MARYLAND PROTON TREATMENT CENTER
AFFILIATED WITH UNIVERSITY OF MARYLAND MARLENE AND STEWART GREENEBAUM COMPREHENSIVE CANCER CENTER

UNIVERSITY of MARYLAND SCHOOL OF MEDICINE

Temperature
~~Heat~~ you can measure: Verification and standards for clinical hyperthermia

CIRMS Annual Meeting 2026
April 13, 2026

Dario Rodrigues, PhD
drodrigues@som.umaryland.edu

Associate Professor of Radiation Oncology
Director, Hyperthermia Therapy Practice School

University of Maryland School of Medicine
Division of Medical Physics
& Maryland Proton Treatment Center

Chair, ASME Thermal Medicine Standards Committee

Talk overview

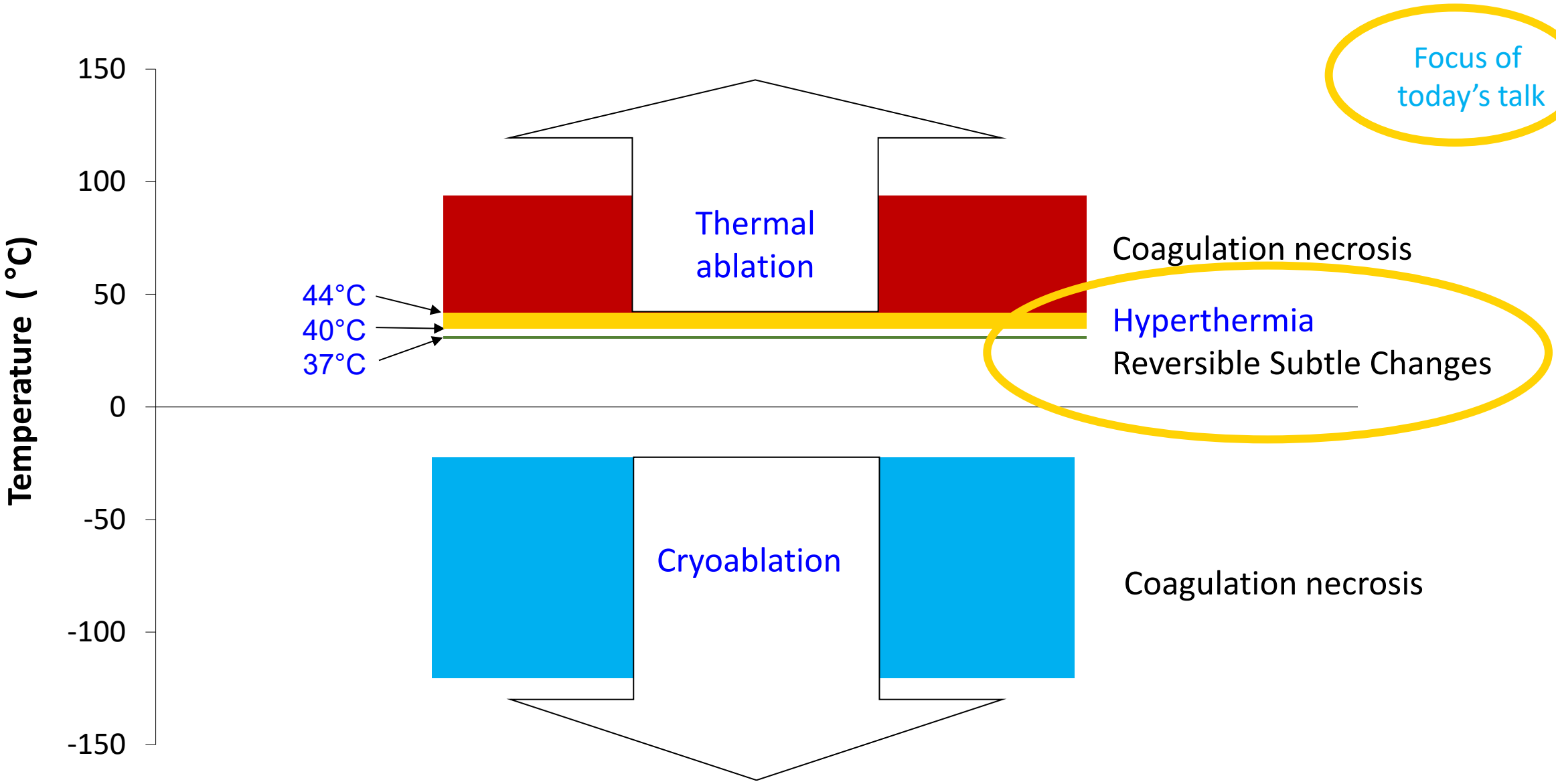
- Introduction to thermal therapy
- Physics and equipment
- Hyperthermia dosimetry
  - Current practice
  - Next steps
- Concluding remarks

"Those who cannot be cured by medicine can be cured by surgery.
Those who cannot be cured by surgery can be cured by fire [hyperthermia].
Those who cannot be cured by fire, they are indeed incurable."

—Hippocrates (460–370 B.C.)

Introduction to Hyperthermia Therapy

Temperature goals for cancer thermal therapies



Thermal therapy = intentional manipulation of temperature to induce therapeutic effect

Hyperthermia therapy (HT)

HT uses non-ionizing radiation, but **metrology needs** are similar to radiation therapy

What is Clinical Hyperthermia?

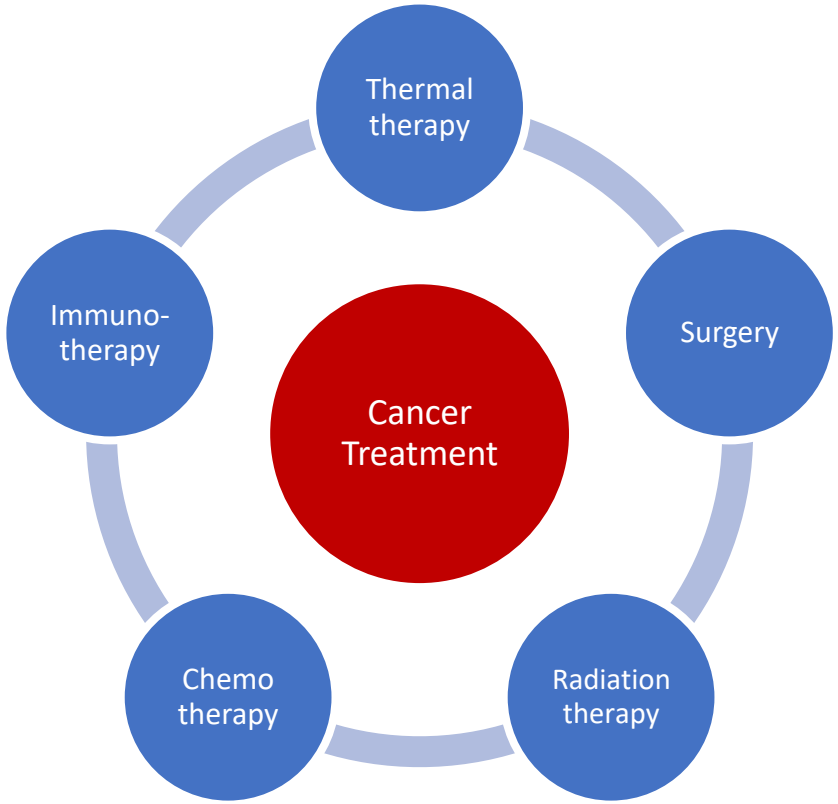
- Controlled heating of tumors to 39-44 °C for ~1h
- Mainly delivered via RF and MW
- Also possible with ultrasound, laser, or magnetic nanoparticles

Clinical Role

- Not a standalone therapy
- Enhances radiation and chemotherapy
- Used within multimodality treatment

Clinical Integration

- Typically 1–3 sessions/week
- Delivered within 0–2 h of radiation

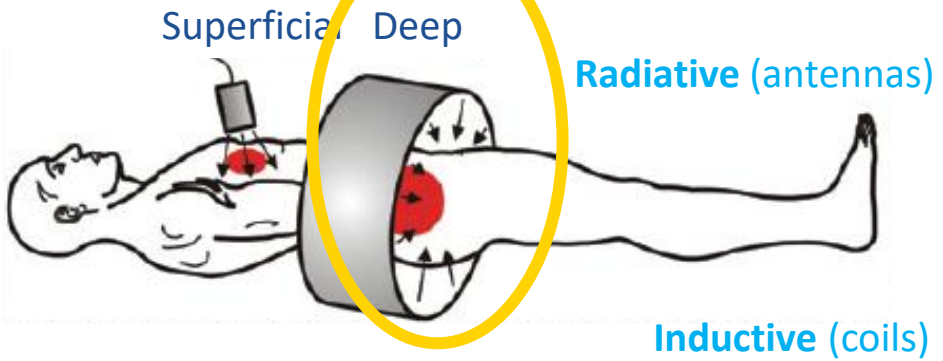


Hyperthermia techniques

Focus of today's talk

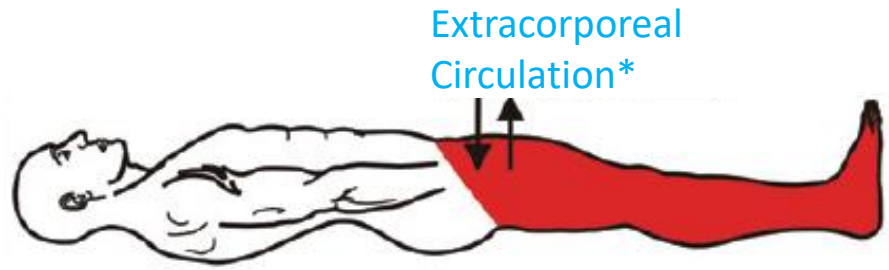
UNIVERSITY of MARYLAND BALTIMORE

LOCOREGIONAL



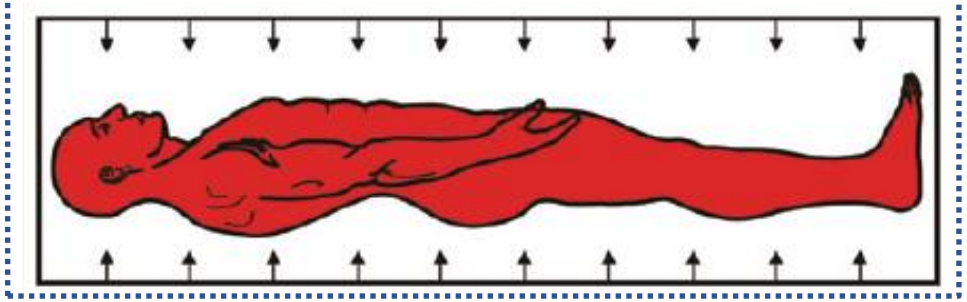
LOCAL INVASIVE

REGIONAL



*Example: Hyperthermic Intraperitoneal Chemoperfusion (HIPEC)

