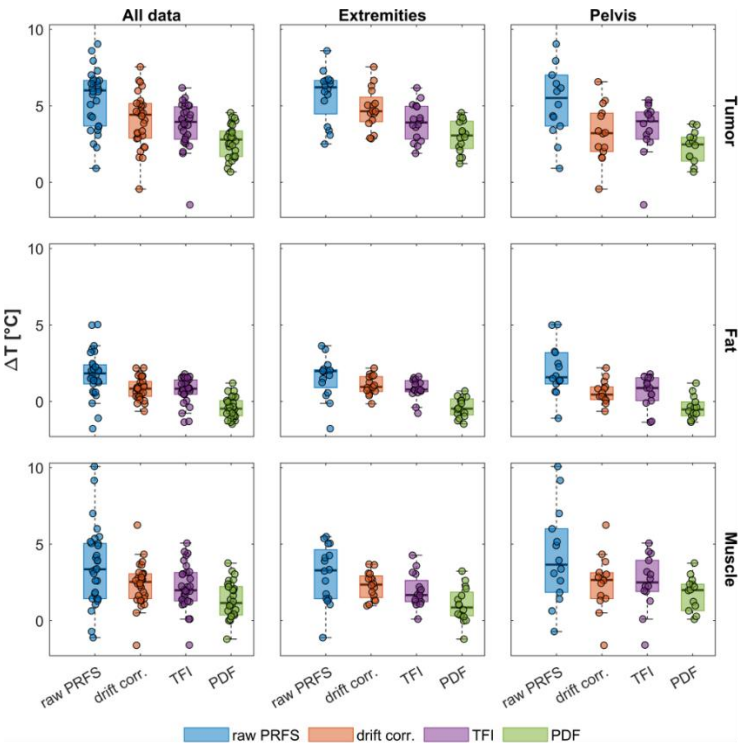

Figure 1: Mean temperature changes (ΔT) in tumor, fat, and muscle ROIs during HT for all patients, and subgroups lower extremities and pelvis. Results are shown for uncorrected (raw) PRFS, standard B_0 drift correction, TFI and PDF.

Fig. 2

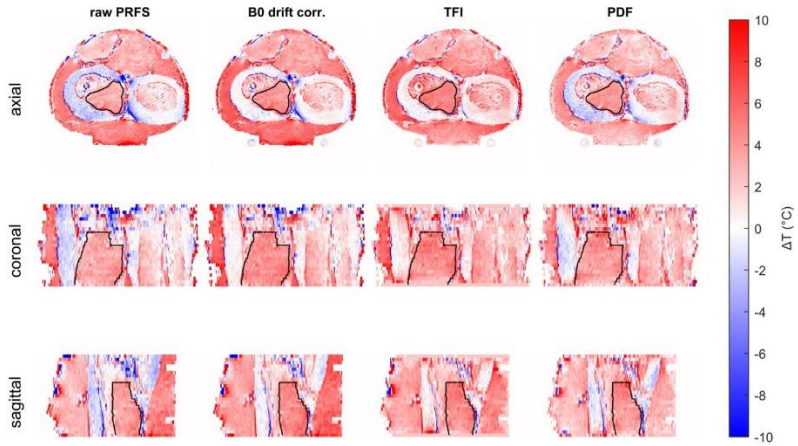

Figure 2: Representative temperature maps reconstructed using raw PRFS, drift correction, TFI, and PDF. TFI most effectively suppresses the dipole-shaped susceptibility artifacts while maintaining tumor heating and near-baseline temperatures in non-heated fat tissue.

OP-020

The need and utility of an independent multichannel measuring system in Hyperthermia

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Introduction. To perform high quality deep hyperthermia it is important that the resulting temperature distribution is accurate and stable. Since applied power and phase result in a specific absorption ration (SAR) and drives the temperature distribution, it is crucial that these entities are accurate.

Commercial hyperthermia systems such as the BSD-2000 (Pyrexar, Utah) record treatment powers and phases but these measurements are mostly not used to provide real-time updates of the resulting SAR/temperature distribution and can be error prone due to phase shifters, read errors, or frequency sensitivities.

At Erasmus MC, we implemented an independent multi-channel measurement system (MMS, Alba, Rome) capable of directly monitoring forward & reflected power, and forward phase across all channels. These measurements are used to generate real-time SAR distribution updates, providing clinicians with visual cues that may indicate potential hotspots in the patient. Due to the independent nature of the MMS system, we believe it can also serve as a valuable quality assurance tool to assess the health and stability of the BSD delivery system.

Goals. The goal of this work is to investigate the value of the MMS system as a quality assurance tool for deep hyperthermia treatments.

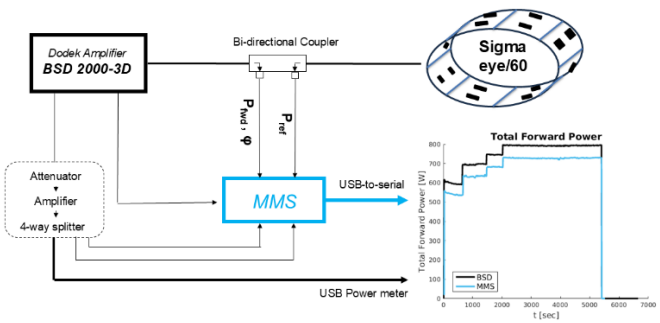
Methods. Equally weighted power and uniform phase treatments were delivered to simple uniform phantoms. A third calibrated power meter (PM) and a vector voltmeter (VVM) were used to verify our MMS against our BSD-2000 system for the Sigma-eye and Sigma-60. Patient treatment data from December 2024 and on were exported from the BSD system. Forward and reflected powers and forward phase were extracted per channel and compared to our MMS system.

Results. For the Sigma-eye, the agreement between the VVM and the BSD, MMS on forward power was 2.6% and 2.8%, respectively; this improved to 1.7% when looking at the combined average of the BSD and MMS against the VVM. For the Sigma-60, this was 6.1% and 5.4%, respectively; this improved to 3.2% for the combined average. The reflected powers and forward phases were 5% and 4 degrees different, both for the BSD and MMS against the VVM for Sigma -eye. For Sigma-60 larger difference in the reflected powers and forward phases were found, these were 8.9%, 9 degrees (BSD vs VVM) compared to 2.7%, 2.6 degrees (MMS vs VVM).

When plotting the difference in total power between BSD and MMS over time from the patient treatment data, this showed that significant increases in the power differences can easily be detected. The difference in power can be plotted per channel, which can quickly reveal if a channel needs adjustments.

Conclusion: An independent, multichannel monitoring system is not only useful to integrate into real-time feedback on measured SAR distributions but can also be used to ensure agreement of the primary delivery system.

Fig. 1



OP-021

Hyperthermia Quality Assurance Program of the SAKK 57/24 TNT-HYPE multicenter phase II soft tissue sarcoma study

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[2] Inselspital, Bern University Hospital, University of Bern, Department of Radiation Oncology, Bern, Switzerland
[3] Ente Ospedaliero Cantonale (EOC), Medical Physics Unit, Institute for Integrated Diagnostics of Switzerland (IDISI), Bellinzona, Switzerland
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[5] Swiss Cancer Institute, Competence Center, Bern, Switzerland

Introduction. The multicenter SAKK 57/24 TNT-HYPE study (NCT06835049) investigates the effect of locoregional hyperthermia (HT) administered concomitantly with neoadjuvant chemotherapy in soft tissue sarcoma. A prerequisite for multicenter studies is a quality assurance (QA) program for all participating centers in order to ensure consistent clinical treatments across all sites.

Goals. For the HT QA program a HT manual was developed defining HT target delineation, treatment planning, and treatment delivery. Compliance was secured using a facility questionnaire and a HT dummy run. Technical equipment QA was ensured through an external heating audit. Three criteria were defined and checked which fulfil the QA requirements of the European Society for Hyperthermic Oncology (ESHO). The ability to create (1) a focal area of the electrical field (E-field) in the center of a homogeneous phantom, (2) to shift the focal area by changing the phase settings of the individual antennas and (3) the ability to increase the temperature in a homogenous tissue equivalent phantom by 6°C within 10 minutes were assessed. The three criteria are part of the upcoming QA guideline developed by the ESHO technical committee currently submitted for publication.

Materials and Methods. All three study centers offering HT use an ALBA4D radiative HT device (MED-LOGIX SRL, Rome, Italy). To evaluate the first and second criterion the E-field distribution in horizontal, vertical and longitudinal direction was recorded using an elliptical phantom filled with a saline solution. Inside the phantom an isotropic E-field probe (EASY4/MRI, SPEAG, Zürich, Switzerland) was moved in three dimensions and the strength of the E-field was recorded.

For the third criterion a tube of 31.5 cm diameter was filled with tissue equivalent wallpaper paste and heated for 10 minutes at 1200 W total emitted power. The temperature increase inside the phantom was recorded with thermometers placed inside tubes in the phantom.

Results. The recorded E-field distribution curves showed a focal area in the physical centre of the homogeneous phantom (criterion 1). By adjusting the phase of each antenna, it was possible to adjust the location of the focal area (criterion 2). All three devices increased the temperature in the phantom by 6°C or higher after a pulse of 1200W for 10 minutes (criterion 3). The results are summarized in the tables below.

Summary. All criteria for technical QA were passed by the three institutes taking part in the study. The measurements of the position of the focal area with the E-field scanning phantom are fast and can be repeated easily within a one-day measurement session. The temperature rise measurements however are very time consuming and therefore critical if measurement time is limited.

Acknowledgements. This study was funded by a Swiss National Science Foundation (SNSF) grant to ES and AK and by the Swiss Cancer Institute

Fig. 1

Criterion 1

Institute	A	B	C
Average deviation from center in X [mm] Tolerance ± 20mm	5.10	-4.34	-1.43
std dev [mm]	0.02	1.15	3.97
Average deviation from center in Y [mm] Tolerance ± 20mm	-2.03	-1.09	-6.81
std dev [mm]	0.51	0.33	2.1
Result	Passed	Passed	Passed

Criterion 2

Institute	A	B	C
Focus can be shifted by phase steering	yes	yes	yes
Result	Passed	Passed	Passed

Criterion 3

Institute	A	B	C
Maximum temperature increase	6.9°C	7.7°C	6.8°C
Required temperature increase	6°C	6°C	6°C
Result	Passed	Passed	Passed

OP-022

Two-layer Hybrid Optimization for Hyperthermia Treatment Planning: Surrogate Optimization Combined with Pattern Search

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Introduction. Optimization is a crucial step in hyperthermia treatment planning. Several optimization algorithms have been proposed, including Particle Swarm Optimization (PSO) and other global or local methods. The selected algorithm influences both the quality of the resulting plan and its reproducibility across repeated runs. Combining a global search algorithm with a local refinement step within a single workflow may improve solution quality while maintaining acceptable computation time.

Goals. The aim of this study was to evaluate a two-layer hybrid optimization strategy for SAR-based HTP in brain tumor and head and neck tumor patient models, combining Surrogate Optimization (SGO) for initial global search with Pattern Search (PS) for deterministic local refinement, and to compare it with standalone SGO and PS in terms of treatment quality, computation time, and stability.

Materials and Methods. SGO+PS was implemented in MATLAB and evaluated on patient-specific 3D models of three brain tumors and three head and neck tumor patients simulated using a 12-channel generic dipole antenna array at 434 MHz. Antenna amplitudes and phases were optimized using THQ as the objective function. In the hybrid workflow, SGO was first run with a reduced evaluation budget to obtain an initial solution, which was subsequently refined by PS within a narrowed search space. Standalone SGO and SGO+PS were repeated five times per patient; standalone PS was evaluated once as a deterministic reference. All computations were performed on CPU without GPU acceleration.

Results. For most evaluated patients, all methods achieved TC25 of 100%, indicating complete target coverage. The only exception was one head and neck patient, where standalone PS achieved notably lower TC25 than both SGO-based methods. THQ was comparable across all methods, with PS refinement improving the initial SGO solution in all 30 runs. SGO+PS substantially reduced computation time compared with standalone PS while remaining comparable to standalone SGO. Key results are summarized in Table 1.

Summary. SGO+PS achieved treatment quality comparable to both standalone methods while substantially reducing computation time relative to standalone PS. TC25 of 100% was reached in five of six patients, with stable and consistent results across repeated runs. These preliminary results suggest that combining surrogate-based global exploration with deterministic local refinement may represent an efficient approach for SAR-based HTP.

Fig. 1: Comparison of optimization strategies.

Metric	Patient group	SGO (median)	PS	SGO+PS (median)
TC25 (%)	Brain	100	100	100
H&N	100	46.2	93.5	
THQ	Brain	0.398	0.432	0.394
H&N	0.358	0.347	0.357	
Runtime (s)	Brain	642	3013	535
H&N	565	2036	528	
Runs per patient	—	5	1	5

OP-023

Compensation of Flow-Induced Thermal Washout in Large-Volume MR-HIFU Hyperthermia Using a Perfusion-Adaptive Control Algorithm in a Dynamic Flow Phantom

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[2] University of Cologne, The Interdisciplinary Program Health Sciences, Cologne, Germany
[3] University of Cologne, Cologne, Germany

Introduction. Mild hyperthermia (41-43 °C) is an established adjuvant cancer therapy. Magnetic resonance-guided high-intensity focused ultrasound (MR-HIFU) enables non-invasive volumetric heating using proton resonance frequency shift (PRFS)-based thermometry, electronic beam steering, and mechanical transducer displacement. However, homogeneous heating of clinically relevant volumes remains challenging due to heat-sink effects, particularly in multi-position sonication cells where temperature control must be maintained across multiple dynamically heated subcells.

Goals. To develop and experimentally validate a perfusion-adaptive control (PAC) strategy for volumetric MR-HIFU hyperthermia capable of compensating flow-induced thermal washout while maintaining temperature stability, spatial accuracy, and thermal coverage under physiological flow conditions.

Materials and Methods. A flow phantom was fabricated using a 3D-printed PVA bifurcated vessel embedded in PAA tissue-mimicking material. Fluid was circulated under physiological conditions (37 °C, 0.26 m/s) using a peristaltic pump. Hyperthermia was delivered using a clinical MR-HIFU system (Profound Medical, Philips Healthcare) operated at 60 W and 1 MHz using a 32 mm treatment cell. PAC used real-time MR thermometry to monitor mean temperature ($\bar{T}_i$), temperature percentiles (T_{10i}, T_{90i}), and a thermal curvature index ($\Lambda_i = \nabla^2 T_i$). Elevated thermal gradients triggered adaptive redistribution of acoustic energy across subcells. Treated volume was defined by 50% time-in-range (TIR50) contours. Volumetric reconstruction from sagittal thermometry assuming rotational symmetry yielded a nominal ellipsoidal volume of 49.8 mL.

Results. Under flow conditions, the conventional controller maintained a mean temperature of 40.8 ± 1.0 °C relative to the 42.5 °C target, while thermal dose (CEM43) decreased by 64%. The TIR50 coverage volume decreased from 49.3 mL to 1.35 mL. The measured heating depth was 86.9 ± 14.0 mm, with an effective diameter deviation of 5.3 ± 2.9 mm from the prescribed treatment cell.Using the perfusion-adaptive controller, the mean temperature was 42.0 ± 0.8 °C, and CEM43 reached 18.7 min. The TIR50 coverage volume measured 32.8 mL and a total energy of 33.8 kJ. Heating efficiency was 0.13 °C/kJ, while spatial temperature variability across subcells decreased from 1.8 °C to 0.9 °C.

Summary. The proposed PAC robustly compensated flow-mediated thermal washout during volumetric MR-HIFU hyperthermia, restoring target temperature, spatial accuracy, and thermal coverage in multi-position sonication cells under physiologically realistic perfusion conditions, supporting clinically efficient large-volume hyperthermia treatment planning.

Fig. 1: Experimental setup: (A) 3D MR model of a human femoral vein. (B) Segmented vessel model. (C) Custom-made perfusion phantom. (D) MR-HIFU experimental setup.

Fig. 2: Thermal dose and TIR contours during 30 min hyperthermia in a 32 mm treatment cell under flow without compensation (A) and with PAC (B).

Fig. 1

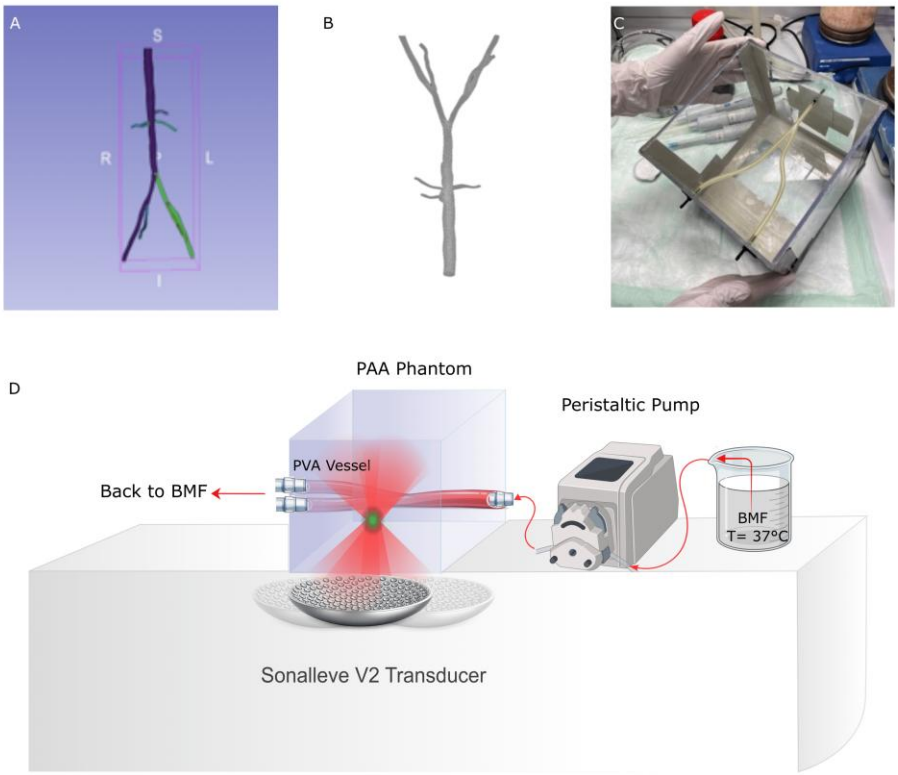
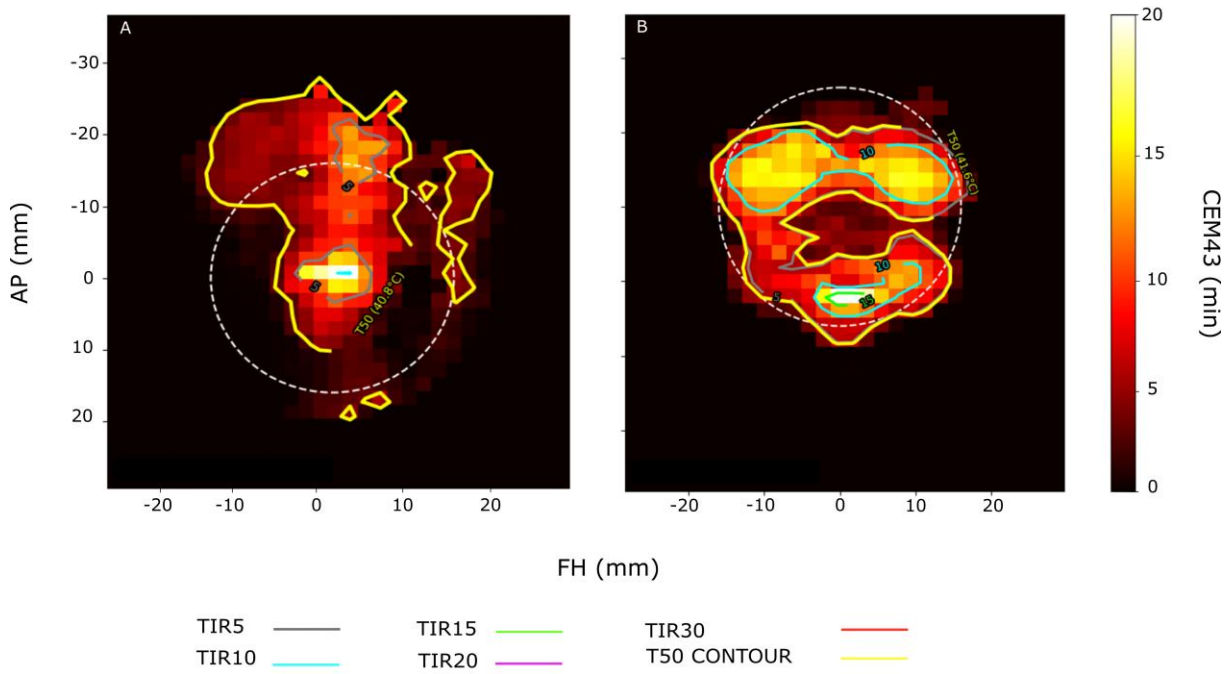

A
S
R
L
I
B
C
D
PAA Phantom
Peristaltic Pump
PVA Vessel
Back to BMF
BMF
T= 37°C
Sonalleve V2 Transducer

Fig. 2


A
B
AP (mm)
FH (mm)
CEM43 (min)
T50 (40.8°C)
T50 (41.6°C)
TIR5
TIR10
TIR15
TIR20
TIR30
T50 CONTOUR

OP-024

Accurate Characterization of ALBA ON 4000D superficial hyperthermia applicators using robotized high-resolution E-field scans

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[1] Amsterdam University Medical Center, Radiotherapy, Amsterdam, Netherlands

Introduction. The Alba On 4000D radiative 434 MHz superficial hyperthermia system uses 5 different sized microstrip applicators to deliver therapeutic heating up to 4 cm depth with a maximum area up to 609 cm^2 for superficial treatments. Characterization of the power deposition by means of quality assurance (QA) measurements of the distribution of these applicators is essential to ensure good control over treatment quality and for reliable treatment planning predictions. Fast routine clinical QA is important and requires automated measurements, similar to the procedure for dosimetric characterization in radiotherapy.

Goals. The characterization of all available Alba applicators by determining the effective field size (EFS), effective penetration depth (EPD) and 3D Specific Absorption Rate (SAR) distribution patterns using robotized high-resolution E-field measurements.

Materials and Methods. The alfa, beta, gamma, delta, omega applicators were characterized; power was delivered using a 434 MHz ALBA ON 4000D generator system (Medlogix SRL, Rome, Italy)

The applicator water bolus thickness is 1.3 cm. The boluses are filled with demineralized water.

The robotized procedure uses a waterproof diode E-field sensor, scanning under the applicator in a tank filled with a tissue-equivalent saline solution (3 gr/L NaCl)[1] (Figure 1). The output of the E-field sensor is linearized to relative SAR values and used to create a SAR distribution scan in X, Y and Z plane with a 1 cm spatial resolution. The X and Y planes pass through the applicator center. The Z plane curvature matches the applicator curvature and is located 1 cm below the applicator. The distribution patterns are used to calculate the EFS and EPD.

Following the ESHO guidelines, the EFS was determined at 1 cm depth by the 50% iso-SAR line, where 100% is the maximum SAR level at 1 cm depth. The EPD was determined by 50% iso-SAR line of the maximum SAR level at 1 cm depth [2].

Results. The measured EFS and EPD values are compared to the specifications for the Alba applicators in Table 1.

After a minor redesign of the water bolus frame of the delta applicator and changing the radius of the omega applicator to 34.4 cm by Medlogix in response to clinical request for less curvature, all applicators comply with the specifications.

Summary. The full range of Alba superficial hyperthermia applicators were characterized using SAR deposition scans using an E-field sensor. All applicators performed according to specifications in terms of EFS and EPD. The accurate EFS, EPD and 3D distributions obtained can serve as a reference for repeated quality control evaluations.

References.

1) Herrera TD *et al. Strahlenther Onkol* **202**, 428–444 (2026).

2) Dobšícek Trefná H et al. *Strahlenther Onkol* 193(5):351–366 (2017).

Footnotes.

1) After replacement of water bolus

2) Modified Curvature radius of applicator is 34.4 cm

Fig. 1: 3D view of the setup

Fig. 2: EFS and EPD of Alba hyperthermia applicators

Fig. 1

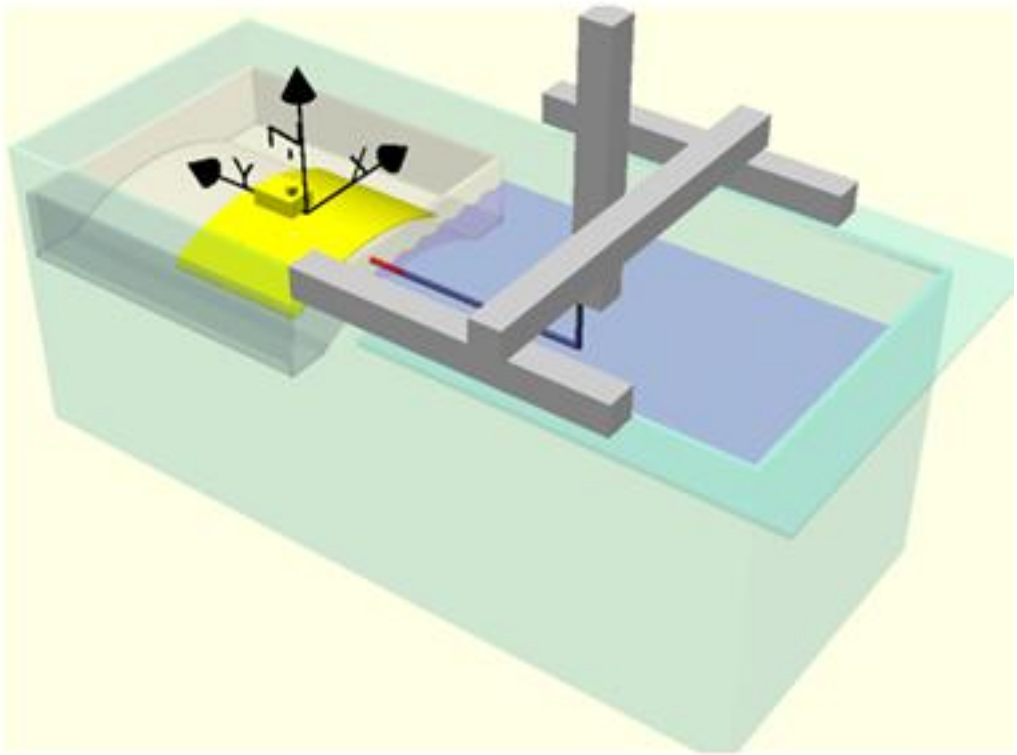

Fig. 2

Applicator	Applicator size (cm2)	EFS (cm^2)	EPD (cm)
Alfa	20 x 7	39	3.5
Beta	15 x 15	63	4.2
Gamma	20 x 20	139	4.2
Delta [1]	21 x 29	173	4.0
Omega[2]	29 x 21	169	4.0

Clinical implementation and multimodal therapies

OP-025

Prognostic value of neutrophil-to-lymphocyte ratio in patients with metastatic melanoma oligoprogression treated with radiotherapy and radiotherapy with hyperthermia

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Objective. To evaluate the prognostic value of post-treatment NLR and ΔNLR in patients with metastatic melanoma (MM) treated with radiotherapy (RT) and RT with hyperthermia (HT).

Methods. Patients with MM who received RT or RT+HT for oligoprogression between 2018 and 2023 were evaluated. Oligoprogression was defined according to ESTRO/EORTC criteria as progression in up to five metastatic lesions. NLR was calculated as the absolute neutrophil count divided by the absolute lymphocyte count, and ΔNLR was defined as the difference between post- and pre-treatment NLR values. To determine the cut-off values, a univariate analysis with repeated Cox regression models was conducted for each NLR value in 0.5–1.0 increments. The assessment of the prognostic value for overall survival (OS) and progression-free survival (PFS) was conducted with the Kaplan–Meier method and the Cox proportional model.

Results. 156 patients were included, 82 patients had RT+HT, 74 had RT only. The median follow-up was 23 months (15.2-34). NLR and ΔNLR cut-off values with the lowest p value and highest HR were 5.5 and 1.5, respectively. In the whole cohort, patients with post-treatment NLR < 5.5 had a better prognosis for OS (NA vs 13.2 m, p<0.0001) and PFS (11.4 vs 3 m, p=0.012). In the cohort treated with RT as the sole method, patients with NLR<5.5 had better prognosis for OS (NA vs 22 m, p=0.0012), also in the cohort treated with HT, patients with NLR<5.5 had better OS (NA vs 13.2 m, p<0.0001). In the cohort treated with RT as the sole method, patients with ΔNLR<1.5 had better prognosis for PFS (18 vs 5 m, p=0.019), also in the cohort treated with HT, patients with ΔNLR<1.5 had better PFS (11 vs 3 m, p<0.04).

Conclusions. Both NLR and ΔNLR may serve as promising prognostic factors in MM treated with RT for oligoprogression. ΔNLR was a better prognostic factor for PFS, while NLR was for OS.

OP-026

Both skin and invasive temperatures should be monitored in locoregional recurrent breast cancer patients treated with postoperative re-irradiation and superficial hyperthermia exceeding 1 cm target depth

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Introduction. Thermoradiation, combining radiotherapy and hyperthermia (40-43°C), is effective for locoregional recurrent (LRR) breast cancer. Skin thermometry is widely used during superficial hyperthermia, but its ability to reflect intratumoral temperatures and predict locoregional tumor control (LRC) in tumors ≥1 cm is unclear.

Goal. To evaluate whether skin temperature measurements are predictive for LRC, compared with invasive temperature measurements in LRR breast cancer with target depths ≥1 cm.

Materials and Methods. We analyzed 112 patients with LRR breast cancer treated (2010-2017) with postoperative re-irradiation (8x4 Gy or 23x2 Gy) and 4-5 weekly hyperthermia sessions. Skin and invasive temperatures were recorded; this cohort was previously reported (Bakker et al 2022; Tello Valverde et al 2025). Hyperthermia was delivered using a 434 MHz ALBA ON 4000D superficial hyperthermia system (Medlogix SRL, Rome, Italy) with microstrip applicators in different sizes (Medlogix SRL, Rome, Italy; SRPC Istok, Fryazino, Russia) (Fig. 1). Based on institutional guidelines moderate bolus cooling (38-40°C) was used to achieve 1-4 cm heating depths. Thermometry used 7-sensor copper-constantan thermocouple probes (Volenec RD Inc., Hradec Králové, Czech Republic) positioned on the skin (80±30 sensors) and in invasive catheters (8±5 sensors, 1-4 cm depth). Pre-heating took 5-15 minutes, steady state heating lasted 60 minutes.

Pearson correlation assessed associations between invasive and skin temperature parameters. Uni- and multivariate analyses evaluated associations between LRC and temperature parameters (mean T50 across sessions and best-session CEM43°CT50; cumulative equivalent minutes at 43°C). Tumor location, lymph node involvement and age were included in the multivariate model.

Results. Mean T50 skin and invasive temperatures were 40.6°C (IQR 40.3-40.8) and 40.7°C (IQR 40.0-41.3), respectively, without correlation between skin and invasive, indicating that skin temperatures do not reflect intratumoral heating. Median CEM43°CT50 was 2.8 (IQR 2.0-4.3) for skin and 7.2 minutes (IQR 3.4-15.9) for invasive in the best hyperthermia session. Infield recurrences occurred in 24 patients. Invasive CEM43°CT50 and T50 were significantly associated with LRC (p=0.015; p=0.021, Fig 2), whereas skin parameters were not (p=0.131; p=0.215).

Conclusion. For tumors ≥1cm depth, invasive thermometry – not skin temperature – predicts LRC. Skin temperature monitoring remains relevant for treatment safety and prevent local hot spots.

References.

Bakker A, et al. Radiother Oncol. 2022;167:149–57 doi: 10.1016/j.radonc.2021.12.036

Tello Valverde CP, et al. Int J Rad Oncol Biol Phys. 2025;122(5):1166–74 doi: 10.1016/j.ijrobp.2025.02.040

Fig. 1: Superficial hyperthermia delivery

Fig. 2: Best session CEM43T50: skin versus invasive

Fig. 1

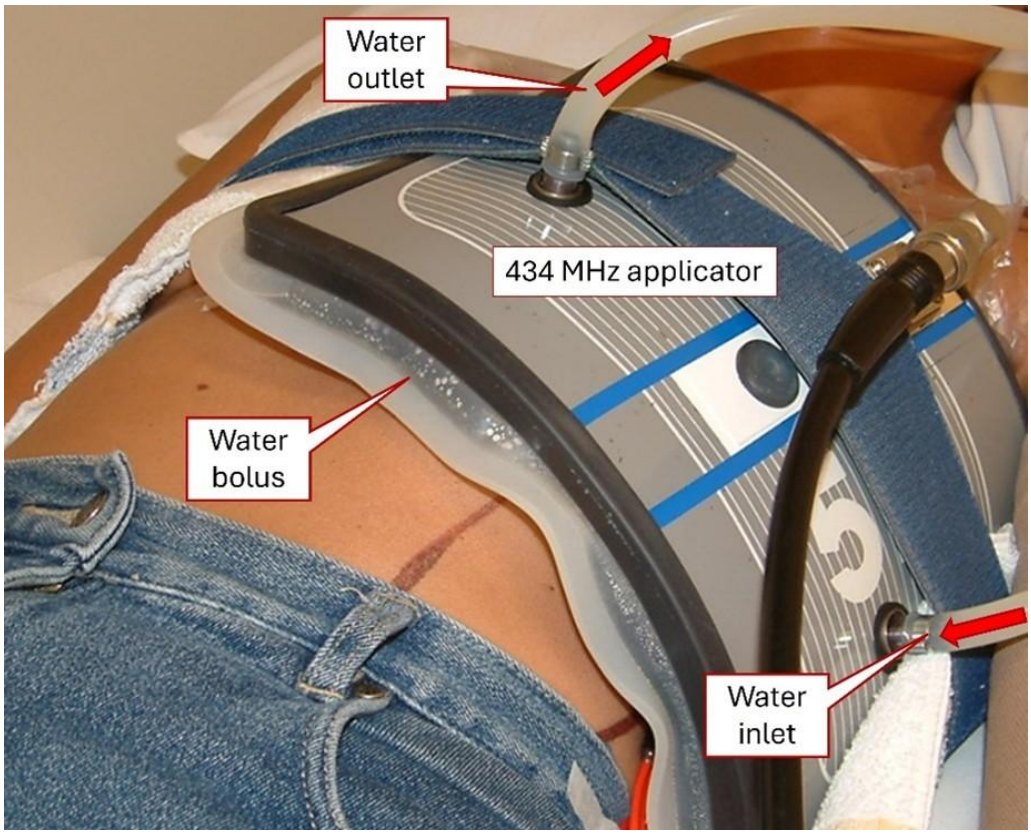
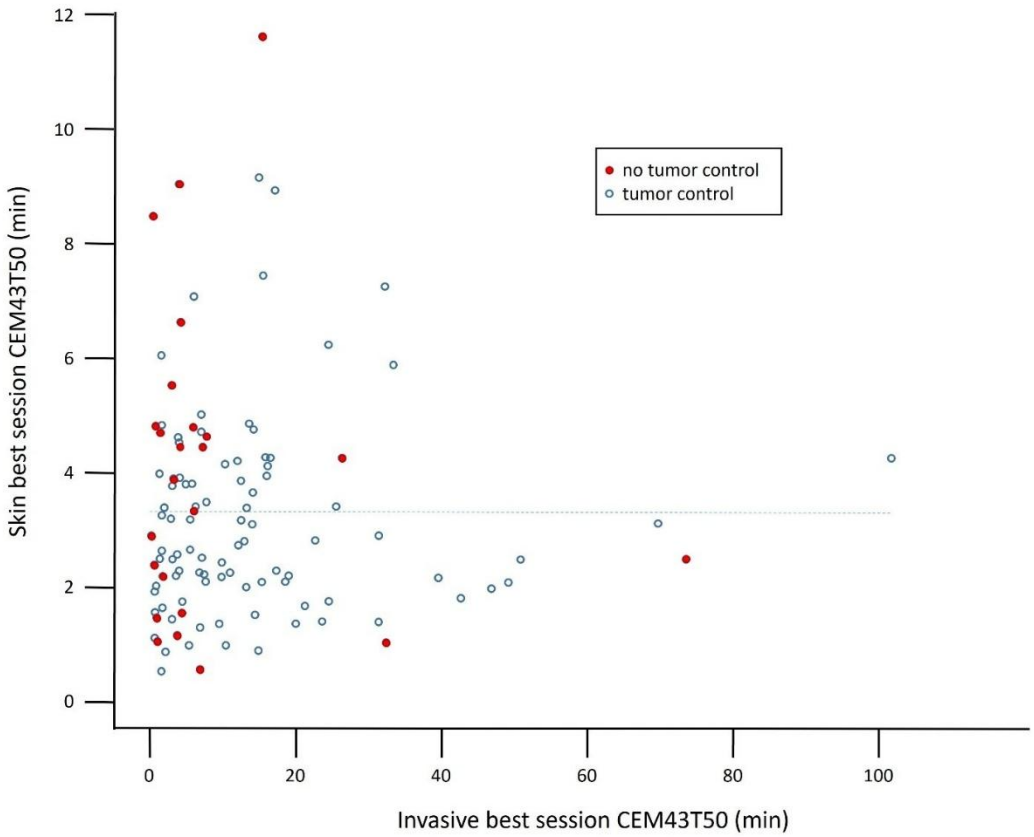

Water
outlet
434 MHz applicator
Water
bolus
Water
inlet

Fig. 2


no tumor control
tumor control
Skin best session CEM43T50 (min)
Invasive best session CEM43T50 (min)
0
2
4
6
8
10
12
0
20
40
60
80
100

OP-027

Transient IL-15 induction following whole-body hyperthermia in patients with solid tumors

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[3] University Hospital of Antwerp (UZA), Antwerp, Belgium

Introduction. Whole-body hyperthermia (WBHT) is increasingly investigated as an adjunct treatment modality in oncology due to its sensitizing effects on conventional therapies, with growing evidence supporting additional immunomodulatory activity. Interleukin-15 (IL-15) is a cytokine with a central role in the activation and proliferation of certain immune players such as NK cells and $CD8^+$ T cells. While cytokine-based immunotherapies, including interleukins such as IL-15, are currently under investigation, the ability of WBHT to induce endogenous cytokine responses in patients remains largely unexplored.

