Oncothermia is a kind of hyperthermia. Hot topics: temperature, dose, selectivity

Andras Szasz, PhD; professor, Chair
Department of Biotechnics, St. Istvan University, Budaors, Hungary

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ESHO'2017

Oncothermia is a kind of hyperthermia.

Hot topics: temperature, dose, selectivity

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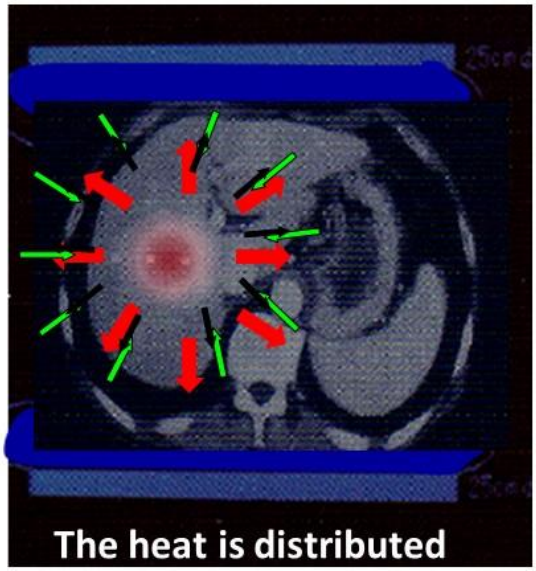
Outline

- ❑ Introduction
- ❑ Temperature
- ❑ Selection
- ❑ Dose

Origin of controversies in clinical results of hyperthermia

Energy could be well focused but the temperature can not be kept focused



Temperature spreads!

It increases the blood-flow trying to compensate the heating.

It is positive for complementary therapies

- radio [reoxygenization]
- chemo [drug delivery, and activity])

It is negative over the tresholds shown

Supplies extra nutrients for tumor

Risks the intensive dissemination

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Oncothermia is thermal

Post-treatment 24 H, 30 min; Each point is 3 independent measurements

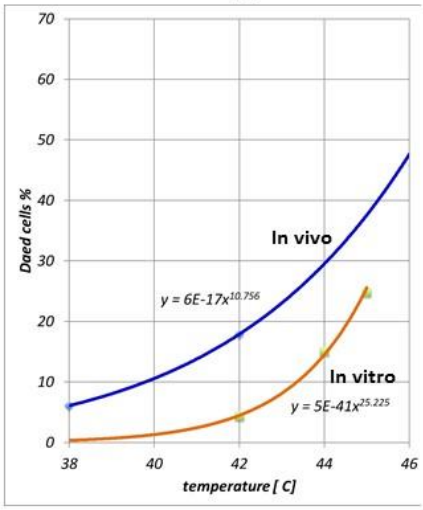
In vitro: U937 human lymphoma cell-line (10^6 cell/ml)

Andocs G, et al, Biology and Medicine 7(4):1-9,

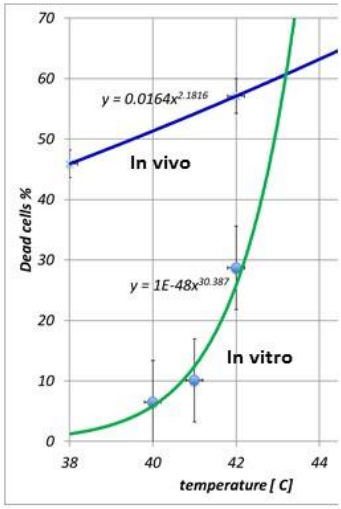
In vivo: HT29 human colorectal cancer xenograft

Andocs G et al. Radiology and Oncology (Strahlentherapie und Onkologie) 185:120-26 , (2009)