WHOLE BODY



Adapted from van der Zee et al. IJH 2008; 24(2):111-122

Biological rationale for HT in cancer treatments

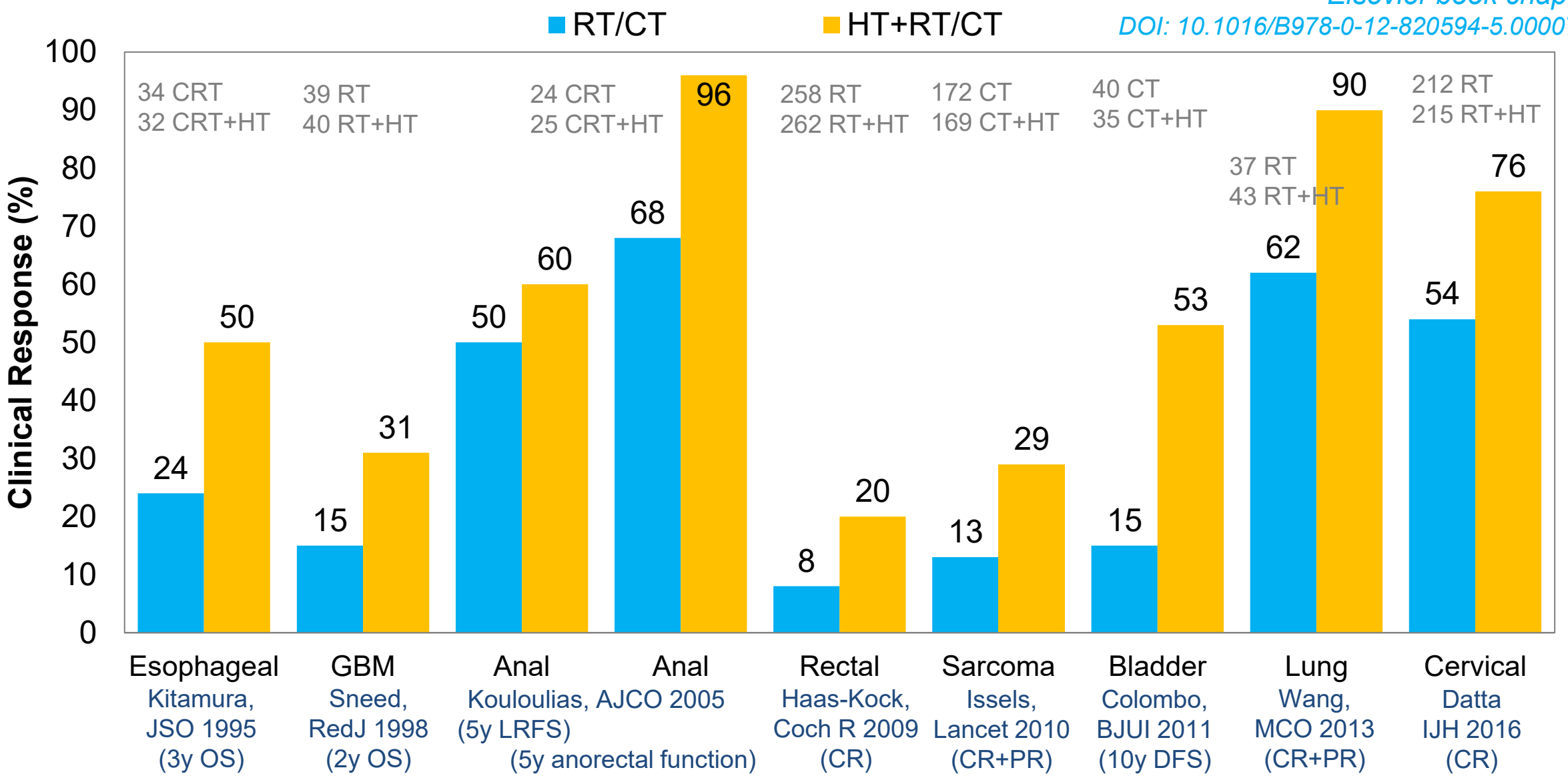
- **Radiosensitization**
  - ↑ Perfusion and oxygenation
  - Inhibits radiation-induced DNA repair
  - Direct cytotoxicity (including S-phase cells)

- **Immunomodulation**
  - Stimulates tumor-specific immune responses

- **Chemosensitization**
  - ↑ Drug delivery to tumor (↑ perfusion and ↑ permeability)
  - ↑ Drug uptake into tumor cells (↑ membrane fluidity)
  - ↓ Drug resistance (inhibits DNA repair and cellular stress responses)

Randomized phase II/III deep HT clinical trials

Rodrigues et al. 2022
Elsevier book chapter
DOI: 10.1016/B978-0-12-820594-5.00007-1



Poor QA

ELSEVIER

International Journal of Radiation Oncology*Biology*Physics

Volume 34, Issue 5, 15 March 1996, Pages 1097-1104

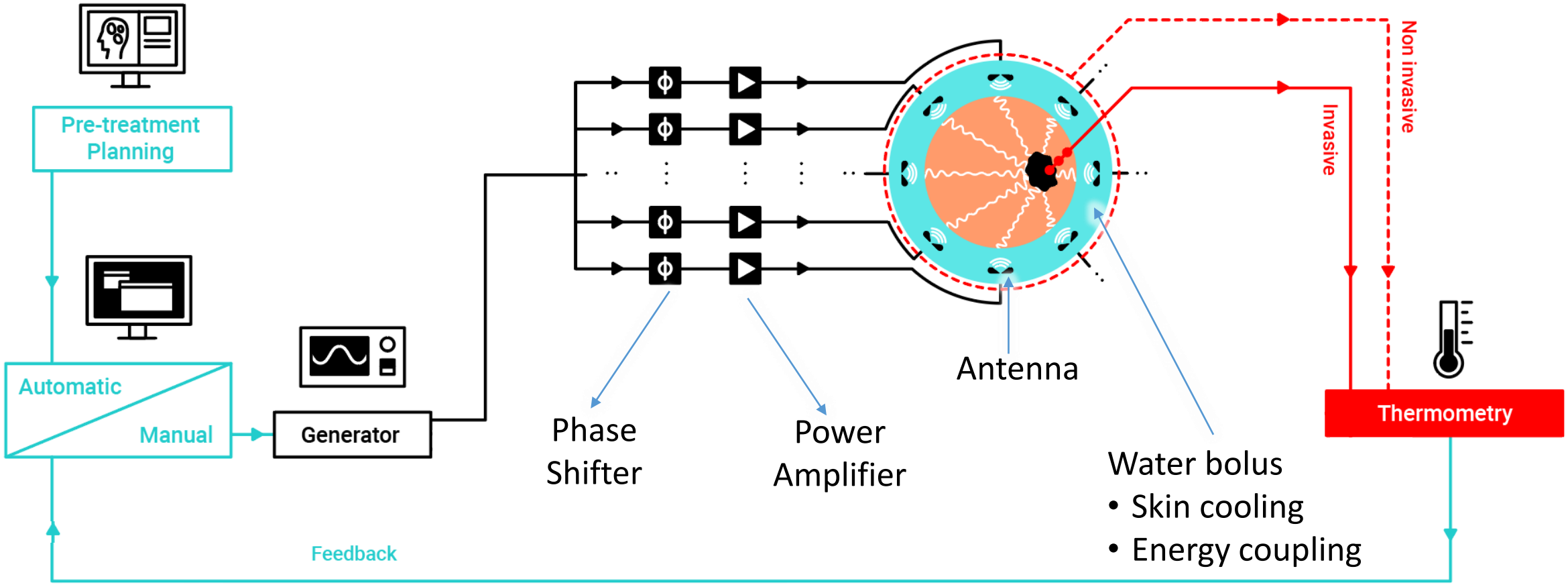
UNIVERSITY of MARYLAND BALTIMORE

Abstract

- **Purpose**: The objectives of this randomized trial were to determine if interstitial thermoradiotherapy (ITRT) improves tumor regression/control in accessible lesions in comparison with interstitial radiotherapy (IRT) alone and to assess the skin and soft tissue complications with either modality.
- **Methods and materials**: From January 1986 to June 1992, **184 patients** with persistent or recurrent tumors after previous radiotherapy and/or surgery, which were amenable to interstitial radiotherapy, were accessioned to a protocol developed by the Radiation Therapy Oncology Group (RTOG). One hundred seventy-three cases were analyzed (87 patients in the IRT group and **86 in the ITRT arm**). The two arms were well balanced regarding stratification criteria. Most tumors were in the head and neck (40% in the IRT group and 46% in the ITRT group), and pelvis (42% and 43%, respectively). Eighty-four percent of patients in both arms had prior radiation therapy (> or = 40 Gy); 50% and 40%, respectively, had prior surgery, and 34% in each arm had prior chemotherapy. The dose of radiation therapy administered was dependent on the previous radiation dose and did not exceed a total cumulative dose of 100 Gy. Hyperthermia was delivered in one or two sessions, either before or before and after interstitial implant. The intended goal of the hyperthermia was to maintain a minimal tumor temperature of 42.5 degrees C for 30 to 60 min.
- **Results**: There was no difference in any of the study end points between the two arms. Complete response (CR) was 53% and 55% in both arms. Two-year survival was 34% and 35%, respectively. Complete response rate for persistent lesions was 69% and 63% in the two treatment arms as compared with 40% and 48% for recurrent lesions. **A set of minimal adequacy criteria for the delivery of hyperthermia was developed. When these criteria were applied, only one patient had an adequate hyperthermia session.** Acute Grade 3 and 4 toxicities were 12% for IRT and 22% for ITRT. Late Grade 3 and 4 toxicities were 15% for IRT and 20% for ITRT. The difference was not significant.
- **Conclusions**: Interstitial hyperthermia, as applied in this randomized study, did not show any additional beneficial effects over interstitial radiotherapy alone. Delivery of hyperthermia remains a major obstacle (since only one patient met the basic minimum adequacy criteria as defined in this study). The benefit of hyperthermia in addition to radiation therapy still remains to be proven in properly randomized prospective clinical trials after substantial technical improvements in heat delivery and dosimetry are achieved.