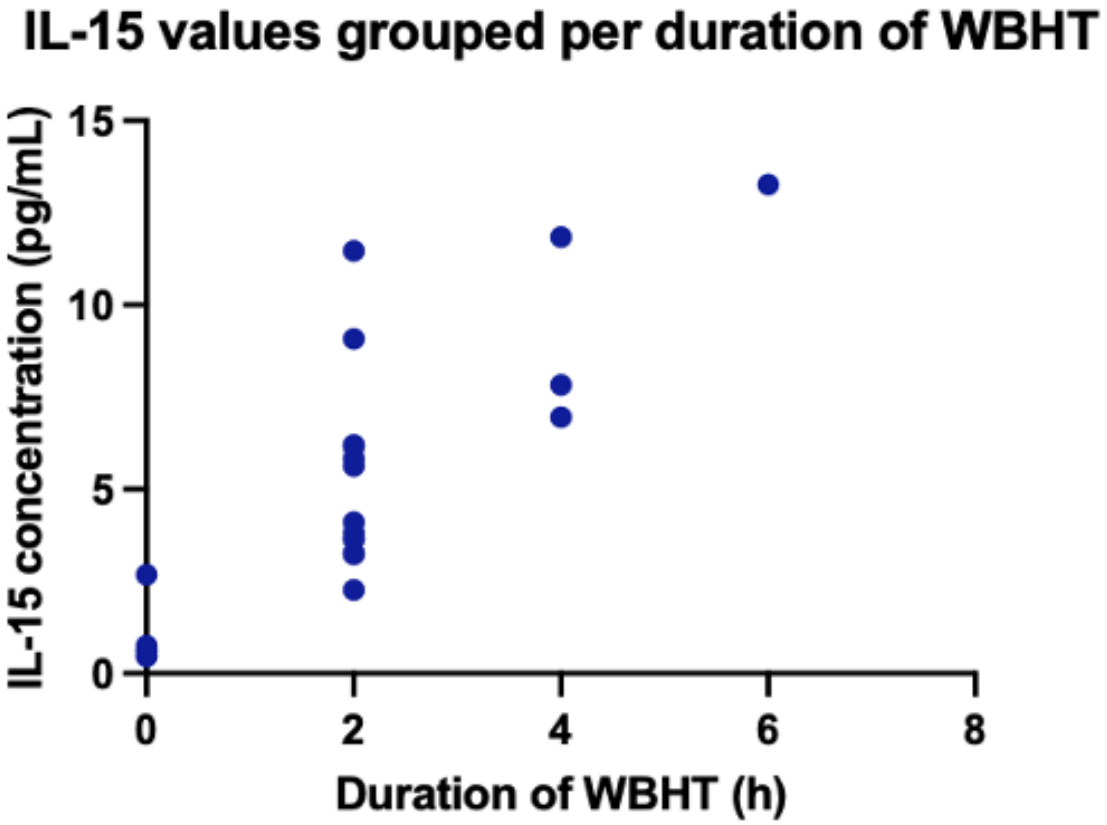
Methods. Serum samples were collected from patients with advanced solid tumors undergoing WBHT (41.5 °C) as part of the MATTERS trial. Patients received treatment sessions of varying durations (2 h, 4 h, and 6 h), either as monotherapy or in combination with subsequent chemotherapy. IL-15 concentrations were measured using a multiplex electrochemiluminescence (MSD) assay. Samples were obtained at baseline (day prior to treatment), on the day of WBHT at the end of treatment plateau phase, and on the second day post-treatment. Changes in IL-15 levels over time and associations with treatment duration were explored using statistical analyses and correlation testing.

Results. Across patients, IL-15 levels consistently demonstrated a transient increase on the day of WBHT administration. Concentrations were lowest at baseline, peaked on the treatment day, and returned toward baseline by day +2. This pattern was observed irrespective of tumor type or chemotherapy. While group comparisons did not reach statistical significance, correlation analysis indicated a moderate-to-strong positive relationship(Spearman"s $\rho = 0.64$; 95% CI, 0.21–0.86; $p = 0.006$; $n = 17$) between WBHT duration and IL-15 induction.

Conclusion. WBHT is associated with a reproducible, transient increase in circulating IL-15 in patients with solid tumors. These findings suggest that WBHT may induce endogenous cytokine responses relevant to immune activation. The observed kinetics indicate a short-lived biological effect, highlighting the importance of treatment timing in relation to potential combination strategies. This study is limited by the early safety focus of the trial, small number of patients (particularly at longer WBHT durations), and the limited number of collected cytokine data points around treatment. These limitations preclude assessment of whether the observed IL-15 elevation was associated with clinical outcomes. Therefore, further studies are warranted to determine whether such transient IL-15 induction translates into functionally meaningful immune activation and to explore its relevance for combination strategies with immunotherapy.

Fig. 1: Increases in IL-15 plotted against the duration of WBHT exposure.

Fig. 1


IL-15 values grouped per duration of WBHT
IL-15 concentration (pg/mL)
15
10
5
0
0
2
4
6
8
Duration of WBHT (h)

OP-028

Absorbed SARhotspot as a predictor of treatment-limiting complaints in deep hyperthermia

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Introduction. Deep hyperthermia (DHT) aims to achieve therapeutic tumor temperatures of 40–44 °C. However, treatment delivery is frequently limited by patient-reported complaints (pain or discomfort) or side effects (fat necrosis or burnings) rather than temperature thresholds, with wide inter-patient variability complicating real-time power decisions. At Erasmus MC, hyperthermia treatment planning includes assessment of the SAR hotspot, defined as the highest SAR within 1% of healthy tissue, with the objective of minimizing it. The location of the SAR hotspot corresponds with patient-reported complaint locations in approximately 80% of treatments, indicating its potential as a marker of treatment tolerance. This study investigates whether the SAR hotspot predicts treatment-limiting complaints during DHT and whether a clinically useful threshold can guide individualized and safe power modulation.

Methods. Between February 2021 and February 2026, 141 patients [HW1] treated with DHT were retrospectively analyzed. Applied net power, absorbed SARhotspot, BMI, WHO status, smoking status, side effects and patient-reported complaints were collected from the electronic patient records. Associations were evaluated using generalized linear mixed models (GLMMs) with patient-level random intercepts. Predictive performance and clinically relevant thresholds were assessed using ROC analysis. [HW2]

Results. Treatment-related complaints during DHT were reported in 35.6% of treatments, whereas side effects occurred in 11.7%. Higher absorbed SARhotspot values were associated with an increased likelihood of patient complaints in univariable GLMM analysis (Table 1). Although this association was modeled as linear on the log-odds scale, the resulting relationship on the probability scale was non-linear, with a steeper increase in absolute complaint risk at higher SAR-hotspot values. ROC analysis showed good discriminative performance (AUC = 0.88) (Figure 1), with an optimal Youden-based threshold of approximately 104 W/kg. At this level, the estimated baseline probability of complaints was 39%. A further 10 W/kg increase corresponded to an estimated probability of approximately 87%. In the multivariable GLMM adjusting for BMI, WHO performance status, and smoking, SARhotspot was still the dominant independent predictor. In addition, WHO performance and, to lesser extent BMI, were independent predictors for complaints. The multivariable model showed excellent discrimination (AUC = 0.91).

Conclusion. A high absorbed SARhotspot is a strong and independent predictor for treatment-limiting complaints during DHT. A clinically relevant threshold of 104 W/kg offers a practical tool for real-time safety monitoring and individualized power modulation. These findings support incorporating SAR-guided decision thresholds into routine DHT workflows to improve treatment safety, consistency, and personalization. In clinical practice, this threshold has been implemented as an alert level.

Fig. 1

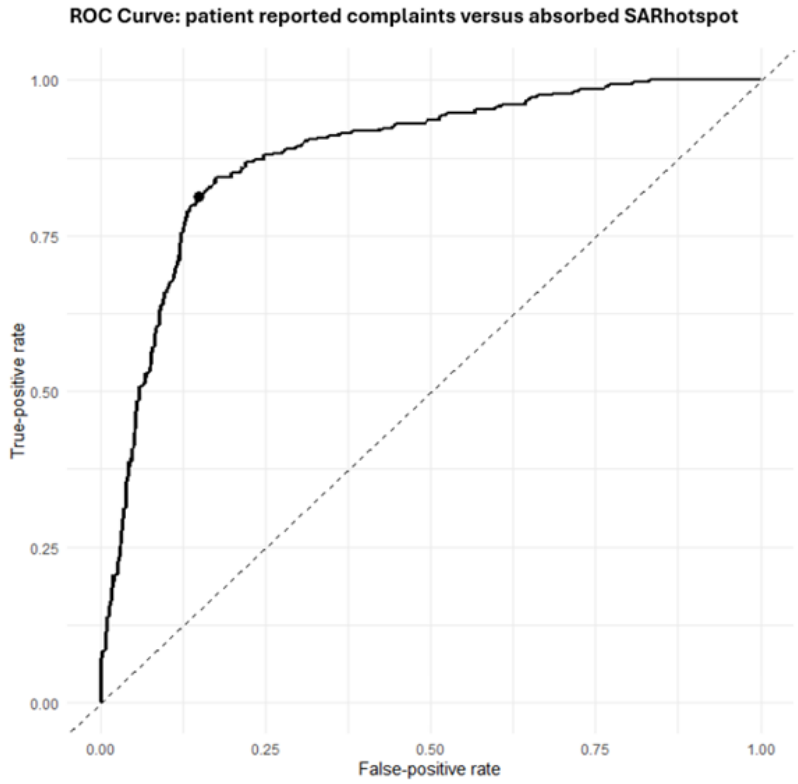

Figure 1: ROC curve for predicting patient-reported complaints based on absorbed SARhotspot during deep hyperthermia treatment with an area under the curve (AUC) of 0.88. An absorbed SARhotspot threshold of 104 W/kg yielded a Youden index of 0.66.

Fig. 2

Table 1: GLMM results demonstrating the association between absorbed SAR hotspot intensity (W/kg) and reported complaints, with patient-level random effects. ICC = interclass coefficient.

	GLMM: Complaint ~ SARhotspot			
Predictors	*Odds Ratios*	*std. Error*	*CI*	*p*
(Intercept)	0.00	0.00	0.00 – Inf	**<0.001**
SAR hotspot (W/kg)	1.29	0.04	0.00 – Inf	**<0.001**
Random Effects				
σ^2	3.29			
$\tau_{00\ Patient}$	5.87			
ICC	0.64			
$N_{Patient}$	141			
Observations	793			
Marginal R^2 / Conditional R^2	0.684 / 0.887			

OP-029

Clinical utility of quality assurance approaches for phased-array hyperthermia applicators

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Objective. Quality assurance (QA) of phased-array radio-frequency (RF) hyperthermia applicators is essential for safe and reproducible clinical heating. In practice, however, the major challenges extend beyond measurement accuracy: clinically meaningful validation also depends on time, workflow burden, and compatibility with existing hardware and staff routines. Although electric-field (E-field) and temperature-based techniques are technically mature, their adoption varies widely, and no prior work has compared the total cumulative effort across QA modalities or examined how workflow constraints influence clinical choices.

Approach. We reviewed and analysed QA methods based on E-field (LED matrix, sensor-arrays, robotic scanning systems, fiber-optic E-field/phase sensor) and temperature (T-probes, IR thermography, MRT) measurements. For each, we compare the sensing principle, primary role in the QA workflow, QA metrics (EFS, EFV, and 3 focus-steering settings), phantom configuration, and task-level contributors to cumulative QA time (preparation, phantom dielectric properties characterization, cooling, and disassembly), enabling direct comparison of setup- versus scan-dominated workflows.

Results. Across all modalities, the largest contributors to total QA time were not the measurements but the surrounding tasks: phantom preparation and positioning, water-bolus management, catheter routing, phantom dielectric verification, and disassembly, as addressed in Table 1.

• Routine QA (daily/weekly): Fast EM-based tools such as LED matrices and sensor-arrays enable immediate qualitative verification of beam steering with minimal handling effort.

• Periodic quantitative QA (monthly/semi-annual/annual): Robotic E-field scanning, T-probes, and MR thermometry provide the detailed quantitative or volumetric data required for applicator characterization and treatment-related verification.

• Targeted troubleshooting: Fiber-optic E-field sensors are particularly valuable for diagnosing and resolving channel-specific or applicator-specific issues. **Significance:** By linking each sensing principle to its QA role and full workflow burden, this study provides a practical, clinically scalable QA blueprint for RF phased-array hyperthermia systems. The step-wise workflow-time template supports institutions in benchmarking their own processes, planning QA schedules more efficiently, and moving toward more transparent, consistent, and standardized QA reporting across centres.

Fig. 1

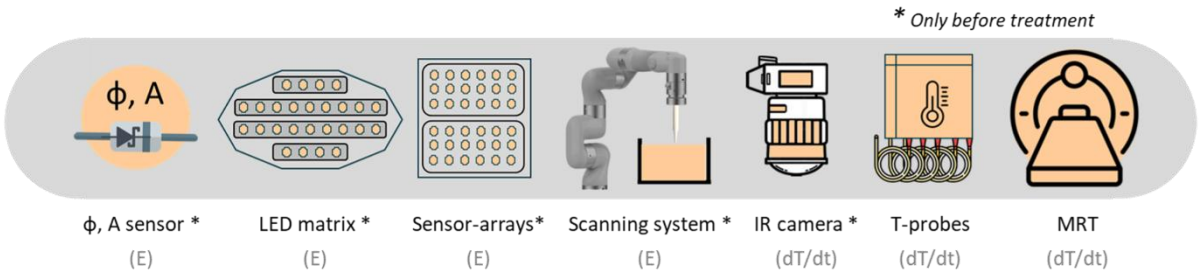

Figure 1QA methods used at Erasmus MC

Fig. 2

Table 1: Approximate contribution of major workflow phases to cumulative QA time for each QA method used in RF hyperthermia. Values are approximate and rounded to reflect typical Erasmus MC workflows; actual times may vary with applicator type, number of steering settings, and operator experience.

Workflow phase	LED matrix	Sensor-arrays	Scanning systems	IR Camera	T-probes	MRT
Phantom preparation						
Weighing, Mixing, Heating	2 min	1 hr	2 min	1 hr	1 hr	1 hr
Cooling / equilibrium	-	6 hrs	-	6 hrs	6 hrs	6 hrs
Filling, bubbles-removal	10 min	1 hr	10 min	1 hr	1 hr	1 hr
Dielectric properties measurement	15 min	15 min	15 min	15 min	15 min	15 min
Thermal properties measurement	-	-	-	15 min	15 min	15 min
Total preparation time	27 min	8.25 hrs	27 min	8.5 hrs	8.5 hrs	8.5 hrs
Experimental setup						
Phantom positioning	5 min	5 min	5 min	5 min	5 min	5 min
Water bolus filling	15 min	15 min	15 min	15 min	15 min	15 min
Equipment handling/prep.	1 min	5 min	5 min	1 min	15 min	15 min
Calibration / zeroing	1 min	5 min	5 min	5 min	5 min	5 min
Heating time per measurement	-	-	-	6 min	6 min	6 min
EFS measurement	1 min	2 sec	40 min	2 sec	-	4sec
EFV measurement	-	-	3.5 hrs (5 slices)	-	-	84sec (25 slices)
3 Focus-steering measurements	3 min	6 sec	2 hrs	6 sec	-	5 min
Cooling between measurements	-	-	-	6 hrs	6 hrs	6 hrs
Total experimental time	26 min	30 min	6.75 hrs	18.5 hrs	18.75 hrs	19 hrs
Disassembly						
Water bolus emptying	5 min	5 min	5 min	5 min	5 min	5 min
Phantom removal / storage	10 min	5 min	10 min	5 min	5 min	5 min
Miscellaneous Equipment cleanup	10 min	10 min	10 min	5 min	5 min	15 min
Total disassembly time	25 min	20 min	25 min	15 min	15 min	25 min
Total cumulative QA time	1.5 hrs	7 hrs	8 hrs	27.25 hrs	27.5 hrs	28 hrs

OP-030

Superficial Hyperthermia and Hypofractionated Palliative Radiotherapy in locally advanced, metastatic or recurrent Head-and-Neck Cancer

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Introduction. Approximately 25–30% of patients with head-and-neck cancer (HNC) present with locally advanced or metastatic disease and are not eligible for curative treatment. These patients frequently experience significant locoregional symptoms and are commonly treated with high-dose hypofractionated palliative radiotherapy (RT). Although these RT schedules can provide symptom relief, durable tumor control remains limited. Hyperthermia (HT) has previously demonstrated clinical benefit as a tumourselective radiosensitizer in combination with RT in HNC and other tumor types, without increasing treatment-related side effects.

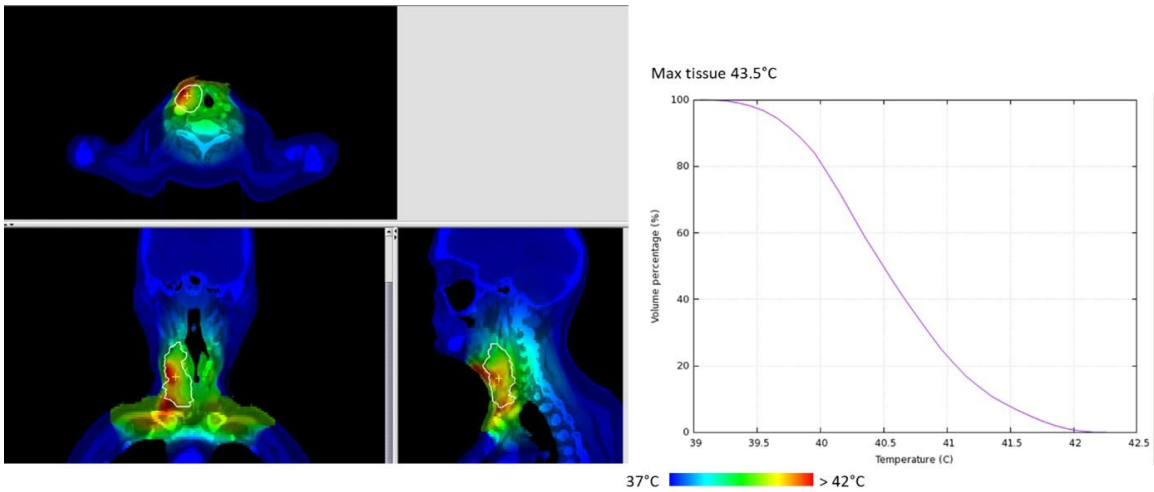
Goals. To prospectively evaluate feasibility, side effects and clinical outcomes of combined superficial hyperthermia and high-dose hypofractionated palliative RT in patients with HNC.

Materials and Methods. This prospective study aims to include 40 patients with locally advanced, metastatic, or recurrent HNC who are not eligible for curative surgery or (chemo)radiotherapy and have an indication for high-dose palliative RT. Patients will be treated according to standard clinical protocol using either 6 RT fractions (with 6 Gy/fx) or 16 RT fractions (with 3.25 Gy/fx), combined with weekly superficial HT sessions. Hyperthermia treatment planning will be performed using Plan2Heat software and delivered using the ALBA ON 4000D hyperthermia system equipped with up to 2 dedicated head-and-neck applicators and newly developed dedicated phase control and positioning holders to optimize reproducibility and focused energy delivery. Prospective data collection includes locoregional control, treatment-related toxicity, survival outcomes, and patient reported outcomes on dysphagia and xerostomia.

Results. This study was approved by the local Medical Research Ethics Committee in May 2026. Patient inclusion is expected to start following AmsterdamUMC approval of the dedicated hyperthermia phase steering and head-and-neck positioning holders. An example simulation for an HNC patient demonstrated focused heating of the target region using a dedicated antenna setup and patient-specific treatment planning, see **Fig. 1**, reaching a conservatively estimated RT enhancement factor of ~1.2. Preliminary simulation studies demonstrated increased estimated equivalent tumor dose distributions with the addition of HT compared with RT alone, supporting the rationale for combined treatment in HNC.

Summary. In this prospective study, we will investigate the integration of superficial HT into high-dose hypofractionated palliative RT for patients with HNC. This combined treatment approach may improve oncological outcomes and symptom control in this challenging patient population.

Fig. 1: A simulated HT heatmap for a HNC patient



Innovative multimodal delivery techniques

OP-031

Thermosensitive Liposomal Irinotecan Combined with Regional Hyperthermia in Pancreatic Cancer: A Preclinical Proof-of-Concept Study

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[2] Bavarian Cancer Research Center (BZKF), Munich, Germany
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[5] Technical University of Munich, School of Medicine, Institute of Pathology, Comparative Experimental Pathology, Munich, Germany
[6] University Hospital Erlangen, FAU Erlangen, Translational Radiobiology, Department of Radiation Oncology, Erlangen, Germany
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[9] LMU University Hospital, Department of Radiation Oncology, Munich, Germany

Introduction. Pancreatic ductal adenocarcinoma (PDAC) is characterized by a dense desmoplastic stroma, resulting in impaired intratumoral drug delivery and limited responsiveness to systemic therapies. Thermosensitive liposomal (TSL) drug formulations, in combination with regional hyperthermia (RHT), enable temperature-triggered intratumoral drug release and may overcome these barriers. Preclinical studies indicate increased intratumoral concentrations of irinotecan and its active metabolite SN-38 with TSL-irinotecan (TSL-IRI) compared to conventional formulations, while RHT enhances tumor perfusion, vascular permeability, and may promote an immunogenic tumor microenvironment (TME). However, the combined effect of TSL-IRI and RHT has not yet been demonstrated in PDAC.

Goals. To establish and provide preclinical proof-of-concept for the combination of TSL-IRI plus RHT as a novel treatment strategy in PDAC.

Materials and Methods. We established a preclinical PDAC platform using a syngeneic C57BL/6 mouse model with subcutaneous KPC1050 PDAC tumors. A dedicated, 3D-printed radiofrequency-based RHT applicator was developed to enable controlled tumor heating (42–43 °C) using the BSD-500 RHT device (Pyrexar Medical, Salt Lake City, UT, USA). Tumor-bearing mice were treated with TSL-IRI + RHT and compared to free irinotecan + RHT and control groups. Endpoints include treatment feasibility, tumor growth kinetics, survival, histopathological response, and pharmacokinetic analyses assessing drug distribution and metabolism (including SN-38) in tumor tissue, blood, and organs.

Results (ongoing). The combined TSL-IRI and RHT approach was successfully implemented in vivo. Early tumor growth kinetics and survival analyses indicate improved outcomes in TSL-IRI-treated animals. Preliminary histopathological and immunohistochemical evaluation demonstrates a treatment-associated response in tumor reaction, characterized by tumor necrosis, apoptosis, and immune cell infiltration patterns. Ongoing translational and pharmacokinetic studies are evaluating the impact of TSL-IRI + RHT on the TME, as well as intratumoral drug accumulation and systemic distribution of irinotecan and SN-38, in comparison to free irinotecan and liposomal irinotecan (Onivyde®).

Summary. This ongoing study provides emerging preclinical evidence supporting the feasibility and therapeutic potential of TSL-IRI–based strategies in PDAC. By improving intratumoral drug delivery and potentially modulating the TME, this approach may represent a promising strategy to overcome therapeutic resistance. Further analyses will define underlying pharmacological and biological mechanisms and support rational combination strategies, including integration with immunotherapy, to enable clinical translation.

OP-032

Beyond Heat: Multimodal Nanotechnology Strategies to Redefine Magnetic Hyperthermia

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Magnetic hyperthermia–mediated cancer therapy (MHCT) is a minimally invasive approach for localized tumor ablation, yet its therapeutic efficacy is often limited by tumor hypoxia, adaptive heat-stress responses, and insufficient reactive oxygen species (ROS) generation. This work presents a series of sustainable, nanotechnology-enabled strategies designed to overcome these biological barriers and enhance MHCT outcomes through multimodal therapeutic integration.

We report the development of shape-engineered magnetic nanoparticles (MNPs) synthesized using green chemistry approaches. Among these, cubic MNPs exhibit superior magnetothermal efficiency, translating into enhanced magneto-chemotherapeutic efficacy in both in vitro and in vivo tumor models. To address intratumoral hypoxia and limited penetration, we engineered self-propelling biohybrid "nanobacteriomagnets" by integrating magnetic nanocubes within *Escherichia coli*, enabling active tumor navigation and achieving complete tumor regression within 30 days.

Mechanistic investigations revealed that modulation of the cellular heat-stress response significantly improves MHCT efficacy. Co-treatment with the HSP90 inhibitor 17-DMAG markedly enhances glioma cell death and tumor inhibition through increased immunogenic activation. In parallel, a vitamin K3–loaded copper–zinc ferrite nanoplatform was designed to synergistically induce ROS generation and immune modulation, resulting in complete tumor regression in lung adenocarcinoma models.

Overall, these multimodal approaches encompassing green nanoparticle synthesis, biohybrid delivery, stress-pathway modulation, and magnetothermodynamic therapy that demonstrate the transformative potential of sustainable nanotechnology in advancing MHCT toward effective and environmentally responsible cancer treatment.

Recent Publications.

1. Kaur T, Sharma D. E. coli as a Smart Thermo-Vector for Combating Solid Tumors: A Synergistic Heat-Induced Cancer Therapy Approach. *Bioconjugate Chemistry,* 2025, 36, 4, 867–880.

2. Gupta R, Sharma D, et al. Enhancing Magnetic Hyperthermia Efficacy through Targeted Heat Shock Protein 90 Inhibition: Unveiling Immune-Mediated Therapeutic Synergy in Glioma Treatment. *ACS Nano*, 2024, 18, 26, 17145–17161.

3. Chauhan A, Sharma D, et al. Vitamin k3-Loaded Magnetic Nanoparticle-Mediated Synergistic Magnetothermodynamic Therapy Evokes Massive ROS and Immune Modulation for Augmented Antitumor Potential. *ACS Applied Materials & Interfaces*, 2023, 15, 23, 27515–27532.

4. Kaur T, Sharma D. Self-Propelling Bacteria-Based Magnetic Nanoparticles (BacMags) for Targeted Magnetic Hyperthermia Therapy against Hypoxic Tumors. *Nanoscale*, 2024, 16, 7892-7907.

Fig. 1

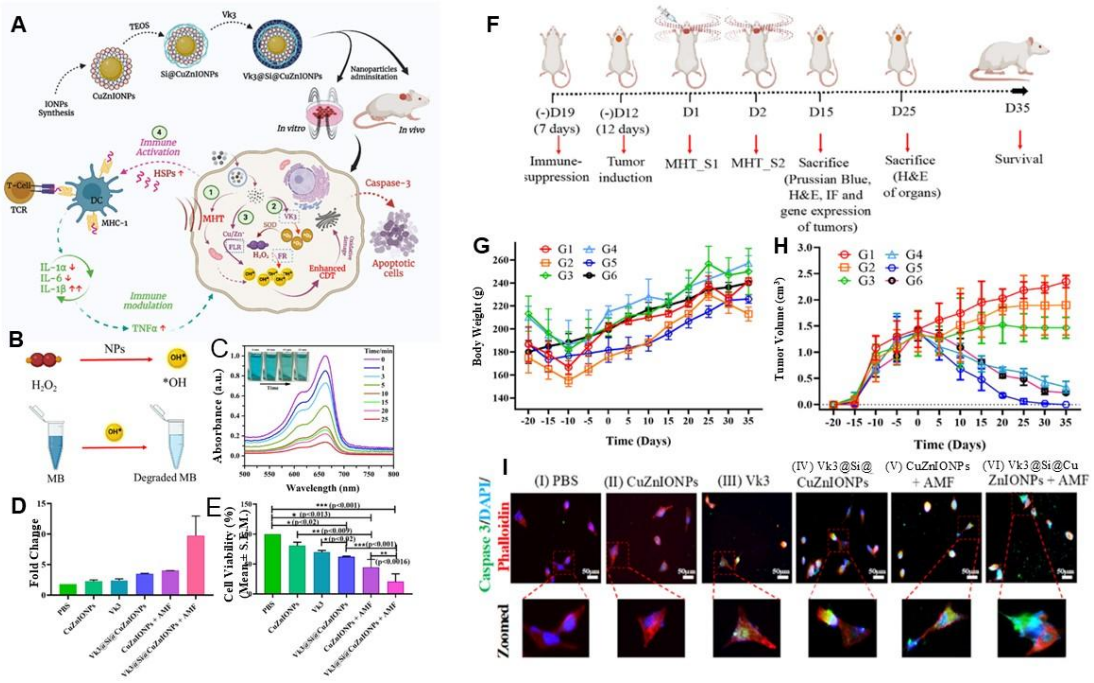
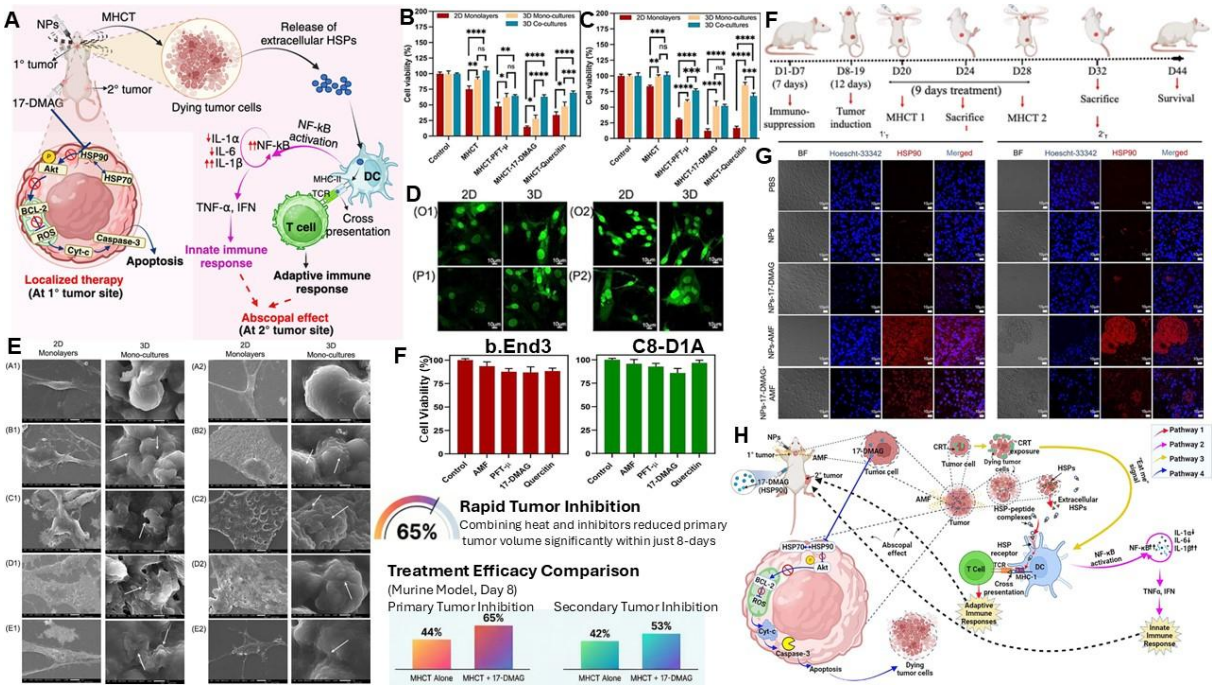

A
TEOS
Vk3
IONPs Synthesis
CuZnIONPs
Si@CuZnIONPs
Vk3@Si@CuZnIONPs
Nanoparticles administration
In vitro
In vivo
Immune Activation
HSPs
T-Cell
TCR
DC
MHC-I
MHT
Caspase-3
Apoptotic cells
Enhanced CDT
IL-1α
IL-6
IL-1β
Immune modulation
TNFα
B
NPs
H_2O_2
*OH
MB
Degraded MB
C
Absorbance (a.u.)
Wavelength (nm)
D
Fold Change
E
Cell Viability (%) (Mean ± S.E.M.)
F
(-)D19 (7 days)
(-)D12 (12 days)
D1
D2
D15
D25
D35
Immune-suppression
Tumor induction
MHT_S1
MHT_S2
Sacrifice (Prussian Blue, H&E, IF and gene expression of tumors)
Sacrifice (H&E of organs)
Survival
G
Body Weight (g)
Time (Days)
H
Tumor Volume (cm³)
Time (Days)
I
(I) PBS
(II) CuZnIONPs
(III) Vk3
(IV) Vk3@Si@CuZnIONPs
(V) CuZnIONPs + AMF
(VI) Vk3@Si@CuZnIONPs + AMF
Caspase 3/DAPI/Phalloidin
Zoomed

Fig. 2


A
NPs
MHCT
1° tumor
2° tumor
17-DMAG
Dying tumor cells
Release of extracellular HSPs
NF-kB activation
IL-1α
IL-6
IL-1β
TNF-α, IFN
DC
T cell
Cross presentation
Innate immune response
Adaptive immune response
Apoptosis
Localized therapy (At 1° tumor site)
Abscopal effect (At 2° tumor site)
B
C
2D Monolayers
3D Mono-cultures
3D Co-cultures
Cell viability (%)
Control
MHCT
MHCT-PFT-α
MHCT-17-DMAG
MHCT-Quercitin
D
2D
3D
E
F
b.End3
C8-D1A
Control
AMF
PFT-α
17-DMAG
Quercitin
Rapid Tumor Inhibition
65%
Combining heat and inhibitors reduced primary tumor volume significantly within just 8-days
Treatment Efficacy Comparison
(Murine Model, Day 8)
Primary Tumor Inhibition
Secondary Tumor Inhibition
44%
65%
42%
53%
MHCT Alone
MHCT + 17-DMAG
F
D1-D7 (7 days)
D8-19 (12 days)
D20
D24
D28
D32
D44
(9 days treatment)
Immuno-suppression
Tumor induction
MHCT 1
Sacrifice
MHCT 2
Sacrifice
Survival
G
BF
Hoescht-33342
HSP90
Merged
PBS
NPs
NPs-17-DMAG
NPs-AMF
NPs-17-DMAG-AMF
H
Pathway 1
Pathway 2
Pathway 3
Pathway 4
Tumor cell
Dying tumor cells
Extracellular HSPs
HSP-peptide complexes
Abscopal effect
Adaptive Immune Responses
Innate Immune Response
Apoptosis

OP-033

MR-HIFU mediated Hyperthermia for Targeted Chemotherapy: Dose and Duration Optimization of doxorubicin containing $DPPG_2$-TSLs

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Introduction. The delivery of doxorubicin (DOX) via temperature-sensitive liposomes (TSLs) has demonstrated significant efficiency when combined with local mild hyperthermia. Drug concentrations in the target region can exceed those of untreated tissue by a factor of up to fifteen. However, the exact correlation between duration of the hyperthermic treatment, the injected dose of DOX encapsulated in TSLs and the obtained amount of DOX in the tumor tissue is unknown.

Goals. The objective of this work is to treat rats bearing subcutaneous tumors, using DOX containing $DPPG_2$-based TSLs in combination with a clinical MR-HIFU system for hyperthermia. The tissue concentration of DOX in the tumor is quantified to assess the relationship between the dose of doxorubicin and the hyperthermia duration.

Materials and Methods. A clinical MR-HIFU system (3T Achieva®, Philips Healthcare; Sonalleve® V2, Profound Medical) was used to treat rats bearing subcutaneous soft tissue sarcoma (BN175 cells). We applied different doses DOX containing DPPG2-based TSLs (1-10 mg/kg body weight) and durations of hyperthermia (5-60 min). After 24 hours, the animals were sacrificed and the amount of doxorubicin was quantified in different tissue types via HPLC (Agilent 1260 Infinity III series).

Results. We established a novel small animal setup that enables prolonged and stable hyperthermia using a clinical MR-HIFU device. This system achieved consistent hyperthermic conditions for 5–60 minutes in rats treated with 1-10 mg/kg body weight doxorubicin encapsulated in DPPG2-containing temperature-sensitive liposomes. In addition, control experiments were performed in the absence of hyperthermia and/or with free doxorubicin.

Summary. To investigate the relationship between hyperthermia duration, drug dose, and tissue uptake, a novel MR-HIFU-based small-animal setup was developed, enabling stable hyperthermia for up to 60 min. Rats with subcutaneous tumors were treated with varying doses of doxorubicin and hyperthermia durations. Tissue drug quantification via HPLC is ongoing and will be available soon. Control experiments without hyperthermia or with free doxorubicin will be included.

Acknowledgements. This project is supported by the Innovative Health Initiative Joint Undertaking (IHI JU) under grant agreement No 101112053.

OP-034

Magnetic Hyperthermia 2.0: Improving Therapy Response through the Lens of Immunogenic Cell Death

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Introduction. The evolution of cancer therapeutics has shifted toward the induction of immunologically "hot" tumor microenvironments. Traditional hyperthermia has long been valued for its radio-sensitizing effects; however, a new paradigm is emerging where regulated cell death (RCD) pathways—such as ferroptosis and pyroptosis—are leveraged to trigger systemic anti-tumor immunity. Magnetic Nanoparticles (MNPs) offer a unique platform for this approach due to their dual role as controllable heat mediators and versatile delivery vehicles.

Goals. Present talk highlights the tumor homing, magnetic hyperthermia and multi-modal therapy efficacy of a patented, tumor-targeted liposomal magnetic nanocarrier termed as "T-LMD". Mechanistic insights pertaining to the role of immunogenic cell death (ICD) in improving the therapeutic response by T-LMD will also be discussed.

Materials and Methods. Synthesis and characterization of T-LMD (Indian Patent No. 441803) by different bio-physical techniques such as cryo-transmission electron microscopy [Fig. 1(i)], dynamic light scattering, zeta analysis, etc would be discussed. Furthermore, the tumor homing of T-LMD was studied in live mice solid tumors using near infrared red probe and in vivo fluorescence imaging. Effect of ICD on lung metastasis of triple negative breast carcinoma (TNBC) has been studied by micro-computed tomography.

Results. T-LMD demonstrated superior tumor-homing capabilities1 and magnetic hyperthermia mediated significant improvement of chemo-radiation therapy efficacy in murine fibrosarcoma tumors [Fig. 1(ii)]. Mechanistic studies revealed that T-LMD facilitates ICD, specifically triggering ferroptotic2 and pyroptotic pathways in TNBC models. This localized intervention resulted in a profound systemic effect, significantly inhibiting lung metastasis. Safety data confirmed a favorable pharmacological profile; T-LMD was well-tolerated with no significant cardiotoxicity observed (Fig. 2).

Summary. T-LMD represents a sophisticated multi-modal platform that bridges the gap between physical thermal medicine and immunotherapy. By successfully integrating MHT with the induction of ICD and metastasis inhibition, this approach provides a promising future for metallic nanoparticles in revitalizing conventional cancer treatments. Our results underscore the potential for T-LMD to serve as a next-generation targeted nano-formulation in the clinical management of solid tumors.

References.

1. Neena G. Shetake*, Sourav Kumar Das, Amit Kumar, et al., Biomat. Adv., 2024, 161, 213868.
2. Neena G. Shetake, Manjoor Ali, Amit Kumar, et al., Biomat. Adv., 2022;142:213147.

Fig. 1 (i) Composition of T-LMD and its visualization by Cryo-TEM. (ii) Tumor homing of T-LMD in murine fibrosarcoma model as studied by live in vivo fluorescence imaging.

Fig. 2 (i) Evaluation of cardiac toxicity after indicated treatments as assessed by hematoxylin & Eosin (H&E) staining and (ii) trichrome staining.