Conventional hyperthermia

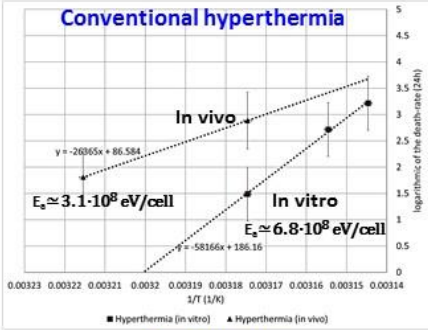


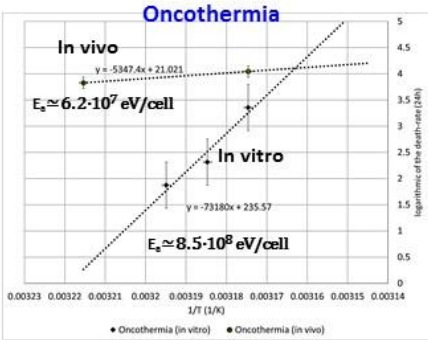
Oncothermia



Power-function

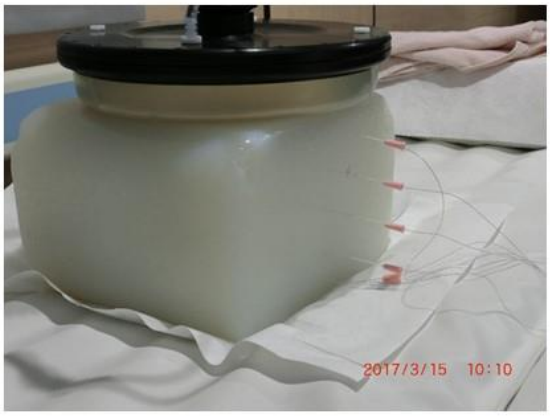
Arrhenius plots (thermal effect)

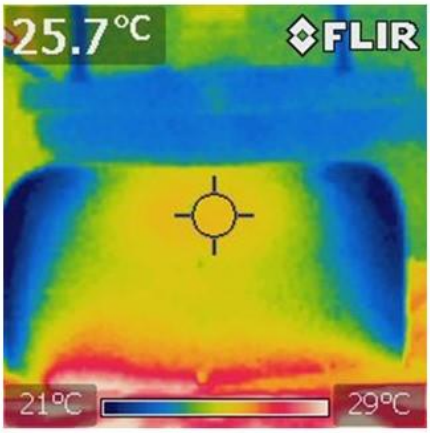




The activation energy is calculated

Temperature measurement Agar phantom





Device: EHY2000+; Applicator: 30cm
Power: 150W; treatment time:30 min
Agar-phantom: 6 kg, Size: 24*24*8.5 cm

Heating for ten minutes with 150 W with 30 cm electrode by EHY2000+ device

Observations:

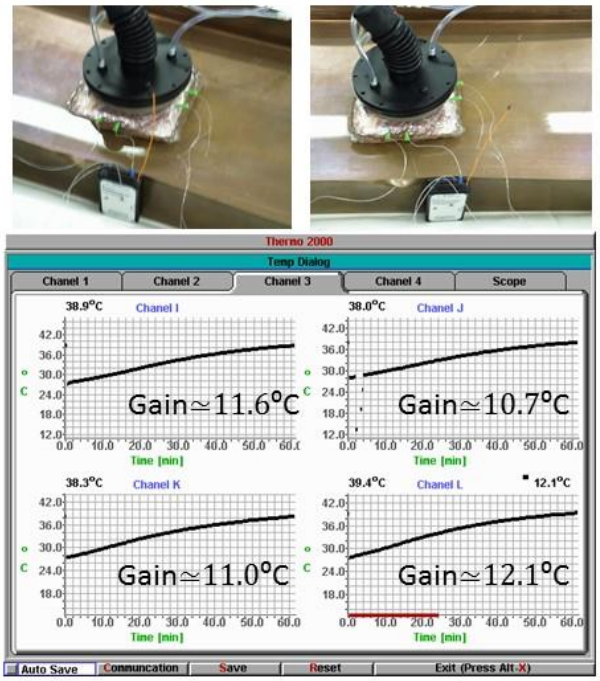
- The temperature was increased >3.5°C (with 150W, 10 min)
- The bulk material was heated, not the surface
- The heating shape is a truncated cone
- Spreading of the heated volume is less than 50% at the bottom