Hyperthermia Physics and Equipment

Deep hyperthermia



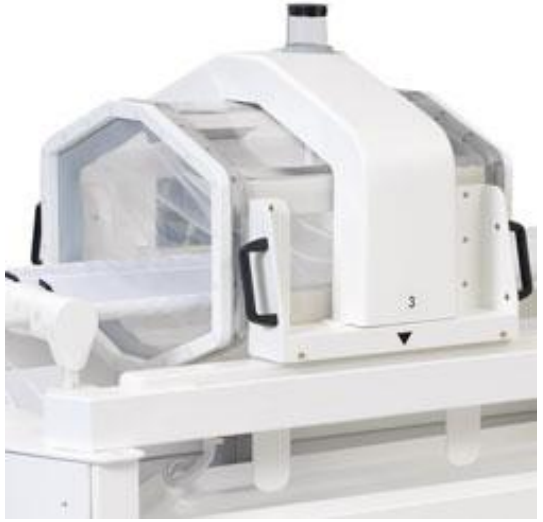
Rodrigues, Molitoris et al. 2022
Elsevier book chapter
DOI: 10.1016/B978-0-12-820594-5.00007-1

Deep hyperthermia equipment

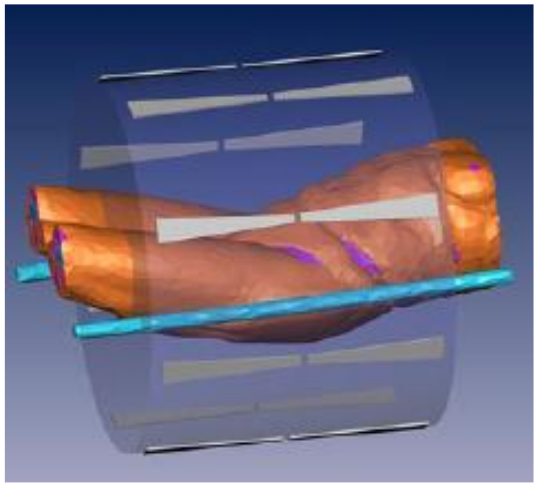
- Applicator
  - Concentric ring RF phased array of 4 pairs dipole radiators
  - Forward power 0-2000 Watts
  - Frequency 80-120 MHz (requires faraday cage)
  - Phase & amplitude for 2D steering
  - Generates a focus with Φ_{radial} = 8-18 cm and Φ_{long} = 22-28 cm
  - Water bolus for skin cooling and energy coupling

- Thermometry
  - 8 high-resistance carbon lead thermistors (RF-insensitive)
    - 1-3 internal (bladder, rectum and vagina) ← Tumor Surrogates
    - 5-6 external (spine, inner thigh, groin, abdomen, etc.)
    - 0-1 interstitial (not common)
  - Thermal mapping
    - 1 cm increments along the tumor or surrogate (via catheters)

Sigma-Ellipse
(51×38×48 cm^3)



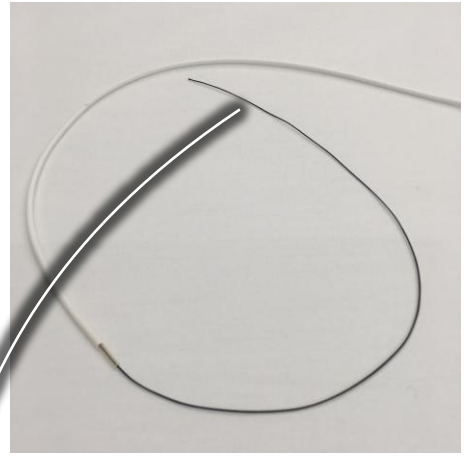
Sigma-60
(Ø=60 cm, L=48cm)



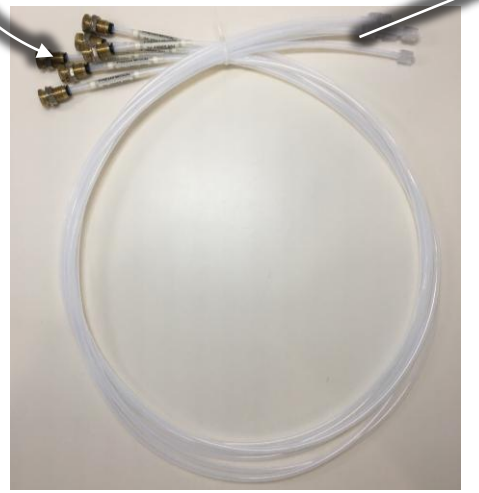
Temperature monitoring hyperthermia

Probe type	Therm-istors	Fiber optics	Thermo-couples*
Max length	25cm	14cm	14cm
Spacing		0.5-2cm	
#sensors	1 ↔	4-8	14

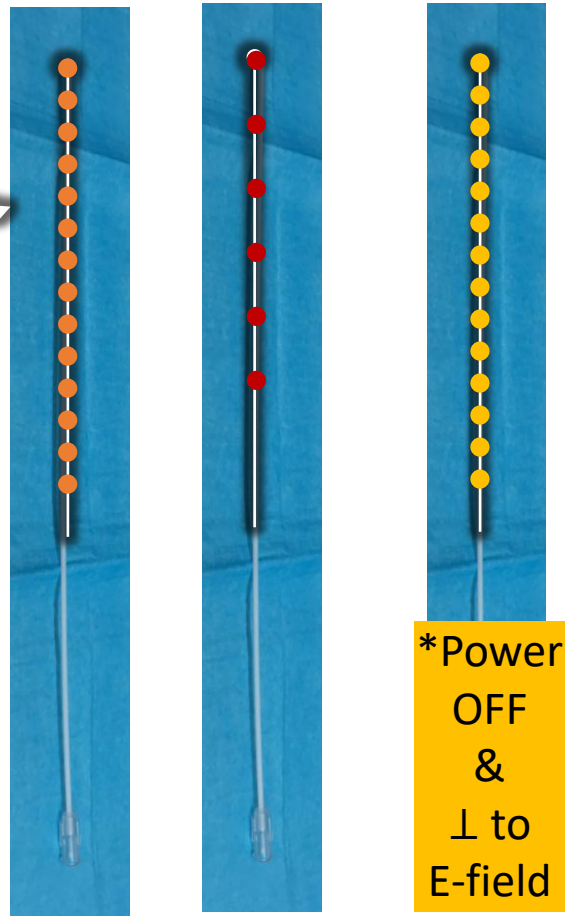
Temperature probe



Temp. probe sleeve

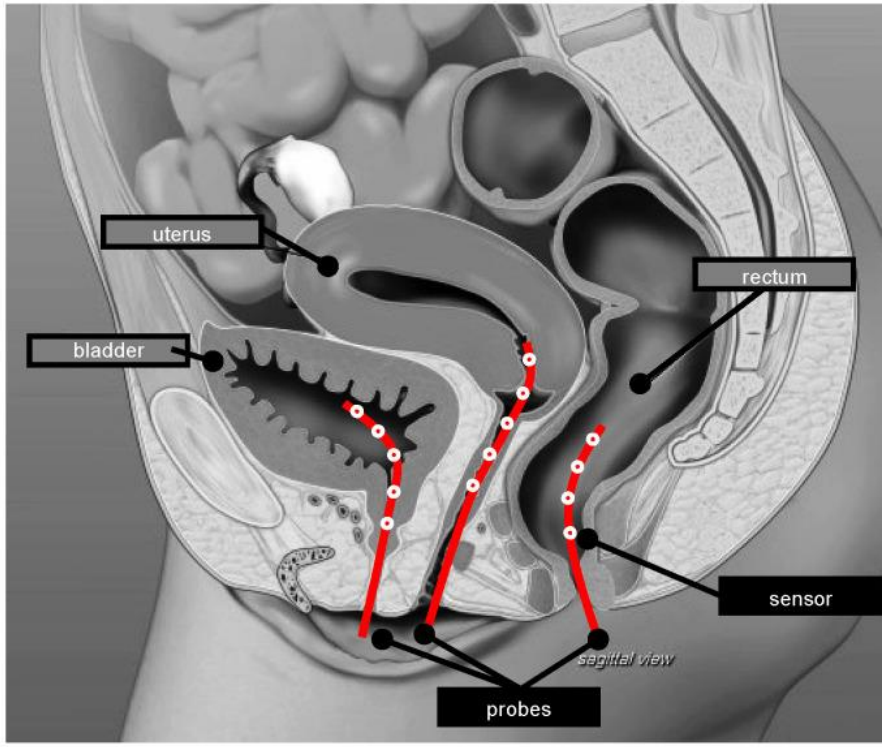


Thermal Mapping (↔)



*Power OFF & ⊥ to E-field

Probe placement



Hyperthermia – A multiphysics problem

- **Electromagnetism**
  - Maxwell Equations to determine the heating pattern as measured by the **Specific Absorption Rate** (W/kg)

$$SAR = \frac{\sigma}{2\rho}|E|^2, \quad E \propto \varepsilon_r$$

- **Heat transfer in tissues**

$$\rho c \frac{\partial T}{\partial t} = \nabla \cdot (k \nabla T) - \omega_{blood} \rho_{blood} c_{blood} (T_{blood} - T) + Q_{metabolism} (T) + \rho SAR$$

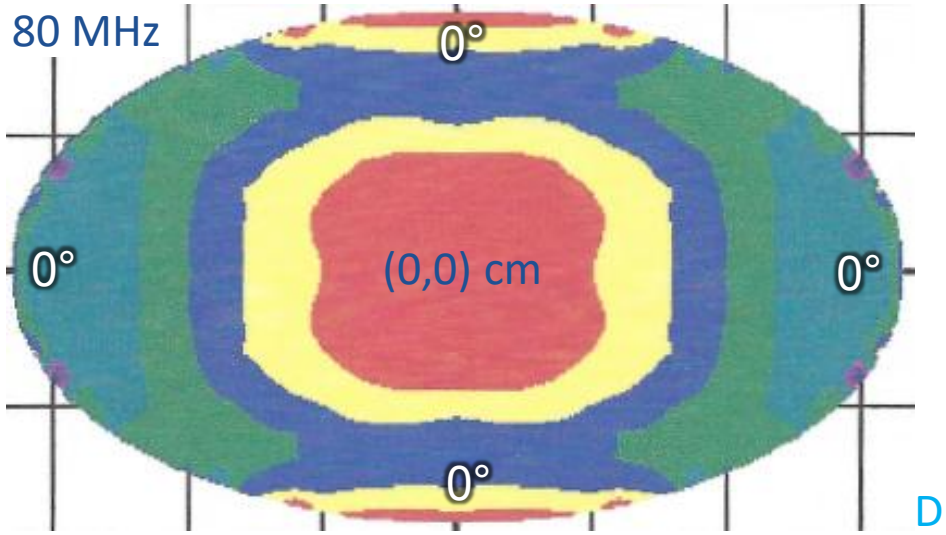
Heat storage = Heat conduction − Blood perfusion (heat sink) + Internal heat source + External heat source