Fig. 1

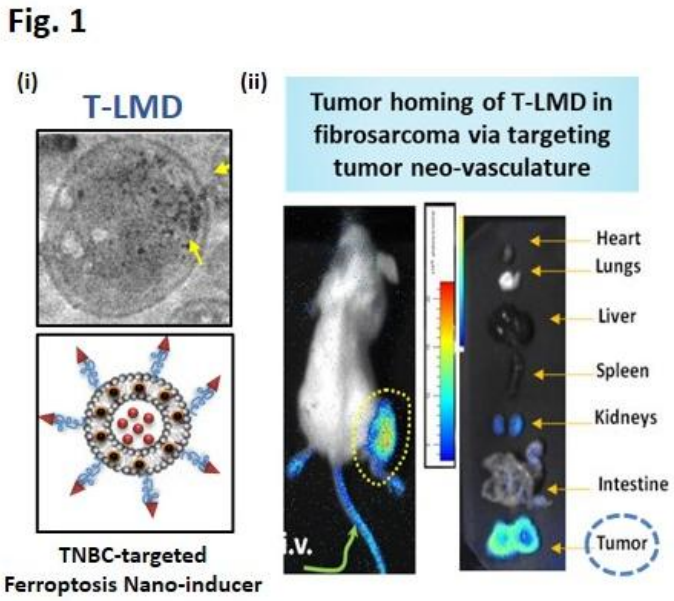
Fig. 1
(i)
T-LMD
TNBC-targeted
Ferroptosis Nano-inducer
(ii)
Tumor homing of T-LMD in fibrosarcoma via targeting tumor neo-vasculature
i.v.
Heart
Lungs
Liver
Spleen
Kidneys
Intestine
Tumor

Fig. 2

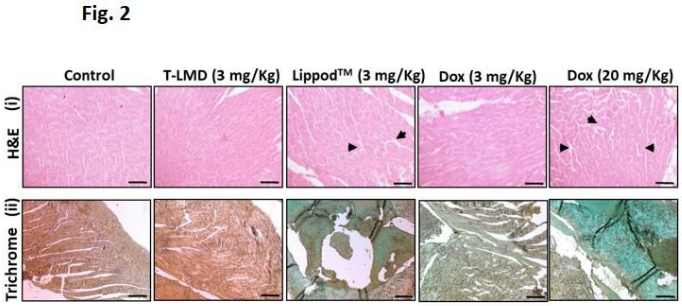
Fig. 2
Control
T-LMD (3 mg/Kg)
Lippod™ (3 mg/Kg)
Dox (3 mg/Kg)
Dox (20 mg/Kg)
H&E (i)
Trichrome (ii)

Technical, clinical, innovative, educational, legal and economic aspects

OP-035

Hazard Assessment of Breast Implants During Regional Hyperthermia (RHT)

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Introduction. RHT at temperatures between 41–43 °C has been demonstrated to enhance radiosensitivity in patients with chest wall recurrences of breast cancer. Following primary tumor resection, many patients undergo breast reconstruction using silicone implants. In the event of local recurrence, a clinically relevant question is whether adequate heating of lesions located between the skin and the implant can be achieved without inducing thermal damage to the implant material. The present study investigated the impact of RHT on specific absorption rate (SAR) and temperature distribution within breast implants under hyperthermic conditions.

Materials and Methods. SAR and temperature distribution were evaluated in commercially available modern breast implants composed of cohesive, dimensionally stable medical-grade silicone gel. Invasive temperature measurements using Bowman probes, which were moved along the implants diameter to obtain intraprosthetic temperature profiles. A spiral applicator of the BSD2000-3D hyperthermia system (Pyrexar, USA) was used as heating device. A power of 50 W at 115 MHz was applied to a 250 g implant, corresponding to approximately eight times the power administered during clinical treatment conditions (20 W/kg).

Results. The maximum invasive temperature increase within the implant was approximately 5 °C during a 40-minute heating session (Tinitial = 23 °C; Tfinal = 28 °C). The maximum superficial temperature reached 32.4 °C. No localized temperature peaks or excessive heating effects within the implant were observed.

Conclusion. Breast implants do not appear to represent a contraindication for RHT treatment. Effective hyperthermia of the chest wall appears to be possible in cases of tumor recurrence without the removal of the breast implant.

OP-036

MR-guided Hyperthermia for Breast Cancer: Effects of Coil Integration on Heating Performance

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Introduction. Accurate thermal dose delivery during hyperthermia therapy (HT) is essential for therapeutic efficacy while sparing healthy tissue[1]. MR thermometry (MRT) enables real-time, 3D temperature mapping, with superior spatial resolution compared to invasive probes. Integrating MR receive coils into an HT device has the potential to improve MRT accuracy by increasing the signal-to-noise ratio (SNR). However, electromagnetic coupling between the MR coils (64MHz at 1.5T) and HT antennas (434MHz) may alter antenna impedance and radiation patterns, potentially compromising heating performance[2].

Goal. Quantitative assessment of the impact of integrating MR receive coils into a 1.5 T breast hyperthermia applicator on heating performance using simulations and phantom experiments.

Methods. An 8-channel MR receive coil array (two 4-element arrays with overlapping 80 × 55 mm loops) was integrated medially and laterally around the prone breast within a 12-element breast HT applicator (Fig. 1). Heating performance with and without MR coils was assessed via thermal simulations and validated experimentally using a cylindrical tissue-mimicking phantom (110mm diameter, 250mm height) (Fig. 1D) composed of deionized water, agar, polyethylene powder, TX-151, and NaCl[3] (σ = 0.57 S/m, εr = 58.92; k = 0.02 W/m/K; c = 3296 J/kg/K). Temperature distributions were recorded via infrared thermography immediately before and after heating with 180W total power for 3 minutes. Simulated and experimental temperature maps with and without MR coils were quantitatively compared using gamma analysis.

Results. Simulated and measured temperature distributions with and without the receive coils are shown in Fig. 2. Quantitative comparison of the results was achieved using gamma analysis (distance-to-agreement = 5 mm, temperature difference = 5%). Simulations, which only account for the presence of conductive coil elements, yielded a 100% passing rate with and without coils present. Phantom experiments, which additionally include matching circuitry and housing materials of the coils, resulted in a passing rate of 95.8%, indicating a negligible impact of coil integration on heating performance.

Summary. Quantitative agreement of simulations and phantom experiments demonstrates that integrating MR receive coils into a breast hyperthermia applicator does not meaningfully compromise heating performance. These findings support the technical feasibility of coil-integrated breast applicators for MRgHT. Future work will assess MRT and SNR benefits, advancing adaptive and clinically robust breast cancer treatment.

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Fig. 1

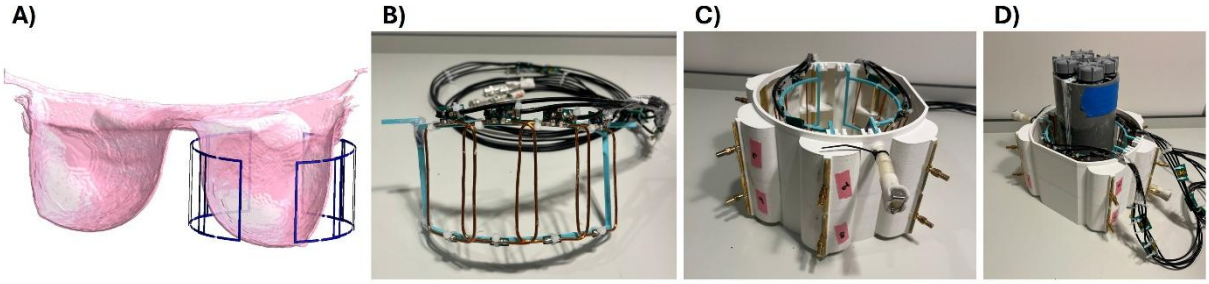

Figure 1: (A) MR receive coil array configuration around prone breast in simulation model, (B) One 4-element MR receive array (C) Both coil arrays inside the breast hyperthermia applicator, (D) Experimental setup with split phantom

Fig. 2

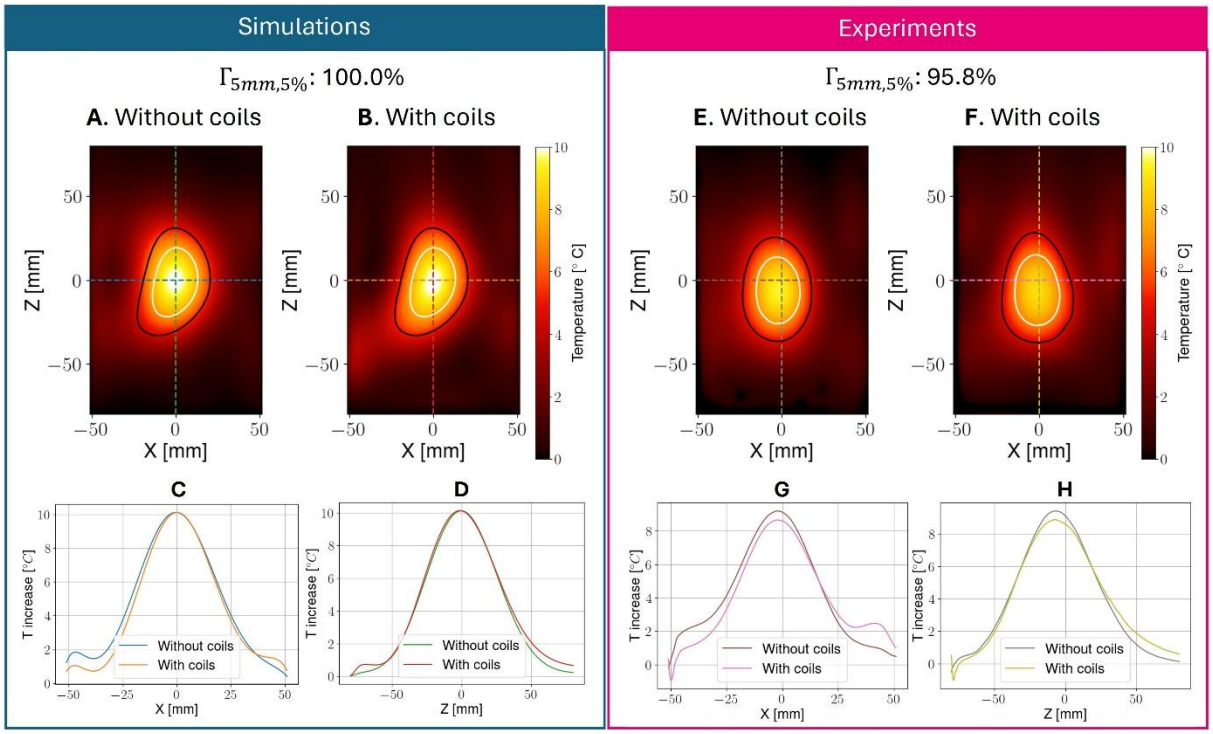

Figure 2: Heatmaps of the temperature simulation (A-D) and heating experiment (E-H). Subfigures (A), (B), (E), and (F) show the spatial temperature distributions, while (C) and (G) present temperature profiles along the line at z=0mm, and (D) and (H) show profiles along the line at x=0mm.

OP-037

The Landscape of Hyperthermia in European Radiation Oncology: Practice Patterns and Barriers to Implementation – Results from the ESTRO Hyperthermia Focus Group Survey of 48 Centers

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Introduction. Hyperthermia (HT) is an effective radiosensitizer that is gaining increasing attention in radiation oncology. In 2025, a HT Focus Group was established within the European Society for Radiation Oncology (ESTRO).

Goals. This ESTRO HT Focus Group initiative aimed to systematically identify European centers delivering HT combined with radiotherapy (HT+RT), characterize institutional features and patterns of care, and establish a framework to enhance coordination of HT development and support collaborative prospective studies and databases.

Materials and Methods. HT device manufacturers active within the European Society for Hyperthermic Oncology (ESHO) were asked to provide lists of centers applying HT+RT. A structured survey comprising 39–47 items, depending on availability of superficial and/or deep HT devices was distributed among these centers.

Results. Of 53 identified centers across 10 European countries, 49 (92.4%) completed the survey; 48 provided consent for data publication. A marked expansion in HT installations was observed, with the number of active centers increasing from 29 to 48 over the past five years. Among the 48 centers, 25% (12/48) use water-filtered infrared-A (wIRA) superficial, 31% (15/48) capacitive, 44% (21/48) radiative superficial, and 44% (21/48) radiative deep HT systems, including 19% (4/21) with MR-guidance. The mean annual number of patients per center treated with combined superficial HT+RT was 22.8 (median 17, range 1–73) and with deep HT+RT 35.5 (median 27,range 3-160). Overall Europe, recurrent breast cancer accounted for the majority (44.8%,368/822) of the annual superficial HT+RT cases, while soft tissue sarcoma (31.9%,261/817) and cervical cancer (17.1%,140/817) predominated in deep HT+RT. In addition, 38.8% (19/49) of centers participate in prospective HT trials. Across all participating centers, 65% (31/48) involve medical physicists in quality assurance (QA). ESHO QA guidelines for HT application are implemented in 80%(39/48) of centers, and temperature monitoring systems are present in 94%(45/48). Reported major barriers to the broader clinical adoption of HT included insufficient reimbursement (20%), skepticism regarding effectiveness (17.6%), and high initial investment costs (14.8%).

Summary. This first comprehensive survey on HT activity in Europe provides evidence for rising use of HT, with 66% increase in device installations over the past five years and approximately 1600 patients treated annually with HT+RT. Ensuring consistent well-controlled high-quality HT delivery requires adherence to standardized QA protocols and mandatory temperature monitoring to enable reliable data comparison. This patterns-of-care analysis will help informing the development of harmonized clinical practices and foster collaborative research to strengthen the evidence base for HT in modern radiation oncology.

Acknowledgments. We thank the 49 HT centers for completing the survey.

OP-038

Therapeutic Integration of Hyperthermia in Modern Oncology: Establishing the First National Practice Standards and Regulatory Roadmap in Romania (The SRHO Whitepaper)

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Background. Despite Level 1A evidence supporting oncological hyperthermia (HT) as an adjunctive cancer treatment, it remains excluded from practical national protocols and reimbursement mechanisms in many European countries. This is primarily due to a shortage of qualified centers, experienced professionals, adequate thermometry, and financial support. In Romania, a critical paradox exists: while HT is theoretically acknowledged, there is a historical lack of practical acceptance and institutional certification. Consequently, hospitals receive no dedicated funding, physicians risk accusations of exceeding their formally certified competencies, and patients are denied both reimbursement and equitable access. To overcome this void, the Romanian Society of Oncological Hyperthermia (SRHO) developed a comprehensive National Whitepaper. It shifts the focus from theoretical guidelines to safe practical implementation, aiming to secure National Health Service recognition.

Methods. The document was developed through a systematic synthesis of Phase III randomized controlled trials and large-scale network meta-analyses (incorporating over 9,800 patients in locally advanced cervical cancer, plus STS, NMIBC, and HNC trials). To guarantee therapeutic safety, the framework explicitly adopts the QA/QC protocols established by ESHO, DGHT, and the SEOR 2019 Consensus.

Results. The Whitepaper outlines a pragmatic, multi-phase roadmap, deliberately adopting the successful regulatory pathway utilized by Hyperbaric Medicine in Romania to secure Ministry of Health approval. Regarding treatment application and QA/QC, temperature control is desirable insofar as it is technically and ethically possible and also necessary. This principle supports a tiered approach to applicator calibration and thermal dosimetry metrics (SAR, CEM43°C), ensuring safety without creating unethical technical barriers. To bridge the gap between theoretical knowledge and safe clinical execution, the document establishes a 140-hour continuing medical education (CME) curriculum mirroring European benchmarks. Guided by an international Scientific Advisory Board, this framework serves as the official dossier for the accreditation of a "Certificate of Complementary Studies" in HT.

Conclusions. The SRHO Whitepaper provides a legally viable blueprint for integrating HT into emerging healthcare systems lacking formal regulations. Similar to the Spanish SEOR consensus, SRHO paves the way for standardizing the practical application of HT in Romania, proposing a regulatory model conceivable for other European countries seeking institutional recognition and government reimbursement for hyperthermia.

Fig. 1

Section 6: Bridging the Implementation Gap

Moving from clinical validation to systemic integration in oncology protocols.

- **Level 1A Evidence (with and without thermal dosimetry):** Clinical leaps are undeniable and historically proven, including **doubling Overall Survival (OS)** in Cervical Cancer and **tripling median OS** in Soft Tissue Sarcoma.
- **Standard of Care:** Hyperthermia is no longer experimental; it is a **MANDATORY** pillar of modern multimodal oncology *(proven effective even before advanced thermometry)*.
- **The Goal:** Immediate integration into national oncology protocols to ensure every patient has access to the synergistic power of Precision Heat.

> ***"It is recommended that oncology centers administering RT/CHT for Level 1A indications integrate Hyperthermia (HT) as a Standard of Care, provided that thermal dosimetry is utilized to maximize precision."***

Hyperthermia: The 4th Pillar of Cancer Treatment

Radiotherapy | Chemotherapy | Surgery | **Hyperthermia**

The Weight of Evidence: Beyond Dispute (Level 1A)

Shifting from isolated trials to the highest echelon of Evidence-Based Medicine (EBM).

The Ultimate Validation

Network Meta-Analysis (NMA) by Datta et al. (2019).

9,894 Patients

Locally Advanced Cervical Cancer Cohort

Clinical Conclusions

- **Survival Benefit:** Conclusive proof that the addition of Hyperthermia significantly improves Overall Survival (OS) and Local Control.
- **Toxicity Profile:** Zero compounding of severe systemic toxicity.

The Paradigm Shift: Hyperthermia is unequivocally validated by the highest standards of global EBM.

Fig. 2

The SRHO Roadmap & Call for Institutional Synergy

Overcoming the regulatory vacuum in Romania despite Level 1A evidence.

1. THE REGULATORY ROADMAP

- Implementation of a structured **140-hour CME Curriculum**.
- Formal accreditation goal: **"Certificate of Complementary Studies"** by the Romanian Ministry of Health.

2. CALL FOR SYNERGY

- We formally invite our esteemed colleagues from **SIIO**, **DGHT eV**, **SEOR** & **ESHO** to:
  - **review and co-sign the SRHO Whitepaper.**
  - **help develop and teach the 140-hour university curricula**
- **The Goal:** Transform European clinical evidence into national health policy through unified institutional weight.

"Let's turn science into standard of care through a unified approach."

ROMANIAN SOCIETY OF HYPERTHERMIC ONCOLOGY (SRHO)

OP-039

The European School of Thermotherapy: advancing clinical education in hyperthermia combined with radiotherapy

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Introduction. While the number of European hospitals offering hyperthermia (HT) as part of cancer treatment is increasing, the technique remains relatively underutilized and requires specialized training. Despite the availability of HT, intergrating HT into clinical practice and delivering high-quality HT treatments can be challenging, particularly when background knowledge of HT biology, physics, and practical implementation is limited. To advance knowledge of HT across Europe and provide practical guidance for initiating high-quality treatments, experts from Erasmus MC and Amsterdam UMC (The Netherlands) developed the European School of Thermotherapy (ESOT). This abstract share the educational experience of the ESOT.

Methods. The first ESOT meeting took place from 14-16 April 2025, and was endorsed by ESTRO and ESHO. The primary aim of this comprehensive three-day course was to provide essential knowledge for the delivery of high-quality HT treatments. The program included the biological rationale, physics, and clinical fundamentals, next to practical implementation, case discussions including clinical challenges, overview ofclinical trials, and live demonstrations in treatment rooms. Lectures were delivered by 25 HT experts from five European countries. The course was designed to meet the needs of a diverse group of professionals interested in HT: radiation and medical oncologists, physicists, radiation therapists (RTTs), nurses and researchers. Participants evaluated the course bya 19-item questionnaire.

Results. A total of 36 participants from 14 countries attended the first edition of ESOT. Eighteen participants had prior HT experience (median 2 years; range 0.2–26 years). The participants consisted of 11 radiation oncologists, 8 physicists, 7 PhD candidates, and 3 medical oncologists. Additional attendees included 2 radiation therapists (RTTs), 2 medical doctors, 2 researchers, and 1 nurse. The overall appreciation of ESOT was rated 8.5 out of 10, with the combination of practical training, clinical discussions, and theoretical background being considered the most valuable aspects. Participants suggested that future editions could include lectures and workshops on capacitive HTsystems, adverse events, and water-filtered infrared HT.

Conclusion. ESOT provided participants with the initial and essential theoretical and practical knowledge required to deliver high-quality HT treatments. It was highly valued for its combination of hands-on training and solid background education, clearly addressing an existing educational gap. The activities of the ESTRO hyperthermia focus group, particularly workgroup 2 (training, education, awareness, and communication), align very well with this initiative and further support its relevance. With the involvement from ESTRO, a second ESOT edition, to meet the evident and growing demand, will be planned in April 2027.

OP-040

Role of CRS-HIPEC in Carcinoma Ovary: Where Do We Stand Today? Experience from a Tertiary Referral Oncology Centre in India

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Background. Advanced epithelial ovarian cancer (EOC) is associated with high rates of peritoneal recurrence despite standard multimodality treatment. Cytoreductive surgery (CRS) remains the cornerstone of management, while Hyperthermic intraperitoneal chemotherapy (HIPEC) has emerged as a potential adjunct to reduce peritoneal relapse and improve disease-free survival (DFS). This study evaluated the role of CRS-HIPEC in upfront, interval, and secondary cytoreduction settings.

Methods. This was a large single-centre retrospective study based on a prospectively maintained database from 2014 to 2025. A total of 510 patients with EOC underwent upfront, interval, or secondary CRS with or without HIPEC. HIPEC was delivered using cisplatin 75 mg/m² for 60 minutes in upfront and interval settings, and cisplatin 75 mg/m² plus doxorubicin 15 mg/m² for 60 minutes in the secondary setting. The primary endpoint was DFS.

Results. The median age was 52 years. Most patients had stage III disease (81.7%), while 18.3% had stage IV disease. Upfront, interval, and secondary CRS were performed in 21%, 54%, and 25% of patients, respectively. Overall, 63.4% underwent CRS-HIPEC. Complete cytoreduction was achieved in the majority, with CC-0 in 79%, CC-1 in 15%, and CC-2/3 in 6% of patients. The median follow-up was 65 months. Median DFS with CRS-HIPEC versus CRS alone was 47 versus 45 months in the upfront setting ($p=0.1465$), 27 versus 14 months in the interval setting ($p<0.0001$), and 22 versus 16 months in the secondary setting ($p<0.0001$). Among CRS-HIPEC patients, DFS was significantly higher in the upfront than interval setting.

Conclusion. CRS-HIPEC was associated with improved DFS in interval and secondary cytoreduction settings. In upfront surgery, complete CRS appears to remain the dominant determinant of outcome, with no statistically significant additional DFS benefit from HIPEC. Larger prospective validation is required.

Biology, translation and model systems

OP-044

Profiles of therapeutically relevant thermophysical and oxygenation-related traits of tissue layers exposed to combined thermo-radiotherapy of breast cancers

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[3] Charité – Universitätsmedizin Berlin, Department of Anesthesiology and Intensive Care Medicine, Berlin, Germany

Introduction. Control of locally recurrent breast cancer (BC) can be achieved using thermo-radiotherapy e.g., mild wIRA-HT, immediately followed by hypofractionated RT). Thermo-physical properties and the oxygenation status of the tissues in the treatment field distinctly influence therapeutic efficacy.

Goals: Update of data on relevant parameters in the different tissue layers of the female breast is crucial for computational modeling of the treatment area, therapy planning and treatment success.

Methods. Reliable pretreatment data on key thermophysical parameters and on O_2 supply to tissue layers exposed to HT+RT during BC-treatment are presented. Tissue water content (Cw), specific heat capacity, thermal conductivity, diffusivity, effusivity, and tissue temperature are presented for tissue layers, tissue components of healthy female breast, pectoralis muscle, and breast cancer, which are exposed to irradiation upon HT+RT treatments. Averaged values of parameters are presented as profiles from peripheral (epidermis) to central tissue layers (pectoralis muscle).

Results. Tissue layers show highly variable values for most traits. *Thermophysical parameters* increase almost linearly with rising water content, and are highest in breast cancers. Increases are similar when comparing different breast tissue components and skin layers. *Blood flow rates* [ml/g/min], which greatly determine O_2 delivery and the oxygenation status are 0.08 in dermis, 0.015 in subcutis and adipose tissue, 0.06 in normal breast *vs.* 0.24 in breast cancers, and 0.03 in pectoralis muscle. *Tissue oxygenation status:* Median pO_2 values [mmHg] are 80 in outer, 5 in central, and 35 in deep layers of the epidermis, 43-48 in dermis, subcutis and adipose tissue, 65 in healthy breast, 10 in breast cancers, and 30 in pectoralis muscle. Hypoxic tissue fractions (HFs) are 50% in cancers *vs.* <5% in normal breast or subcutis. Oxygen enhancement ratios (OER) are 2.80-2.85 in healthy tissues *vs*.1.85 in cancers. O_2 diffusion coefficients D [cm^2/s] rise almost linearly with increasing Cw- values

Summary. Clinically relevant thermophysical and oxygenation properties of tissue layers exposed to HT+RT of breast cancers vary greatly: Hyperhydration of cancers result in higher absorption of electromagnetic radiation (i.e., increased thermal energy uptake). This is counteracted by higher thermal conductivities, diffusivities and effusivities, causing temporary conductive heat fluxes into normal tissues adjacent to breast cancers, i.e., greater heat fluxes from cancers into surrounding tissues until thermal steady states are reached. Thus, adjusted irradiances and adequate exposure times are required to enhance therapeutically relevant effects, and to avoid hot spots (especially relevant for HT levels T>41°C). With the exception of HFs, all O_2-related parameters listed and O_2-extractions increase upon mild HT, thus sensitizing for radiotherapy and some chemotherapy, and activating antitumor immune responses.

OP-045

Cryo-thermal therapy reprograms myeloid cells into CCL5+ mature phenotype to increase T-cell infiltration and potentiates anti-PD-1 therapy

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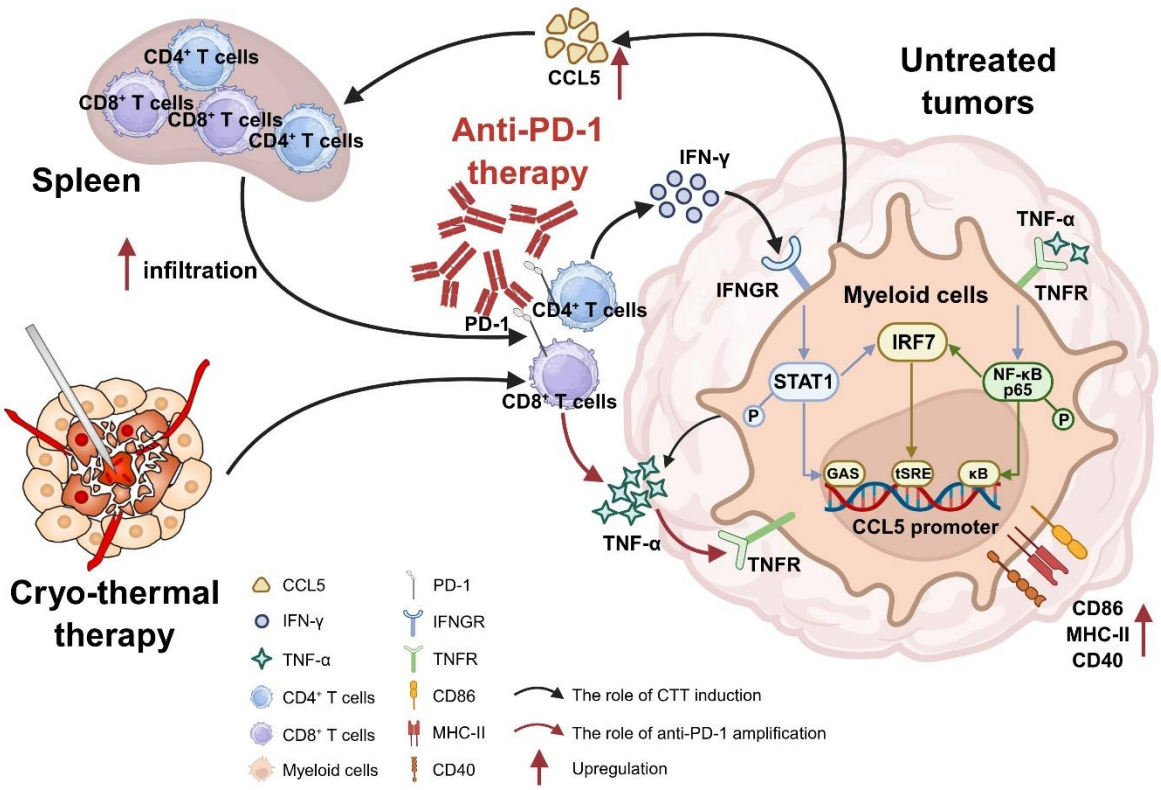
[1] Shanghai Jiao Tong University, School of Biomedical Engineering and Med-X Research Institute, Shanghai, China

Although immune checkpoint blockade (ICB) represented by anti-PD-1 therapy has demonstrated significant clinical benefits, its efficacy remains limited by the immunosuppressive tumor microenvironment (TME). Cryo-thermal therapy (CTT) not only completely ablates local solid tumors by pre-freezing before radiofrequency heating, but also reverses immunosuppression and triggers strong systemic anti-tumor immunity to inhibit tumor recurrence and metastasis. Our present study revealed that the combination of CTT and anti-PD-1 therapy potently enhances myeloid cell maturation and simultaneously promotes the infiltration and functional activation of T cells in distal tumors, resulting in superior suppression of distal tumor growth compared to either cryoablation or radiofrequency ablation combined with anti-PD-1 therapy. Mechanistically, CTT specifically induces TNF-α production in mature myeloid cells, triggering autocrine CCL5 secretion that recruits peripheral IFN-γ+ T cells induced by CTT in distal tumors, creating a cytokine loop in which IFN-γ derived from T cells and TNF-α derived from myeloid cells collectively promote CCL5 secretion in myeloid cells to increase effector T-cell recruitment in distal tumors. After CTT, anti-PD-1 treatment amplifies this cascade by enhancing TNF-α production in T cells, and high levels of IFN-γ and TNF-α in distal tumors promotes increased secretion of CCL5 in myeloid cells, resulting in robust infiltration of T cells. The parallel activation of STAT1 by IFN-γ and NF-κB by TNF-α in myeloid cells converges to drive IRF7-dependent CCL5 upregulation to create a local immune enhancing environment via CCL5-mediated recruitment of T cells. Our study demonstrates that CTT establishes an immunologically favorable TME by reprogramming immunosuppressive myeloid cells into mature myeloid cells with high CCL5 production, thereby facilitating effector T-cell recruitment, providing an efficient therapeutic strategy to promote the response to anti-PD-1 therapy.

Fig. 1



OP-046

Transient necroptosis induction combined with chemo- or thermoradiotherapy as a synergistic immune inducer for low toxicity, sustained cervical cancer therapy

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Question. Patients with locally advanced cervical cancer (LACC) are typically treated with chemoradiotherapy or in case of contraindications for chemotherapy, treated with radiotherapy combined with hyperthermia (thermoradiotherapy). Although immunotherapeutic drugs are now indicated for recurrent and metastatic cervical cancers, many tumors remain immunologically "cold", thus fail to respond. Strategies that enhance tumor immunogenicity are therefore of increasing interest. A potential mechanism to promote the anti-tumor immune responses through the release of damaged-associated molecular patterns and enhanced antigen presentation is the induction of necroptosis, is a regulated form of inflammatory cell death.

We have explored ways in which necroptosis can be enhanced for synergistic outcomes with thermoradiotherapy and immunotherapy.

Methods. To better characterize the involvement of necroptosis in cervical cancer, experiments were performed in an in vitro setting using four cervical cancer cell lines and a panel of seven patient-derived organoids in biomimetic conditions. The intracellular signal transduction and necroptotic machinery were measured at the protein level under various conditions, including treatment with the standard of care chemo- (+/- thermo)radiotherapy and a necroptosis induction cocktail. These experiments were performed in an in vitro setting using cervical cancer cell lines and patient derived organoids in biomimetic conditions.

Results. Necroptosis seems to occur in a highly context-and patient-specific manner, with substantial basal differences between different cell lines and patient-derived organoids. Patient-derived cervical cancer organoids have proven a suitable platform for the study of necroptosis and have clearly demonstrated the biological variation present in this process. We have included responders and non-responders which do not correlate to the basal expression of RIP3, as has been widely proposed in literature.

Conclusions. Our previous clinical data suggest that poorer survival in high-risk cervical patients may result from a suppressed tumor immune microenvironment. We have also preliminarily observed durable responses from patients having received thermoradiotherapy.

We postulate that the addition of transient necroptosis induction through specific caspase 8 blockade to hyperthermia or thermal ablation, would be highly effective in facilitating immune cell recruitment to the tumor site. Restoration of immunologically "cold" cervical cancers provides for a less toxic and more durable response with the potential for immune memory and abscopal effects through the increased antigenicity and adjuvanticity associated with necroptosis.

OP-047

Effect of Hyperthermia and Radiotherapy Combination on DNA Damage Repair and Immune Phenotype of Breast Cancer Cells

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Question. Hyperthermia (HT) is an established radiosensitizer that enhances the efficacy of radiotherapy (RT) through multiple biological mechanisms, including inhibition of DNA repair pathways. However, the impact of HT-RT sequencing on DNA damage and its potential immunological consequences remains not fully understood. This study therefore investigated the effects of HT and RT combinations on DNA damage repair, micronuclei (MN) formation, and immune checkpoint molecule expression in breast cancer cells.

Methods. Human breast cancer cell lines MCF-7 and MDA-MB-231, as well as murine 4T1 cells, were treated with HT (41°C, 1 h), RT (2 × 5 Gy), in different sequences of both modalities (HT first then RT, and vice versa). The interval between HT and RT was 1h. γH2AX foci formation, MN frequency in tumor cells, mean nuclear area, and HVEM immune checkpoint molecule expression were analyzed at 24 h, 72 h, and 120 h post-treatment using high-throughput fluorescence imaging and customized image-analysis pipelines.

Results. HT followed by RT induced significantly higher persistent γH2AX foci at 120 h compared to RT or HT alone, suggesting delayed DNA damage repair. Combined HT+RT treatments also increased MN formation across all examined cell lines, but with the strongest effects observed when HT was applied before RT. Furthermore, increased MN prevalence is strongly correlated with elevated HVEM expression in MDA-MB-231, MCF-7, and 4T1 cells. Nuclear enlargement, which is one of the signs suggesting senescence-like changes, was also modestly correlated with HVEM upregulation.

Conclusions. HT enhances RT-induced DNA damage and MN formation in breast cancer cells, particularly when administered before RT. The observed association between MN formation and HVEM expression suggests a potential link between DNA damage responses and immunosuppressive signaling pathways. These findings support further investigation of HT-RT combinations as modulators of anti-tumor immunity and for additional combination with immune checkpoint inhibitors.

OP-049

Immunomonitoring of patients with anal carcinoma treated with deep regional hyperthermia in combination with standard radiochemotherapy – first results of the HYCAN trial

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Introduction. Anal cancer represents approximately 1.6% of all malignancies of the digestive system, with increased incidence observed in specific high-risk populations. Established risk factors include tobacco use, infections with sexually transmitted pathogens (e.g., HIV, HPV), and chronic immunosuppression. For more than three decades, the standard of care has been radio-chemotherapy (RCT) with 5-fluorouracil and mitomycin C. Emerging evidence suggests that the addition of regional hyperthermia may improve overall survival, local control, and colostomy-free survival. In this context, the prospective randomized HYCAN trial (NCT02369939) was initiated to evaluate the impact of combining hyperthermia with standard RCT in patients with anal carcinoma.

Goals. As part of the accompanying translational research program, comprehensive longitudinal immunophenotyping of peripheral blood is conducted to assess potential immunostimulatory effects of hyperthermia and to identify predictive and/or prognostic immune biomarkers.

Materials and Methods. A total of 118 patients with locally advanced anal cancer will be randomized into two treatment arms. Patients in the control arm receive standard RCT. In the experimental arm, patients receive an additional six sessions of regional hyperthermia. Peripheral blood samples for immune monitoring are collected at baseline, on day 8 of treatment, and on day 29 (post-hyperthermia). Comprehensive immunophenotyping is performed using a validated multicolor flow cytometry assay, enabling the identification of seven major immune cell populations and multiple subpopulations directly from whole blood. In addition, the activation status of immune cells is assessed.

Results. A first interim analysis of the longitudinal immune monitoring was performed after the recruitment of 50 patients. As expected, RCT impacts significantly on the number of circulating immune cells, especially on lymphocytes. Even though the number of immune cells is reduced, certain immune cell populations show a modulation of their respective activation status during RCT. Further, hyperthermia was found to induce certain immune modulations, that are exclusively found in the experimental arm. These modulations include higher counts of circulating polymorphonuclear cells, especially neutrophils and different patterns of activation in specific immune cell types.

Summary. Deep regional hyperthermia combined with RCT results in distinct modulations of the peripheral immune status of patients with anal carcinoma. These immune alterations will be analyzed in relation to treatment response and toxicity, thereby supporting the future identification of predictive and prognostic immune signatures. Moreover, longitudinal immune monitoring may help to elucidate the immunomodulatory mechanisms of hyperthermia in multimodal tumor therapies.

OP-048

Mitochondria-targeted precision hyperthermia therapy in triple negative breast cancer cells by bioengineered gold nanoparticles

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Introduction. Conventional modalities for treatment of highly aggressive triple negative breast cancers (TNBCs), such as chemo and radiotherapy lacks tumor specificity. Gold nanoparticle (AuNP)-based hyperthermia is one of the emerging cancer treatment modalities. However, application of mitochondria-specific green synthesized AuNPs for laser-based hyperthermia therapy has not been explored in detail. As mitochondria is essential for cells" bioenergetic, biosynthetic and signalling demands, their targeted destruction can starve cells to death. Moreover, apoptosis resistant cancers can be sensitized by enhanced production of reactive oxygen species and cytochrome C release.

Goals. This study explores the anti-cancer efficacy of mitochondria-targeted green synthesized AuNPs in combination with hyperthermia. The targeted action of the combinatorial therapy has the potential to overcome resistance and elevate cancer cell death.

Materials and Methods. AuNPs were prepared by green synthesis route using Bacopa monnieri (Brahmi) extract and functionalized with Rhodamine 123(RhoBm@AuNPs). The AuNPswere characterized by UV-visible spectroscopy, dynamic light scattering (DLS), zeta potential analysis, Fourier transform infrared spectroscopy, thermogravimetric analysis, and transmission electron microscopy (TEM). Laser hyperthermia therapy efficacy was evaluated using NIR laser light of 808 nm. The cellular uptake of the particles was confirmed by confocal and TEM, whereas combinatorial efficacy was evaluated in MDA-MB-231 cells by crystal violet, clonogenic and PI cell viability assays.

Results. RhoBm@AuNPswerefound to have a hydrodynamic diameter of 120nm by DLS, with a zeta potential of -34±0.5mV, suggesting good colloidal stability. TEM analysis showed a mean core size of 17nm with predominantly spherical shape. Both RhoBm@AuNPsand Bm@AuNPs showed significant heating after laser irradiation suggesting laser hyperthermia therapy efficacy.Confocal imaging confirmed the mitochondrial targeting of RhoBm@AuNPs in MDA-MB-231 cells as observed by co-localization with mitotracker red. Furthermore, this observation was validated by cellular ultrastructure analysis which showed dark contrast of AuNPs inside mitochondria for RhoBm@AuNPs, however, Bm@AuNPs were predominantly visualized inside endosomes and cytoplasm. The selective mitochondrial damage by RhoBm@AuNPs was evident as mitochondrial bulging, reduced number and loss of cristae, characteristic features suggesting mitophagy mode of cell death. PI and crystal violet assays showed increased killing of TNBC cells after treatment of RhoBm@AuNPs, which was further enhanced in combination with hyperthermia. Enhanced thermal sensitization efficacy of RhoBm@AuNPs was also corroborated by clonogenic survival assay as well.

Summary. Mitochondria targeted RhoBm@AuNPs showed enhanced anti-cancer efficacy after laser hyperthermia.