SAR≃24.5 W/kg

≈4.5 kg is heated, 110W was absorbed, ≃74 %

Prof. Dr. Kwan-Hwa Chi* and Dr. Samuel Yu-Shan Wang**
*Department of Radiation Therapy & Oncology Shin Kong Wu Ho-Su Memorial Hospital
**Molecular Medicine and Biochemical Engineering, National Chiao Tung University, Hsinchu, Taiwan

Meat-phantom experiements

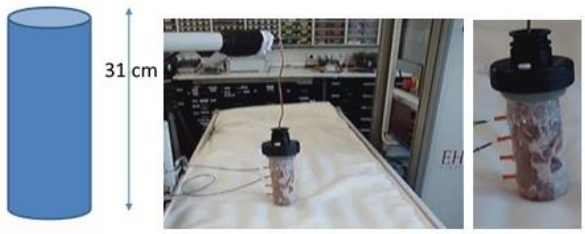


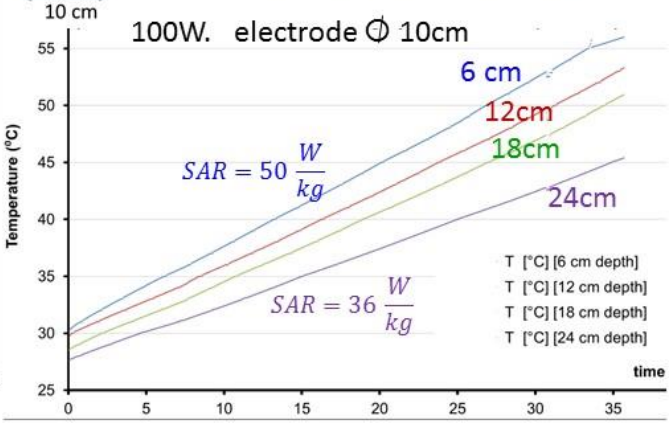
5 kg Pork meat

Start 27.3°C

Power 100W, 60 min

Muscle-fat mixture model





Complete absorbed power $= 92W$

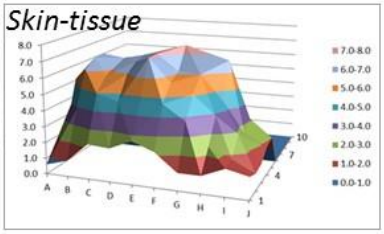
Nagy G. Meggyeshazi N. Szasz O (2013) Deep temperature measurements in oncothermia processes. Hindawi ;Conference Papers in Medicine. Volume 2013. Article ID 685264

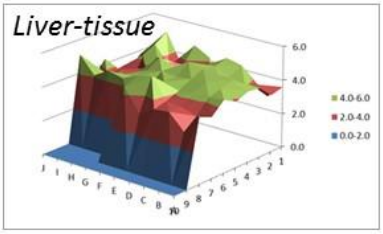
Local Hyperthermia – Oncotherm (Dr.Herzog)

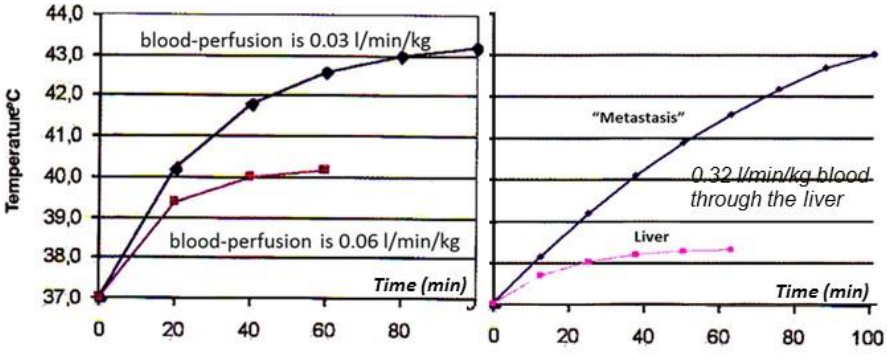
Herzog A (2008) Messung der Temperoturverteilung om Modell der nicht perfundierten Schweineleber bei lokoler Hyperthermie mit Kurzwellen mit I3,56 MHz; Forum Hyperthermie, Forum Medicine, 1/10, pp.30-36

electrode 20cm, 100W

Measurement results after 15 minutes			
Measurement point		Temperature rise °C	
			(from - to)
△T	Skin	5.4	2.6 - 7.1
△T	Liver surface	4.1	2.6 - 5
△T	Liver inside	2.4	2.4 - 3.9