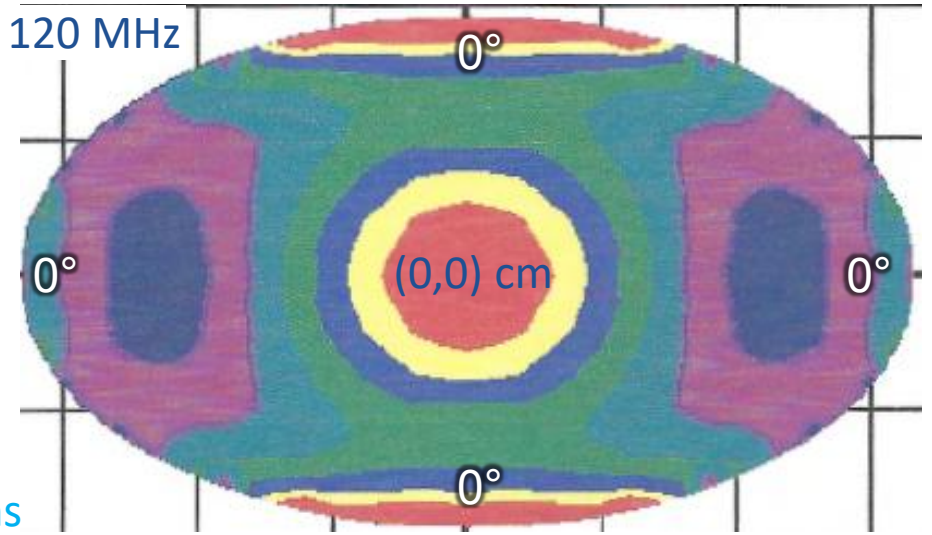
- **Fluid flow**
  - Heat transfer in air and liquids
  - Continuity equation (mass conservation)
  - Momentum equation (momentum conservation)

Units	
ω_b	kg/s/m³
SAR	W/kg
Q_{met}	W/m³

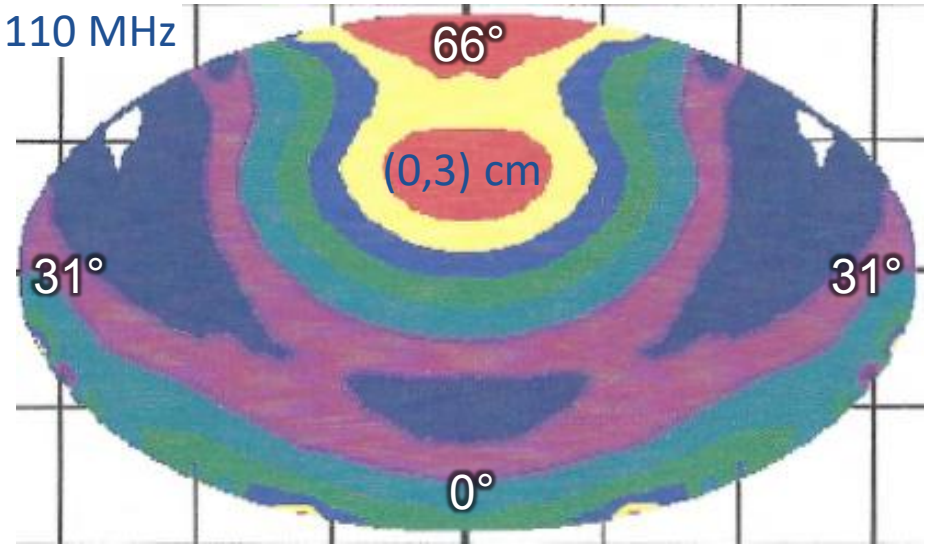
"It is said that mathematics is the language of Nature. If so, then physics is its poetry." Hermann Weyl

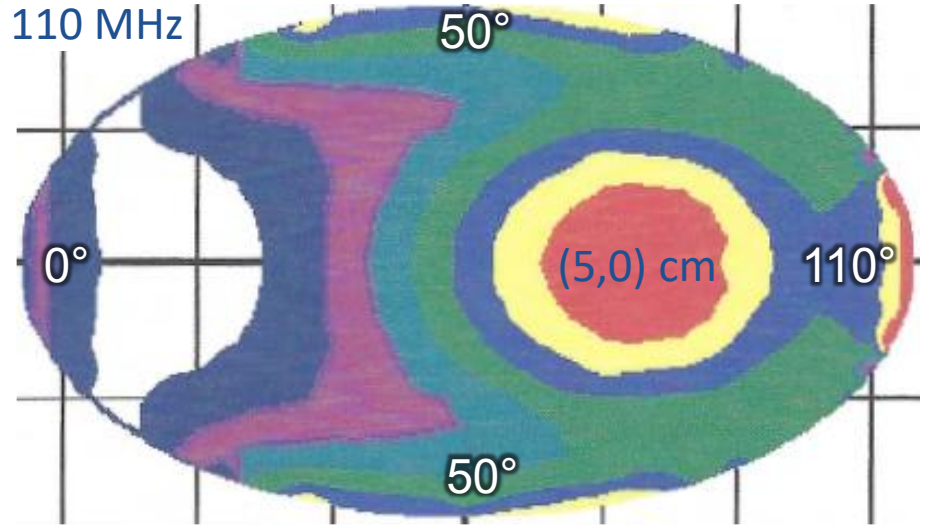
2D SAR-based treatment planning

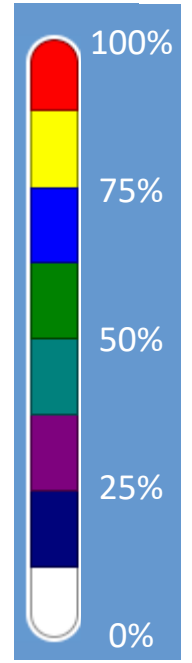




Patient Dimensions
19 cm × 33 cm







Antenna phase

Hyperthermia Dosimetry (Current Practice*)

*some clinical centers

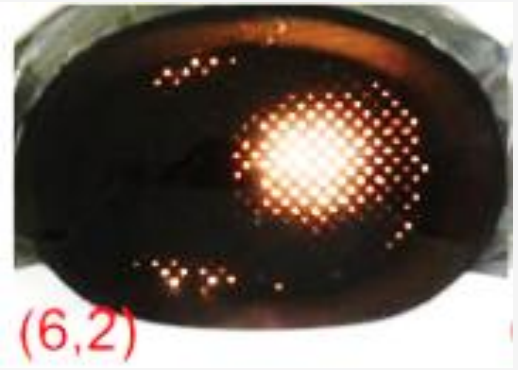
Phantom dosimetry: the QA backbone for device performance

- Phantoms verify applicators work as designed — at installation and periodically thereafter

LED / lamp phantoms

Qualitative

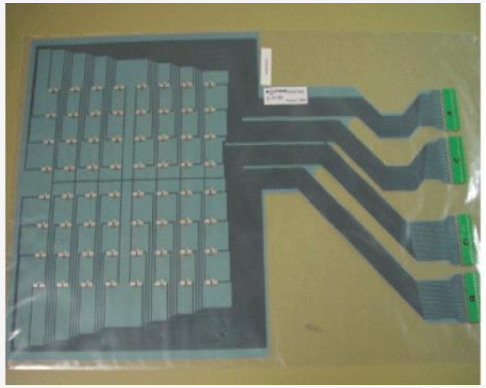
- Saline-filled elliptical shell
- Diode/lamp matrix lights up with E-field
- Fast steering & symmetry check



Schottky diode sheet

Quantitative (2D)

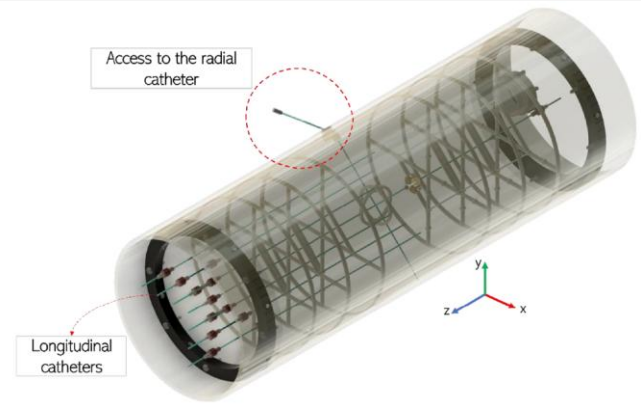
- Planar E-field mapping
- Calibrated SAR distribution
- Focus & hotspot verification



Tissue-mimicking gel

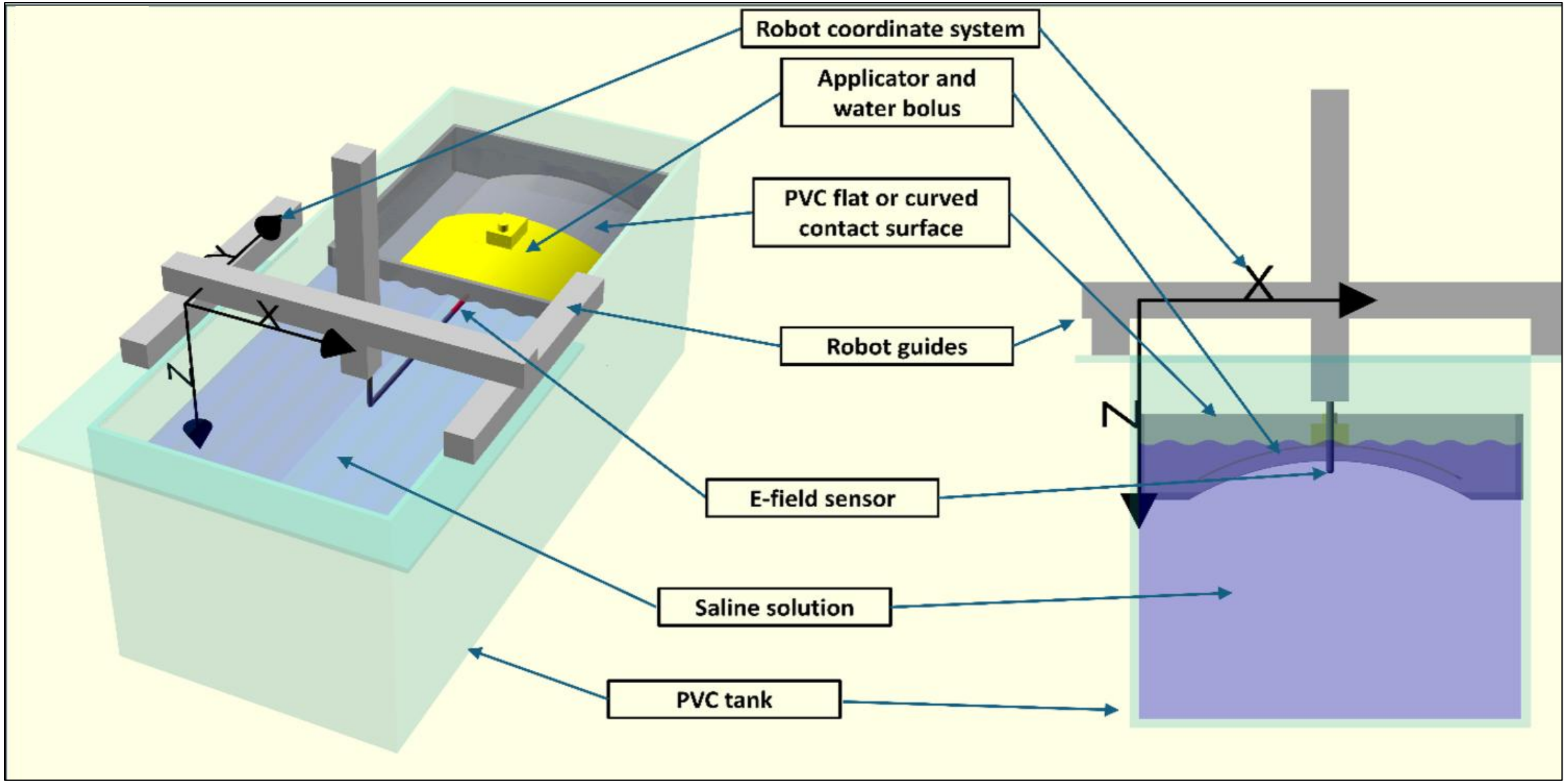
Quantitative (3D)