Fig. 1: Cellular TEM of MDA-MB-231 cells treated with (1) Bm@AuNP, (2) RhoBm@AuNP

Fig. 1

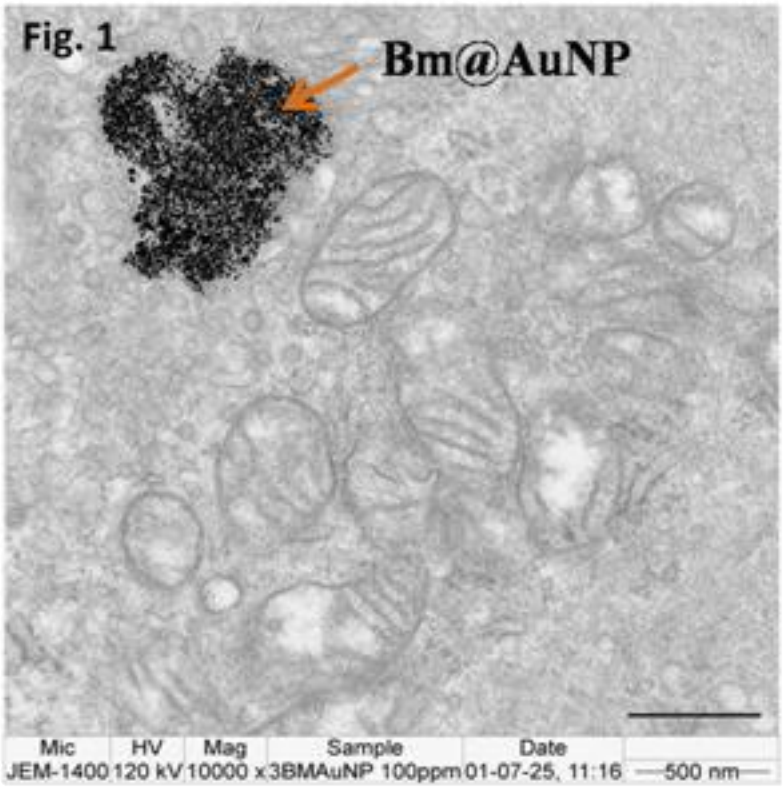
Fig. 1
Bm@AuNP
Mic
HV
Mag
Sample
Date
JEM-1400
120 kV
10000 x
3BMAuNP 100ppm
01-07-25, 11:16
500 nm

Fig. 2

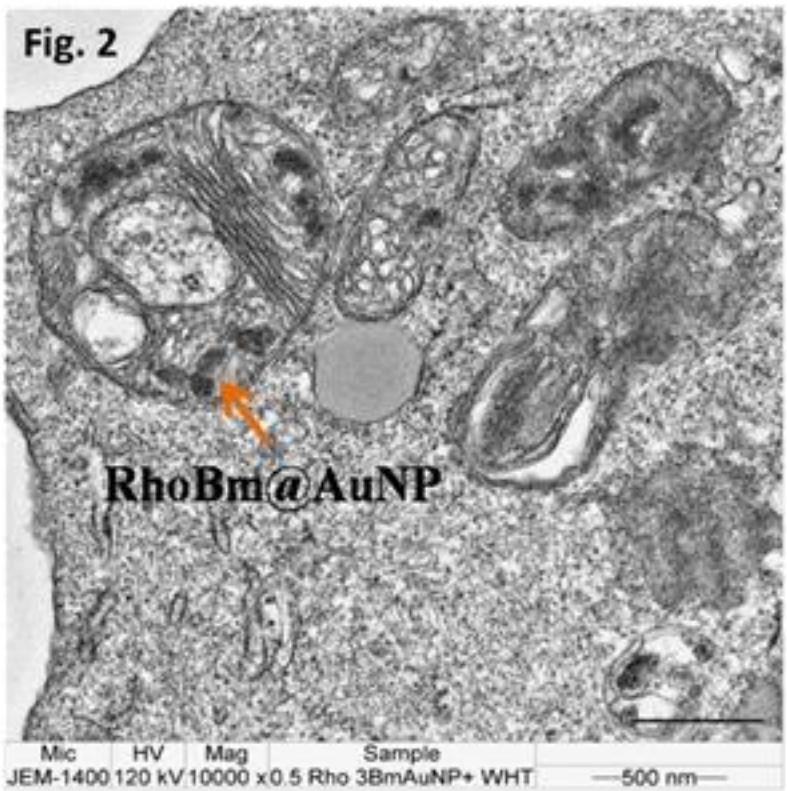
Fig. 2
RhoBm@AuNP
Mic
HV
Mag
Sample
JEM-1400
120 kV
10000 x
0.5 Rho 3BmAuNP+ WHT
500 nm

Clinical trials

OP-050

Phase II feasibility study of MR-guided hyperthermia combined with chemoradiotherapy for locally recurrent rectal cancer: Integration of ctDNA methylation as a biomarker of hypoxia-driven resistance

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Question. LRRC occurs in 5–11% of rectal cancer patients, affecting 60,000 patients worldwide and 300 annually in the Netherlands(1). LRRC is associated with poor prognosis and limited locoregional treatment options(2-3). Neoadjuvant chemoradiotherapy (CRT), including reirradiation in previously irradiated patients, is standard of care in many institutions. Although extensive downstaging may result in a pathologic complete response (CR) associated with improved survival(4), CR occurs in only ~5% of patients, while many experience substantial toxicity with limited benefit(5-6). More effective and less toxic treatment strategies are therefore needed. Tumor hypoxia is a major driver of CRT resistance by impairing DNA damage repair and inducing characteristic DNA methylation patterns detectable in circulating tumor DNA (ctDNA)(7-8). Deep regional HT heats tumors to 39–45°C for 60–90 minutes, enhancing perfusion, reoxygenating hypoxic regions, inhibiting DNA repair, and sensitizing resistant tumor cells to CRT without substantial additional toxicity(9).

Methods. This phase II feasibility study will enroll 42 patients with LRRC eligible for curative-intent neoadjuvant CRT. Patients will receive standard CRT combined with weekly HT. Radiotherapy consists of either 50 Gy in 25 fractions or, for previously irradiated patients, 30 Gy in 15 fractions, both administered with concurrent daily capecitabine and combined with 5 or 3 weekly HT sessions, respectively. HT treatments will be monitored using MR thermometry and/or intraluminal temperature probes. Feasibility endpoints include treatment adherence, thermal stability, workflow integration, toxicity, and patient-reported quality of life. Tumor response will be assessed clinically by MRI during treatment and at 3 months after treatment, and pathologically following surgery when applicable. ctDNA samples will be collected at baseline, during treatment, and at 3 months to evaluate hypoxia-associated methylation patterns and their association with thermal dose, tumor response, and locoregional control. The study is powered to detect an increase in CR rate from 5% with CRT alone to 17% with CRT+HT.

Impact. This study introduces a biologically rational, low-toxicity strategy to overcome hypoxia-driven CRT resistance in LRRC. CRT+HT is expected to improve CR and local control while maintaining quality of life. Longitudinal ctDNA methylation profiling may provide a minimally invasive biomarker for hypoxia, enabling personalized treatment by identifying patients most likely to benefit from CRT+HT. Findings may advance understanding of epigenetic mechanisms underlying treatment resistance and support broader implementation of HT in clinical practice.

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OP-051

Sequencing of Hyperthermia and Re-irradiation in Locoregional Recurrent Breast Cancer – A Pilot Randomized Trial (SEQUENCE)

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Background. There are no clinical data that show that treatment sequencing of hyperthermia (HT) and radiotherapy (RT) or timing have a significant effect on clinical outcomes. As a result, substantial heterogeneity exists in the clinical application of both treatments across centers, often depending on local practice patterns, administrative factors, and team availability.

Aim. The SEQEUNCE study is a multicentre pilot randomized trial designed to investigate the effect of treatment sequencing and time interval between HT and reirradiation (reRT) in patients with breast cancer recurrences.

Methods. Patients with operable or inoperable breast cancer recurrences will be included. All patients will receive reirradiation, either adjuvant (subcohort 1) or definitive (subcohort 2) and will be randomized to HT before or after reRT The primary endpoint is acute grade ≥3 toxicity, assessed according to CTCAE version 6.0 from the start of treatment until 4 weeks after completion of radiotherapy in patients with recurrent operable and inoperable breast cancer (Figure 1). Secondary endpoints include local control, disease-free survival, distant metastasis (DM) or progression, overall survival, adverse events, and quality-of-life outcomes assessed using the EORTC QLQ-C30 and BR23 questionnaires. These endpoints will be evaluated at 1-, 2-, and 3-year timepoints in both recurrent operable and inoperable breast cancer cohorts. In addition, thermometric parameters recorded either on the skin surface or invasively within the target volume during HT sessions will be evaluated. This is the first randomized clinical trial investigating the sequencing of HT and RT in locoregional recurrent or inoperable breast cancer. Therefore, the study is designed as a pilot trial with the primary objective of generating estimates to inform the design assumptions of a future confirmatory study. The primary estimand is the between-arm absolute risk difference (RD) in the rate of acute grade ≥3 toxicity within the primary assessment window. No formal confirmatory hypothesis testing is planned; statistical inference will focus on point estimates and confidence intervals. A total sample size of 100 patients (50 per arm) is planned. Using simulation analyses, the precision of the estimated absolute difference in toxicity between treatment arms was assessed based on the width of the 95% confidence interval.

Conclusion. The SEQUENCE study will evaluate whether delivering HT before versus after RT fractions influences clinical outcomes in patients with recurrent operable and inoperable breast cancer. Furthermore, the study will prospectively assess the impact of additional parameters, including thermometry type, the time interval between treatment modalities, and tumor depth, within a controlled multicentre study setting.

Fig. 1

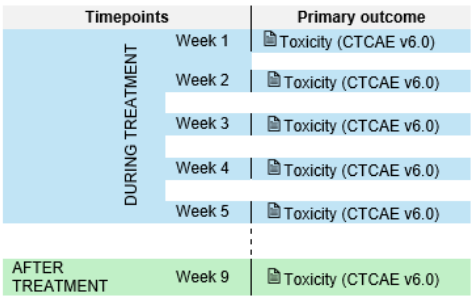

Figure 1. Evaluation timepoints for the primary outcome.

OP-052

Proposed new study: ThermoRad-BC study, a randomised phase 2 study of the addition of Thermotherapy (superficial hyperthermia by wIRA) with palliative Radiotherapy plus systemic treatment versus systemic treatment in patients with local recurrent Breast Cancers (LRBC)

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Background and question. Locoregional recurrent breast cancer (LRBC) remains a major therapeutic challenge, particularly in patients with previously irradiated disease. Local disease progression often leads to distressing symptoms including pain, ulceration, bleeding, malodour and substantial deterioration in quality of life. The water-filtered infrared A radiation (wIRA) superficial hyperthermia in combination with re-irradiation has been used to treat LRBC at centres across Europe for many years. However, in the UK and many other countries, re-irradiation with wIRA hyperthermia is not accepted as standard of care for LRBC due to lack of randomized clinical data. To change practice in the UK and other parts of the world, evidence based on randomized data is required. In addition, with the advancement of systemic treatments in different subtypes of breast cancers, question remains whether superficial hyperthermia in combination with re-irradiation plus systemic treatment would offer additional local tumour control compared to systemic treatment alone in LRBC.

Methodology.

Study design
We proposed to do a randomized phase 2 study of superficial hyperthermia with palliative radiotherapy plus physicians" choice of systemic treatments versus physician"s choice of systemic treatments in patients with inoperable or locally recurrent breast cancer

PICO
Patient population
Local recurrent breast cancers +/- other metastases
Main inclusion criteria
• Aged ≥18 years old
• Eastern Cooperative Oncology Group (ECOG) performance status 0 to 1
• Capacity to consent
• Previously histologically confirmed breast cancers with known ER/PR and HER2 status
• Previous adjuvant radical radiotherapy to breast/chest wall

Intervention
Re-irradiation (20Gy/5 fractions/5 weeks) of locally-recurrent breast cancer with superficial hyperthermia using (wIRA) superficial hyperthermia machine

Comparator
Arm 1 (control): SACT (standard systemic treatment as per physicians" choice)
Arm 2 (experimental): SACT + re-irradiation (20Gy/5F/over 5 weeks) with hyperthermia

Outcomes
Primary outcomes: Local Objective Response rate (ORR) rate according to RECIST 1.1
Secondary outcomes:
• Median PFS
• Rate of adverse events assessed by CTCAE version 5.0
• Median and 12-month PFS
• Median and 12-month OS
• Best Objective response rate (ORR)

• Loco-regional control rate and control rates at 6 and 12 months
• Quality of Life (QoL) assessment using Patient Reported Outcome Measures

Results and conclusions. We will be sharing the preliminary results from breast cancer cohorts of patients treated in ThermoRad wIRA study, which is a prospective real-world implementation study in the UK. The results from this study will highlight the importance of combining systemic treatment with superficial hyperthermia and palliative radiotherapy in order to achieve a durable locoregional tumour control, which will provide justification for the proposed randomized phase 2 study (ThermoRad-BC study).

OP-053

Feasibility of Total Neoadjuvant Treatment with Hyperthermia in Patients with Sarculator high-risk Extremity and Trunk Soft Tissue Sarcoma (TNT-HYPE). A Multicenter, Single Arm, Open Label, Phase II Trial of the Swiss Cancer Institute (SAKK 57/24)

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[2] LMU University Hospital, Department of Internal Medicine III, Munich, Germany
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[9] Cantonal Hospital St. Gallen, Department of Medical Oncology and Hematology, St. Gallen, Switzerland
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Introduction. Extremity and trunk soft tissue sarcomas (eSTS) are rare cancers. While local control rates exceed 90%, patients with high-risk eSTS remain at significant risk of systemic relapse. Currently, there is no accepted international standard of care for this population. However, three cycles of neoadjuvant anthracycline-based ChT combined with ifosfamide are commonly used in clinical practice. The previous phase III trial from Issels/Lindner et al. 2010/2018 demonstrated that adding regional HT to anthracycline-based ChT (administered as 4 neoadjuvant and 4 adjuvant cycles), followed by surgery and RT, improved 10-year overall survival by 10%.

Goals. The aim of the present recruiting study is to administer HT concurrently with the most commonly used three-cycle neoadjuvant ChT-based regimen for high-risk eSTS and to integrate it into a total neoadjuvant treatment (TNT) approach together with RT and surgery.

Methods. SAKK 57/24 TNT-HYPE is a single-arm, national, multicenter phase II trial investigating the feasibility and efficacy of a TNT approach in patients with resectable, non-metastatic high-risk eSTS, as defined by the Sarculator nomogram. Included patients receive three 3-weekly cycles of neoadjuvant ChT following the STRASS 2 study regimen with doxorubicin (d1, 75mg/m2) and ifosfamide (d1-d3, 3g/m2) simultaneously applied with two sessions of radiative HT on d1 and d3 of each cycle. For leiomyosarcoma, ifosfamide is replaced by dacarbazine (d1-3, 300mg/m2). This is followed by RT, and subsequent surgical resection. As this new TNT approach has not yet been prospectively evaluated, feasibility is defined as primary endpoint, defined as percentage of patients who complete treatment according to protocol. Eight Swiss sarcoma centers are currently participating. Three of these centers have their own HT facilities for the concurrent chemo-HT part, while the other five centers refer their patients to the HT centers for the concurrent chemo-HT part. RT and surgery are performed at the respective referring centers. 24 patients will be enrolled. A RT and HT quality assurance program ensures reproducible RT and HT delivery. An HT manual defines the procedures for invasive temperature measurements and data reporting in order to enable thermal dosimetry analysis for all patients. In addition, the translational research program includes peripheral blood immune phenotyping in collaboration with the Translational Radiobiology Unit in Erlangen, Germany, as well as paired biopsies obtained at three time points during trial treatment (baseline, second cycle, and surgery).

Summary. If this approach is shown to be feasible and safe—and gains attraction within the international sarcoma community—it may serve as a foundation for a future randomized international trial.

Funding and trial number. This study (NCT06835049) is currently recruiting and funded by a Swiss National Science Foundation grant to ES and AK and by the SAKK.

OP-054

Ongoing 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 5 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.

OP-055

Mild Superficial wIRA-Hyperthermia Combined with Hypofractionated Radiotherapy in Locally Recurrent Breast Cancer – First Results of the HISTOTHERM study

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Introduction. Locoregional recurrences of breast cancer pose a significant therapeutic challenge, especially in previously irradiated areas where treatment options are limited. Mild hyperthermia acts as radiosensitizer by improving tumor oxygenation, inhibiting DNA repair mechanisms, and improving anti-tumor immune responses. The HISTOTHERM study investigates the combination of mild superficial hyperthermia with hypofractionated radiotherapy to enhance local tumor control in recurrent breast cancer.

Goals. The study aims (a) to evaluate clinical and histological tumor response, and (b) to identify underlying predictive markers and cellular processes associated with therapy response.

Methods. The HISTOTHERM study is a monocentric, prospective, longitudinal study. Patients with locally recurrent breast cancer receive a combination treatment of 60 min of mild superficial hyperthermia (39–43°C) using water-filtered infrared A (wIRA) irradiation, immediately followed by hypofractionated radiotherapy (weekly fractions of 4 Gy, total dose 20–24 Gy). Tumor biopsies are collected prior to treatment, during therapy (at a dose of 12 Gy), and at follow-up. Comprehensive analyses include patient characteristics, disease pathology, and treatment course documentation. Tissue samples undergo immunohistological characterization to evaluate histological regression and identify key regulated processes. The primary endpoint is the clinical local tumor response at first follow-up.

Results. Recruitment for the HISTOTHERM study is almost completed (38/40 prospective patients + 14 retrospective patients). Patients received one to five HT+RT cycles in different treatment sites. Preliminary analysis of 40 patients shows that 74 % of patients presented with large lesions (Rclass III/IV according to Notter et. al. [1]). Complete disappearance of all macroscopic tumor was achieved in 25% of patients at first follow-up in the first treatment cycle. 53 % presented with partial control, while stable or progressive disease was observed in 23 % of patients six weeks after completion of HT+RT. Analysis of biopsies revealed complete disappearance of tumor cells in 41 % of treated regions in follow-up biopsies. In samples containing tumor cells only sparse cells were identified in 49 %. The proliferating fraction was reduced in average from 49 % to 36 %.

Summary. The HISTOTHERM trial provides a prospective evaluation of the synergistic effects of hyperthermia and hypofractionated radiotherapy in recurrent breast cancer. By integrating clinical outcomes with tissue- based marker analyses, the study aims to provide a mechanistic basis for therapy responses. The results are expected to clarify the value of this combined approach in achieving local tumor control and to guide future treatment strategies for locoregional recurrences.

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Posters

Hyperthermia in the clinics: clinical implementation and multimodel therapies

P-018

Local Hyperthermia + Intravenous-Vitamin-C: Patient outcomes at an integrative medicine clinic in Australia

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Background. Hyperthermia treatment (HT) for cancer has a long history of more than 50 years worldwide, and is incorporated in mainstream oncology in the USA, Germany, and South Korea. In Australia, the National Institute of Integrative Medicine (NIIM) is one of only two institutions offering local hyperthermia. Hyperthermia has been shown to increase the response rate to chemotherapy and radiotherapy by up to 80% in more than 55 clinical trials worldwide.

Methods. Between Aug 2012 - Jun 2015 and between Jun 2025 – Apr 2026 NIIM treated two cohorts of n=32+21 cancer patients, who had at least 8-16 HT sessions 1-2x weekly for 8 weeks – as recommended for best effect -, using the Celsius42-TCS local hyperthermia device (Germany). Alternatively to chemo- or radiotherapy, 57% of NIIM"s patients combined HT with Intravenous-Vitamin-C (IVC) therapy.

Results. A 10-year follow-up study of our first cohort (2012-2015) revealed local hyperthermia to be a safe and effective adjunctive treatment for cancer, achieving a greater than 2-year survival in 60% (n=18/32) of patients with a variety of cancers, including 30% (n=9/32) who survived 5-11 years, (average 9 years). In this cohort, 56% (16/32) of patients had IVC therapy adjunctive to HT, with 94% (17/18) surviving 3-11 years (average 9 years). Types of cancers treated with HT+IVC included pancreatic (survival 9+ years), prostate (11 years), breast (10+ y), colorectal (16 y), cervical cancer (5+ y) or melanoma (10+ y).

At time of abstract submission, in our second cohort (2025-2026), 21 cancer patients had completed 8-16 HT sessions in 2 months, with promising results at 3 months, whereby 55% had improved, and 40% were considered stable. About half of these patients 57% (12/21) underwent HT+IVC treatment, and 43% underwent HT+chemo/radio treatment. Treatment areas included metastatic liver cancer (n=5^{C}, 3 improved, 2 stable), metastatic lung cancer (n=5, 2^{IVC} improved, 2^{IVC} stable, 1^{C} worse), and prostate cancer n=5, 2^{IVC} improved, 1^{IVC} stable, 1^{R} pending). The presentation will provide further updates.

Conclusions. Our data provides evidence for intravenous Vitamin-C (IVC) as an integrative medical therapy to be a suitable and effective adjunctive therapy with local hyperthermia.

P-019

Metastatic breast ACC progressed after chemo-immunotherapy. Multimodal treatment with hypofractionated SBRT, hyperthermia, and integrative therapies led to partial regression of lung lesions, suggesting a feasible, well-tolerated option for oligoprogressive disease

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Adenoid cystic carcinoma (ACC) of the breast is an extremely rare tumor accounting for <0.1% of all breast cancers diagnosed. ACC usually has favorable prognosis despite being a triple negative tumor: estrogen- progesterone- and human epidermal GFR2- negative. ACC is an anomaly with indolent behavior with a better prognosis rather than other triple negative tumors. Metastasis from ACC is uncommon, but when it does, the lungs are most affected with the liver, bones and kidneys. Despite ACC is well-known worldwide, literature is poor about any treatment of oligoprogressive metastatic ACC treated with hypofractoined Stereotactic Body Radiotherapy (SBRT) synergized with hyperthermia and integrative therapies as such combined with chemo-immunotherapy, ozone therapy. A 62-year-old woman diagnosed with grade 2 breast ACC (pT2 pN0) in 2022 underwent right mastectomy with reconstruction for grade 2 adenoid cystic carcinoma (pT2, 4.5 cm; pN0 sentinel node). Histology showed nipple and inferolateral dermal involvement, focal lymphovascular invasion, no perineural invasion and negative margins (ER−, PgR−, HER2−, Ki-67 24%). In Jan 2024, CT scan revealed millimetric lung nodules; a left lung segmentectomy confirmed metastatic triple-negative ACC (BRCA1−, PD-L1 >10%). Systemic therapy with Atezolizumab plus Nab-Paclitaxel was initiated and concluded in Dec 2024. In Jan 2025, CT scan and FDG-PET documented lung disease progression, showing both metabolic and dimensional advancement. Following disease progression, subject refused capecitabine treatment, and multidisciplinary approach was initiated. Patient has been treated with SBRT for multiple lung lesions between Sep 2025 and Jan 2026. The simulation CT was acquired using a breath-hold technique with 1 mm slice thickness to ensure maximum spatial precision. Clinical target volume was contoured on CT data set fused with PET-CT. The dose prescription was 30 Gy to the 70% isodose (42.85 Gy at isocenter) in three fractions. Treatment was delivered through multiple coplanar and no coplanar VMAT arcs by 6MVfff Linac. Isocenter position was verified before each fraction using CBCT co-registered to planning CT, setup rotation errors were corrected using the Exapod 6-degree-of-freedom (6DOF) robotic couch. In Sep 2025, four nodules were treated (two in the right lower lobe, one in the left upper lobe, and one in the right upper lobe). In Oct 2025, three additional nodules were targeted (right lower lobe, left lower lobe, and right middle lobe). This high-dose SBRT was integrated with ozone therapy and complementary treatments to optimize local control and patient tolerability. The whole treatment was integrated with 12 sessions of oncologic hyperthermia, ozonotherapy and oral immune-supporting therapies.

Combined treatment with precise hypofractionated SBRT, synergized with hyperthermia and integrative supports, showed significative reduction of three lesions lesions (Figure 1). This oncologic integrative approach showed a robust and well-tolerated option for oligoprogressive metastatic ACC.

Fig. 1

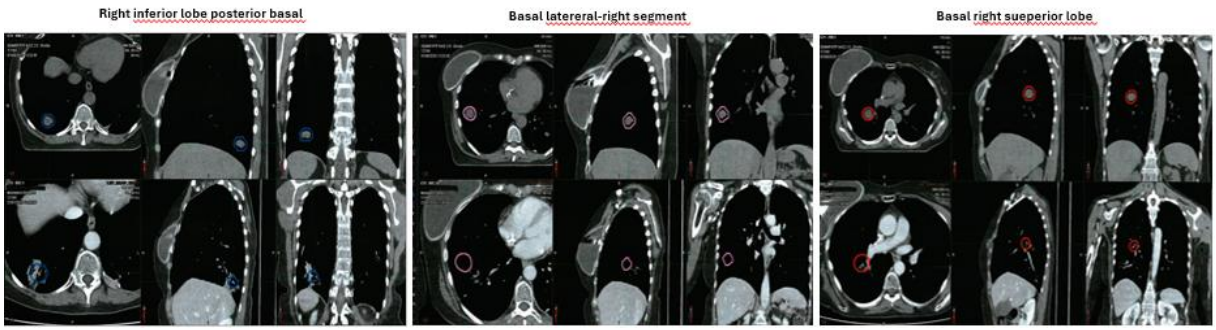

Fig. 2

P-020

Quality of life measurement during modulated electrohyperthermia as part of individualized multimodal immunotherapy

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Question. Over the last ten years, glioblastoma patients were treated with individualized multimodal immunotherapy (IMI) during and after first line standard of care (PMID40075726; PMID38548421). Throughout the complete IMI, modulated electrohyperthermia (mEHT, EHY2000, www.oncotherm.com) was repetitively performed in blocks of 5 days using 40-60 Watt for 50 minutes. Real World Data on 104 well-documented patients suggest a meaningful improvement in overall survival (OS) of both MGMT promoter unmethylated and methylated patients: median OS is 20 resp. 31 months; 2-year OS is 37% resp. 70%. Alongside extension of OS, Health-Related Quality of Life (HRQoL) becomes an important factor.

Methods. Since October 2021, the European Quality 5 Dimensions 5 Levels (EQ-5D-5L, https://euroqol.org) questionnaire was included at time of each treatment. The EQ-5D-5L consists of a self-reported descriptive system and EQ visual analogue scale (EQ-VAS). Data for reference health state were derived from mean values for Belgium, the Netherlands and England. Health utility indices (HUI) per patient per measurement were calculated. The time interval between each consecutive questionnaire was translated to quality-adjusted life months (QALM) using the corresponding HUI.

Results. A subgroup of 33 out of the 104 patients was selected for in-depth HRQoL analysis based on: availability of 1/ HRQoL data at time of the first IOZK intake, and 2/ at least 5 HRQoL measurements. Patient response rate was 96%. In total, data from 310 questionnaires, given at each treatment course, were sampled. A more varied functioning was reflected in patient-reported EQ-VAS compared to the Karnofsky Performance Index assessed by the treating physician. The EQ-VAS and EQ-5D-5L patient-reported outcome reflect patient HRQoL stability between first and last contact. For EQ-5D-5L, the dimension of mobility and self-care was considered less problematic in comparison to the dimensions of usual activity, pain/discomfort and anxiety/depression. Loss of HRQoL was most reported in the dimensions of usual activity and anxiety/depression. Level 5 was most noticed in the dimension of usual activity, but absent in the pain/discomfort dimension. Before progressive disease, median HUI was 0.83, resulting in median QALM of 6.2 months (ranging 0.8 – 37) versus median 6.9 calendar months (ranging 0.9 – 37). After progressive disease, a deviation of the QALM from calendar months only occurred for a minority of patients.

Conclusion. The data suggest that IMI, including repetitive mEHT, can prolong OS of glioblastoma patients while maintaining HRQoL. Implementation of the EQ-VAS and EQ-5D-5L is easy in daily routine and provides vital information for the medical community as well as for health policy decisions.

P-022

A deep hyperthermia dry-run workflow with patient-facing physics consultation to improve treatment readiness and reduce anxiety

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Question. Deep hyperthermia (DHT) is technically complex and unfamiliar to most patients. DHT simulation and treatment require patient loading into a sling, applicator positioning, abdominal pressure from the water bolus, thermometry setup, and prolonged close interaction with specialized equipment. We asked whether a dedicated DHT dry run, combined with a patient-facing physics consult, could improve readiness for treatment and reduce patient anxiety.

Methods. A DHT dry-run workflow was implemented 6 months after the start of our clinical program and iteratively refined during 2018-2026. It includes a physics consultation conducted in the treatment room, where the physicist reiterates the purpose of adjuvant DHT with radiation or chemoradiation and explains the role of the DHT applicator and water bolus; the need for RF shielding, thermometry, and safety monitoring; as well as expected sensations, communication during treatment, and the step-by-step workflow from simulation to treatment. The patient is then positioned in the applicator, supported by the sling, to obtain setup measurements and assess treatment feasibility, tailored comfort strategies, and workflow barriers. This report summarizes empirical observations across more than 130 DHT patients, including ~100 who completed the dry run.

Results. The dry run consistently identified practical issues before treatment, including positioning challenges, patient discomfort, sling or applicator-access constraints, thermometry access challenges, and surgeries missing from the chart (e.g., knee implants). Patients commonly presented with anxiety related to unfamiliar equipment, duration, confinement, heat sensation, and probe placement. Use of plain language, analogies, and carefully chosen humor helped address these concerns; for example, explaining the RF shield by noting that "we do not have a license to broadcast" made this safety feature understandable. After the consult and dry run, patients generally appeared more prepared, asked more specific and actionable questions, and demonstrated clearer expectations for treatment. Compared with patients who did not undergo a dry run, who often demonstrated moderate to high anxiety during the first treatment, this workflow substantially reduced observed first-treatment anxiety and uncertainty. The dry run also allowed technical and logistical barriers to be addressed before the first treatment.

Conclusions. A DHT dry run with a patient-facing physics consult is a practical, low-risk workflow intervention that improves treatment readiness and reduces observed first-treatment anxiety. Prospective patient-reported outcome data are still needed, but our experience in more than 130 patients supports incorporating this step into routine DHT practice. This extends direct patient care by medical physicists to hyperthermia, where patient understanding, comfort, and technical preparation are inseparable from safe and effective treatment delivery.

P-023

Clinical outcomes following radiotherapy combined with water-filtered infrared-A hyperthermia for superficial tumor manifestations: a retrospective real-world analysis

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Background. Superficial tumor manifestations may require local treatment for symptom palliation and/or durable local control. Outcome data following ultrahypofractionated radiotherapy (uhRT) combined with water-filtered infrared-A hyperthermia (wIRA-HT) are limited. We evaluated time-related objective response, symptom relief, local control (LC) and tolerance. Methods: We retrospectively analyzed 63 uhRT/wIRA-HT-treated lesions in 50 patients. Median age was 74.6 y (43.3–92.0). Entities were melanoma (39.7%), breast cancer (34.9%), non-melanoma skin cancer (9.5%) and others (15.9%). Prior same-site RT was performed in 62%. Prior systemic therapy was documented in 34/53 evaluable lesions (64.2%; median 1 line, range 0–9), concomitant systemic therapy in 34.9%. Pre-RT ulceration/open wounds were present in 22/63 (34.9%) and 14/63 (22.2%). uhRT regimens were 20 Gy/5 fractions in 26/63 (41.3%) and 30 Gy/6 fractions in 13/63 (20.6%). wIRA-HT was applied once weekly in 45/63 lesions (71.4%) and twice weekly in 18/63 (28.6%). Objective response was assessed in 58 lesions by clinical examination, imaging and/or photographic documentation; symptom relief in 34 lesions with documented baseline and follow-up symptoms. Exploratory analyses were performed by ulceration status and lesion depth. **Results.** Mean/median follow-up after RT was 37.9/13.0 weeks (0-177). Estimated 1-year overall survival was 60.0% (22 patients at risk). Best objective response within 6 months was evaluable in 58 lesions and showed an ORR of 46/58 (79.3%): complete response (CR), assessed clinically and/or by imaging when available, in 21/58 (36.2%), partial response in 25/58 (43.1%), stable disease/no change in 6/58 (10.3%) and progressive disease in 6/58 (10.3%). In previously irradiated lesions (n=34), ORR was 73.5%. Median time to first/best response was 1.8/3.3 weeks. Ulcerated lesions showed lower CR rates (2/21, 9.5% vs. 19/37, 51.4%), with ORR of 16/21 (76.2%) vs. 30/37 (81.1%). In lesions with depth data (n=40), CR was 11/22 (50%) for lesions ≤20 mm versus 3/18 (16.7%) for lesions >20 mm; ORR was 19/22 (86.4%) versus 13/18 (72.2%). LC was evaluable in 60/63 lesions (95.2%); local failure, defined as progression or recurrence of the treated lesion, occurred in 26/60 (43.3%) after a median of 9.1 weeks (IQR, 3.9–21.1). Median LC duration was 43.0 weeks, LC at 12 months was 47.6% (14 lesions at risk). Symptom improvement occurred in 28/34 symptomatic lesions (82.4%): bleeding in 11/12 (91.7%), wound-care burden in 16/21 (76.2%), pain in 13/20 (65.0%) and exudation in 9/14 (64.3%). Acute skin/soft-tissue toxicity was grade 1/2/3/4 in 34/48 (70.8%)/13/48 (27.1%)/1/48 (2.1%)/0%. Late toxicity (>3 months, n=12) did not exceed grade 2. Conclusion: In this real-world cohort of elderly, pretreated patients, uhRT/wIRA-HT was well tolerated and achieved fast objective responses and symptom improvement in ~80% each, with a median LC duration of >10 months.

Fig. 1

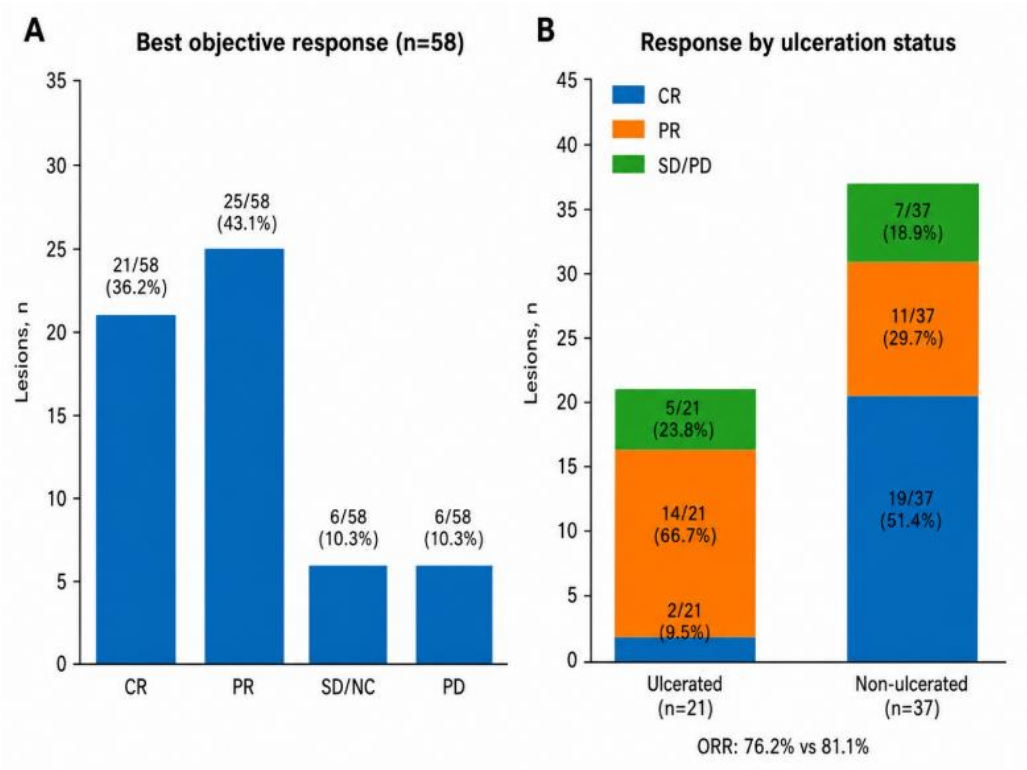
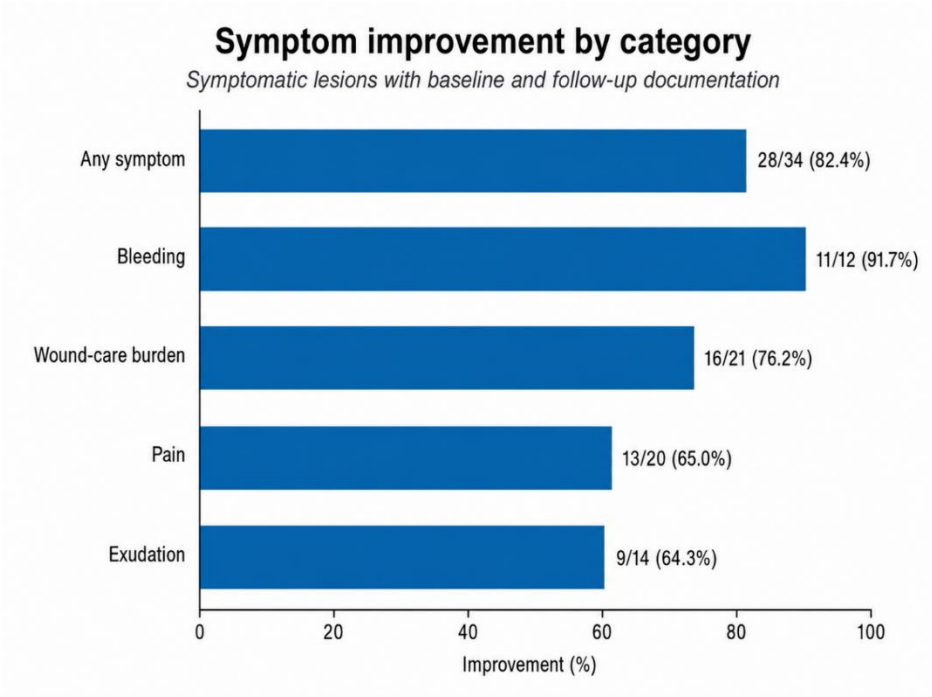

A
Best objective response (n=58)
Lesions, n
21/58 (36.2%)
25/58 (43.1%)
6/58 (10.3%)
6/58 (10.3%)
CR
PR
SD/NC
PD
B
Response by ulceration status
CR
PR
SD/PD
5/21 (23.8%)
14/21 (66.7%)
2/21 (9.5%)
7/37 (18.9%)
11/37 (29.7%)
19/37 (51.4%)
Ulcerated (n=21)
Non-ulcerated (n=37)
ORR: 76.2% vs 81.1%

Fig. 2


Symptom improvement by category
Symptomatic lesions with baseline and follow-up documentation
Any symptom
28/34 (82.4%)
Bleeding
11/12 (91.7%)
Wound-care burden
16/21 (76.2%)
Pain
13/20 (65.0%)
Exudation
9/14 (64.3%)
Improvement (%)

P-024

Chemoradiotherapy with IMRT and Regional Hyperthermia Combined with Durvalumab Therapy for Stage III Non-Small Cell Lung Cancer

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Question. Reports on hyperthermia for Non-Small Cell Lung Cancer (NSCLC) primarily involve Japanese-developed capacitive heating devices, as thoracic tumors remain technically challenging for radiative deep hyperthermia systems preferred in Western countries. Since the 1990s, our institution has achieved high local control with capacitive hyperthermia, particularly in apical lung cancers. Our past research established that tumor-adjacent intra-esophageal temperature significantly correlates with radiofrequency (RF) output, and maintaining an RF output of 1200 W or higher significantly improved local control and survival. However, the safety and efficacy of combining hyperthermia with modern regimens remain unelucidated. Therefore, this study evaluated adding this high-power capacitive hyperthermia to modern IMRT-based chemoradiotherapy followed by durvalumab consolidation for stage III NSCLC.