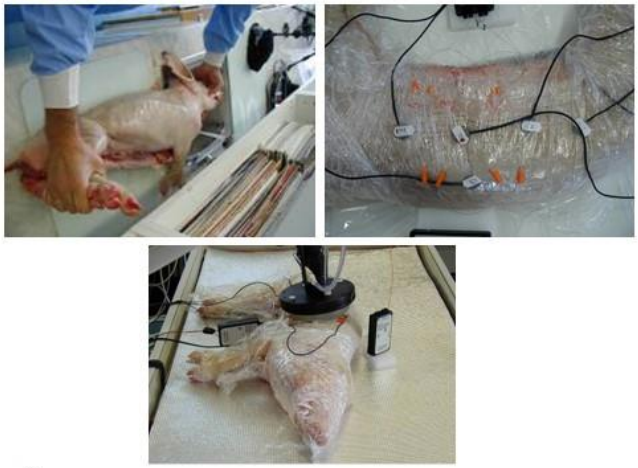


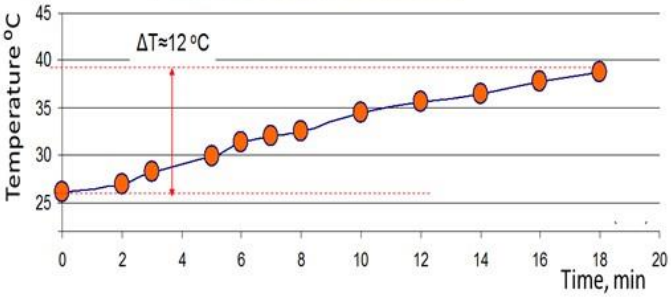




Pig experiments

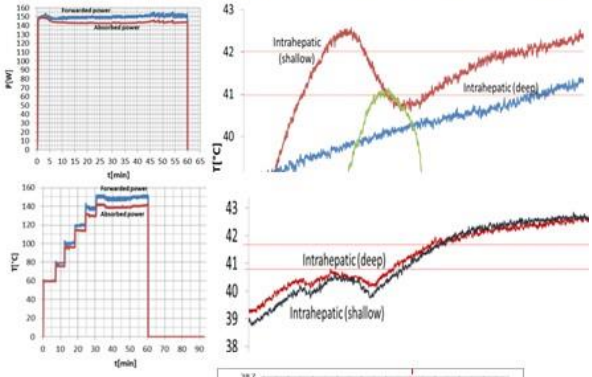
Ex vivo



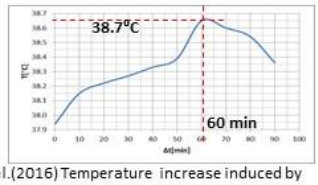


In vivo

Intrahepatic temperature measurement (alive)