- Dielectric-matched gel
- Multi-probe thermal mapping
- Validates SAR and T models



- No widely adopted commercial solution provides the quantitative SAR assessment needed to assure simulation accuracy
- Rigorous, traceable device-performance verification is a prerequisite for treatment planning and multi-center clinical trials

Phantom dosimetry: Automated 3D SAR measurements



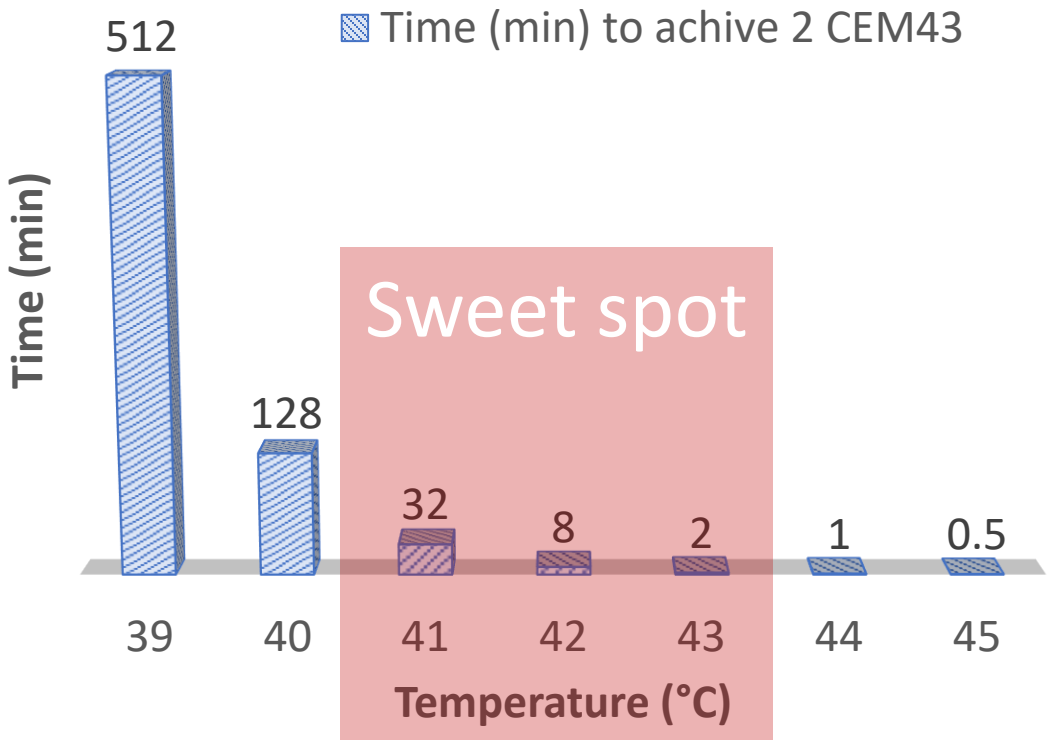
Daniel Herrera 2026 Strahlenther Onkol.

Thermal dose

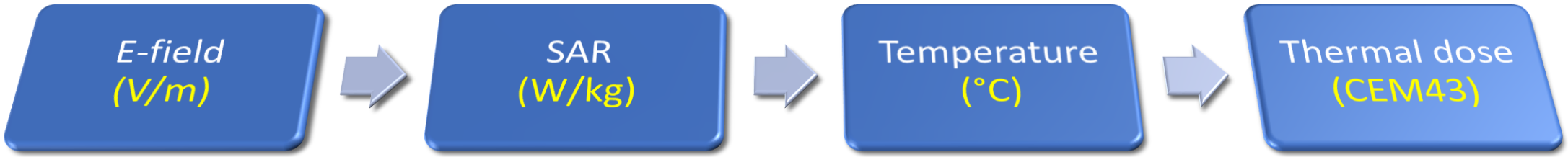
- Thermal dose increases in direct proportion with temperature and heating time
- Units of “equivalent minutes at 43°C” or CEM43
- Concept derived from an Arrhenius model of cell survival *f(T)* not radio or chemo sensitization
- Can only be calculated after tx delivery

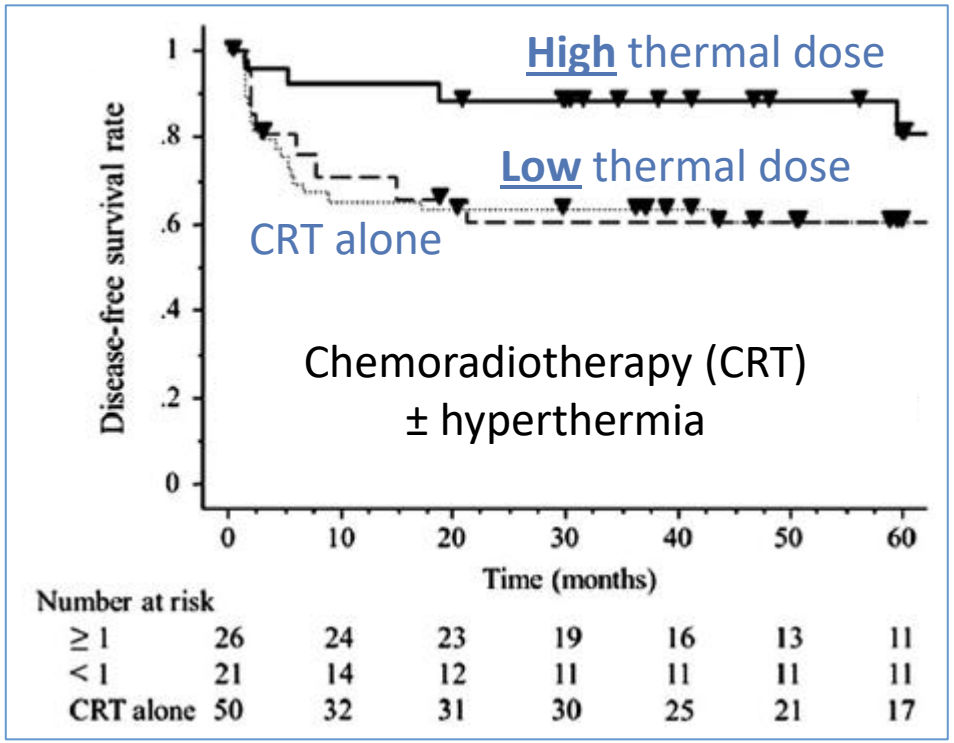
$$TD = \begin{cases} \sum_i \Delta t_i \frac{1}{4^{43-T_i}}, T_i < 43℃ \\ \sum_i \Delta t_i 2^{T_i-43}, T_i \geq 43℃ \end{cases}$$

Temperature Ti (°C)	Thermal dose after 60 min of treatment at Ti (min)
39	0.2
40	0.9
41	3.8
42	15
43	60
44	120



The thermal dosimetry chain: from field to biological effect





Ohguri 2018 (PMID: 28679349); Locally advanced cervical cancer
Multicenter randomized clinical trial

Efficacy (tumor)

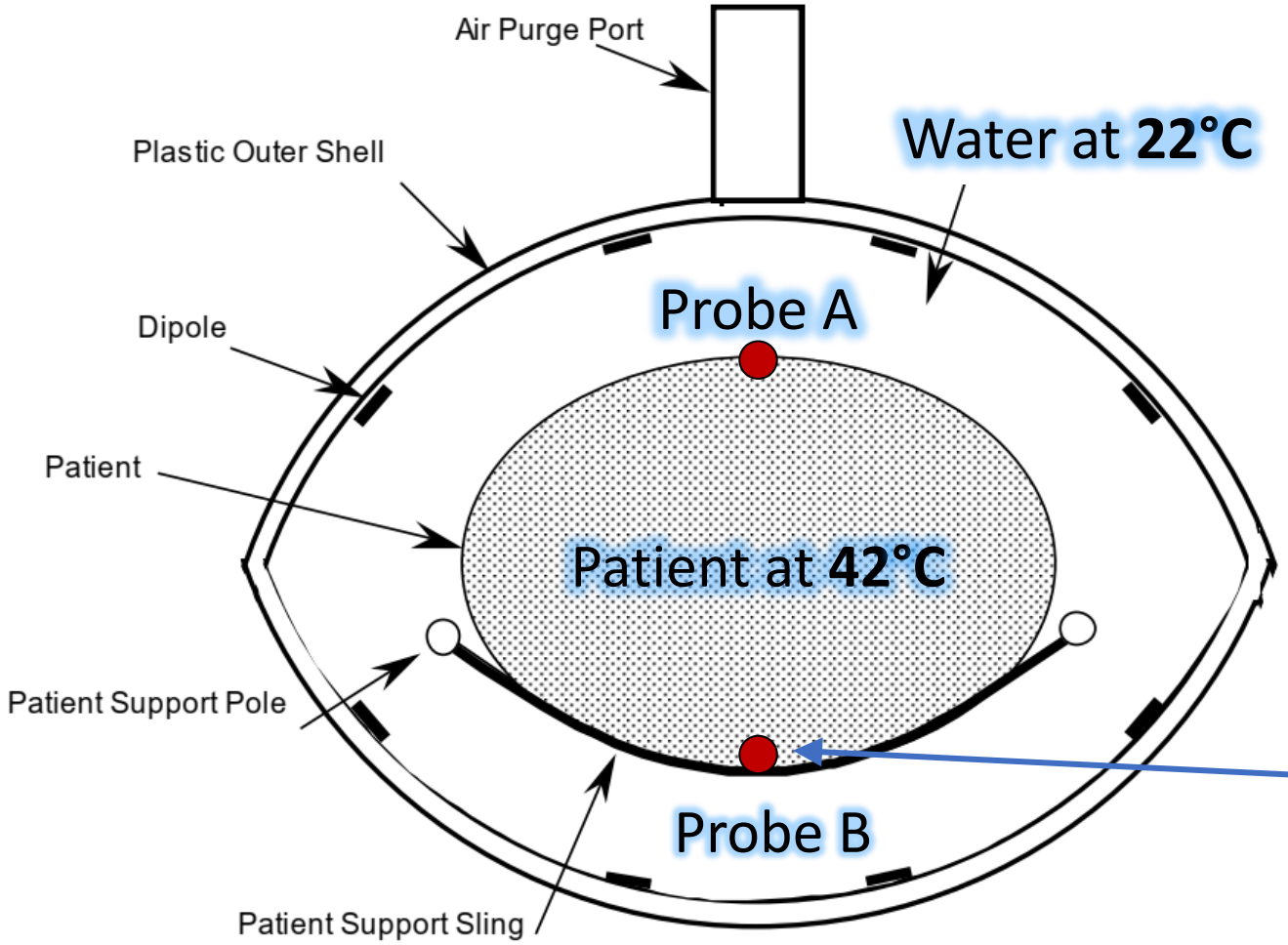
- T50 ≥ 41 °C
- T90 ≥ 40 °C
- CEM43T90 ≥ 1min