Methods. This retrospective study evaluated 27 patients with stage III NSCLC treated with definitive IMRT (60 Gy in 30 fractions; IFRT/ENI: 25/2) and concurrent chemotherapy (CBDCA+PAC/CDDP+S-1/CDDP+PEM: 23/3/1) followed by durvalumab consolidation between August 2019 and July 2024. Patient characteristics included: stage IIIA/IIIB/IIIC (10/10/7) and squamous cell carcinoma/adenocarcinoma/others (10/9/8). During chemoradiotherapy, 8-MHz capacitive hyperthermia (Thermotron-RF8TM, Yamamoto Vinita, Osaka) was administered to 16 patients. Patients were dichotomized into a compliant group (defined as ≥3 sessions maintaining an RF output ≥1200 W for ≥20 minutes; n=7) and a control group (≤2 sessions or no hyperthermia; n=20, including 11 who did not receive hyperthermia). The median number of durvalumab cycles was 8 in the compliant group and 6 in the control group.

Results. The 3-year local control, progression-free survival, and overall survival rates were 85.7%, 28.6%, and 80.0%, respectively, in the group receiving 3 or more hyperthermia sessions, compared to 70.6%, 28.6%, and 58.4% in the group receiving 2 or fewer sessions or no hyperthermia. Acute adverse events included 1 case of Grade 3 dermatitis, as well as Grade 2 esophagitis and dermatitis in other patients. Late complications included one case each of Grade 3b empyema and Grade 3 radiation pneumonitis, and six cases of Grade 2 radiation pneumonitis.

Conclusions. Serious acute complications and high-grade radiation pneumonitis were infrequent, and treatment outcomes tended to be more favorable in patients who received adequate hyperthermia. High-power capacitive hyperthermia may represent a feasible and promising adjunct to modern chemoradiotherapy followed by immunotherapy for stage III NSCLC.

P-025

Feasibility and Limitations of MR-Guided Hyperthermia in Soft Tissue Sarcomas of the Pelvis and Lower Extremities

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Introduction. Tumor temperature is predictive for treatment outcome in regional hyperthermia (RHT) combined with chemo- and/or radiotherapy in several tumor entities. While invasive thermometry is considered the gold standard for temperature assessment, it is limited by restricted spatial coverage and invasiveness. Since 2018, an MR-guided hyperthermia system (Pyrexar BSD 2000-MR with Universal and Sigma-30-MR applicators integrated into a 1.5 T Philips Ingenia MRI system) has been implemented in clinical routine at LMU University Hospital.

Goal. To evaluate the performance of the hybrid system regarding MRI-based temperature monitoring in soft tissue sarcomas (STS) of the thigh and pelvic region.

Materials and Methods. A total of 100 patients with STS of the lower extremities or pelvic region underwent 839 hybrid hyperthermia treatments (mean: 8.8 treatments per patient; range: 1–16). MR thermometry data were retrospectively analyzed in 32 patients with STS of the lower extremities and 28 patients with pelvic STS treated between 2020 and 2025.

Results. MR-based thermometry was feasible in most treatments; however, image quality and temperature accuracy strongly depended on tumor localization, tissue composition, and physiological motion. Reliable temperature mapping was achieved particularly in homogeneous soft-tissue regions with limited motion, such as the thigh and gluteal region, whereas temperature assessment in the deep pelvis was frequently impaired by susceptibility artifacts caused by bowel gas motion.

The mean T50 achieved was (4.4 ± 1.6)°C for tumors of the lower extremities and (2.8 ± 1.5)°C for pelvic tumors. MRI guidance enabled visualization of intratumoral temperature distribution as well as early detection of hot spots. This information allowed treatment adaptation during ongoing hyperthermia sessions and improved treatment quality, particularly in patients with postoperative seromas or impaired sensory perception. No severe treatment-related adverse events were observed.

Conclusion. MR-guided hyperthermia with non-invasive MR thermometry is clinically feasible in patients with soft tissue sarcomas and provides clinically relevant information beyond that obtainable with conventional temperature monitoring techniques. MR thermometry showed the highest reliability in anatomically stable and homogenous soft-tissue regions, such as the thigh and gluteal area, weheras image quality in the deep pelvis remained limited by motion- and susceptibility-related artifacts. Real-time visualization of intratumoral temperature distribution and early hot-spot detection enabled adaptive treatment optimization during therapy and contributed to improved treatment safety, particularly in vulnerable patients. These findings support the clinical utility of hybrid MR-guided hyperthermia systems for individualized treatment monitoring and quality assurance in regional hyperthermia.

P-029

Development and Ambispective Validation of a Selection and Prognostic Scoring System in Recurrent Epithelial Ovarian Cancer

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Background. Secondary cytoreductive surgery (SCS) may improve outcomes in selected patients with recurrent epithelial ovarian cancer; however, reliable selection criteria remain inadequately defined. This study aimed to develop and ambispectively validate a practical prognostic scoring system to stratify patients according to expected benefit from SCS.

Methods. An ambispective cohort study was conducted, including a retrospective derivation cohort of 96 patients and a prospective validation cohort of 26 patients with recurrent epithelial ovarian cancer. Clinicopathological, biochemical, and treatment-related variables were analyzed for their association with peritoneal recurrence-free survival (PRFS) and overall survival (OS). Multivariate Cox regression was used to identify independent prognostic factors. Significant variables from the retrospective cohort were incorporated into a numerical scoring model, which was subsequently evaluated in the prospective cohort.

Results. In the retrospective cohort, platinum-free interval, peritoneal cancer index (PCI), histological grade, use of Hyperthermic intraperitoneal chemotherapy (HIPEC), and completeness of cytoreduction independently predicted OS. Ascites, PCI, histological grade, CA-125 level, and HIPEC were significantly associated with PRFS. Median disease-free survival was 20 months in the retrospective cohort and 16 months in the prospective cohort, while median OS in the retrospective cohort was 51.7 months. A scoring system based on ascites, PCI, histological grade, CA-125 level, and platinum-free interval stratified patients into favorable, intermediate, and poor prognostic groups using score cut-offs of ≤8, 9–12, and >12, respectively.

Conclusion. This novel scoring system provides a clinically applicable framework for risk stratification and selection of patients for SCS in recurrent epithelial ovarian cancer. Larger multicentric validation is warranted.

P-030

The aim of this report is to highlight how hyperthermia combined with integrated oncologic therapies may contribute not only to tumor disease control, but also to improve quality of life, in patient wit Invasive Ductal Carcinoma

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Oncologic hyperthermia is increasingly used as an integrated treatment approach in advanced and metastatic cancer, potentially enhancing the effects of systemic therapies. We report the case of a patient with metastatic breast cancer (Invasive Ductal Carcinoma 2) treated with hyperthermia combined with supportive infusion therapy.

A 58-year-old woman was diagnosed in July 2023 with grade 2 infiltrating ductal breast carcinoma according to Hartveit classification. The patient underwent radiotherapy and chemotherapy. Whole-body FDG-PET/CT performed in June 2025 revealed multifocal pathological uptake involving the entire spine, distal sternum and xiphoid process, both iliac bones, ischiopubic branches predominantly on the right side, posterior column of the right acetabulum, and hepatic involvement in segments III and IV. Additional tracer uptake was observed in both pulmonary hilar regions and in the subsacral area.The patient subsequently underwent integrated treatment consisting of oncologic hyperthermia and infusion therapy with antioxidants and immunostimulant agents. The hyperthermia protocol included three treatment cycles, each consisting of 12 sessions, delivered with power settings ranging from 180 to 350 watts.

Follow-up FDG-PET/CT performed in September 2025 showed progression of hepatic disease, with increased liver lesions and new focal uptake in the left hepatic lobe and in segment VII. Overall metabolic activity appeared substantially stable compared with the previous examination; however, skeletal lesions demonstrated marked metabolic suppression, except for persistent pelvic involvement. Previously described bilateral pulmonary hilar lymph nodes were no longer detectable. A mild bilateral pleural effusion was also reported.Hyperthermia has been investigated for its potential synergistic effects with chemotherapy, radiotherapy, and supportive treatments, especially in patients with progressive disease and limited therapeutic options. The aim of this report is to highlight how hyperthermia combined with integrated oncologic therapies may contribute not only to tumor disease control, but also to improved quality of life in metastatic cancer patients.

In this case, integrated treatment including oncologic hyperthermia was associated with reduced metabolic activity of skeletal metastatic lesions despite hepatic disease progression. These findings suggest a potential role of hyperthermia in the metabolic control of bone metastases and locoregional disease management. Further clinical investigations on larger patient cohorts are warranted to better define the therapeutic contribution of hyperthermia in metastatic breast cancer.

P-031

Response analysis for radiotherapy (RT) and RT with hyperthermia (HT) in patients with metastatic melanoma (MM) oligoprogression

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Objective. The aim is to evaluate responses, time to response (TTR), and duration of response (DOR) for RT and RT with hyperthermia (HT) in patients with oligoprogressive metastatic melanoma (MM) under systemic treatment.

Methods: Patients treated at the referral center between 2018 and 2023 were included. Oligoprogression was defined as up to five progressive metastases. Systemic treatment included immunotherapy (ITH) and BRAF/MEK inhibitors, and RT was employed as the sole method or with HT. Response to RTH in different evaluation intervals according to response evaluation criteria in solid tumors 1.1 (RECIST1.1), TTR, and DOR were analyzed. Factors that may influence DOR were evaluated.

Results. 156 patients were included, 82 pts had RT+HT while 74 had RT only, and 184 lesions were irradiated. The median follow-up was 23 months (15.2-34m). ITH was used in 82.7%, and BRAF/MEK inhibitors in 17.3% of patients. The median total dose of RT was 32 Gy (10-50), and the median biologically effective dose (BED) was 108.8 Gy. There were 27 (14.7%) complete responses (CR) and 62 (33.7%) partial responses (PR) at the last follow-up. The overall response rate was 48.3%. CR increased from 2.2% to 14.7% at 1.4 and 13.3 months following RTH. Only two patients who initially achieved CR had PD at the last follow-up. TTR was 4.2 months (95% CI: 0.4-79 m), and DOR was 38.5 months (95% CI: 36-NA m) for pts with RT only. TTR was 2.7 months (95% CI: 0.2-57.4 m), and DOR was not reached at the time of the analysis for pts with RT+HT. There were no statistical differences between groups for TTR (p=0.13) and DOR (p=0.62). Total dose>; median (p=0.1), and systemic treatment (ITH vs. BRAF/MEK inhibitors; p=0.57) did not influence DOR. Patients with BED ≥ to the median exhibited significantly inferior DOR outcomes (p=0.006).

Conclusion. Both RT+HT and RT alone provide long-lasting local responses in nearly half of the patients. Early post-radiotherapy evaluation (1-2 months) may not correlate with the final local response to treatment. Optimal radiological evaluation occurs 3-4 months after treatment.

P-032

Comparative analysis of local efficacy of radiotherapy for oligoprogression in metastatic melanoma with or without locoregional hyperthermia

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Objectives. Further comparison of the local outcomes and safety of radiotherapy (RT) vs RT combined with hyperthermia (HT) in metastatic melanoma (MM).

Methods. Patients with oligoprogressive MM treated with RT+HT between 2018 and 2023 were included. Oligoprogression was determined as up to 5 progressive lesions. The inclusion criteria were the availability of follow-up imaging after radiotherapy and concomitant systemic therapy. The comparison of RT vs RT+HT was evaluated in terms of local control (LC), which was defined as the percentage of patients who met the RECIST1.1 criteria for stable disease (SD), partial response (PR), and complete response (CR), and local benefit (LB) was defined as the percentage of patients who met the criteria for PR and CR. Adverse events (AEs) were evaluated.

Results. 156 patients were included in the study; 82 patients had RT+HT, while 74 had RT only. Median follow-up was 17.5 months (12.7-21.4). Most patients (82.7%) were irradiated during immunotherapy (ITH), and 17.3% during BRAF/MEK inhibitors. Median LC was not reached at the time of analysis in both groups. The 1- and 2-year LC rates for the RT group were 92.8% and 90.9%, respectively. In the RT+HT group were 94.6% and 87.5%, respectively. Median LB was 64.7 months (95% CI, 61.7-NA months). The 1- and 2-year LB rates for the RT group were 80.7% and 77%, respectively. In the RT+HT group were 88.7% and 78.2%, respectively. No statistically significant differences were observed between the study groups for either the LC ($p = 0.99$) or the LB ($p = 0.48$). 41 pts (26.3%) patients experienced an increase, relapse, or new AEs within 1 month of RT+HT, among which 18 pts (11.5%) had RT+HT. Of these, 13 (8.3%) had AEs ≥ grade 3 according to Common Terminology Criteria for Adverse Events (CTCAE) 5.0.

Conclusion. RT and RT+HT are effective local treatments for patients with oligoprogressive MM. Both types of therapy are well tolerated, and systemic treatment based on both ITH and BRAF/MEK inhibitors can be safely used concurrently.

P-033

Achieving national consensus in thermoradiation protocols for treatment of patients with locoregional recurrent breast cancer in the Netherlands

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[1] Amsterdam University Medical Center, Radiation Oncology, Amsterdam, Netherlands
[2] Princess Máxima Center/ UMCU, Utrecht, Netherlands
[3] Erasmus MC, Rotterdam, Netherlands
[4] Instituut Verbeeten, Tilburg, Netherlands

Background. Hyperthermia combined with re-irradiation has shown substantial efficacy in locoregional recurrent breast cancer and can be applied as a standard treatment in the Netherlands. Until recently, variations in hyperthermia delivery, temperature monitoring, and data reporting between Dutch centers hindered consistent outcome evaluation.

Aim. Nationwide harmonization of hyperthermia protocols in preparation for the RT-HYPE study (NCT06452485, funded by KWF).

Methods. A structured three-step consensus process was implemented between the three Dutch radiotherapy centers (Amsterdam UMC, Erasmus MC, Institute Verbeeten) delivering hyperthermia combined with re-irradiation. First, an inventory of existing hyperthermia devices, thermometry systems, treatment protocols, and documentation procedures was conducted through on-site audits and structured interviews. Differences and similarities were recorded in a comprehensive item list. Next, consensus was achieved using the nominal group technique, a structured face-to-face method for small-group decision-making. Four multidisciplinary meetings were held in 2023 to align clinical delivery, quality assurance, and data registration, in accordance with ESHO guidelines for superficial hyperthermia clinical trials. The final step was protocol implementation across all centers from January 2024 onward (Figure 1).

Results. All centers employed radiofrequency hyperthermia systems (434 MHz) suitable for target depths up to 4 cm, with invasive thermometry applied for deeper targets. Consensus was reached on key clinical and delivery treatment parameters (Table 1). Institutional differences (thermometry type, timing between radiotherapy and hyperthermia) were accepted and will be recorded for subsequent analysis.

Conclusion. Successful harmonization of hyperthermia treatment protocols was achieved across the three Dutch hyperthermia centers. This standardization is essential for valid multicenter comparison of treatment outcomes and will contribute to establishing evidence-based standards of care for patients with locoregional recurrent breast cancer requiring postoperative re-irradiation with or without hyperthermia. The harmonized protocols have been implemented not only for the RT-HYPE study participants but also for all patients receiving hyperthermia treatment at these centers.

Fig. 1

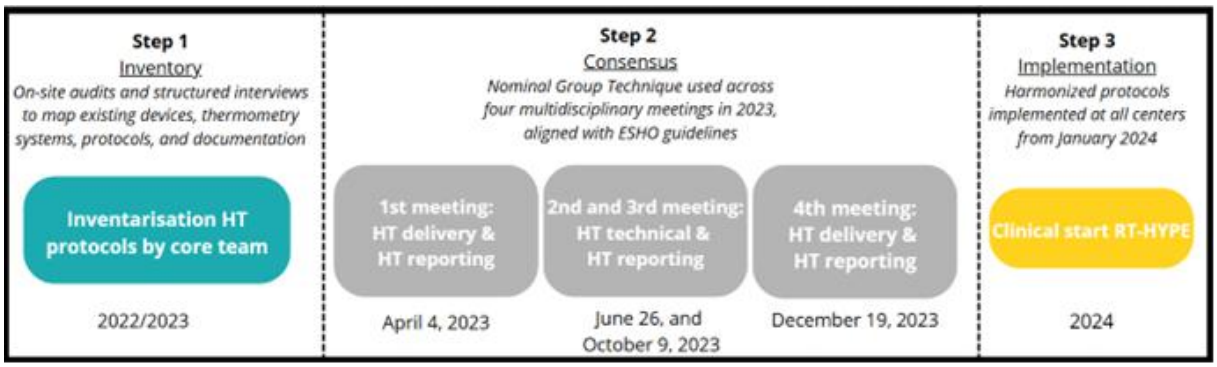

Fig. 2

	Status	
	04-04-2023	19-12-2023
Clinical topics / considerations		
Consensus clinical indications	☑	☑
HT field ≥ reRT field	☑	☑
reRT schedules 23x2Gy/8x4Gy*	☑	☑
HT 1x/week		☑
Interval HT sessions ≥ 72 hours		☑
Delivery		
Preheating 15 minutes	☑	☑
Steady state heating 60 minutes	☑	☑
Maximum HT depth 4 cm**		☑
Definitions time interval reRT-HT	☑	☑
Sequence: first reRT, then HT	☑	☑
Goal 41-42°C, accepted range 40-43.5°C	☑	☑
Skin thermometry	☑	☑
Invasive thermometry if tumor depth ≥ 1 cm	☑	☑
Invasive thermometry in seroma	☑	☑
Priority invasive temperature rise	☑	☑
Uniform documentation framework		☑

Running and planned clinical trials (including clinical trial ideas)

P-044

Hyperthermia and Radiotherapy in Arthritis and Osteoarthritis (Hyperart-1 and Hyperart-2 Studies)

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[2] University Hospital Erlangen, FAU Erlangen, Translationale Strahlenbiologie, Strahlenklinik, Erlangen, Germany
[3] University Hospital Frankfurt, UniversitKlinik für Unfallchirurgie und Orthopädie, Dr. Rolf M. Schwiete Forschungsbereich für Arthrose, Frankfurt a. M., Germany

Introduction. Painful joint disorders are highly prevalent across Germany, and radiotherapy in this setting has a long tradition. However, recent consensus work by the ASTRO–ESTRO–DEGRO–RANZCR group [1] highlights a lack of high-level evidence in this field. Published controlled studies have demonstrated heterogeneous results regarding pain reduction and joint function when comparing 3.0 Gy in 6 fractions with sham or very low-dose irradiation [2,3].Hyperthermia has demonstrated potential analgesic effects in both in vivo and clinical studies[4,5].

Goal. The aim of our studies is to evaluate the clinical efficacy of superficial hyperthermia alone and in combination with low-dose radiotherapy (LDRT) in patients with painful joint disorders compared with the radiotherapy as a standart of care.

Materials and Methods. Two randomized trials are planned, with different weighting of inflammatory versus degenerative components in joints. Each study will enroll 168 patients, randomized into three treatment arms:

Group 1: Radiotherapy: 3.0 Gy in 6 fractions over three weeks; Group 2: Superficial hyperthermia: three times weekly for 30 minutes over three weeks; Group 3: Combination therapy: hyperthermia followed by radiotherapy within 15 minutes.

The primary endpoint is pain reduction. Secondary endpoints include toxicity (NCI-PRO-CTCAE), quality of life (SF-12), analgesic consumption, proportion of patients achieving ≥20% reduction on the Numeric Rating Scale (NRS), and changes in inflammatory and cartilage-specific biomarkers (TNFα, IL-1β, TGFβ, IL-18, COMP, MMP-3, MMP-9, CTX-II, hyaluronan).

Results. The studies have been initiated in collaboration with the University Hospital Erlangen and the University Hospital Frankfurt. Patient recruitment is ongoing; no evaluable results are available at this time.

Summary. These studies aim to contribute to the evidence base for the use of superficial hyperthermia alone and in combination with low-dose radiotherapy in painful joint disorders.

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Fig. 1

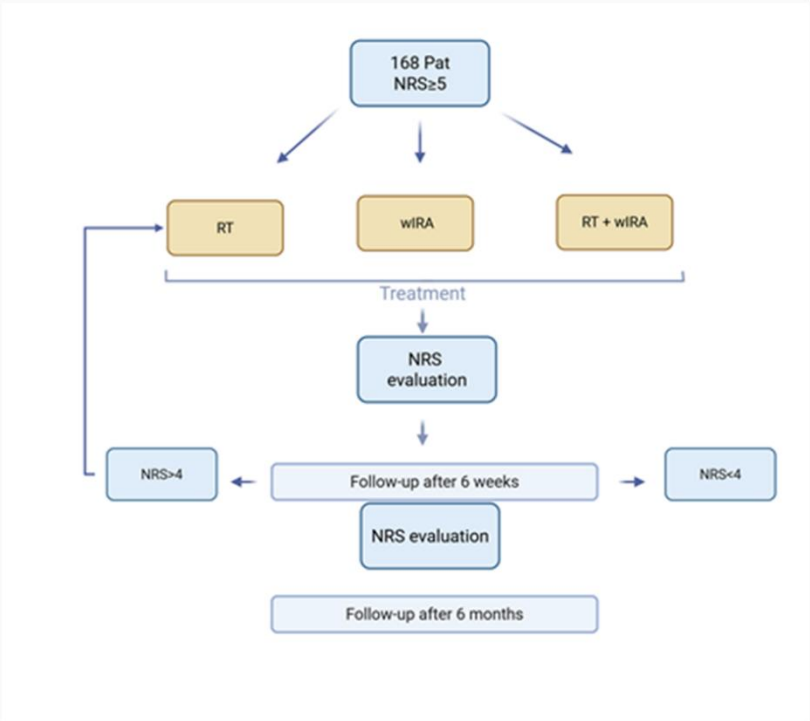
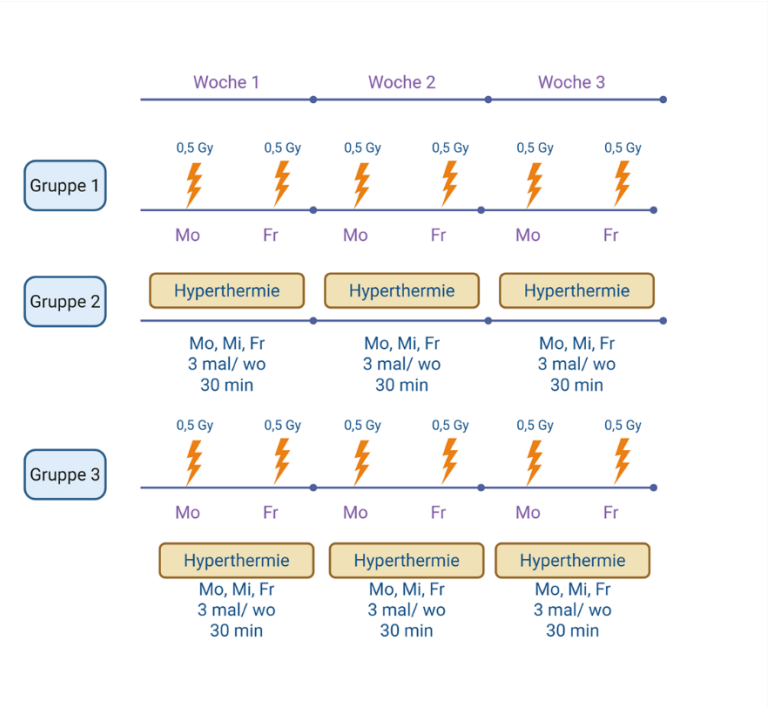

168 Pat
NRS≥5
RT
wIRA
RT + wIRA
Treatment
NRS
evaluation
NRS>4
Follow-up after 6 weeks
NRS<4
NRS evaluation
Follow-up after 6 months

Fig. 2


Woche 1
Woche 2
Woche 3
Gruppe 1
0,5 Gy
Mo
Fr
Gruppe 2
Hyperthermie
Mo, Mi, Fr
3 mal/ wo
30 min
Gruppe 3

P-045

Consolidative MR-guided adaptive radiotherapy combined with hyperthermia in locally advanced pancreatic cancer patients not suitable for resection after induction chemotherapy (HOTPANC): a prospective phase I trail

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Background. Locally advanced pancreatic cancer (LAPC) remains associated with poor prognosis despite advances in systemic therapy. A substantial proportion of patients remain unresectable after induction chemotherapy and have limited local treatment options. Stereotactic and hypofractionated radiotherapy approaches have demonstrated encouraging local control rates but are constrained by the proximity of critical gastrointestinal organs at risk. Magnetic resonance-guided online adaptive radiotherapy (MRIgRT) allows superior soft-tissue visualization and daily plan adaptation, while regional hyperthermia (RHT) has radiosensitizing and perfusion-enhancing effects. The combination of MRIgRT and RHT may therefore enable safe dose intensification and improved local tumor control in LAPC.

Methods. HOTPANC is a prospective, open-label, single-arm, single-center phase I trial to establish a proof of concept regarding the feasibility and tolerability of consolidative MRIgRTcombined with RHT in patients with unresectable LAPC without disease progression after induction chemotherapy. Sixteen patients will be enrolled. Radiotherapy is delivered on an MR-Linac using a hypofractionated schedule of five fractions with a simultaneous integrated boost to the gross tumor volume and a lower dose to an elective volume, administered twice weekly. RHT is applied in close temporal proximity to each radiotherapy fraction. Follow-up visits are scheduled every three months for one year after treatment completion. The primary endpoint is treatment-related grade ≥ 3 toxicity according to CTCAE, assessed from the start of radiotherapy until 12 months after completion. Secondary endpoints include local control, freedom from distant progression, overall survival, systemic therapy-free interval, and patient-reported quality of life assessed with EORTC QLQ-C30 and PAN26 questionnaires.

Discussion. HOTPANC is the first prospective clinical trial to systematically investigate the combined use of MRIgRT and RHT in LAPC. The study aims to establish preliminary safety data and provide initial signals of clinical efficacy for this multimodal consolidative treatment concept.

Fig. 1: Trail Overview

Fig. 2: Study assessments

Fig. 1

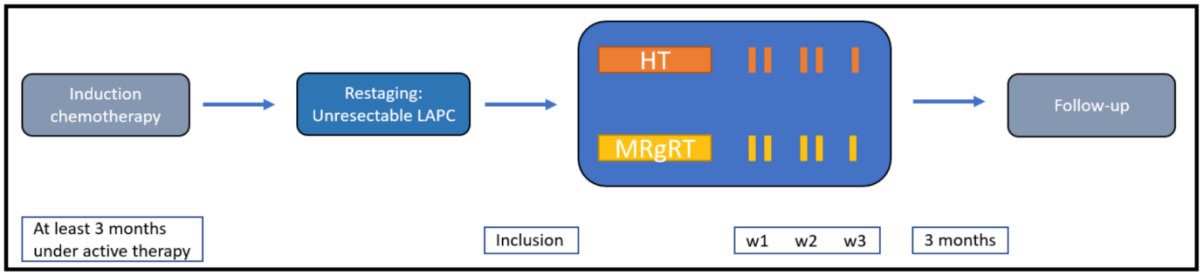

Fig. 2

Workflow	Baseline visit	During Therapy	Follow-up			
	T_0	T_1	T_2	T_3	T_4	T_5
	30 d prior to enrollment	After last fx of MRIgRT / RHT	3 mo after MRIgRT	6 mo after MRIgRT	9 mo after MRIgRT	12 mo after MRIgRT
Check of in- and exclusion criteria	x	-	-	-	-	-
Patient information, informed consent	x	-	-	-	-	-
Documentation of demographic data, medical history and baseline symptoms	x	-	-	-	-	-
Documentation of medication	x	x	x	x	x	x
Physical examination	x	x	x	x	x	x
Documentation of Performance Status (ECOG)	x	x	x	x	x	x
Documentation of toxicities and adverse events (CTCAE v6.0)	-	x	x	x	x	x
Diagnostic imaging of the abdomen (CT / MRI)	x	-	x	x	x	x
CT of the chest	x	-	-	-	-	-
CA 19-9 level	x	-	x	x	x	x
Documentation of local control, freedom from distant progression, survival status and systemic therapy-free interval	-	-	x	x	x	x
QoL-Assessment (QLQ-C30, PAN26)	x	x	x	-	-	x

Abbreviations: CT: computed tomography; CTCAE: Common Terminology Criteria for Adverse Events; d: days; fx: fractions; ECOG: Eastern Cooperative Oncology Group; mo: months; MRI: magnet resonance imaging; Tx: timepoint x (0-5)

P-046

Preliminary data from ThermoRad wIRA study, a prospective study to assess the real-world implementation of Thermotherapy using wIRA (water-filtered infrared A superficial hyperthermia) in addition to standard of care palliative Radiotherapy in patients with inoperable or incurable cancers

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Background and Question. The water-filtered infrared A radiation (wIRA) superficial hyperthermia system has been used for many years at centres across Europe to treat patients with superficial tumours, although most clinical experience has been on previously irradiated, locally recurrent breast cancers (LRBC). Guy's Hospital is the first cancer centre to acquire wIRA superficial hyperthermia for patient use in the National Health Service (NHS). In the UK, superficial hyperthermia in combination with radiotherapy is not the standard of care for any recurrent cancers including LRBC. In addition, there is uncertainty whether the retrospective evidence and the dose used in LRBC (Notter M et al, 2000) is applicable to other non-breast cancer patients. There is a need for prospective data to support the evidence needed to use wIRA hyperthermia in combination with palliative radiotherapy for LRBC and other tumours in the UK and other countries where wIRA hyperthermia is not funded or is not part of the standard of care. Therefore, a prospective study is needed to collect the real world evidence of superficial hyperthermia treatment in combination with radiotherapy in order to change the clinical practice in the UK.

Methods. ThermoRad wIRA is a prospective real-world implementation study of superficial hyperthermia (wIRA) in addition to standard of care (SOC) palliative radiotherapy in cancer patients. Biological samples are collected to conduct translational research to understand the biomarkers that could predict treatment response. The study populations include inoperable/incurable or recurrent/metastatic head and neck squamous cell carcinoma (HNSCC), cutaneous squamous cell carcinoma (cSCC) and LRBC. In addition to the efficacy endpoints such as objective response rate and survivals, the study will evaluate the real-world implementation by the NASSS (non-adoption, abandonment, and challenges to scale-up, spread, and sustainability) framework using NASSS-CAT (complexity assessment tool) (Greenhalgh T et al, 2020).

Results. The ongoing study commenced in October 2024 and is expected to complete recruitment in Sept 2027. We will share the experience of setting up wIRA hyperthermia service in the NHS in the UK. We will present the efficacy (response rate, survival outcomes) as well as toxicity profiles on the recruited patients treated with wIRA and radiotherapy +/- anti-PD1 checkpoint inhibitor as part of the standard of care. We will present the characteristics on the patients who responded and those who did not respond. The preliminary assessment on the recruited patients showed that the combination treatment has an acceptable toxicity profile.

Conclusions. Superficial hyperthermia (wIRA) in combination with palliative radiotherapy can be implemented at centres and in countries where it is not yet of standard of care but practical and logistic challenges need to be overcome for successful implementation.

P-047

From trial concept to clinical reality: lessons learned from TANCA-I to the redesigned TANCAP-I study integrating thermotherapy with curative treatment for primary locally advanced head and neck cancer

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Locoregional recurrence remains a major challenge in patients with locally advanced head and neck cancer (LAHNC), reflecting the limitations of current curative-intent radiotherapy (RT) or chemoradiotherapy (CRT). Thermotherapy is a potent radiosensitizer with a favorable toxicity profile, but its integration into primary LAHNC treatment, using deep-heating devices, has not been established. Our original TANCA-I trial was designed to evaluate thermotherapy plus RT monotherapy in LAHNC patients. However, during early accrual, we encountered substantial and unexpected barriers that caused us to redesign the trial.

The eligible patient population was smaller than anticipated. In our centre, LAHNC patients aged ≥70 years are treated with RT alone, as the benefit of cisplatin in this group is uncertain. As a result, our study population consisted of older, frail patients with significant comorbidities. These patients frequently presented with large dental metal implants which we stated as an exclusion criterium, and experienced difficulty tolerating prolonged supine positioning required for the thermotherapy treatments. Furthermore, this RT-only population does not reflect broader European practice, where most patients receive concurrent chemoradiotherapy (CRT), limiting external validity.

Combining RT monotherapy and CRT within one cohort, conflicted with the requirement for a homogeneous population in early-phase toxicity studies. At the same time, excluding RT-only patients, who have an even greater unmet clinical need, was considered unethical.

With these challenges in mind, we modified the study design to include two parallel cohorts: (1) a primary dose-finding cohort combining thermotherapy with platinum-based CRT, aligned with current standard of care, and (2) a secondary prospective RT-monotherapy registration cohort. Dose escalation in the primary cohort is guided by a Time-to-Event Bayesian Optimal Interval design using SAR-based dose definitions in healthy tissues. Patient safety is prospectively overseen by an independent Data Safety Monitoring Board. Eligibility criteria have been refined, including a more flexible, treatment-planning–based approach to dental metal implants.

This shift in indications, highlighted the importance of early multidisciplinary alignment, particularly with medical oncology, as well as the need for a clearly structured study design. Finally, this redesigned protocol was submitted as a new clinical trial: TANCAP-I.

TANCAP-I is a direct result of the challenges we encountered in the original study. By adapting the design to clinical practice and incorporating multidisciplinary input, we created a more robust study setup. This highlights the importance of designing early-phase trials that reflect real-world care. By incorporating these lessons, the current study provides a robust framework for the safe integration of thermotherapy into standard curative treatment for LAHNC.

P-048

Combined Hyperthermia and SBRT Reirradiation for Radio-Recurrent Prostate Cancer: The Multicenter Prospective Phase II Hyper-SBRT Study

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Introduction. Intraprostatic recurrence after primary external beam radiotherapy (EBRT) occurs in a substantial proportion of patients with prostate cancer (PCa) and represents a challenging clinical scenario. Salvage treatment options remain heterogeneous, and consensus on the optimal approach is lacking. Local recurrence is closely linked to subsequent metastatic progression, underscoring the importance of durable local control. Stereotactic body radiotherapy (SBRT) is an emerging salvage strategy; however, its use in the reirradiation setting is limited by the risk of genitourinary (GU) and gastrointestinal (GI) toxicity. Deep hyperthermia (HT) has a strong radiobiological rationale as a radiosensitizer and may allow radiation dose de-escalation on healthy tissue while maintaining tumor control.

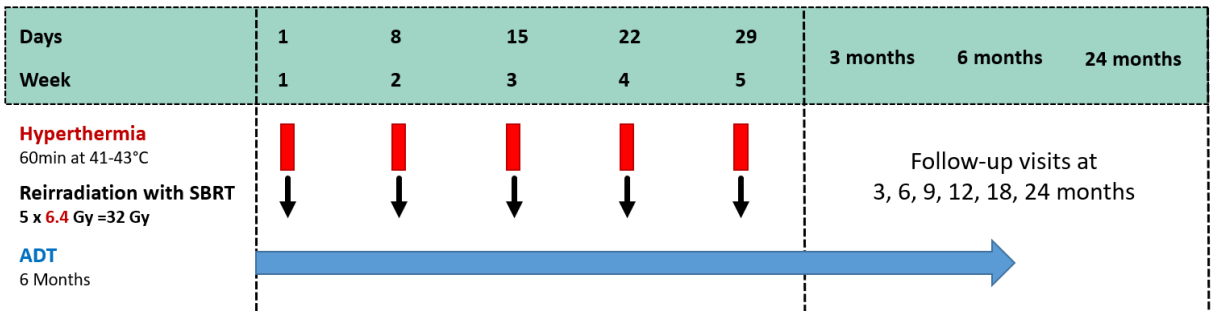
Goals. Hyper-SBRT is a planned single-arm, multicenter, prospective phase II trial evaluating deep HT combined with dose-reduced salvage SBRT in patients with radio-recurrent PCa. Based on literature data and an expected 2-year biochemical relapse-free survival (bRFS) of approximately 65% with salvage SBRT alone, Hyper-SBRT tests the hypothesis that SBRT plus deep HT can increase 2-year bRFS to 85%.

Materials and Methods. The study will enroll 38 patients with biochemical recurrence and biopsy-proven intraprostatic recurrence occurring at least 2 years after primary EBRT, no pelvic or distant metastases on PSMA-PET/CT, PSA doubling time >10 months, IPSS ≤12, and performance status WHO 0–1. Patients will receive SBRT to a total dose of 32 Gy in 5 weekly fractions of 6.4 Gy, combined with weekly deep HT sessions aiming for 41–43°C in the target volume for 60 minutes (Fig. 1). Androgen deprivation therapy (ADT) will be initiated at study start and continued for 6 months. An interim safety analysis is planned after enrollment of the first 12 patients, with predefined stopping rules for unacceptable toxicity. The primary endpoint is 2-year bRFS, defined according to the Phoenix criteria (nadir PSA + 2 ng/mL). Secondary endpoints include acute and late GU/GI adverse events according to CTCAE v5.0, progression-free survival, time to further anticancer therapy, prostate cancer-specific survival, overall survival, and quality of life assessed using EORTC QLQ-C30, EORTC QLQ-PR25 and IPSS questionnaires.

Current Status. The study is currently in the protocol finalization phase, with partial funding already secured (Fond"Action Grant to MS). First patient enrollment is planned for Q4 2026.

Summary. Hyper-SBRT addresses an important unmet clinical need in patients with radio-recurrent PCa. By combining the radiosensitizing effect of deep HT with dose-reduced SBRT, this trial aims to establish a biologically optimized salvage strategy that maintains durable local tumor control while minimizing treatment-related toxicity.

Fig. 1: Hyper-SBRT trial treatment schedule



Quality assurance: thermometry, treatment planning, image guidance

P-001

Inherent hyperhydration of malignant tumors decisively modulates key thermophysical parameters determining the effectiveness of clinical hyperthermia by radiofrequencies, microwaves or water-filtered infrared-A (wIRA) irradiation

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Introduction. Since half a century it is known that the water contents (C_w) of normal tissues are

(a) highly variable, and (b) up to approx. 1.5- times higher in corresponding malignancies, due to a 3- times larger interstitial fluid space in solid tumors [1,2]. C_w affects the absorption and penetration of radiofrequencies (RF), microwaves (MW) or water-filtered infrared-A radiation (wIRA), in tissues, and heat exchanges between different tissues in the treatment field.

Goals. Assessing the impact of inherent high water content of malignant tumors on parameters responsible for assessment of therapeutically relevant hyperthermia levels using electromagnetic waves.

Methods. Published data on the absorption coefficient of electric resistivity, relative permittivity, dielectric loss and penetration depth for clinically applied radiofrequencies, microwaves and wIRA, as well as thermophysical tissue parameters (density, specific heat capacity, thermal conductivity, thermal diffusivity, thermal effusivity) of normal tissues and corresponding malignant tumors were correlated with associated tissue water contents.

Results. On average, heat gain by absorption of wIRA rises linearly with increasing water content for $C_w > 60$ wt.%. Depending on the frequency of RFs and MWs, the relative permittivity, dielectric loss and heat gain by induction of conduction and displacement currents in all tissues increased exponentially with C_w, while the electrical resistance decreased exponentially. When C_w increased from 60 to 85 wt.%, the mean penetration depths decreased accordingly by factors of ≈ 1.5-1.9 (wIRA) and ≈ 1.8-1.9 (RF and MW). Thermophysical tissue parameters increased approx. linearly with C_w and were maximal in malignant tumors. Increases were similar when comparing different tissue types, normal whole breast tissue components and skin layers. High C_w values in cancers resulted in (a) higher absorption of electromagnetic radiation and thus (b) greater accumulation of thermal energy, but also in (c) higher thermal conductivity, (d) thermal diffusivity, and (e) thermal effusivity than in normal tissues or in tissues in close vicinity of the tumor.