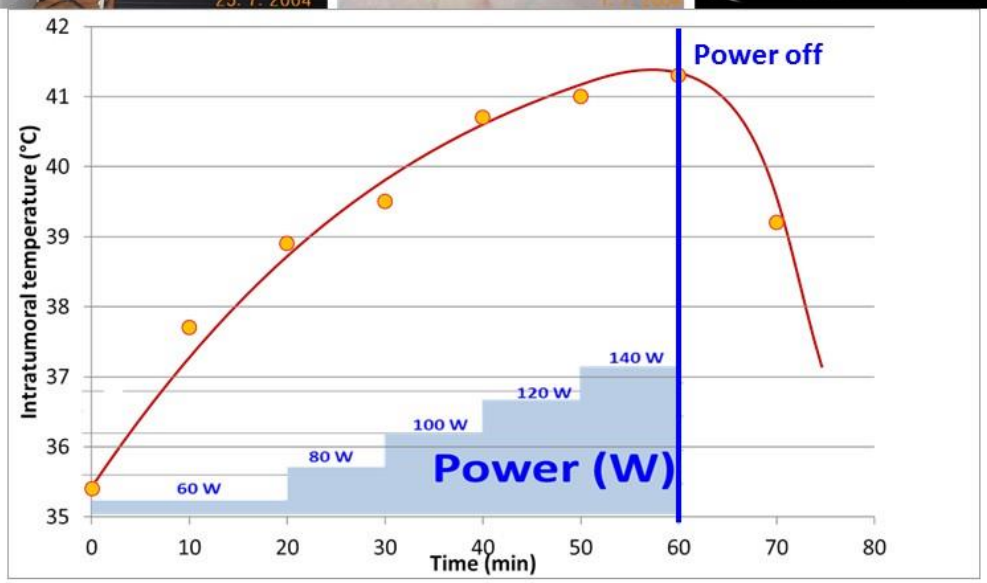


rectal

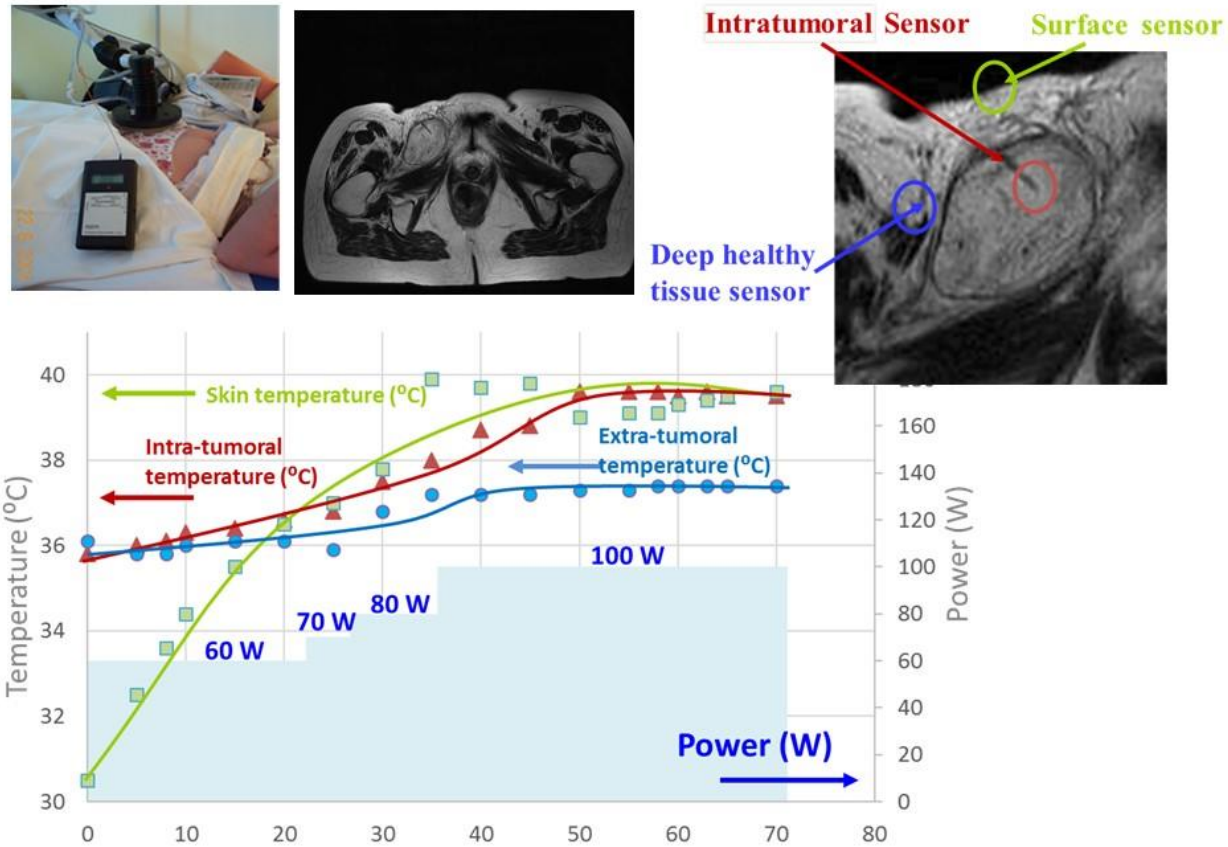


Balogh L, Polyak A, et al.(2016) Temperature increase induced by modulated electrohyperthermia (oncothermia®) in the anesthetized pig liver, Journal of Cancer Research and Therapeutics, 12(3):1153-1159