Safety (normal tissue)

- Tmax < 42-43 °C (pain, edema, blistering)
- 43–44 °C tolerable only for short periods

Txx: temperature exceeded by xx% of the tumor volume
CEM43T90: thermal dose reached by ≥90% of tumor volume

Interpretation of surface temperature readings



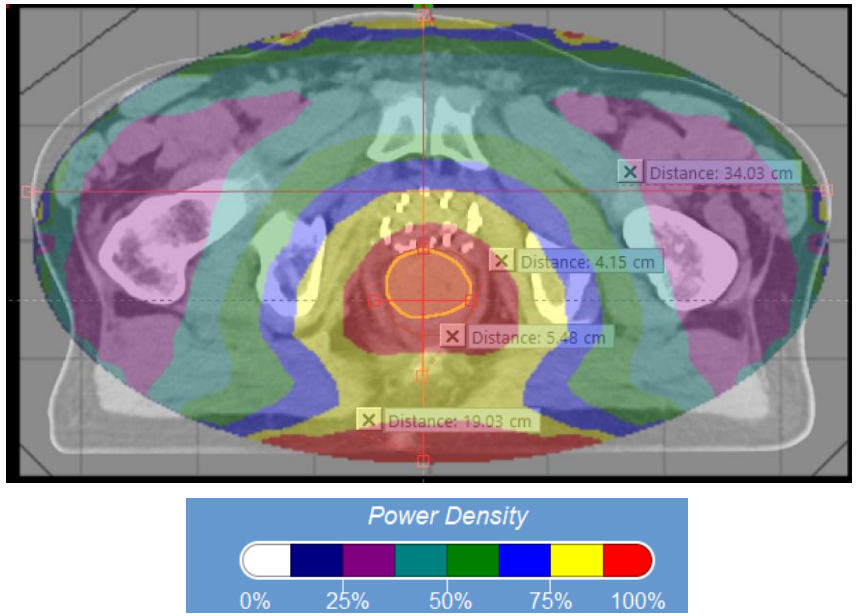
Patient feedback is critical:
- They "measure" temperature in 3D(t)
- Cannot report exact location or °C

Insulation layers:
- Bed pads (chucks)
- Sling
- Bolus membrane

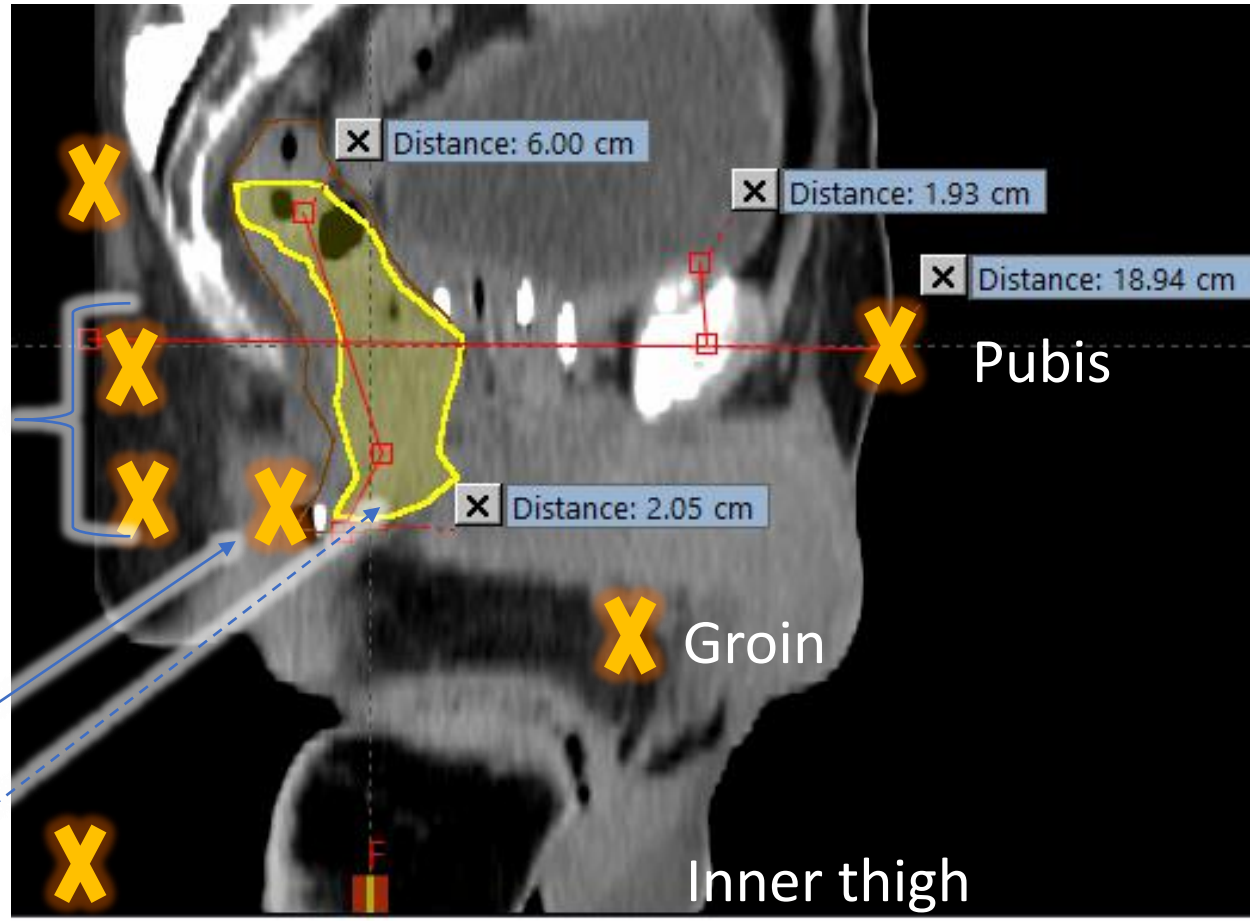
Probes read ~ average temperature of all contacting surfaces
- Temperature (Probe A) ~ 32°C, ~average between Tbolus and Tskin
- Temperature (Probe B) ~ 40°C, closer read to Tskin due to insulation layers

Using surrogate temperatures: case example

75 y.o. male with history of prostate cancer treated with low-dose rate (LDR) brachytherapy, now found to have high grade, low rectal adenocarcinoma

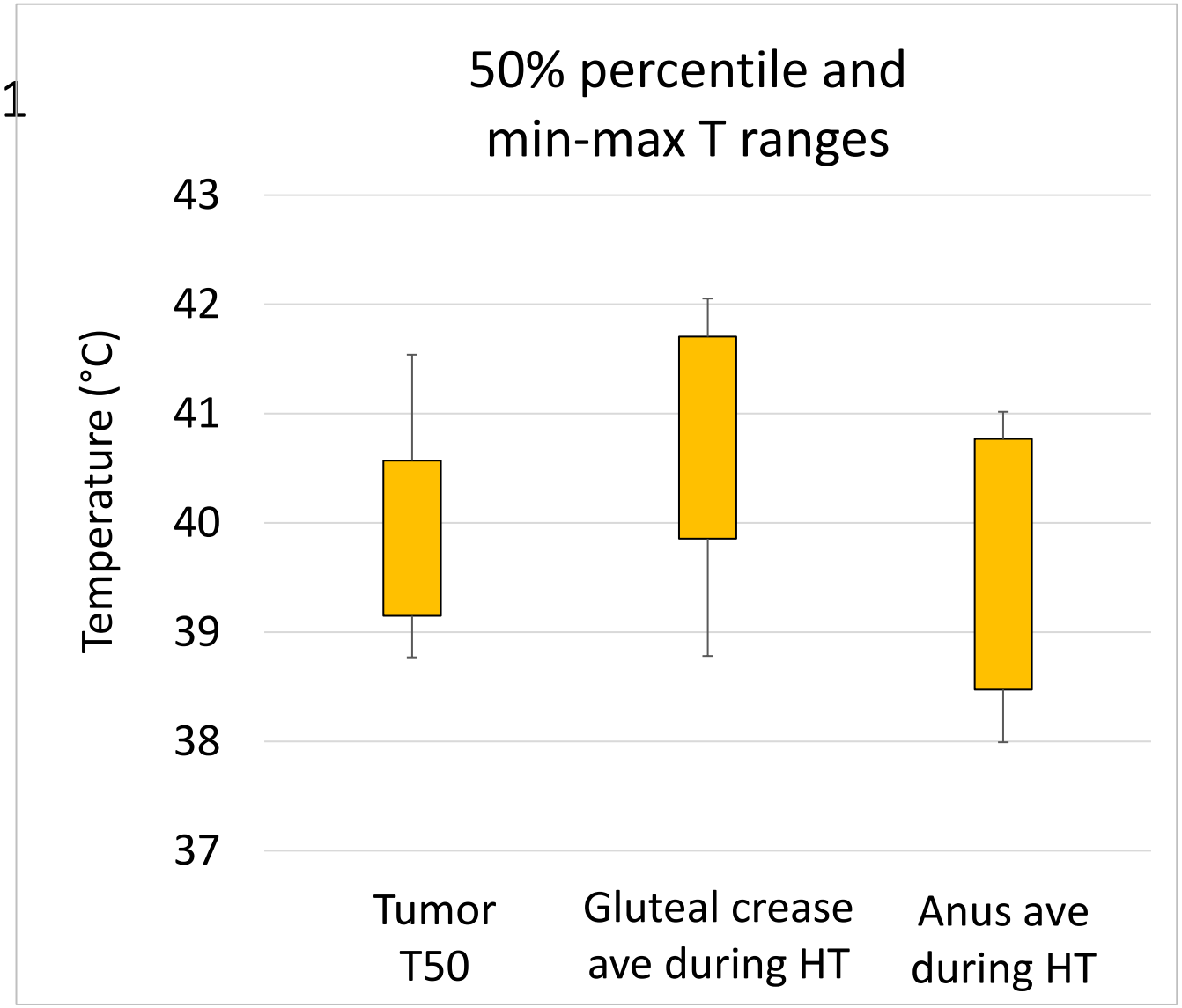


Can gluteal crease be a surrogate for rectal temperature?