Summary. Adjusted irradiances and/or electric field strengths are required in tissues with different water contents to (a) prevent hot spots, and to (b) induce therapeutically relevant effects, i.e., clinically relevant hyperthermia levels.

References.

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P-003

Temperature-Dependent Electric Field Drift in a Breast Hyperthermia Applicator: Implications for Quality Assurance

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Objective. Electric field (E-field) distributions in radiofrequency (RF) hyperthermia applicators are typically characterised at room temperature, yet during treatment the phantom or tissue heats substantially. This study investigates whether and to what extent E-field patterns shift as phantom temperature rises during continuous RF exposure in a breast hyperthermia applicator, with the goal of quantifying the thermal drift that may affect quality assurance (QA) reproducibility.

Approach. A cylindrical phantom (radius 50 mm, length 120 mm) was positioned in a breast hyperthermia applicator and power of 120W was applied. Robotic E-field scanning was performed at a fixed axial depth of 6 cm, acquiring 120 points per slice in approximately 6 minutes per scan. A repeated measurement protocol was applied: RF ON → scan → RF OFF (1 min cooldown) → temperature reading → RF ON, yielding five consecutive scans over a total duration of approximately 34 minutes. Phantom surface temperature was recorded after each RF-off interval. E-field magnitude maps from successive scans were compared, and the fraction of measurement points deviating by more than 5 V/m and 10 V/m between consecutive scans and across the full measurement series was quantified.

Results. Phantom temperature increased from 37.7 °C at scan 1 to a peak of 43.3 °C at scan 5, while the peak E-field magnitude declined from 314 V/m to 300 V/m over the same period. Between consecutive scan pairs, 95–100% of measurement points remained within a 10 V/m window, indicating good short-term stability. However, cumulative drift across all five scans (37.7 °C to 43.3 °C, ~5.6 °C rise) was more pronounced: 48.8% of points shifted by more than 10 V/m and 24.8% by more than 5 V/m relative to the baseline scan. The largest single-step change occurred between scans 1 and 2 (37.7 °C → 39 °C), with 60% of points exceeding the 5 V/m threshold.

Significance. These results demonstrate that thermal drift of the E-field distribution is measurable and clinically relevant even over a moderate temperature rise of ~6 °C. While scan-to-scan variation is modest, the cumulative shift across a 30-minute QA session is substantial enough to affect reproducibility benchmarks if the applicator has not reached thermal equilibrium. This highlights the importance of standardising phantom temperature at the start of E-field QA procedures and of reporting the thermal conditions under which measurements are obtained. Accounting for temperature-dependent drift will support more accurate and consistent QA of RF hyperthermia applicators across institutions.

Fig. 1

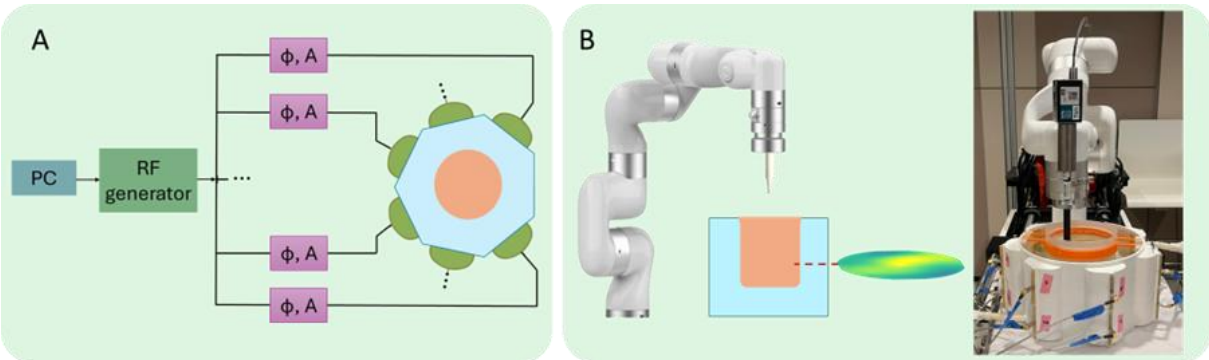

Fig. 2

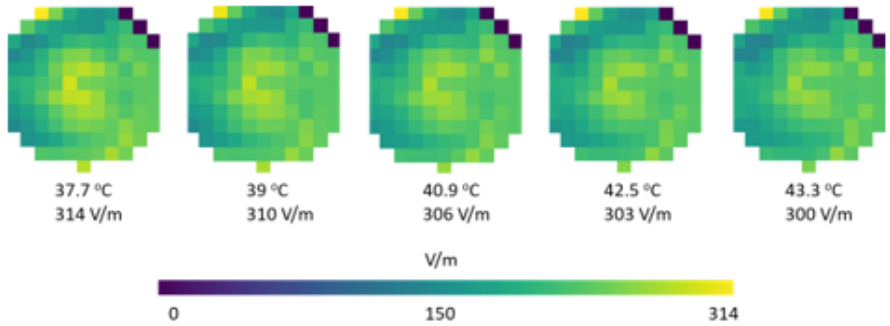

Figure 2E-field magnitude distributions at increasing phantom temperatures (37.7–43.3 °C), showing a gradual decline in peak field from 314 to 300 V/m across five consecutive scans.

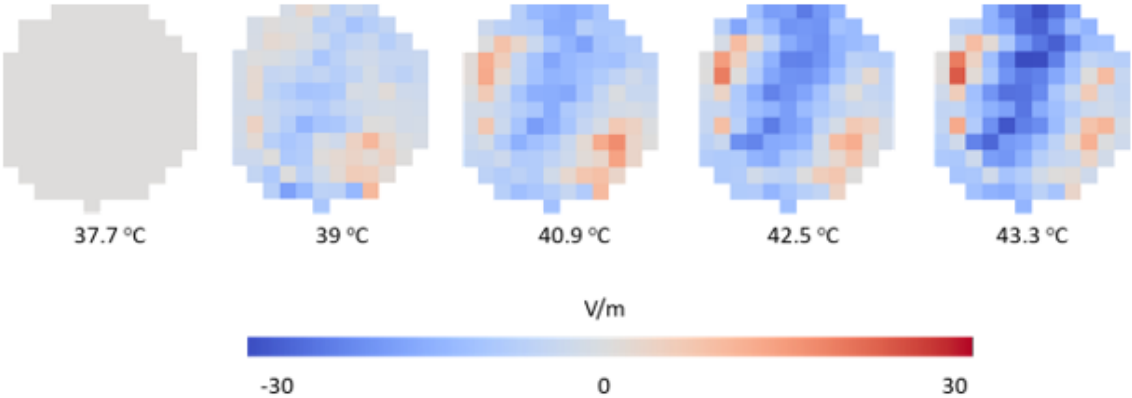

Figure 3Cumulative E-field deviation relative to the baseline scan, revealing progressive spatial drift as phantom temperature increases.

P-004

A Clinically Realistic Pipeline for Computer Based Testing of Deep-Regional Hyperthermia Technology

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Introduction. The development of new hyperthermia (HT) technology and treatment strategies requires reliable tools to predict clinical performance. Yet, current computational models, e.g. the ESHO benchmarks, are typically restricted to static pre-treatment planning and ignore the dynamic realities in the clinic: warm-up behavior, real applied power and phase adjustments, treatment interruptions, patient dependent variables, and temperature-dependent physiological responses. As a result, the field lacks a virtual environment for evaluating new applicators or treatment concepts under true clinical conditions.

Goals. We present a dynamic, end-to-end simulation pipeline that models the full HT treatment, from power-on to steady state, using patient specific anatomy and actual clinical control settings. We validate simulated temperatures against intraluminal measurements. We also demonstrate how this workflow can function as a virtual testbed for future HT technology by analyzing the impact of perfusion models.

Materials and Methods. One treatment session per patient (n = 12) with locally advanced cervical carcinoma treated at Erasmus MC (BSD-2000 3D MR-compatible system) was modeled. Each session included a 30 min warm-up (WU) and a 60 min steady-state, divided into SS1 and SS2 for analysis. Patient-specific anatomical models, including all temperature probe locations, were segmented from T1-weighted MRI. Electromagnetic and thermal simulations were performed in Sim4Life. The Pennes bioheat equation was solved using:

the constant-stress perfusion model from the ESHO benchmark study [1], and a temperature-dependent perfusion model [2].

Crucially, simulations were driven by the measured power and phase settings recorded during each treatment (Fig. 1). To demonstrate the clinical relevance of the pipeline, simulated temperatures were compared with all measured probe temperatures.

Results. Across all patients and probes (Fig. 2), the temperature-dependent perfusion model produced lower mean errors than the constant-stress model:

1. Constant-stress model: –1.4 ± 1.0 °C

2. Temperature-dependent model: 1.1 ± 1.2 °C

The negative error indicates that the model underestimated the temperatures. Unlike static planning models, the dynamic pipeline reproduced clinically observed warm-up behavior and intra-treatment temperature variations.

Summary. We developed and validated a fully dynamic, end-to-end HT treatment simulation pipeline that incorporates measured power and phase, and perfusion changes. Beyond improving temperature prediction, this workflow serves as a clinically realistic virtual test environment for evaluating treatment concepts before clinical deployment. We believe, this framework represents an important step toward personalized HT and multi-institutional benchmarking of emerging HT technology.

References.

[1] Paulides, MM. et al., *Int J Hyperthermia*, 38(1), 1425 (2021)
[2] Lang, J.et al., *IEEE Trans. Biomed. Eng.*, 46(9), 1129 (1999)

Fig. 1

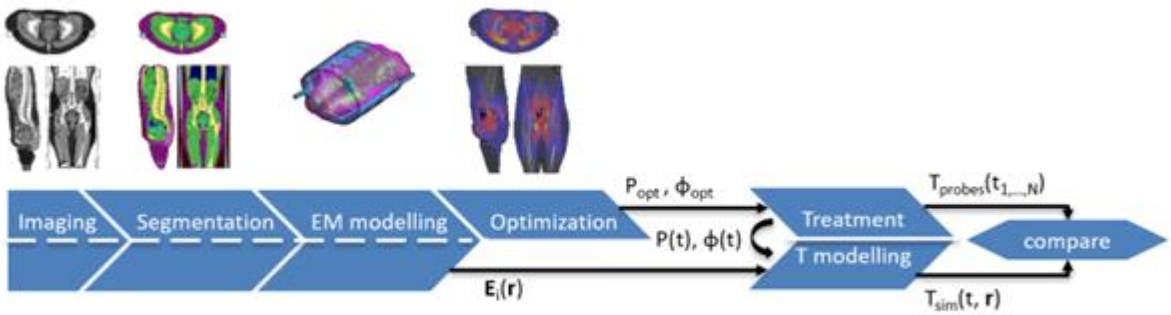

Fig. 1. Flowchart explaining the entire modeling pipeline. $\mathbf{E}_i(\mathbf{r})$ is the electric field of each antenna. P_{opt} is the optimal power settings determined by the optimization, and ϕ_{opt} is the optimal phase settings. P(t) and ϕ(t) are the powers and phases applied during the treatment.

Fig. 2

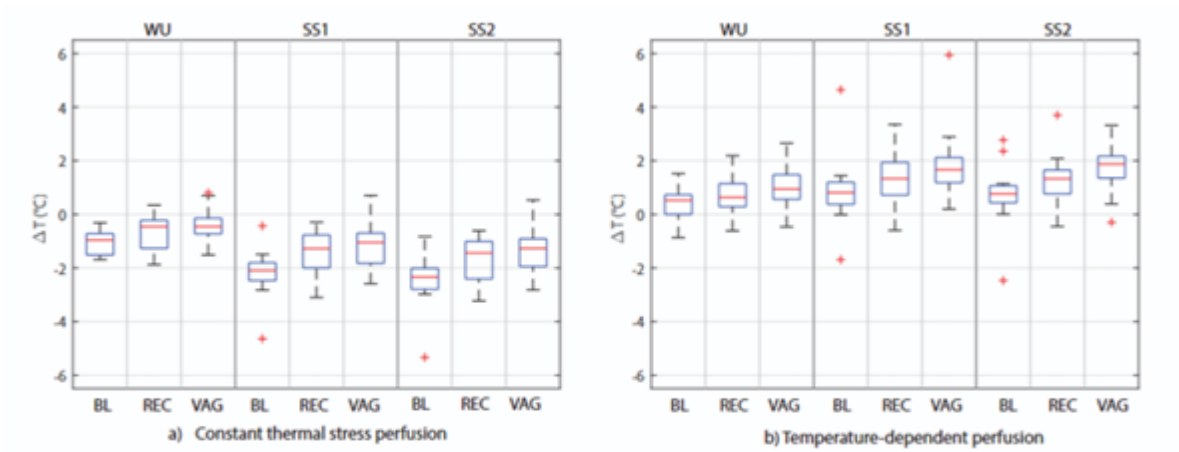

Fig. 2. The mean error for the two different perfusion models, where probe measurements in the bladder, rectum and vagina were compared against simulations. With 30 min warm up (WU) and a 60 min steady state, divided into SS1 and SS2.

P-005

A Robust MR Thermometry in Large-Volume MR-HIFU Mild Hyperthermia using Third-Order B_0 Drift Correction and SNR Masking

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[2] University of Cologne, The Interdisciplinary Program Health Sciences, Cologne, Germany

Introduction. Proton resonance frequency shift (PRFS)-based MR thermometry is the gold standard for real-time temperature monitoring during magnetic resonance-guided high-intensity focused ultrasound (MR-HIFU) hyperthermia. However, prolonged treatments remain vulnerable to temperature bias caused by B0 drift, susceptibility artifacts and spatial signal-to-noise ratio (SNR) variations, compromising thermometry accuracy, spatial stability, and reliable thermal control1.

Goal. To develop and experimentally validate a hybrid correction framework combining third-order B0 drift correction and Otsu-based SNR masking for robust in vivo MR thermometry during prolonged MR-HIFU hyperthermia.

Materials and Methods. A temperature feedback control algorithm based on the approach of *Tillander et al.* 2 was extended by integrating Otsu-based SNR masking and third-order polynomial B0 drift correction into the commercial software of the Sonalleve® MR-HIFU system. Otsu mask was applied to magnitude images to automatically separate signal from background noise, followed by binary erosion. Spatial B0 drift was modeled using a 3rd Order polynomial expansion of voxel coordinates implemented through a Vandermonde matrix including higher-order spatial terms, and polynomial coefficients were estimated using least-squares fitting. The refined algorithm was first evaluated during 30 min *in vitro* in a custom-made tissue mimicking phantom then validate *in vivo* during a 30-minutes MR-HIFU hyperthermia in a porcine hind-leg model using an 18 mm treatment cell, and compared with conventional 0th-Order drift correction without masking.

Results. The 0th-Order drift correction showed pronounced spatial temperature distortions and temporal fluctuations, particularly in non-focal regions. The hybrid correction reduced spatial drift artifacts and stabilized temperature control throughout the treatment. Mean target temperature was maintained at 42.2± 0.4 °C without systematic bias during the 30 minutes sonication. Otsu-based SNR masking suppressed low-signal noise and reduced temperature overshoot in peripheral regions. The combination of masking and 3rd-order drift correction resulted in more homogeneous temperature distributions and improved spatial consistency of PRFS-based MR thermometry.

Summary. Hybrid third-order B0 drift correction combined with Otsu-based SNR masking improves the robustness, spatial accuracy, and temporal stability of PRFS-based MR thermometry during prolonged in vivo MR-HIFU hyperthermia. These findings support the clinical implementation of advanced drift compensation strategies for reliable temperature monitoring and precise thermal control during extended hyperthermia treatments.

References.

[1] Bing et al., 2016. International Journal of Hyperthermia, 32(6), 673–687. https://doi.org/10.1080/02656736.2016.1179799
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Fig. 1: Algorithmic workflow of the refined masking and third-order B_0 drift correction algorithm

Fig. 2: Temperature Mapping Overlaid on T1w Images during 30-minute MR-HIFU hyperthermia in a porcine hind leg, with 0th-order correction (A, B, C) and 3rd-order correction (D, E, F)

Fig. 1

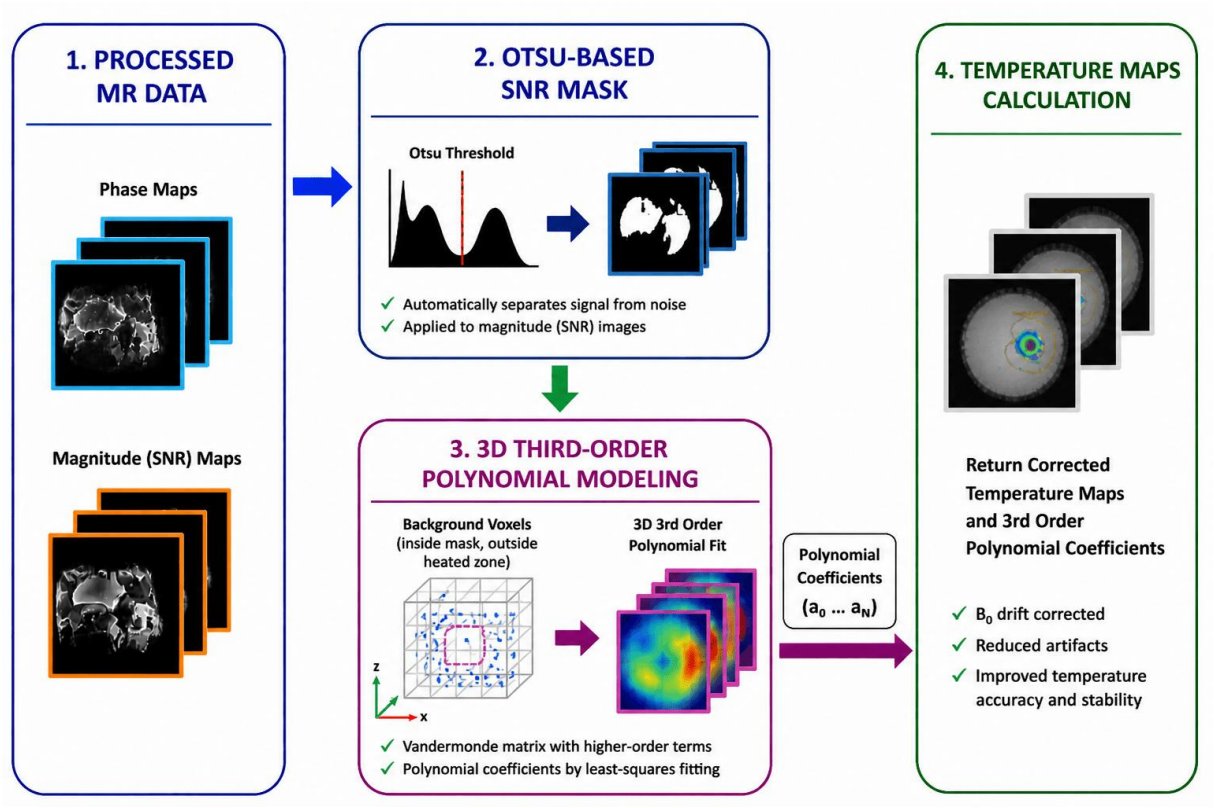
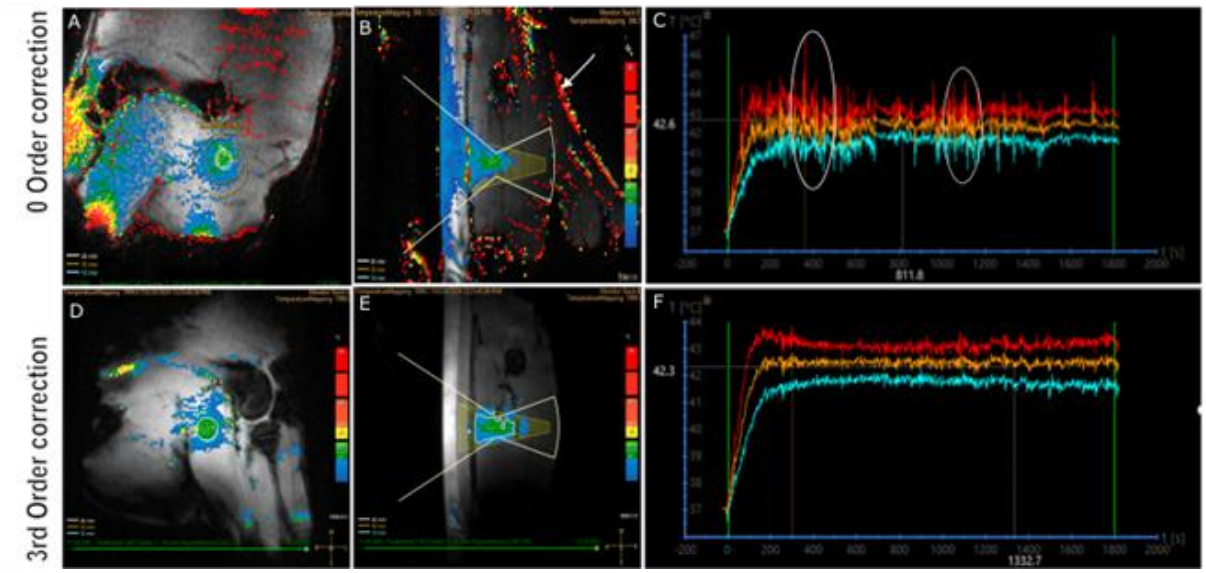

1. PROCESSED MR DATA
Phase Maps
Magnitude (SNR) Maps
2. OTSU-BASED SNR MASK
Otsu Threshold
✓ Automatically separates signal from noise
✓ Applied to magnitude (SNR) images
3. 3D THIRD-ORDER POLYNOMIAL MODELING
Background Voxels (inside mask, outside heated zone)
3D 3rd Order Polynomial Fit
z
x
✓ Vandermonde matrix with higher-order terms
✓ Polynomial coefficients by least-squares fitting
Polynomial Coefficients (a_0 ... a_N)
4. TEMPERATURE MAPS CALCULATION
Return Corrected Temperature Maps and 3rd Order Polynomial Coefficients
✓ B_0 drift corrected
✓ Reduced artifacts
✓ Improved temperature accuracy and stability

Fig. 2


0 Order correction
3rd Order correction
A
B
C
D
E
F

P-006

Thermal dose evaluations based on skin temperature data in recurrent breast cancer patients treated with superficial hyperthermia in combination with adjuvant radiotherapy: a retrospective analysis

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[1] Cantonsspital Aarau, Aarau, Switzerland

[2] University of Zürich, Institute of Physics, Science Faculty, Zurich, Switzerland

Aim. In breast cancer patients, skin temperature is commonly used to guide superficial hyperthermia (HT) treatments. However, it remains unclear to what extent skin temperature represents the temperature achieved in the planning target volume (PTV). This retrospective analysis was performed to evaluate the correlation between maximal PTV depth and thermal dose parameters, and to assess the efficacy of combined HT and adjuvant radiotherapy (RT) in patients with recurrent breast cancer.

Methods. A total of 41 patients with recurrent breast cancer (median age: 66 years; range: 24–85), with recurrence sites in the breast, nodal lymphatic drainage, parasternal region, and chest wall, treated between October 2014 and September 2024 at Kantonsspital Aarau, were included in this retrospective analysis. Among these patients, 70% and 56% were estrogen receptor (ER) and progesterone receptor (PR) positive, respectively, while 12% were HER2 positive. The median prescribed total RT dose was 46 Gy (range: 36–50.4 Gy), and patients received a median of 7 (range: 4–10) weekly HT sessions. Overall, 95% of patients underwent reirradiation, having previously received a median dose of 60 Gy (range: 50–70 Gy). The primary endpoint was to evaluate the correlation between maximal PTV depth and thermal dose parameters, expressed as cumulative equivalent minutes at 43 °C (CEM43Tx), where x represents the 10th, 50th, and 90th percentiles of measured skin temperature points during each HT session. Secondary endpoints included variation in thermal dose (CEM43Tx) and temperature metrics across HT sessions, as well as local recurrence-free survival (LRFS), progression-free survival (PFS), overall survival (OS), and acute toxicity.

Results. Pearson correlation analysis showed a statistically significant, moderate positive correlation between maximal PTV depth (4.53 ± 2.29 cm) and CEM43T50 (r = 0.39, p = 0.046) and CEM43T10 (r = 0.39, p = 0.043), as shown in Figure 1. The thermal dose parameter CEM43T90 showed non-significant but moderate positive correlations with maximal PTV depth (r =0.38, p=0.053). As shown in Figure 2, there were no significant differences among sessions for CEM43T10 (p = 0.6, W = 0.1), CEM43T50 (p = 0.3, W = 0.2) and CEM43T90 (p = 0.2, W = 0.2). The median follow up of patients was 50 (95%CI: 43-61) months. The 3-year OS and LC rates were 87% (95% CI: 77-98 %) and 94% (95CI: 85%-100%), respectively. There were seven patients who had distant progression, leading to a 3-year PFS rate of 79% (95% CI: 65-96 %). The rates of acute toxicity of grades 2 and 3 were 19% (46%) and 3% (7%), respectively.

Conclusion. The recurrent breast cancer patients were treated with reproducible thermal dose parameters across HT sessions, which were positively correlated with maximal PTV depth, indicating that the thermal dose at a given PTV depth may be higher than that monitored or calculated based solely on skin temperature data.

Fig. 1

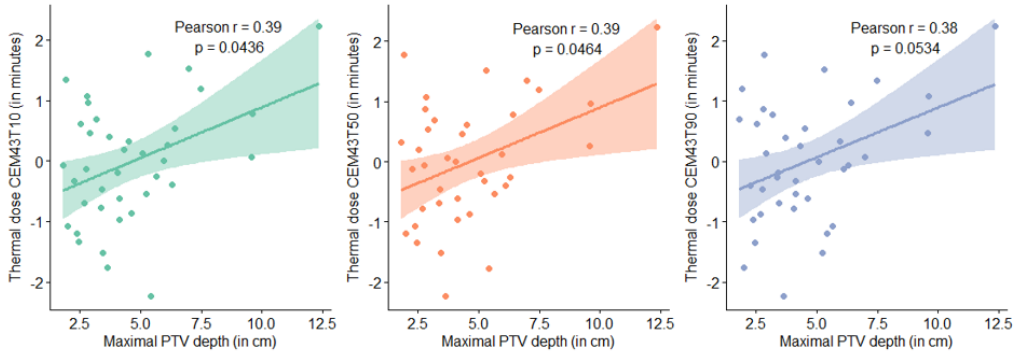

Figure 1. Scatter plots showing the correlation analysis between maximal planning target volume (PTV) depth and rank-based inverse normal transformed median thermal dose parameters ($CEM43T_{10}$, $CEM43T_{50}$ and $CEM43T_{90}$). Each subplot displays individual patient data points (dots), a linear regression line with 95% confidence interval (shaded area), the Pearson correlation coefficient (r) and Bonferroni-adjusted p-value annotated on the plot.

Fig. 2

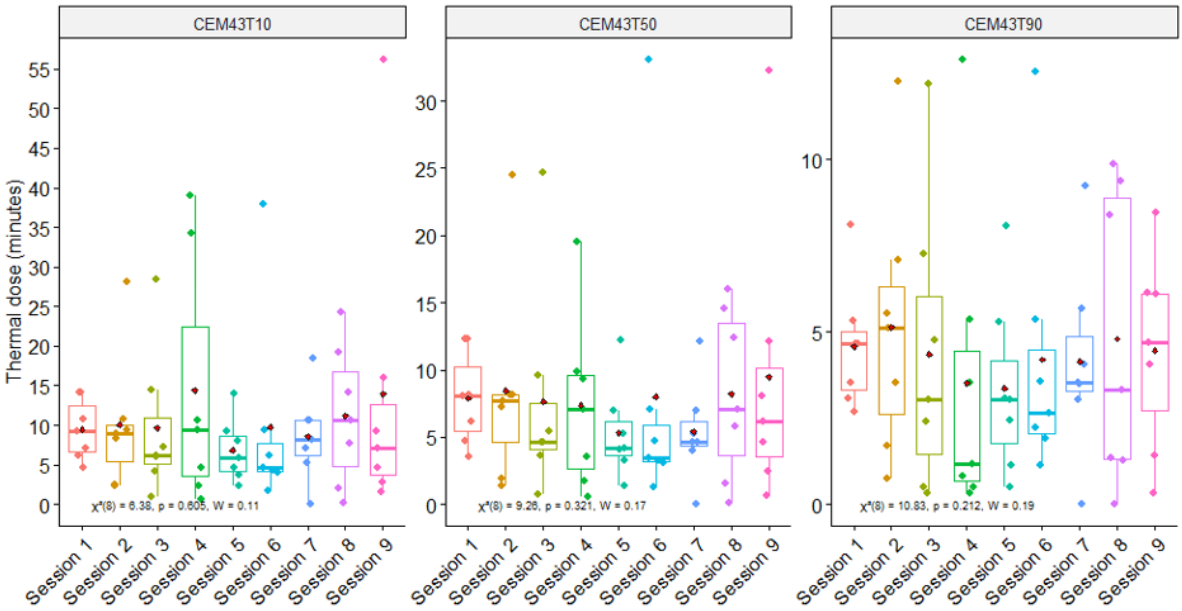

Figure 2. Variation of thermal dose $CEM43T_{10}$, $CEM43T_{50}$, $CEM43T_{90}$ parameters among hyperthermia sessions. Boxplots represent the interquartile range where the horizontal line shows the median and the red diamonds indicate the mean value. Friedman test results (χ^2, p, Kendall's W) are shown. Note that the data for Session 10 are not shown because there was only one patient treated with 10 superficial hyperthermia sessions combined with radiotherapy.

P-007

Spatial versus temporal variability of thermometric parameters in locally advanced rectal cancer patients treated with neoadjuvant chemoradiotherapy in combination with deep regional hyperthermia

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[1] Cantonsspital Aarau, Department of Radiation Oncology, Aarau, Switzerland
[2] Universitätsklinikum Erlangen, Department of Radiation Oncology, Erlangen, Germany
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Aim. Thermal dose, expressed as cumulative equivalent minutes at 43°C (CEM43), has been reported as a predictive parameter of treatment response of combined radiotherapy (RT) and hyperthermia (HT). In patients with locally advanced rectal cancer (LARC), invasive thermometry is routinely performed and can be used to evaluate thermal dose parameters. Using the Hyperboost REC study data, we aimed to assess the spatial and temporal variability of CEM43 thermal dose metrics.

Methods. In total, 206 LARC patients treated with neoadjuvant chemoradiotherapy (CRT) and HT (median age: 62 years, male 66%) were included in this analysis. RT was given with a median dose of 50.4Gy (95%CI:50.4–56) delivered in 1.8 Gy per fraction in combination with either 5-FU only (46% of patients) or as different doublets containing oxaliplatin. The median number of HT sessions was 7(1-11). For each HT session, thermometry data from the BSD-2000 3D/MRI system (Pyrexar Medical Corporation, Salt Lake City, USA) were used to compute thermal dose CEM43 metrics, derived at the 10th, 50th, and 90th percentiles of measured temperature points, denoted as CEM43T10, CEM43T50, and CEM43T90, respectively. The dose metrics were evaluated using both temporal and spatial thermometry. Temporal thermometry was based on a single measurement point (i.e., the tip of the temperature probe inserted in rectum during HT) recorded every 5 seconds, whereas spatial mapping was derived from temperature measurements along the catheter length in 1-cm increments up to a maximum depth of 10 cm, acquired at 5- or 8-minute intervals. Comparisons of thermal dose metrics between measurement approaches were performed using paired Wilcoxon signed-rank tests. To account for multiple testing, Bonferroni correction was applied.

Results. There was no significant difference between spatial and temporal evaluations of the thermal dose parameters CEM43T10 and CEM43T50, as shown in Figure 1. However, significant variability was observed for the high-temperature parameter CEM43T90. Subgroup analyses stratified according to the median number of HT sessions revealed similar results for spatial and temporal evaluations. Furthermore, the analysis according to treatment period (before versus after 2015) showed that patients treated after 2015 received higher CEM43T10 thermal doses than those treated before 2015 (5.29±7.88 vs 3.66±3.19, $p = 0.03$), while CEM43T50 and CEM43T90 were comparable between groups. Figure 2 shows the map distribution of complete responders across thermal dose and HT session strata, indicating that complete responders tended to receive higher thermal doses (CEM43T50> 1.3 min and CEM43T10> 3.4 min) and more HT sessions (>7).

Conclusion. This analysis shows that the type of thermometry influences the evaluation of maximum thermal dose, expressed as CEM43T90. In addition, a trend toward complete response was observed in patients who received both higher thermal doses and a higher number of HT sessions.

Fig. 1

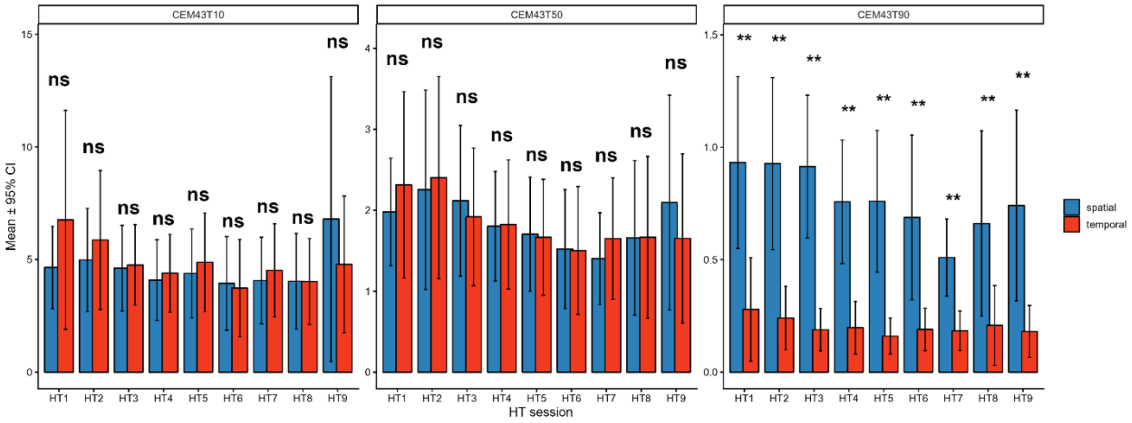

Figure 1. Bar plots represent mean values of CEM43 parameters with 95% confidence intervals, and significance levels between spatial and temporal evaluations are indicated by asterisks.

Fig. 2

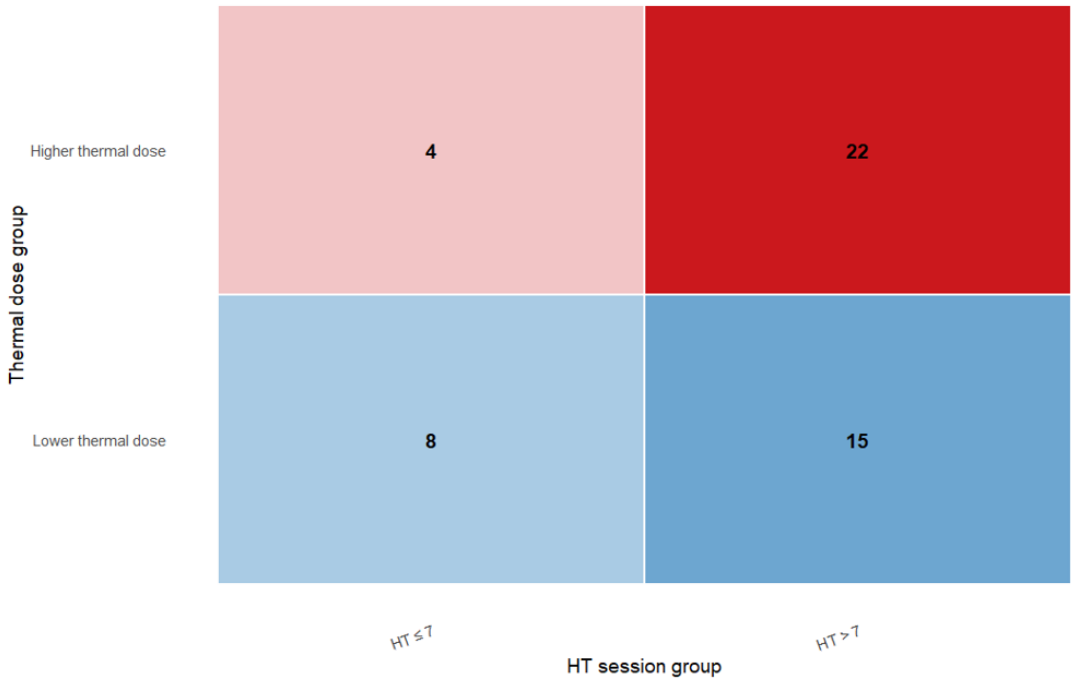

Figure 2. Heatmap distribution of complete responders (n=49) according to thermal dose and hyperthermia (HT) session groups. The heatmap displays the proportion of complete responders within each combined treatment group. Color represents the median thermal dose CEM43T50 and color intensity represents the number of patients.

P-008

Well-controlled and Reproducible Hyperthermic Treatments of Cell Cultures using Ultrasound: Challenges for Quality Assurance

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Introduction and Goals. Mild and moderate hyperthermia therapy at temperatures between 41 and 43 °C is commonly delivered through tissue absorption of energy carried in electric and/or magnetic fields. More recently, the use of ultrasound, sometimes combined with the administration of nanoparticles, has been investigated as an alternative to this approach [1,2]. Ultrasound-based hyperthermia does, however, present particular challenges especially when high ultrasonic frequencies are used, as the short wavelength makes it inherently susceptible to interference on millimeter scales. Consequently, hot spots and energy voids occur, leading to uneven exposure. Yet, homogeneous exposure of cells under well-controlled conditions is essential for investigating thermal and non-thermal (micromechanical) effects in vitro.

Methods. To meet the aforementioned requirements, an in vitro setup for exposing cells to ultrasound at 1 MHz while tightly controlling acoustic pressure and temperature was developed. This setup is designed to ensure reliable and reproducible measurements. It consists of an ultrasonic source, a water bath maintained at a set temperature, a holder for the vessel containing the cells, and an absorber to minimize undesired reflections.

Results. We present a comparison between measured data and results simulated in COMSOL Multiphysics with a focus on the associated quality assurance process and highlight how seemingly minor mistakes can lead to significant deviations in predicted acoustic fields. In particular, we address the intrinsic limitation that any measurement inevitably perturbs the system under investigation, making it impossible to fully observe the undisturbed wave field. Finally, we discuss the practical challenge that the exact operating conditions of the system cannot always be measured. In the present case, the cell-containing vessel is sealed, thus pressure measurements within the sealed compartment are unfeasible, yet most critical. These limitations necessitate careful inference, calibration, and validation strategies to ensure reliable model predictions.

Summary. An in vitro ultrasound hyperthermia setup was developed to expose cells under controlled conditions. Measurements and simulations were compared to validate the system and identify sources of error. The study highlights challenges such as inaccessible pressure measurements in sealed cell vessels.

References.

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[2] Yang, Mengyao, et al. "Nanomaterials enhanced sonodynamic therapy for multiple tumor treatment." *Nano-Micro Lett.* 17.1 (2025): 157.

P-009

Comparative analysis of numerical tools for radiative hyperthermia applications

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Question. Radiative hyperthermia (HT) uses electromagnetic (EM) fields to raise tumour temperatures to 40–44 °C. To preliminarily assess EM field and temperature (T) distributions in the body, numerical treatment planning (TP) is widely used in clinics; thus, the validation of TP software is essential. This work compares an industry-standard simulation tool (CST Microwave Studio, Dassault Systèmes, France) and a clinically adopted software (Plan2heat, MedLogix Srl, Italy) in simulating a superficial HT scenario.

Methods. The simulation scenario consists of a superficial HT antenna (β antenna, MedLogix Srl) placed on a muscle-equivalent model, as shown in Fig.1.

The density, dielectric and thermal properties of muscle tissue were used for the model [1], including the perfusion coefficient. Its initial T was set at 37.0 °C.

The specific absorption rate (SAR) and T distributions were evaluated. To compute EM results, the transient solver, based on the Finite Integration Technique, and the finite difference time domain (FDTD) method were used in CST and Plan2heat, respectively. The thermal steady-state solver was used to compute the T distribution in both software. A grid of 1×1×1 mm³ resolution was used in the muscle tissue.

The SAR profiles along the central x, y and z axis were compared. A region of interest (ROI) was defined as the area of the model within the 50% iso-SAR contour in the central xy plane. Within the ROI, SAR and T distributions obtained with the two software were compared using CST results as reference, according to:

$$\Delta X_{\%}=[(X_{Plan2heat}-X_{CST})/X_{CST}]\cdot 100$$

where X = SAR or T. The mean value ± standard deviation was considered.

For the T distribution, also the γ-matrix was computed. For each point $\mathbf{r_e}$ of the Plan2heat distribution, the Γ value was calculated with respect to every point $\mathbf{r_r}$ of the CST distribution [2] according to:

$$\Gamma(\mathbf{r_e},\mathbf{r_r})=\{[(T(\mathbf{r_e})-T(\mathbf{r_r}))^2/\Delta T^2]+[|\mathbf{r_e}-\mathbf{r_r}|^2/\Delta d^2]\}^{1/2}$$

where Δd = 1 mm and ΔT = 3 % of $T(\mathbf{r_r})$ are the acceptance criteria for distance and temperature [2]. For each $\mathbf{r_e}$, the γ value was defined as the minimum Γ value. The percentage of points in the ROI with γ≤1 ($P_{\leq 1}$), i.e. satisfying both acceptance criteria, was evaluated resulting in a local gamma analysis [2].

Results. The resulting $\Delta SAR_{\%}$ and $\Delta T_{\%}$ in the ROI were 6.81±2.58 % and 0.74±0.49 %, respectively. Within the ROI, where T ranged from 38.0 to 45.7 °C, the absolute variation of the studied T distributions was 0.30±0.21 °C, and $P_{\leq 1}$ was 99.92 %.

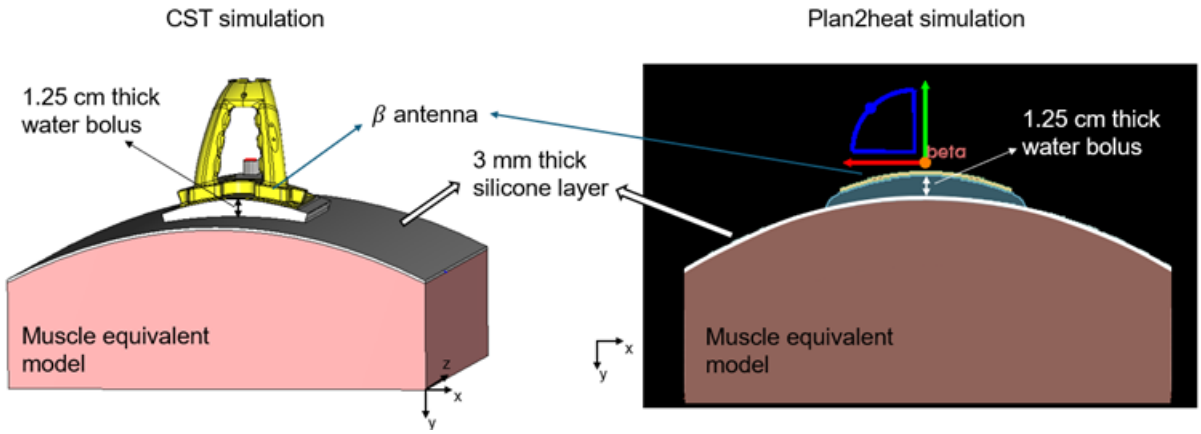
Discussion. The results show a strong agreement between the SAR and temperature distributions obtained with the two software in a homogeneous muscle-equivalent model. The future development will consist in the use of multilayer media to perform the comparison in case of multiple dielectric interfaces and more realistic anatomical conditions.

References.

[1] Paulides et al., Int. J. Hyperthermia 38, 1425–1442 (2021).
[2] Wendling et al., Med. Phys. 34, 1647–1654 (2007).

Fig.1: Simulation scenario.

Fig. 1


CST simulation
Plan2heat simulation
1.25 cm thick
water bolus
β antenna
3 mm thick
silicone layer
Muscle equivalent
model
z
x
y
beta
1.25 cm thick
water bolus
Muscle equivalent
model
x
y

P-010

Normal tissue complication frameworks using Lyman-Kutcher-Burman model in combined RT+HT treatment for realistic CNS tumor

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Introduction. Microwave Hyperthermia (HT) is a well-established radiosensitizer treatment that enhances the efficacy of radiotherapy (RT) by elevating tumour temperature to 40-44°C while maintaining normal tissues within safe thermal limits [1]. Modelling of combined treatments has been largely focused on tumour response, with normal tissue effects often neglected [2]. This simplification is partly motivated by the limited clinical evidence for additional HT-induced toxicity. However, this assumption becomes insufficient when tumours are located near highly radiosensitive structures or when the prescribed RT dose approaches normal-tissue tolerance thresholds.

Goal. This work quantifies the therapeutic enhancement of HT delivered in conjunction with RT for two patients with CNS tumours, as well as possible complications in normal tissues. We propose a framework for modelling thermal radiotherapy, including tumour control and normal tissue complication probability (NTCP), aligned with Swedish radiotherapy protocols (PRO-CNS) [3] and QUANTEC clinical guidelines [4].

Method. CT and MRI data, together with clinical RT plans (prescribed dose ~60 Gy), were used to compute the equivalent dose (EQD; note not EQD2) for RT alone and RT+HT. HT was assumed to be administered one to two times per week. Patient-specific temperature distributions were optimized using an in-house HT treatment-planning system [1] and integrated with RT dose distributions using an adapted linear-quadratic (LQ) model [2]. For each patient, NTCP was evaluated for CNS structures specified in the PRO-CNS [3] using dose–response modelling (Lyman-Kutcher-Burman) consistent with QUANTEC recommendations and parameters [4].

Results. Figure 1 shows the outcomes of the combined treatments for one of the patients. The combined plan demonstrates a therapeutic enhancement in the tumour compared to RT alone (right figure), while the NTCP curve for a nearby sensitive structure indicates a modest, though non-negligible increase in complication risk (left figure). One of the consequences of the results is an easy way of attaining model parameters for predicting tissue complications in combined treatments.

References.

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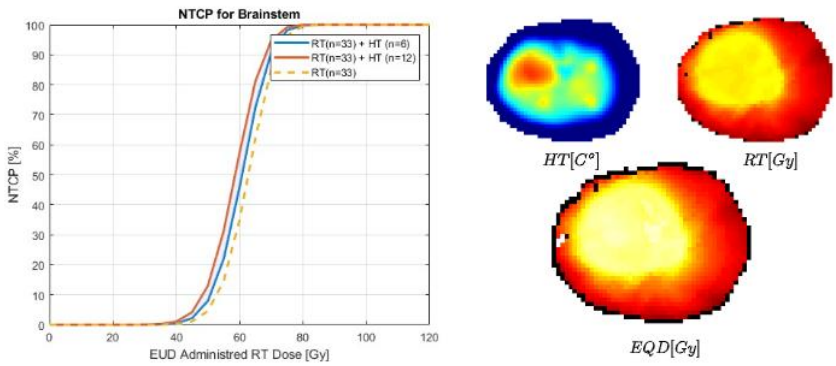
Fig. 1



P-011

Improved target coverage of regional hyperthermia using HyperPlan® for the clinical BSD-2000/3D system for patients with high-risk retroperitoneal sarcoma: a simulation study

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[2] Dr. Sennewald Medizintechnik GmbH, Munich, Germany

Background. Hyperthermia treatment planning is essential for improving treatment quality and consistency. This study presents a simulation-based evaluation of the *HyperPlan®* treatment planning system for regional hyperthermia in patients with retroperitoneal sarcoma.

Methods. Eight patients with high-risk retroperitoneal sarcoma who underwent neoadjuvant chemotherapy combined with regional hyperthermia between 2016 and 2025 were retrospectively analyzed. Patient-specific models were generated in *HyperPlan®* using planning computed tomography (CT) scans and hyperthermia planning contours. The original applicator position, amplitude, and phase settings—determined during clinical quasi-two-dimensional geometrical planning using standard Pyrexar Planing Software Tools for the hyperthermia system BSD-2000/3D (Pyrexar Medical, Salt Lake City, UT, USA)—were replicated in fully voxel-based finite-difference time-domain (FDTD) simulations. Additionally, three-dimensional (3D) optimization was performed based on the gross tumor volume (GTV) contour. Specific absorption rate (SAR) distributions within the GTV were compared between the original and optimized settings.

Results. Simulations of the original treatment settings yielded a median SARMEAN (V) of 31.15 W/kg (range: 18.0-54.0 W/kg) and a SAR90 (SAR in 90% of the GTV) of 16.45 W/kg (range: 10.5-36.2 W/kg). Optimization based on 3D target volume contours significantly improved both SARMEAN (median 34.4 W/kg, range: 21.6-69.8 W/kg; $p = 0.023$) and SAR90 (median 22.7 W/kg, range 14.6-52.2 W/kg; $p = 0.008$). Assessment of SAR values in organs at risk, including the urinary bladder, rectum, and small bowel, proved safety of the *HyperPlan®* planning.

Conclusion. *HyperPlan®* effectively enhances the heating characteristics of phased-array system BSD-2000 /3D for regional hyperthermia of patients with high-risk retroperitoneal sarcoma. These findings support its clinical implementation to improve the quality and consistency of regional hyperthermia treatments.

Fig. 1

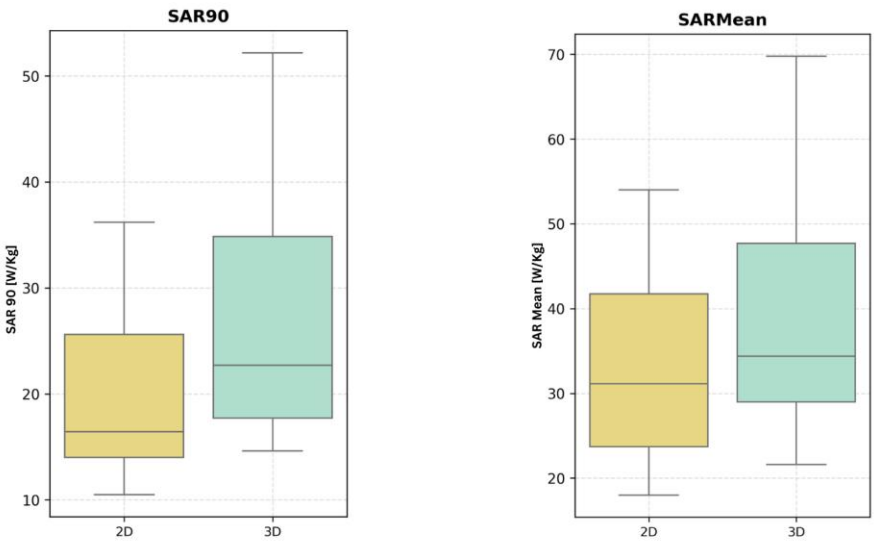

Fig. 1. *Comparison of simulated specific absorption rate (SAR) distributions within the gross tumor volume (GTV) for two-dimensional (2D) and three-dimensional (3D) treatment planning. Boxplots show the SAR_{90} (left) and SAR_{mean} (right) values obtained from retroperitoneal sarcoma patient models. 3D optimization in HyperPlan® resulted in higher median SAR_{90} and SAR_{mean} values compared to the original 2D clinical settings, indicating improved target coverage and heating efficiency.*

Fig. 2

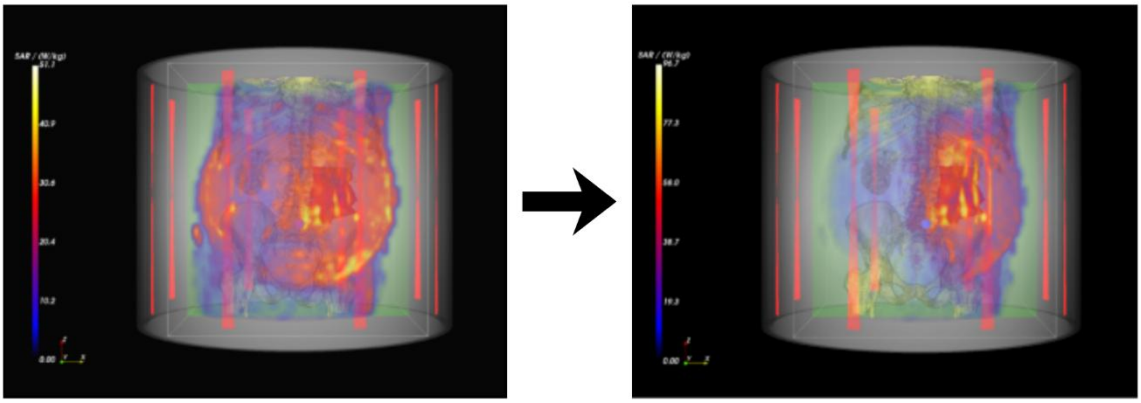

Fig. 2. *Patient positioned within the BSD-2000/3D applicator based on the planning CT image, and corresponding two-dimensional (2D) and three-dimensional (3D) HyperPlan® treatment plans illustrating the simulated specific absorption rate (SAR) distribution in the entire patient, with clear visualization of SAR deposition in relation to the gross tumor volume (GTV).*

P-012

Safety of radiofrequent and microwave hyperthermia treatments in patients with MR-compatible cardiac implantable electronic devices (CIED)

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Introduction. Hyperthermia (HT) at 40-43°C is an adjuvant therapy used to tumour-selectively enhance the effect of chemotherapy and radiotherapy. HT is mostly delivered using radiofrequent/microwave antennas, creating an electromagnetic field in the target region. The presence of a Cardiac Implantable Electronic Device (CIED) is currently a contraindication for HT. The risks of HT include electromagnetic interference (EMI), which could lead to CIED malfunction, e.g. inaccurate pacing or inappropriate shocks and unwanted heating of the CIED leads, potentially resulting in local tissue ablation.

Goals. Evaluating the safety of delivering HT in patients with CIEDs.

Materials and Methods. The effects of the HT EM field were evaluated for an MRI-compatible pacemaker and an ICD in tissue-equivalent phantoms. Three MRI-compatible leads and one abandoned MRI-compatible lead were implanted in ex vivo rat hearts placed within a tissue-equivalent wallpaper-paste phantom. Six thermocouples were positioned along the lead, near the lead tip, at the heart and at the CIED device. Devices were programmed to maximal atrial and ventricular sensitivity, with EMG storage, noise reversion, and high ventricular rate detection enabled. Worst-case conditions were mimicked to test for EMI and heating by aligning leads parallel to the EM field and in the HT focus. Superficial HT was delivered by ALBA ON 4000D with a 434 MHz 3H antenna (power up to 100W), and deep HT with the 70 MHz ALBA 4D system (power up to 4 × 400W). Baseline temperature was 37°C, temperatures were monitored to the therapeutic range of 40-43°C, with additional distance testing if values exceeded the therapeutic. Baseline impedance, sensing, ECG recordings, and abandoned lead behaviour were also assessed, followed by pathological analysis of marked tissue samples.

Results. No temperatures above 43°C were observed under any test condition. Temperature rise at the lead was not greater than that measured in more distant surrounding myocardial tissue, indicating that heating near leads was a result of phantom HT exposure rather than caused primarily by localized lead-related heating. Low-voltage baseline noise below 0.1 mV was occasionally observed, sometimes coinciding with pacing artefacts. However, no difference was found between power-on and power-off conditions, suggesting this did not represent HT treatment-related interference. No lead-related heating or EMI was observed under the worst-case conditions.

Summary. No EMI or lead-specific heating was observed in a tissue-mimicking phantom with ex vivo rat hearts, a pacemaker, an ICD, and an abandoned lead, which were tested during superficial and deep HT. These findings suggest that HT can be delivered safely in patients with an MRI-compatible CIED, the first time preferably in the presence of a pacemaker technician.

P-013

Multi-Center Prospective Standardization and Practical Recommendations for Quality Assurance of Thermometry in Superficial Hyperthermia in the Netherlands

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Question. This study focused on delivering prospective calibration and quality assurance (QA) procedures for superficial hyperthermia across Dutch centers as part of the RT-HYPE project, funded by the Dutch Cancer Society [1]. The goal was to establish standardized procedures to improve the reliability of temperature measurements in all hyperthermia centers in the Netherlands.

Methods. Three Dutch institutes providing clinical superficial hyperthermia—Amsterdam UMC, Erasmus MC, and Institute Verbeeten—participated. Their thermometry systems (multi-sensor thermocouples, fiber-optic probes, and single-sensor thermocouples, respectively) were prospectively assessed for accuracy, bias, precision, and stability over a 3-week period. Benchmarking was performed against a universal reference thermometer across all institutes, with measurements taken between 37°C and 43°C in 0.2°C increments. Temperature stability was evaluated weekly by maintaining 40°C for 2 hours assessing short-term (2 hours) and long-term (3 weeks) stability. One center implemented a new calibration procedure during the study to correct deviations found during preliminary testing. To assess (self-)heating behavior, thermometry probes were placed on a human tissue-equivalent phantom and were exposed to the electromagnetic field of a clinical superficial hyperthermia applicator. Probe orientation was varied relative to the main electric field component of the applicator to evaluate angular misalignment effects on temperature readings.

Results. Accuracy, bias, precision, and stability results are summarized in Table 1. The updated calibration procedure (b) improved accuracy for one center compared to their original procedure (a). All centers met the existing QA guidelines, confirming compliance with clinical standards for superficial hyperthermia thermometry. Thermocouples (Figure 1a,b,c) showed measurable self-heating artifacts when misaligned by more than 15° from perpendicular orientation to the main electric field component. As an example of the procedures, thermocouples (Figure 1d) positioned (nearly) perpendicular per clinical protocol, and fiber-optic probes both exhibited negligible artifacts under electromagnetic exposure.

Conclusions. This multi-center initiative demonstrates that the three Dutch centers implemented standardized prospective calibration and QA protocols, and thereby improved the accuracy, bias, precision and stability of temperature measurements in all Dutch superficial hyperthermia centers. The applied quality assurance procedures can prove helpful for newcomers to application of thermo-radiotherapy.

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Fig. 1

Table 1. Thermometry results with the existing guideline values established by the European Society of Hyperthermic Oncology (ESHO) and American Association of Physicists in Medicine (AAPM). Green indicates compliance with the requirements specified in the applicable guidelines, whereas red denotes non-compliance.

Parameter	Range	Center 1 procedure (a)	Center 1 procedure (b)	Center 2	Center 3	Guidelines	Definition
Accuracy, α [°C]	37 ~ 43 °C	0.27	0.15	0.03	0.04	$\lvert\alpha\rvert \leq 0.2$ [4]	$\alpha(x_i) = \frac{\sum_{i=0}^{i=N-1} \lvert x_i - A \rvert}{N}$
Bias, β [°C]	37 ~ 43 °C	0.27	-0.01	-0.01	0.02	$\lvert\beta\rvert \leq 0.2$ [4]	$\beta(x_i) = \frac{\sum_{i=0}^{i=N-1} (x_i - A)}{N}$
Precision, SD [°C]	37 ~ 43 °C	0.22	0.19	0.03	0.05	SD ≤ 0.1 [4]	$\mathrm{SD} = \sqrt{\frac{\sum_{i=0}^{i=N-1} (x_i - \bar{x})^2}{N-1}}$
Stability (short-term), S_S [°C / hr]	37 ~ 43 °C	-0.03	-0.03	-0.02	-0.01	$\lvert S_S\rvert \leq 0.1$ [5]	$S_S = \frac{\max((x_i - A_i) - \alpha(x_i) - (x_{t=0} - A_{t=0}))}{t}$
Stability (long-term), S_L [°C / wk]	37 ~ 43 °C	-0.09	-0.09	0.03	-0.04	$\lvert S_L\rvert \leq 0.1$ [5]	$S_L = \frac{\sum_{i=0}^{i=N-1} ((x_{t=3,i} - A_{t=3}) - (x_{t=1,i} - A_{t=1}))}{N \cdot t}$

Fig. 2

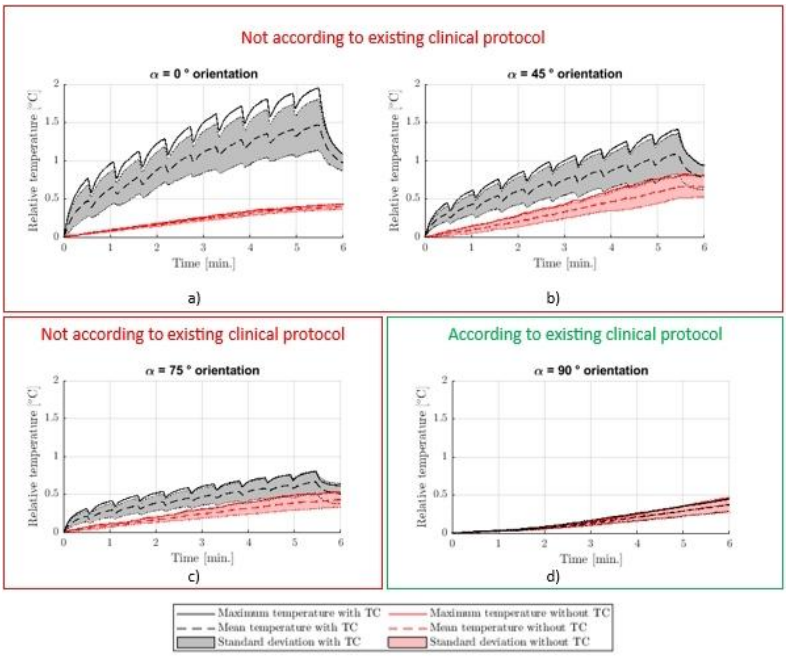

Figure 1. *Fiber-optic temperature readings (in °C) over 6 minutes. Each plot corresponds to a different angle (in °) between the probes and the main component of the electric field of the applicator. 0° angle corresponds to a parallel orientation and 90° corresponds to a perpendicular orientation. Data are shown for 0 cm depth in the fat-muscle phantom. Solid lines represent the maximum relative temperature reported by the fiber-optic probes. Dashed lines represent the average relative temperature reported by the fiber-optic probes. Black curves represent the experiment with the thermocouple (TC) present, and red curved represent the experiment without the thermocouple present. Due to the significant self-heating artefacts present at the orientations in a) and b), the existing clinical protocol has always been to place the thermocouples at the orientation as shown in d). Acceptable effects are shown at the orientations in both c) and d).*

P-014

Magnetic Resonance Thermometry and Biological Modelling to Predict Optimal Hyperthermia Fractionation in Locally Advanced Cervical Cancer

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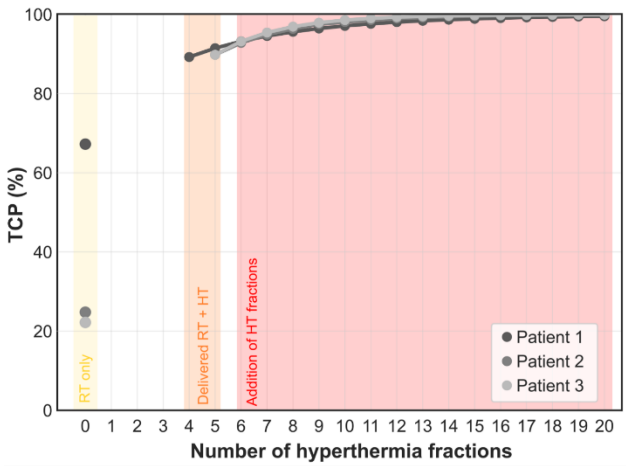
Purpose. Hyperthermia enhances the effects of radiotherapy, but the number of hyperthermia sessions needed to achieve maximal tumour control is not well established. This study evaluated whether biological modelling based on magnetic resonance (MR) thermometry from delivered hyperthermia fractions can be used to estimate the total number of fractions required to reach a predicted tumour control probability (TCP) of ≥ 95 %.

Materials and Methods. Three patients with locally advanced cervical cancer (LACC) treated prior to the introduction of the EMBRACE-II protocol in routine clinical practice were included. At that time, treatment consisted of external beam radiotherapy (EBRT: 23 × 2.0 Gy) combined with weekly magnetic resonance-guided hyperthermia (MRgHT), followed by brachytherapy. One patient received four hyperthermia fractions and two patients received five fractions. MR thermometry data acquired during hyperthermia were combined with patient-specific radiotherapy dose distributions. The potential radiosensitising effect of hyperthermia was quantified voxel-wise in terms of equivalent dose in 2 Gy fractions (EQD2) and tumour control probability (TCP) using an extended linear–quadratic model incorporating temperature-dependent radiobiological parameter. Measured temperature distributions were subsequently used in simulations to extrapolate the impact of increasing the number of hyperthermia fractions, in order to determine the total number of fractions required for each patient to reach approximately ≥ 95% TCP. This analysis assumed that clinically achieved temperatures would remain consistent across additional fractions.

Results. Values of TCP for radiotherapy alone were 67 %, 25 % and 22 %, for patients 1,2 and 3, respectively. Baseline TCP values for the radiotherapy plus the delivered number of hyperthermia fractions were 89 % for patient 1 and 90 % for patients 2 and 3, corresponding to EQD2 values of 3.4 Gy, 7.1 Gy, and 6.6 Gy at mean temperatures of 39.4 °C, 40.3 °C and 40.2 °C. To achieve a TCP of ≥ 95 %, patients 1 and 2 would require 8 hyperthermia fractions, while patient 3 would require 7 fractions. This corresponded to EQD2 values of 6.3 Gy, 10.6 Gy and 9 Gy for patients 1, 2 and 3, respectively. Beyond these patient-specific thresholds, additional hyperthermia fractions provided minimal further TCP improvement.

Conclusion. Biological modelling combined with MR-based temperatures from delivered hyperthermia fractions can estimate the patient specific number of hyperthermia fractions needed to achieve maximal predicted TCP. This approach may support more personalised hyperthermia scheduling by identifying when additional fractions are (un)likely to provide significant benefit.

Fig. 1



P-015

Real-time Hyperthermia Treatment Monitoring, Parameter Inference, and Model Predictive Control (Eurostars Project SENS-THERM: Electromagnetic sensing, video control and metamodelling in thermotherapy of advanced head and neck (H&N) cancers)

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Questions. Hyperthermia has been shown to be a highly effective (adjuvant or stand-alone) therapy for a wide range of cancer types. Electrode arrays generating interfering fields can be used to preferentially focus electromagnetic (EM) energy on the tumor, while avoiding collateral healthy tissue exposure. The highly limited monitoring data accessible, heterogeneous anatomical environment, along with the difficulty of predicting the impact of stimulation parameters, often makes simulation-based treatment planning a necessity. However, modeling uncertainty and dynamically evolving thermoregulatory effects can lead to divergence between the planned and effective administered doses and the occurrence of safety or tolerability limiting hot-spots. The SENS-THERM Project aims to address these concerns using metamodeling techniques, enabling dynamically adaptive treatment control based on sparse real-time temperature feedback.

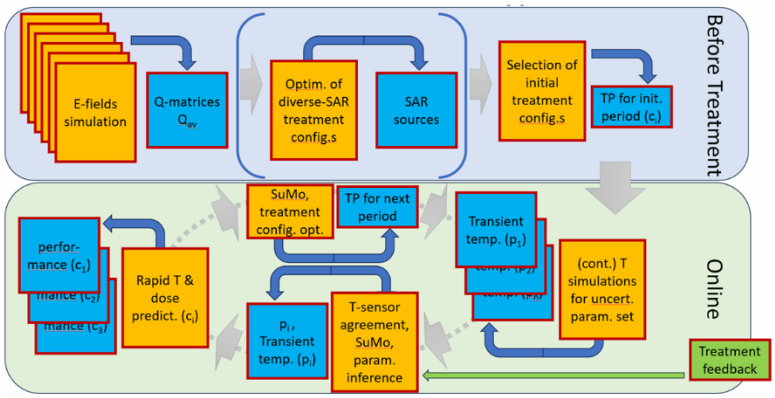
Methods. Our approach adapts treatment parameters every 5min, during which it performs two steps: calibration and control. For calibration, we assume *a priori* probability distributions for a set of model parameters, such as blood perfusion rates in the tumor, muscle, and fat. We then sample from this parameter space and generate an ensemble of computational thermal simulation models that are updated every 5min given the currently applied treatment conditions. At the end of each interval, we compare model predictions with sparse patient data (e.g. thermal point probe measurements) and infer *a posteriori* parameter probabilities. The most likely combination is used to reconstruct the full temperature field evolution.

For treatment control, we leverage the EM superposition principle, along with a novel rapid CEM43 dose predictor and surrogate-modeling, to assess the performance of a large set of treatment options for the forthcoming 5min interval. From these, the configuration that offers the best compromise between achieving the desired target dose and protecting healthy tissue is selected. This process is repeated periodically.

Results. In an *in silico* throat cancer patient model involving a commercial 12-antenna applicator, we run a simulation with "ground truth" tissue parameters and monitor temperature on 20 points along a catheter trajectory. Updating in parallel the ensemble of 200 calibration simulations every 5min and inferring best-fitting parameters takes 2min. Another 2min are spent on exploring 5000 potential treatment parameter configurations for the next 5min interval, the best of which is applied during the next interval. The framework readily infers the ground truth parameters and identifies optimal treatment conditions under these optimal conditions.

Conclusions. Our framework enables adaptive, model-predictive closed-loop controlled hyperthermia treatment. It is expected to handle dynamically changing conditions, but that remains to be tested, before demonstrating its value under research clinical conditions.

Fig. 1



P-016

Determining the minimum requirements to be included in a phased-array deep hyperthermia treatment planning system

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Introduction. A number of studies have demonstrated the clinical value of hyperthermia treatment planning (HTP). However, HPT has remained mostly a niche activity by a few academic centers since commercial software have yet to be approved by regulatory agencies. Now multiple commercial developers have sought certification, and expectations are that they will shortly be available on the European market. At this stage, hyperthermia care facilities should assess whether forthcoming commercial HTP software will meet their needs. Establishing these requirements however, entails considerable preparatory work given the absence of guidance on defining functional or performance metrics for HTP systems.

Goals. The objective of this work is to present the methodology to establish a list of requirements and key aspects of our findings. This list will be freely online accessible. The secondary call is to the community to work to establish a minimum set of safety and reporting requirements that each commercial HTP software should contain.

Materials and Methods. The intended purpose and clinical use of a HTP system was defined. A list of stakeholders and regulatory scope for applicable standards were established. Furthermore, relevant publications were identified and information related to functional or performance related aspects of HTP systems extracted. A user-needs survey was conducted on topics of functional, performance and safety requirements and included 25 proposed requirements where clarity was wanted; users could indicate if the proposed requirement was necessary, desired, or unnecessary. Finally, an initial list of specifications was created and evaluated against our in-house HTP system.

Results. A total of 8 HTP users completed the users-need survey and among the 25 uncertain proposed requirements, an average pairwise agreement (Herfindahl index) of 63% was achieved indicating there was considerable disagreement on some of these items. Nonetheless, based on the intended clinical use, stakeholder input, literature review, and user needs survey, a total of 56 specifications were identified and comprised of 44 required and 12 desired items across functional, performance, and safety domains. When evaluated against our in-house HTP system, 24 of the 44 required specifications were met.

Summary. This work presents a set of specifications for evaluating newly certified HTP systems and identifies gaps in our current in-house system. Defining minimum requirements may help institutions clarify their needs and support manufacturers in developing software suitable for use across multiple institutions. One common thread among surveyed users is the need to be able to verify the intended SAR or temperature distribution. Thorough and common acceptance procedures across platforms would accelerate technological adaptation.

P-017

Enhancing quality of life in bladder cancer patients: leveraging hyperthermia and chemotherapy

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When pathogens become aggressive, the immune system triggers fever, mobilizing natural defenses, supplying tissues with increased oxygen and nutrients, aiding in detoxification, and enhancing infection resolution. Inspired by this natural response, a hyperthermia device using water-filtered infrared-A (wIRA) was developed to control skin burns and body temperature. Fever-range infrared hyperthermia (FRIH) leverages natural self-healing mechanisms to treat chronic conditions and malignant diseases. This study investigates the molecular and cellular mechanisms of FRIH as immunotherapy for cancer, combined with standard chemotherapy and immunotherapy protocols. The protocol included gemcitabine 1000 mg/m² over 30-60 minutes on days 1, 8, and 15, and cisplatin mg/m² on day 2, repeated every 4 weeks for up to 6 cycles. For gemcitabine with carboplatin, dosing was adjusted based on creatinine clearance, with carboplatin dosed at 4.5× [glomerular filtration rate +25] on day 1 over 1 hour IV every 3 weeks. Pembrolizumab 200 mg was administered every 3 weeks for treating distant metastases. For bladder tumors, gemcitabine, cisplatin, and pembrolizumab were combined. On the second day of the course, 1 hour after cisplatin infusion, local hyperthermic therapy was administered for 3 hours at 43-44°C. FRIH enhances the immune system's anti-tumor activity through several molecular pathways. Increased body temperature induces the expression of heat shock proteins (Hsps), which serve as molecular chaperones and play crucial roles in protein folding, repair, and degradation. Hsps also enhance the presentation of tumor antigens by antigen-presenting cells (APCs) such as dendritic cells. These APCs migrate to lymphoid tissues, where they activate cytotoxic T lymphocytes (CTLs), which then target and destroy cancer cells. Additionally, hyperthermia promotes the infiltration of immune cells, including natural killer (NK) cells and macrophages, into the tumor microenvironment. This increased immune cell presence enhances tumor visibility to the immune system, facilitating targeted immune responses. Hyperthermia also upregulates the expression of adhesion molecules and chemokines, supporting the recruitment and retention of immune cells at the tumor site. Preclinical and clinical data demonstrate improved anti-tumor responses with mild hyperthermia. The molecular mechanisms underlying these improvements include the activation of the immune system via Hsps, enhanced antigen presentation, and increased immune cell trafficking to the tumor. Hyperthermia may sensitize tumor cells to treatments like chemotherapy and radiation by disrupting their protein homeostasis and inducing apoptosis. Hyperthermia shows significant potential as an adjunct to cancer immunotherapy.

Fig. 1

Fig. 1

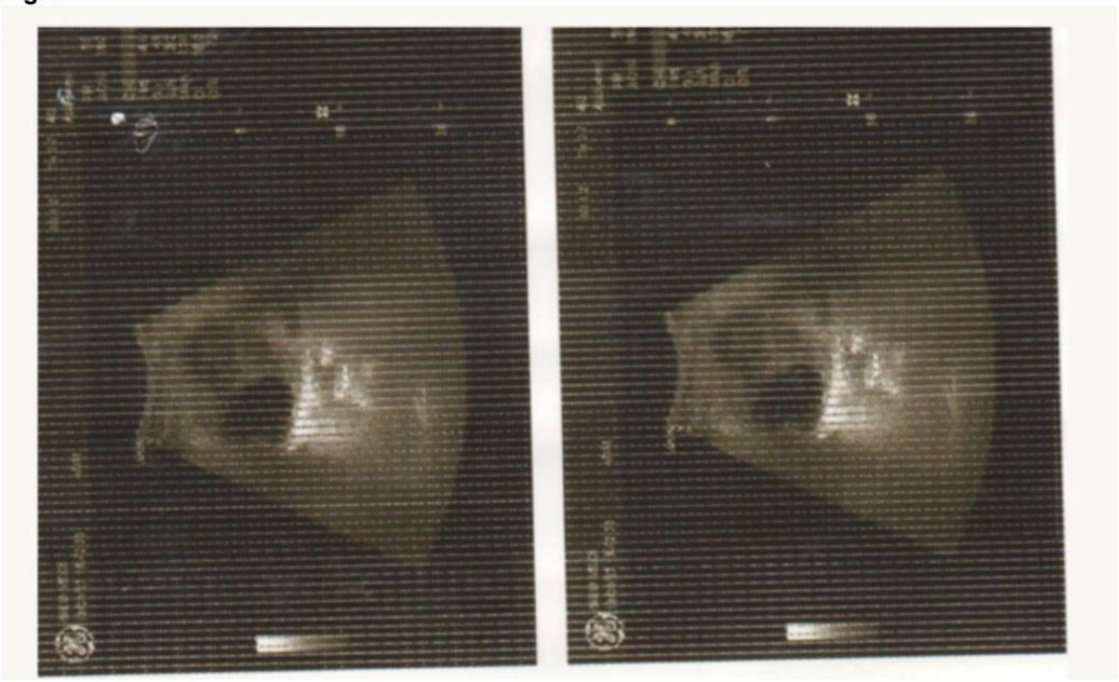
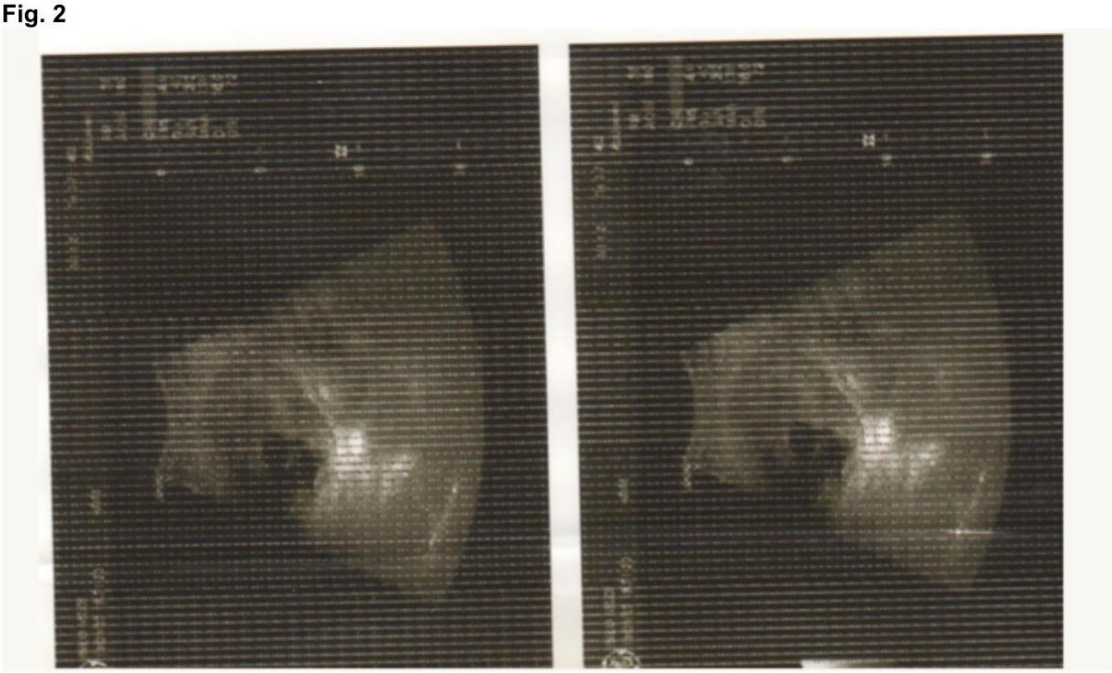


Fig. 2

Fig. 2



Biological modes of action of hyperthermia

P-037

Multicore Iron Oxide Nanoflowers for Magnetic Hyperthermia: Polyol Synthesis, Colloidal Control and CT2A In Vitro Safety

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Methodology. Multicore iron oxide nanoflowers were produced through a solvothermal polyol synthesis in a sealed autoclave using iron precursors and NaOH in a diethylene glycol/N-methyldiethanolamine (DEG/NMDEA) mixture, followed by an oxidation step to improve colloidal stability. Morphology and primary crystallite size were examined by transmission electron microscopy (TEM). Hydrodynamic diameter and dispersity were measured by dynamic light scattering (DLS), and surface charge by zeta potential. Heating capability was assessed calorimetrically under a trapezoidal alternating magnetic field (AMF, 4 mT, 300 kHz), using the temperature rise as a practical indicator of heating efficiency. Initial in vitro safety was evaluated in CT2A glioblastoma cells via XTT metabolic activity and Calcein-AM/propidium iodide (PI) staining after 24–48 h exposure up to 5 $mg \cdot mL^{-1}$.