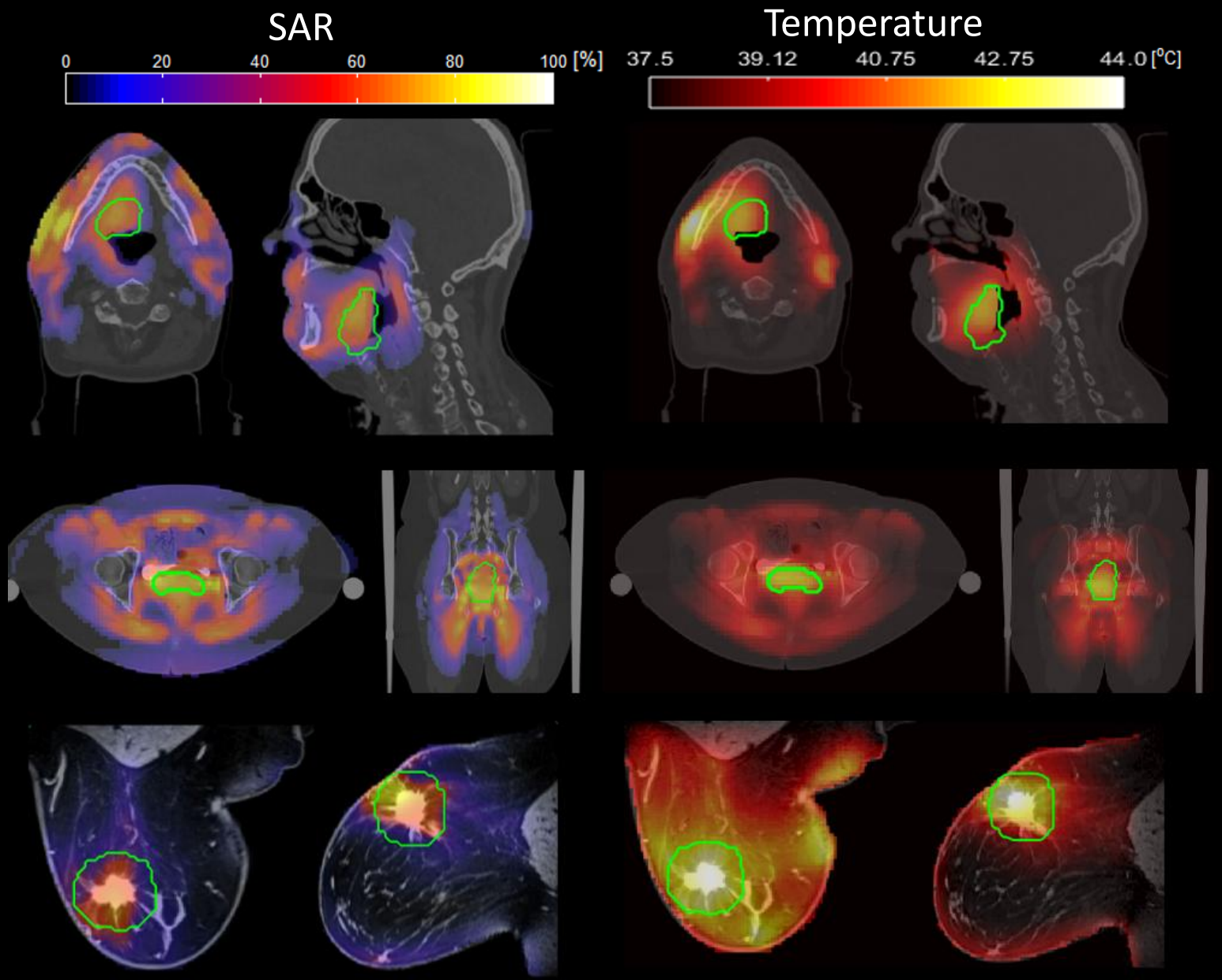
Results - gluteal fold and anus as surrogates?

- T50, **n=56 treatments**
  - Intratumoral distance: 8 (2-13) cm, n=61
  - 39.8 (38.8-41.5) °C
- Gluteal crease Tave during HT (Tg)
  - 1-3 probes/tx, n=50
  - 40.9 (38.8-42.1) °C
  - **Tg=T50+1.0±2.2** (-1.1,2.8)
- Anus Tave during HT (Ta):
  - 39.9 (38.0-41.0) °C
  - 1 probe/tx, n=14
  - **Ta=T50+0.3±1.8** (-1.4,1.1)

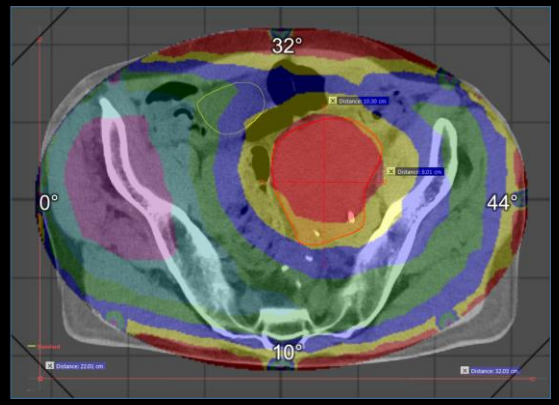


Hyperthermia Dosimetry (Next steps)

Future of Deep HT: 3D patient-specific treatment planning



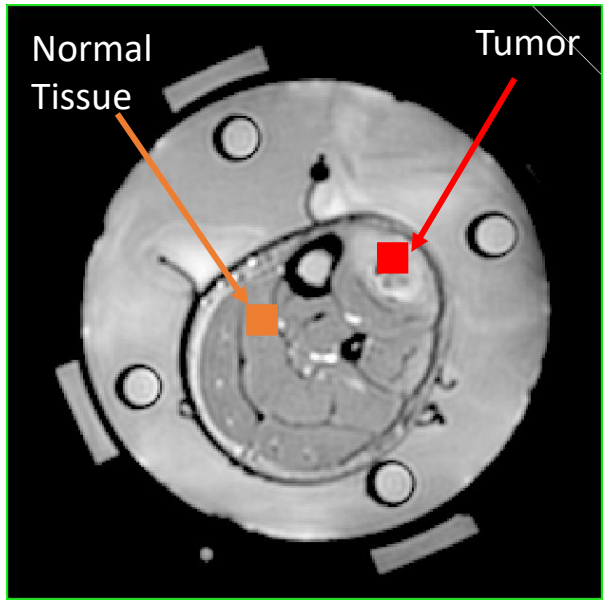
Current SOC

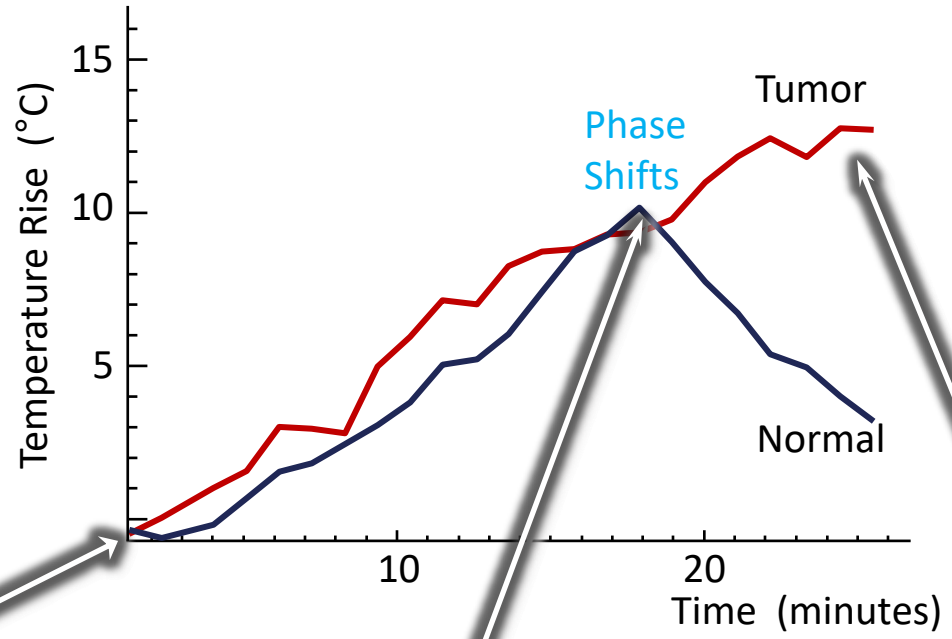


Paulides, Rodrigues et al. Int J Hyperthermia 2021;38(1):1425-42

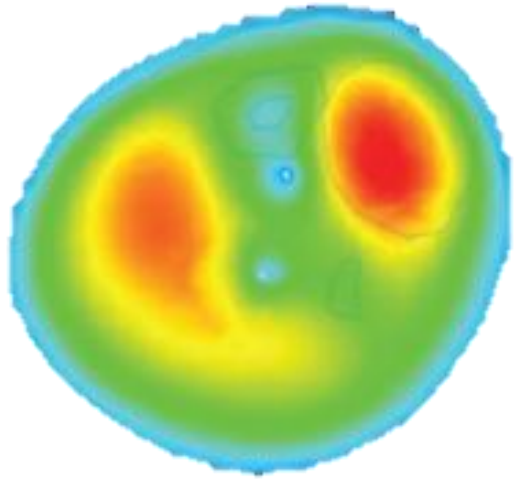
MR thermometry using proton resonance frequency shift

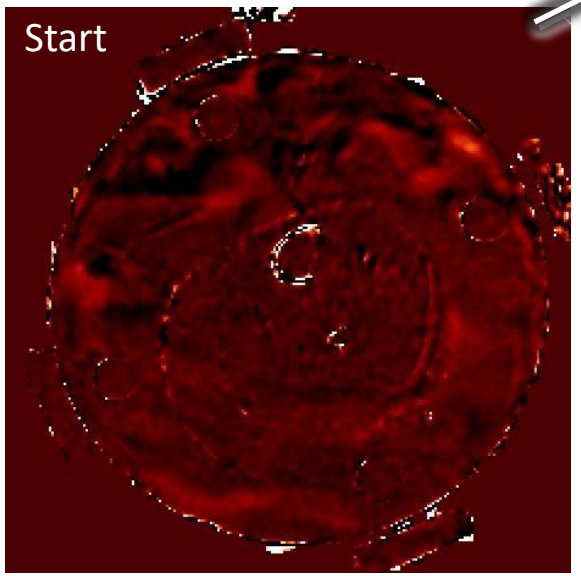
Li, Stauffer, et al. IJH
2011 27(1):86-99

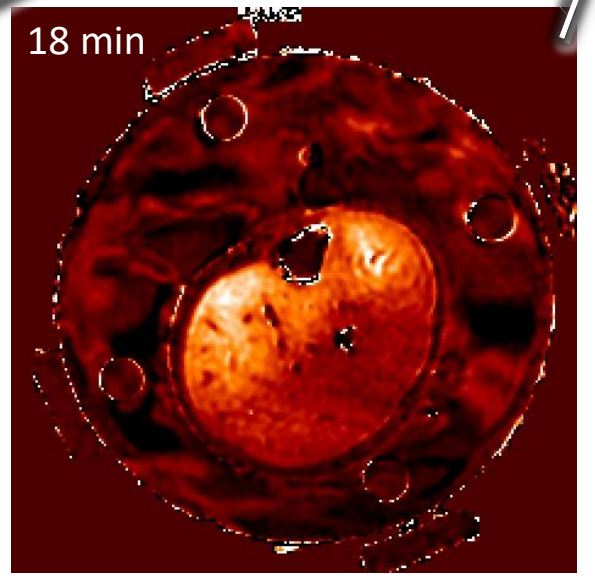


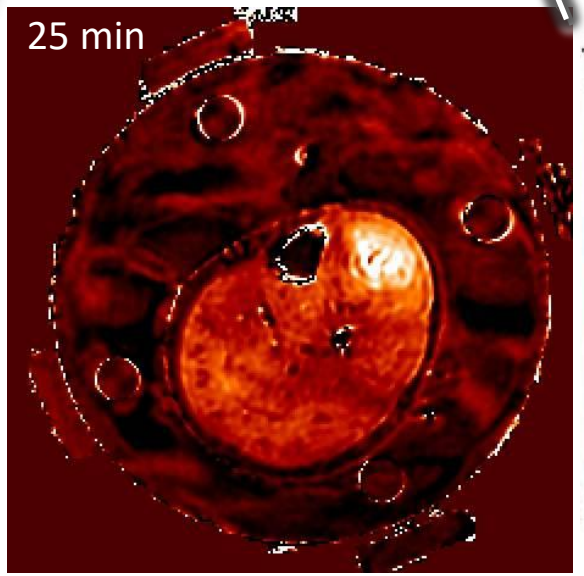


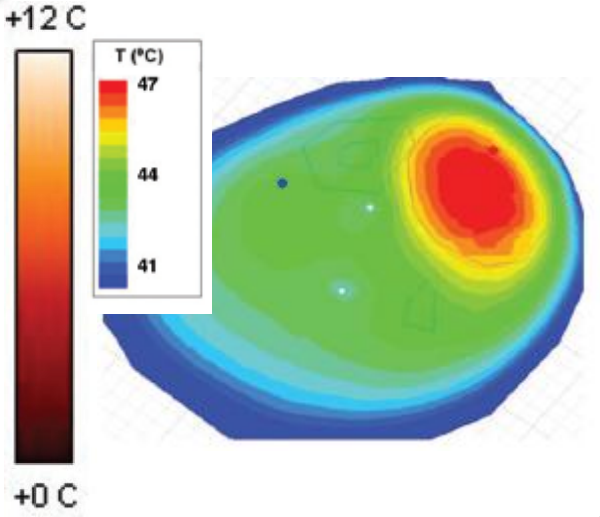
Temperature simulations



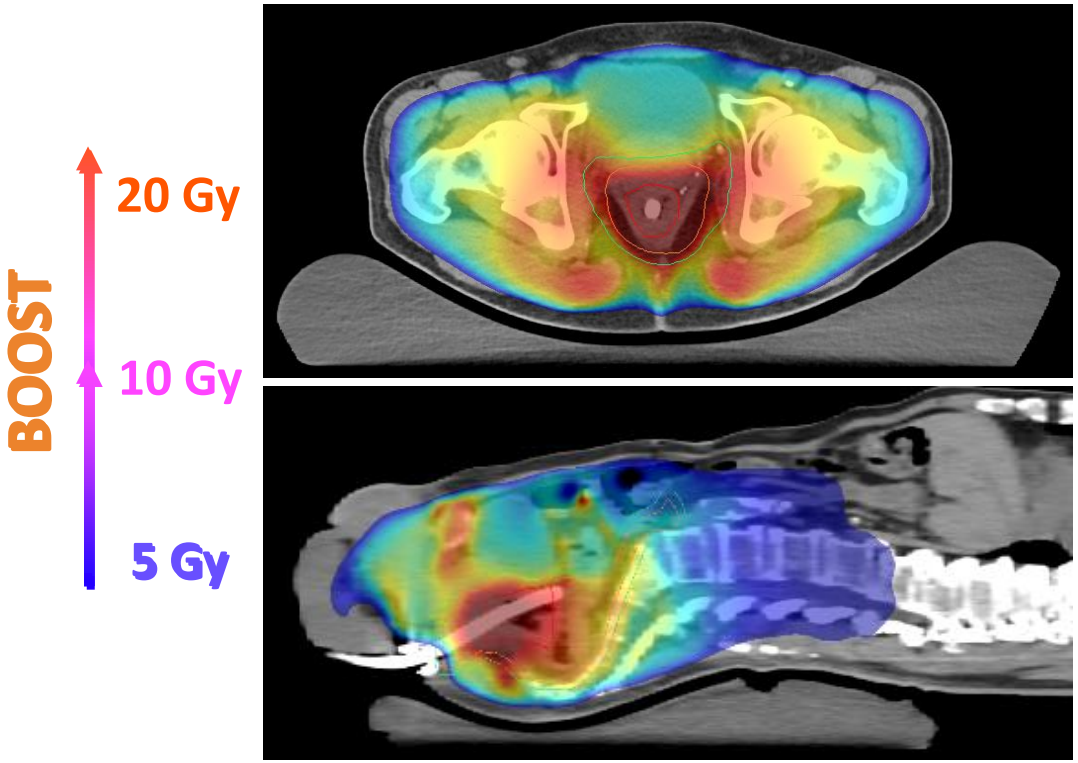








Biological modelling of the HT-induced radiation dose escalation



Courtesy of:

MEDLOGIX medical solutions

Closing the loop: hybrid MR thermometry + treatment planning

Measurement and simulation reinforce each other — neither alone is sufficient

Simulation alone

Limitations

- Tissue EM/thermal properties literature-based
- Position differs from CT/MRI planning (cms!)
- Non-linear and dynamic physiology
- Biological-effect modeling has large uncertainty

→ Useful for device design & relative treatment planning, not for absolute patient-specific thermal dose

MR thermometry alone

Limitations

- PRF shift weak — severe noise sensitivity
- Motion & scanner drift create artefacts
- Low-water tissues (fat, bone) not mapped
- Limited temporal resolution; spatial gaps

→ Direct 3D T measurements, but needs model support to fill the gaps

Hybrid thermal assessment

↓

adaptive HT using patient feedback, probe + 3D thermometry, and real-time replanning

Concluding remarks

Pathway to widespread of hyperthermia therapy into Radiation and Medical Oncology clinics

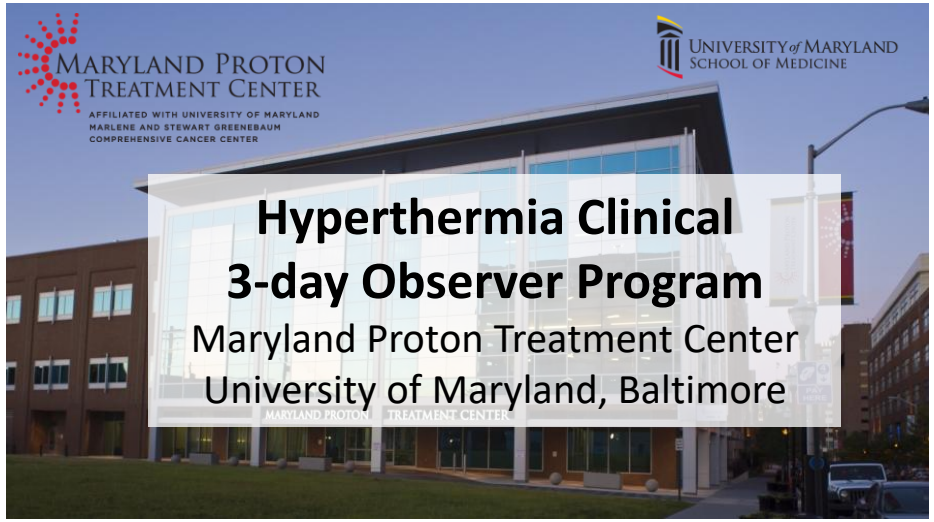
- **Commercialize academic products** that are decades ahead of available technology
- **Formal practical training**
- **FDA reclassification of HT devices**
- **International consensus guidelines and standards**
  - Equipment QA and treatment delivery
    - Trefna et al. under prep. (DHT)
    - Trefna et al. IJH 2019, 36(1):277-94 (IHT)
    - Trefna et al. StrOnkol 2017,193:351-66 (SHT)
    - Trefna et al. IJH 2017, 33(4):471-482 (SHT)
  - 3D treatment planning
    - Paulides et al. IJH 2021;38(1):1425-42
  - **Thermal Medicine Standards Committee** (ASME/STM)
- **Certification** of hyperthermia health professionals
- **Increase recognition and utilization** of HT for the benefit of cancer patients

University of Maryland School of Medicine

Hyperthermia Therapy Practice School

Presented by Department of Radiation Oncology

4th edition: Spring 2027



Society for Thermal Medicine

40th Annual STM Meeting
Savannah GA
May 7-9, 2026

ESHO EUROPEAN Society for Hyperthermic Oncology – 37th Annual Meeting

Erlangen, Germany
Oct 4-6, 2026

Concluding remarks

- **Reproducibility and verification** that the HT treatment met the intended goal are far more complex to document than radiation treatments
- Hyperthermia works, but **metrology remains a major bottleneck** to reproducible delivery and broader adoption
- **Thermal dose prescription and acceptance criteria** are not yet standardized across centers
- **Reliable clinical thermal dosimetry** requires a hybrid measurement + modeling approach in real-time
- **Ultrasound thermometry** may become a viable long-term option for noninvasive 3D thermometry, enabling broader adoption
- **Consensus standards** for reporting, calibration, phantom QA, and device performance are the next step toward routine integration in radiation oncology

Thank you! Dario Rodrigues (drodrigues@som.umaryland.edu)