Results. TEM revealed flower-like aggregates in the 25–50 nm range assembled from ~10 nm crystallites, consistent with a multicore architecture. In water, DLS showed a hydrodynamic diameter around 50 nm with PDI < 0.2, indicating a narrow size distribution and stable dispersion. Under the trapezoidal AMF, nanoflower suspensions achieved a temperature increase of approximately 23 °C, markedly higher than typically observed for comparable single-core SPION formulations at similar magnetic mass. In CT2A cultures, viability remained above 80% at 24 h and above 60% at 48 h even at the highest tested concentration, with no clear membrane disruption by live/dead staining, supporting a workable safety window for ongoing efficacy experiments that combine nanoflowers with AMF exposure.

Conclusion. The combination of multicore morphology, good colloidal control and strong AMF-induced heating supports these iron oxide nanoflowers as efficient mediators for localized magnetic hyperthermia. Their in vitro safety profile in CT2A cells at the tested range motivates further optimization and efficacy testing for brain-tumor-relevant scenarios where maximizing heating per magnetic dose is essential.

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Model systems for hyperthermia research and application

P-039

Decoupling heat and cell death in magnetic hyperthermia: SAR based intracellular temperature estimates might support a mechanical hypothesis

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Methodology. In magnetic hyperthermia experiments in cell cultures, we observed a significantly greater increase in cell mortality with non-sinusoidal alternating magnetic fields than with sinusoidal fields [1]. While we cannot directly measure the temperature reached in the intracellular medium in our experiments, the temperatures captured with thermographic images do not exceed 38.5 °C, with an initial temperature of 37 °C, which does not discard a greater increase at the microscopic scale. To estimate intracellular temperatures in our experiments, we performed a meta-study based on precise intracellular temperature measurements obtained in magnetic hyperthermia experiments with a sinusoidal signal using spherical superparamagnetic nanoparticles similar to ours, but with a larger diameter [2]. To estimate the quantitative relationship between the SAR in both experiments, we used previous studies on the same type of particles that determined the dependence of the SAR on several parameters such as field intensity and shape, diameter, and frequency [3, 4]. We then assumed similar heat dissipation in both cultures to estimate the intracellular temperature in our experiment. We repeated the experiments in cell cultures at lower basal temperatures, a result not yet published, obtaining similar mortality rates.

Results. The temperature increase estimate exhibits significant uncertainty, on the order of the estimated temperature increases themselves, which prevents a precise determination of the final intracellular temperature. However, the estimated values obtained are below 0.2 °C and 0.5 °C, depending on the case. That is, even considering the upper limit given by the uncertainty, it is difficult to imagine that the intracellular increase could be greater than 39.5 °C and, therefore, it appears to be much lower than the lower limit of 41–42 °C required for effective hyperthermia. Furthermore, in the reference experiment, cell death is lower than that obtained in our case, despite reaching an estimated intracellular temperature of around 50 °C.

Conclusion. We propose as a conjecture that cell death could be the direct result of a mechanical, rather than thermal, mechanism. Biomolecules near the nanoparticles would undergo shape alterations induced by mechanical resonance due to the vibration of the nanoparticles' crystalline structure during the initial stages of magnetization and demagnetization processes. Pulsed fields could thus induce a greater transfer of mechanical energy than the smoother sinusoidal fields.[JS1]

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[3] M. Zeinoun, et al. IEEE Access, vol. 9, pp. 105805-105816, 2021, doi: 10.1109/ACCESS.2021.3099428
[4] de la Presa, Patricia et al., The Journal of Physical Chemistry C. 116. 25602, doi. 10.1021/jp310771p.

P-043

Precise Delivery of Water-Filtered Infrared-A Hyperthermia in Mice: Adaptation of a Human Clinical Device

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[2] University of Freiburg, Department of Radiation Oncology, Freiburg i. Br., Germany
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Introduction. Preclinical hyperthermia (HT) models often rely on non-clinical heating methods, such as water bath heating, failing to replicate human conditions. Building on the foundational work of Vaupel et al. (1992) and Kelleher et al. (1995), water-filtered infrared-A (wIRA, 780–1400 nm) radiation offers a clinically available, targeted, non-invasive approach for localized HT in superficial tumors. Adapting clinical devices for small animal models presents challenges in achieving precise, controlled heating of very small targets without affecting surrounding tissues.

Goals. We aimed to adapt the clinical Hydrosun® 750 wIRA device (Vaupel et al., 1992), integrating a flexible light guide to enable precise, localized heating of superficially seated tumors in mice.

Materials and Methods. The Hydrosun® 750 (200 mW/cm² irradiance), was adapted by integrating a flexible light guide to focus wIRA onto a defined small target area: the mouse pinna with or without B16-F10 melanoma (see Figure). The exit of the flexible light guide was positioned 1 cm from the ear, and irradiance was controlled by adjusting the distance between the lamp and the entrance of the flexible light guide (111–187 mm), achieving an irradiance range of 1500–120 mW/cm² at the target, respectively. A Medtherm heat flux transducer connected to an ALMEMO V7 data logger was used for the radiant heat flux measurements. To match clinical HT protocols, 200 mW/cm² was achieved at 157 mm lamp-to-guide distance.

Real-time thermal monitoring used an Optris IR camera and a mini-hypothermic probe (33 Gauge, Omega). HT delivered a surface temperature of 41°C, with the Hydrosun® 750 automatically turning off at 41°C and back on when the IR Camera detected a temperature drop below 40.5°C. Anesthetized mice were maintained at body temperature of 37°C.

Results. The adapted setup successfully delivered controlled wIRA radiation to the mouse pinna and tumor maintaining 41°C surface and 42°C core tumor temperatures. The IR Camera confirmed accurate, localized heating, while the thermoregulation system ensured stable body temperature at 37°C. The flexible light guide enabled fine-tuned irradiance adjustments, ensuring reproducible and targeted treatment.

Summary. This study validates a preclinical wIRA HT model that replicates clinical conditions (200 mW/cm² irradiance). Real-time thermal monitoring with automatic feedback ensures precise control, bridging preclinical and clinical research. This model provides a robust foundation for future wIRA HT studies.

References.

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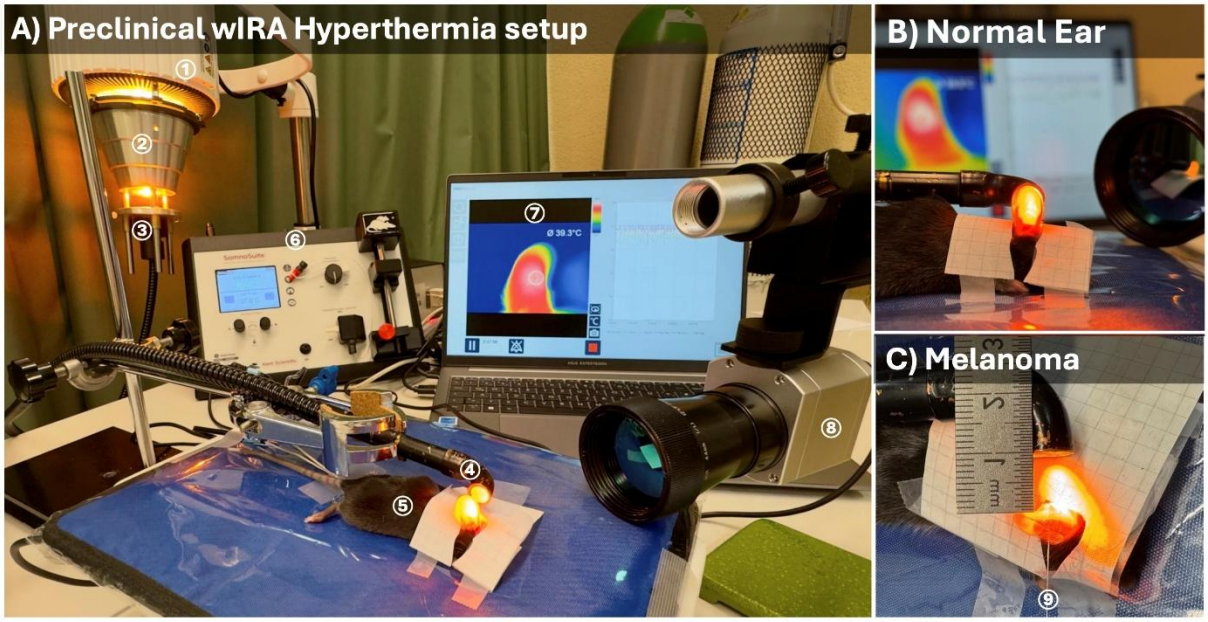
Fig. 1



Preclinical wIRA hyperthermia (HT) experimental setup and application. (A) Preclinical wIRA setup: The experimental apparatus includes: ① Hydrosun 750®, ② Focusing nozzle for directed irradiation, ③ Entrance of the flexible light guide, ④ Exit of flexible light guide, ⑤ Anesthetized mouse positioned for treatment, ⑥ SomnoSuite® system for monitoring and controlling mouse's body temperature, ⑦ Laptop monitor displaying thermal imaging from the infrared camera and Hydrosun software interface, ⑧ Infrared camera for real-time temperature monitoring. **(B) Normal ear pinna undergoing HT treatment. (C) Melanoma model in the ear pinna undergoing HT**: Demonstration of wIRA treatment on a murine melanoma model, with the mini-hypothermic probe (⑨) inserted in the tumor and the light guide exit positioned 1 cm away for precise thermal delivery.

Translational hyperthermia studies

P-040

In Vitro Studies Show that Hyperthermic Intraperitoneal Chemotherapy (HIPEC) Can Overcome Chemoresistance in Ovarian Cancer

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Background. A considerable number of patients develop a resistance to chemotherapy, which can result in relapse and death. Implementation of innovative approaches to overcome drug resistance may facilitate the successful treatment of resistant ovarian cancer. The objective of this preclinical study is to evaluate the efficacy of HIPEC on both parental cells and chemotherapy resistant cells and assess the impact of chemotherapy resistance on HIPEC efficacy.

Method. The selection of subpopulations of chemotherapy-resistant OVCAR3 and COV318 cells was achieved through administration of elevated doses of carboplatin and paclitaxel. The rate in which only 50% of seeded cells have the ability to form clones were achieved at a 10-fold and 3-fold higher drug concentration in OVCAR3, respectively, and 2-fold higher in COV318. The cells were next subjected to hyperthermia combined cisplatin (42°C, 90 minutes). In addition, parental cells and resistant cells were also subjected to carboplatin/paclitaxel treatment at 37°C, followed by HIPEC.

Results. The carboplatin/paclitaxel resistant ovarian cancer cells also demonstrated cisplatin resistance. In the context of carboplatin and paclitaxel treatment, resistant cells showed no detectable reduction in survival. The combination of hyperthermia and cisplatin has been observed to result in significant sensitivity to HIPEC, both in parental cells and in drug-resistant cells. The incorporation of HIPEC has been found to be a successful strategy in overcoming drug resistance.

Conclusions. Combining hyperthermia and cisplatin can overcome carboplatin and paclitaxel resistance in cells. These findings suggest that the hyperthermic conditions make HIPEC clinically effective on all cells, including drug resistant cells.

P-041

Three-Dimensional In Vitro Tumor Microenvironment Models for Combined Hyperthermia and Radiation Studies: Development and Dosimetric Validation

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Aims. To develop and dosimetrically validate a three-dimensional (3D) in vitro tumor model for combined radiobiological and hyperthermia studies, reproducing key features of the tumor microenvironment and improving treatment response assessment.

Methods. Multicellular spheroids were generated from OVCA-433 ovarian cancer cells using 2% agarose microwell platforms to ensure high uniformity and reproducibility. Cells were cultured in supplemented RPMI-1640 medium and seeded at 50,000 cells/well, corresponding to approximately 125 cells per microwell. This protocol enabled the formation of spheroids with an average radius of ~130 µm, ensuring homogeneous culture conditions and experimental consistency.

Before irradiation and hyperthermia experiments, thermal uniformity across the multiwell plates was evaluated using a thermal imaging camera to assess temperature homogeneity. In parallel, real-time temperature monitoring was performed by placing a temperature probe in a dedicated control well, allowing continuous recording during pre-irradiation, irradiation, and post-irradiation phases.

Samples were irradiated with a 6 MV photon beam using a LINAC, delivering a single ablative dose of 10 Gy. The setup included a tissue-equivalent phantom with build-up and backscatter layers to ensure electronic equilibrium. Dosimetric validation was performed through EPID analysis and absolute dose measurements. Radiobiological response was assessed at 2 h and 24 h by flow cytometry, comparing irradiated spheroids with non-irradiated controls.

Results. Dosimetric assessment confirmed high irradiation accuracy, with excellent beam uniformity and a relative dose deviation of 0.75%. Thermal characterization demonstrated homogeneous temperature distribution across the plate, while real-time monitoring confirmed stable temperature maintenance throughout the experimental procedure. Irradiation induced a significant time-dependent reduction in spheroid size and viability compared with controls. Early cellular damage was observed at 2 h, whereas the maximal effect occurred at 24 h, with a marked decrease in viability (~9%) and increased advanced cell death (~73%), consistent with mitotic catastrophe (Figure 1). Preliminary combined hyperthermia–irradiation experiments are currently ongoing.

Conclusions. Agarose-based 3D spheroid models represent a reliable and physiologically relevant platform for radiobiological investigations. The integration of accurate dosimetry, thermal characterization, and advanced in vitro models enables improved assessment of tumor treatment response and may support the development of optimized and personalized therapeutic strategies. Further studies are ongoing to quantitatively evaluate the synergistic effects of hyperthermia on tumor radioresponse.

Fig. 1

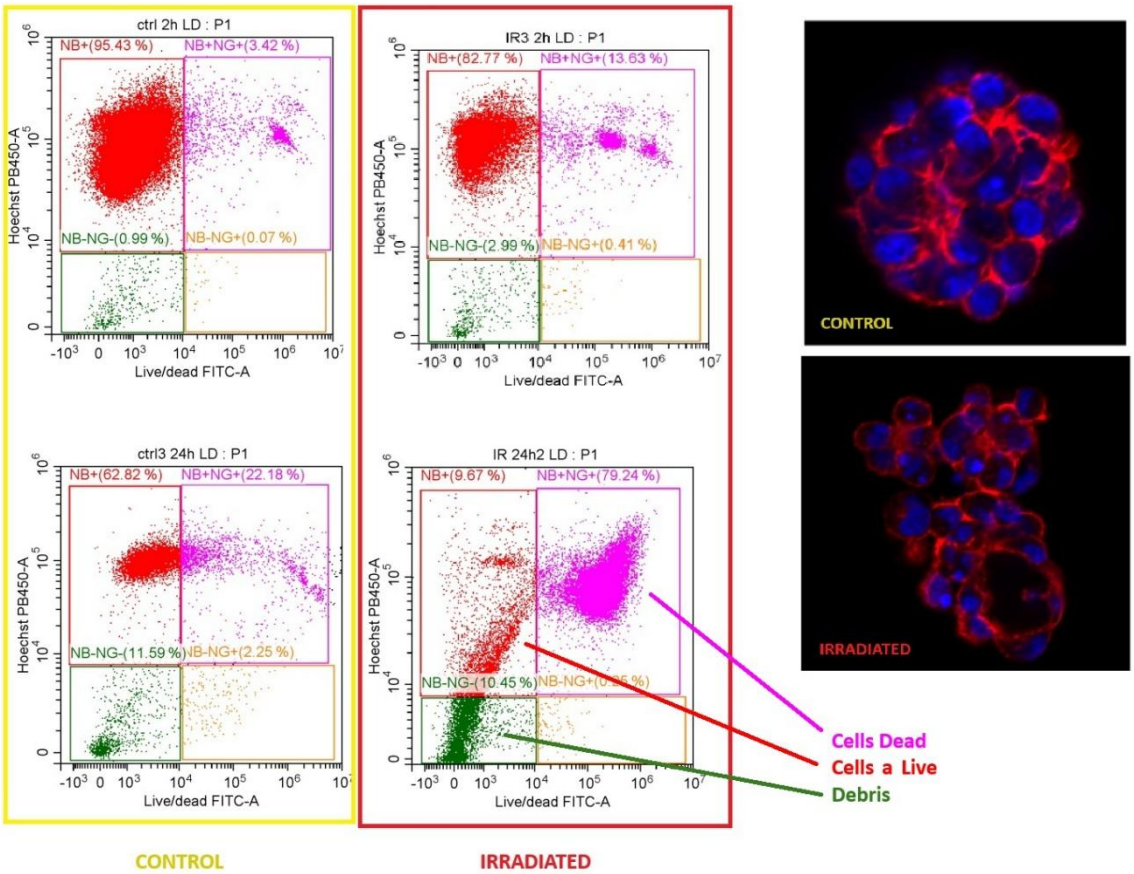

Figure 1: In the left panel, flow cytometry (Hoechst/Live-Dead probes) was utilised to analyse the control culture and the irradiated culture. The upper section of the figure corresponds to two hours after irradiation, while the lower section corresponds to 24 hours after irradiation, respectively. The right-hand image is a 3D volumetric reconstruction of an OVCA spheroid.

P-042

Region-specific antenna positioning for microwave hyperthermia treatment of brain tumors

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Introduction. In previous work, we demonstrated that microwave hyperthermia (MW-HT) delivery to brain tumors can be significantly improved, both in terms of target coverage and maximum achievable temperature, by tailoring the positioning of antennas in the applicator to the patient-specific tumor location and size, beyond conventional treatment planning. Although this represents an optimal solution, implementing fully patient-specific antenna positioning in clinical practice may introduce placement uncertainties, requiring stringent quality assurance procedures to maintain treatment quality. Assuming similar optimal applicator arrangements for tumors within the same brain region (e.g., lobes), this study aims to define a limited set of array configurations ensuring effective whole-brain coverage while remaining clinically practical, and to validate their performance in realistic models.

Methods. To ensure computational feasibility, an in-house-developed field interpolation method was applied to a realistic model of an 11-year-old girl, with artificial spherical tumor targets (30, 50, and 100 mL) placed at multiple intracranial locations representing the four brain lobes and the central brain. For each target location, the antenna arrangement of a helmet applicator with up to 12 elements was optimized, and the resulting configurations were subsequently cross evaluated across all target locations using T10, T50, and T90 to identify generalized region-specific applicator layouts. Optimization was performed using an integrated COMSOL–MATLAB workflow, in which precomputed single-antenna electromagnetic fields were interpolated to evaluate candidate configurations, followed by SAR-based optimization of antenna placement and steering parameters to maximize selective tumor heating while minimizing hotspots in healthy tissue. The generalized configurations were validated in two realistic pediatric cases (parietal ependymoma and medulloblastoma) and one adult case of recurrent meningioma.

Results. Preliminary results identified antenna arrangements providing effective heating for tumors located in the anterior and posterior brain regions. In the adult validation case, the generalized antenna configuration improved target heating compared with a conventional helmet array, increasing T10, T50, and T90 by 0.8 °C, 0.3 °C, and 0.2 °C, respectively. In the pediatric cases, the average improvements were 0.2 °C for T50 and 0.3 °C for T90.

Conclusion. Location-adapted antenna positioning represents a practical compromise between fully patient-specific optimization and standardized applicator designs for brain MW-HT. Defining generalized antenna configurations for groups of tumor locations has potential to improve treatment performance while preserving clinical feasibility, supporting clinical translation. Moreover, ongoing experimental comparison between optimized and conventional helmet configurations will assess practical implementation and reproducibility.

Hyperthermia promoted drug delivery and nanoparticle applications

P-026

Effect of Combining Hyperthermia and Chemotherapy on Head and Neck Cancer Cell Lines

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Introduction. Chemotherapy in head and neck cancer (HNSCC) is effective, yet associated with potentially severe systemic side effects. In this regard, the additional effect of hyperthermia has not yet been conclusively clarified up to now. Targeted drug delivery with nanoparticles carrying chemotherapeutic agnts combined with local hyperthermia could improve treatment efficacy and reduce systemic side effects. This study investigates the impact of hyperthermia combined with various chemotherapeutics in vitro to elucidate possible additive or synergistic effects.

Material and Methods. Four HNSCC cell lines (FaDu, SCC-9, A253. Detroit562) were exposed to temperatures of 42°C, 45°C and 47°C for one hour and to different doses of the chemotherapeutics Cisplatin, Docetaxel and Mitoxantron. The effects of these various treatment combinations were determined using live cell microscopy based on cell growth. Additionally, western blot analyses and immunocytochemistry stainings on relevant targets, such as heatshock proteins, were performed.

Results. Hyperthermia at 42°C did only show a small or even a negative effect on all cells. However, at 45°C, a significant decrease in cell growth was observed in all cell lines. At 47°C, the cell number decreased dramatically in all cell lines followed by a slow recovery of Detroit562 and FaDu after 48 hours. As hyperthermia alone at 45°C is effective already, synergistic effects of hyperthermia and chemotherapeutics can mostly be observed at 42°C and to some extent at 45°C. All chemotherapeutics applied at 47°C led to complete inhibition of cell growth. The levels of heat shock proteins varied with higher temperatures throughout the different cell lines but no direct correlation to cell survival was identified.

Conclusion. In this study, combinations of chemotherapeutics with hyperthermia of 45°C and 47°C were highly effective in exterminating HNSCC cell lines. In contrast, mild hyperthermia at 42°C with low doses of Docetaxel led to enhanced proliferation. These pioneering results indicate that, targeted drug delivery by magnetic nanoparticles and appropriate hyperthermia in the range of 45°C in the tumor site deserves further experimental evaluation as a potentially clinically effective treatment option for HNSCC.

Fig. 1: Confluence of A253 cells measured after 72 hours of treatment using optical live cell imaging (IncuCyte). (A) Effect of 1 h hyperthermia treatment. (B),and (C) Effects of different cytostatic drugs (cisplatin, docetaxel, and mitoxantrone) used at different concentrations and in combination with different temperatures.

Fig. 2: Western Blot analysis of A253 cell lysates. Blots are depicted over their respective integrated volume analysis of bands for HSP60 and HSP70. While HSP60 expression stayed roughly the same, HSP70 expression increased steadily over the applied temperatures.

Fig. 1

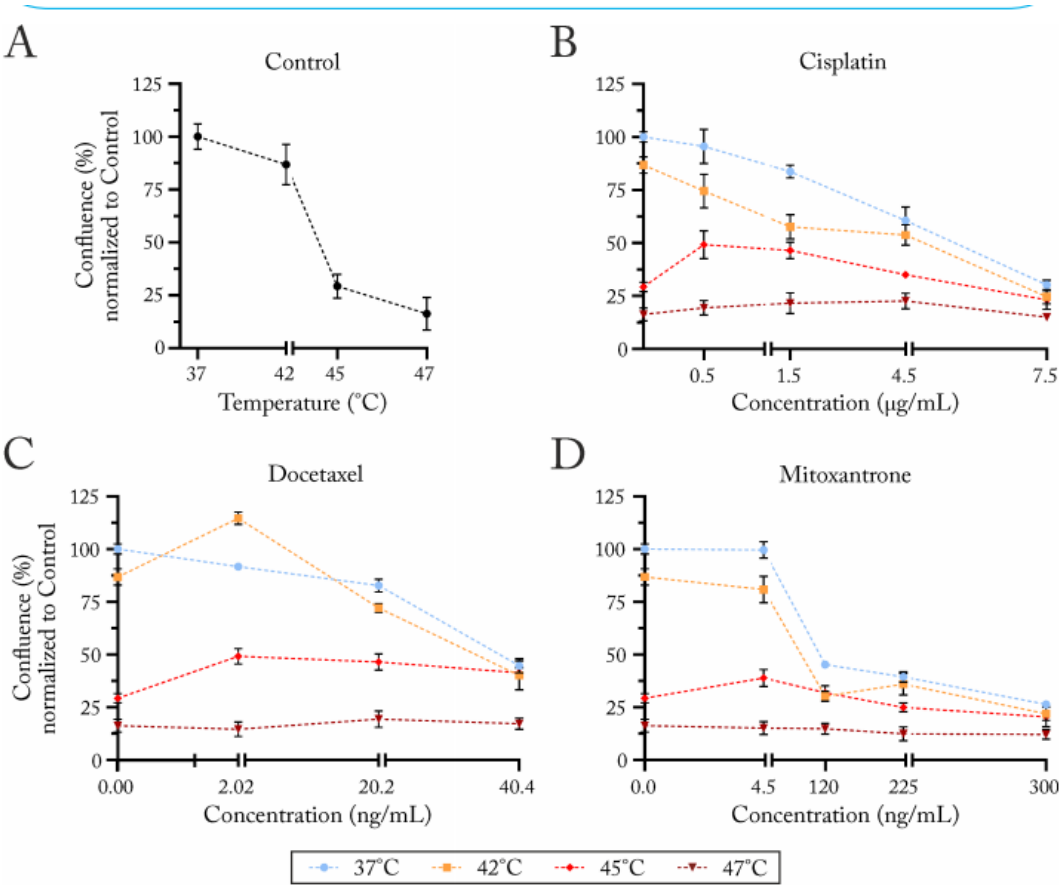
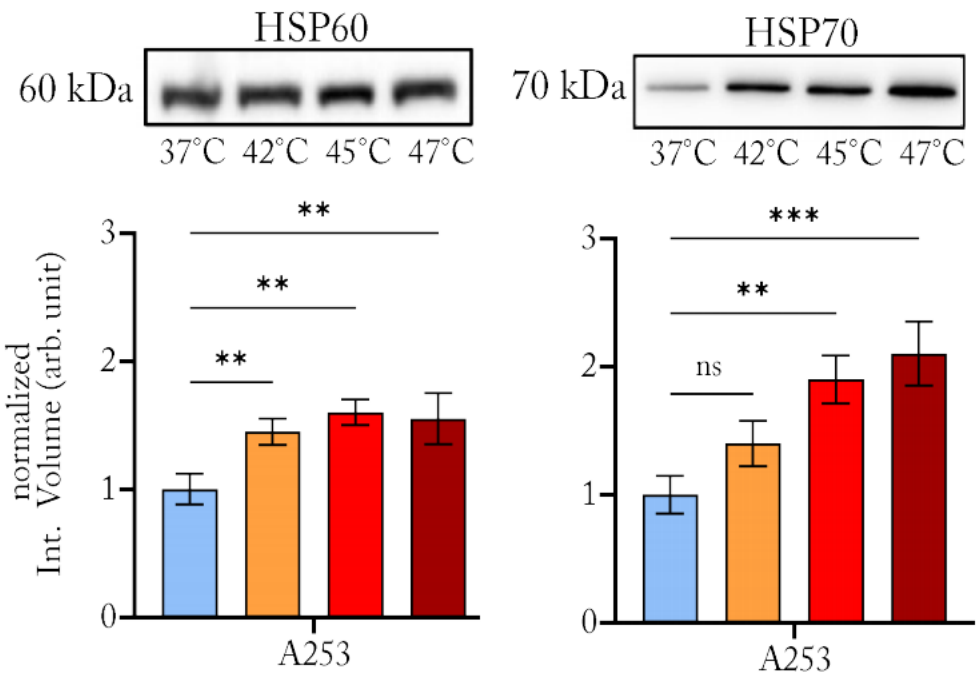

A
Control
Confluence (%) normalized to Control
125
100
75
50
25
0
37
42
45
47
Temperature (°C)
B
Cisplatin
0.5
1.5
4.5
7.5
Concentration (µg/mL)
C
Docetaxel
0.00
2.02
20.2
40.4
Concentration (ng/mL)
D
Mitoxantrone
0.0
4.5
120
225
300
Concentration (ng/mL)
37°C
42°C
45°C
47°C

Fig. 2


HSP60
60 kDa
37°C 42°C 45°C 47°C
HSP70
70 kDa
37°C 42°C 45°C 47°C
normalized Int. Volume (arb. unit)
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ns
A253
A253

P-027

Fractal Tumor Vasculature-on-Chip for In Vitro–In Silico Flow Modeling Toward Magnetic Hyperthermia Optimization

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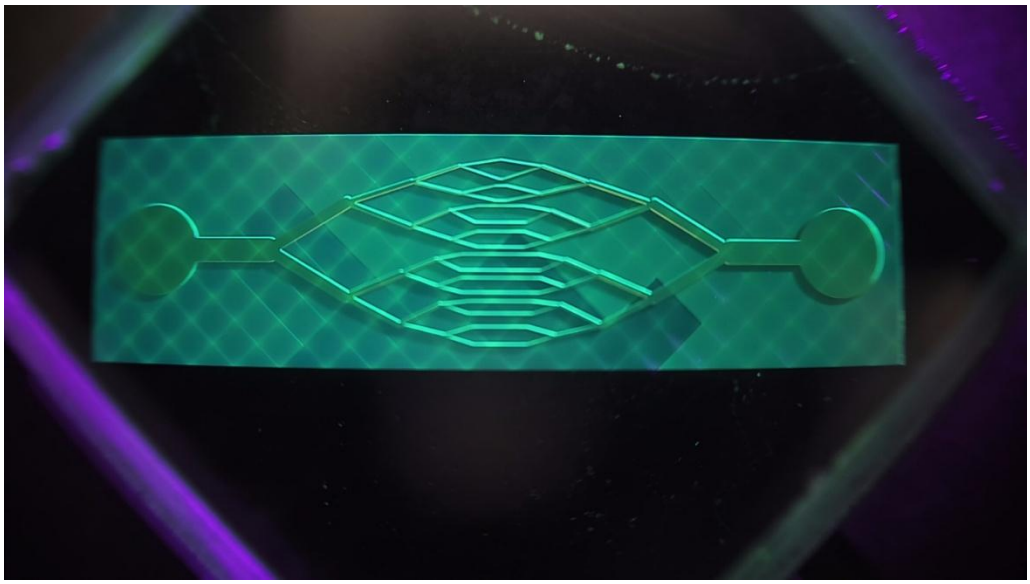
Question. Magnetic hyperthermia outcomes depend on nanoparticle heating and on perfusion-driven heat transport within irregular tumor vasculature. Can a realistic vascular tumor-on-chip coupled with numerical modeling predict flow redistribution in hepatic tumor-like microvascular networks and support future heat-transfer studies?

Methods. A PDMS lab-on-chip device was designed from a custom parametric script reproducing a fractal-inspired hepatic tumor vascular network with target fractal dimension 1.88. The 18 mm network includes hierarchical channels 20–50 µm in diameter with global symmetry and local variations in branch length, vessel diameter and bifurcation angle. Master molds were fabricated by two-photon polymerization and replicated by soft lithography. Laminar, steady, incompressible flow was simulated in COMSOL Multiphysics directly on the generated geometry, using inlet-flow and outlet-pressure boundary conditions. Experimental validation is planned under controlled syringe-pump perfusion by tracking tracer nanoparticles in optical microscopy and comparing measured and simulated velocities across vessel generations.

Results. The platform integrates parametric geometry generation, high-resolution fabrication and numerical analysis in a single workflow. Preliminary simulations show heterogeneous velocity fields and flow partitioning along the vascular hierarchy, from larger branches to capillary-scale channels, indicating that network architecture strongly affects local transport. The same model can be used to quantify percentage errors between predicted and measured velocities and, once validated, to test alternative fractal dimensions and branching morphologies without repeated device fabrication.

Conclusions. This fractal-inspired tumor vasculature-on-chip provides a physiologically relevant in vitro-in silico framework for studying transport in tumor microenvironments. By linking microvascular geometry, perfusion and predictive simulation, it represents a step toward multiphysics models coupling nanoparticle transport and localized heat generation for magnetic hyperthermia optimization.

Fig. 1



P-028

Mathematical modeling of thermochemotherapy drug delivery to study the effects of temperature on pharmacokinetic parameters and drug delivery

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Purpose. Mild Hyperthermia (40-43°C) is known to change blood flow and transport properties both in tumour and normal tissue, increasing drug delivery and cellular uptake. Patient specific mathematical modelling of Temperature effects on pharmacokinetic (PK) parameters can help predict drug uptake in the tumour and treatment outcome. Patient specific perfusion and blood flow parameters are required, these can be collected from clinical imaging to personalize treatment optimization.

Methods. An existing compartment model has been modified to study how temperature dependent changes in PK parameters can affect drug transport and delivery, including extravasation and cellular uptake. The model has been validated against literature data from *in vivo* murine tumor models for free doxorubicin (DOX) and encapsulated in thermosensitive liposomes (TSL-DOX).

The model compartments are systemic plasma, tumor plasma, lumped tissue, tumor EES, and intracellular space of tumor cells. The transport of TSL-DOX is described by: systemic exchange with lumped tissue, systemic elimination, perfusion-driven transport from systemic plasma to tumor plasma, temperature-triggered drug release, transvascular transport into the tumor EES, and cellular uptake.

The parameters with a temperature dependency include blood flow (differentiating between tumor and systemic circulation, to account for abnormal vascular structure in tumor) and tumor vascular permeability of TSL-DOX and free DOX, whose mathematical behavior is reported in literature. All systemic compartment parameters are treated as constants, since systemic temperature is not raised during localized hyperthermia.

Results. The heat-induced increase in tumour blood flow and vascular permeability cause a slightly higher drug concentration in tumour cells for both Fast and Slow TSL formulations. TSLe show instead an higher total tumour concentration, but a lower cellular concentration.

In all delivery types, considering the Temperature effects cause an higher tumour EES concentration with a temporal profile much more similar to that of tumour plasma, since higher permeability allows for a faster extravasation.

Comparison with literature data is satisfactory, concentration profiles from simulation match literature data within standard deviation range.

Conclusions. Hyperthermia influences drug delivery by altering the physical and biological parameters governing the exchange mechanisms between tumour and surrounding system.

For mild hyperthermia these changes are generally beneficial. A precise numerical description of these exchange phenomena allows to predict treatment outcomes and perform a better treatment planning.

Investigation of how pharmacokinetic parameters are affected by temperature is necessary to reach higher precision in treatment planning and for comparison between treatment modalities.

Fig. 1

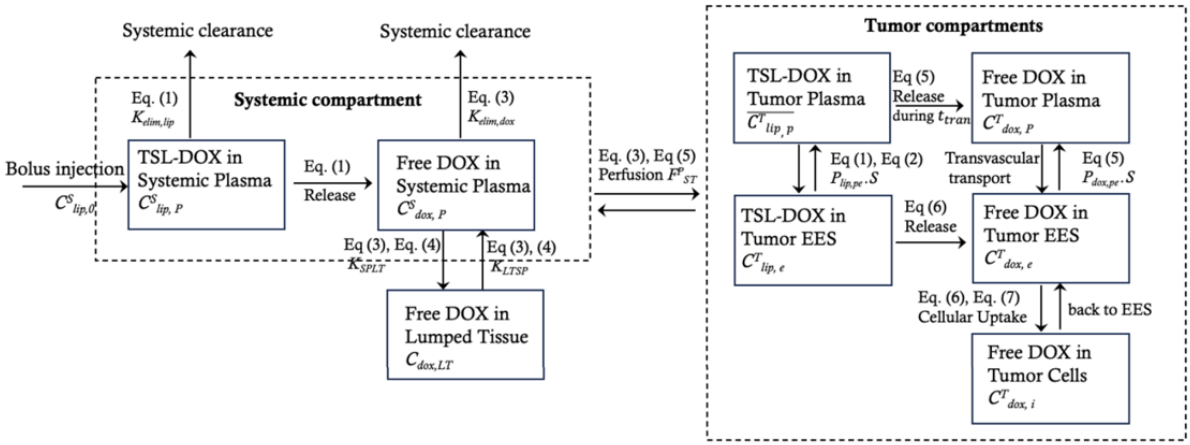
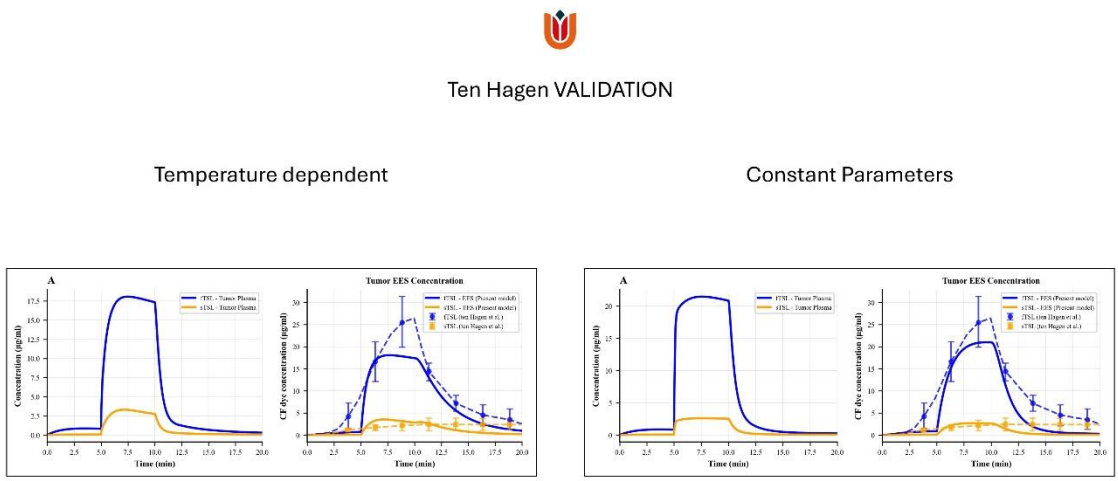

Systemic clearance
Systemic clearance
Eq. (1)
$K_{elim,lip}$
Systemic compartment
Eq. (3)
$K_{elim,dox}$
Bolus injection
$C^S_{lip,0}$
TSL-DOX in Systemic Plasma
$C^S_{lip,P}$
Eq. (1)
Release
Free DOX in Systemic Plasma
$C^S_{dox,P}$
Eq. (3), Eq. (4)
K_{SPLT}
Eq (3), (4)
K_{LTSP}
Free DOX in Lumped Tissue
$C_{dox,LT}$
Eq. (3), Eq (5)
Perfusion F^F_{ST}
Tumor compartments
TSL-DOX in Tumor Plasma
$C^T_{lip,p}$
Eq (5)
Release
during t_{tran}
Free DOX in Tumor Plasma
$C^T_{dox,P}$
Eq (1), Eq (2)
$P_{lip,pe}.S$
Transvascular transport
Eq (5)
$P_{dox,pe}.S$
TSL-DOX in Tumor EES
$C^T_{lip,e}$
Eq (6)
Release
Free DOX in Tumor EES
$C^T_{dox,e}$
Eq. (6), Eq. (7)
Cellular Uptake
back to EES
Free DOX in Tumor Cells
$C^T_{dox,i}$

Fig. 2


Ten Hagen VALIDATION
Temperature dependent
Constant Parameters
A
Tumor EES Concentration
Time (min)
Concentration (µg/ml)
CF dye concentration (µg/ml)

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ESHO