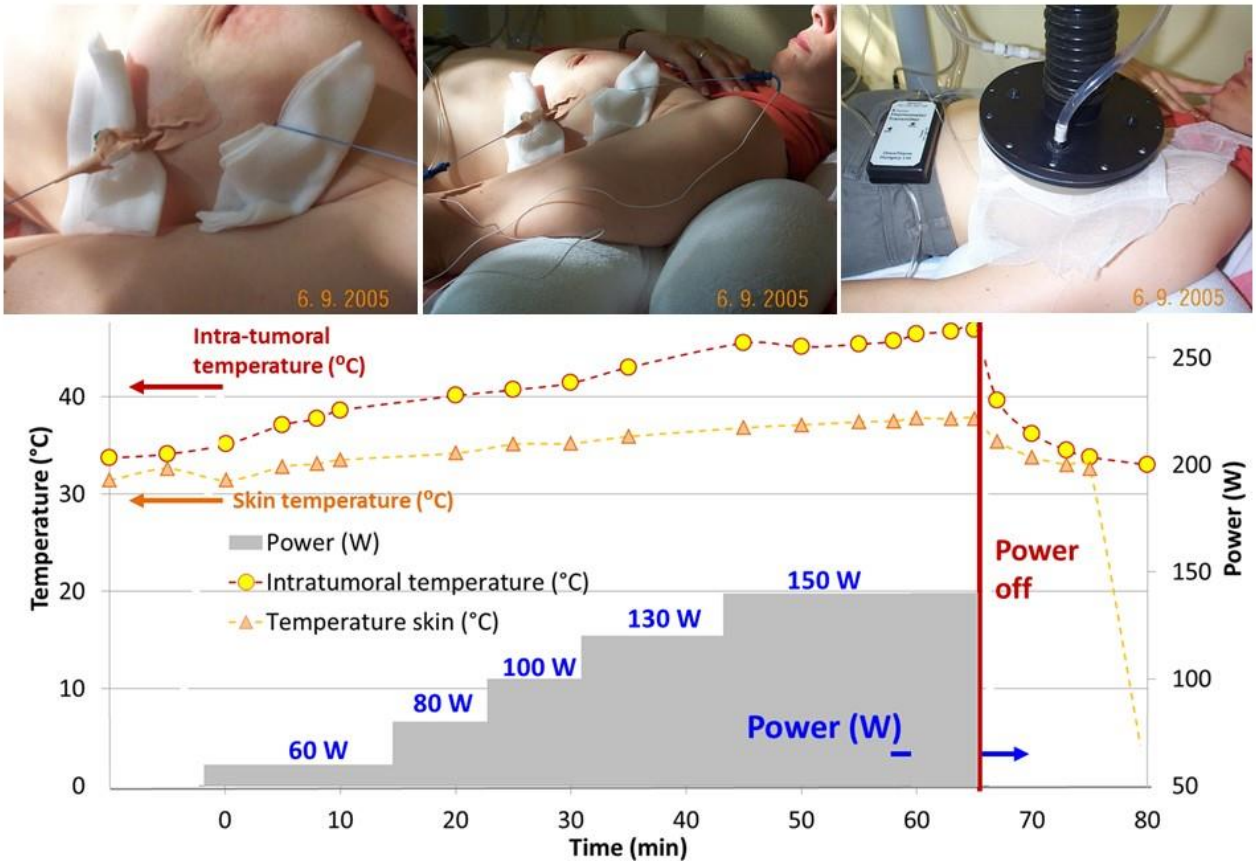
Human abdominal temperature measurement



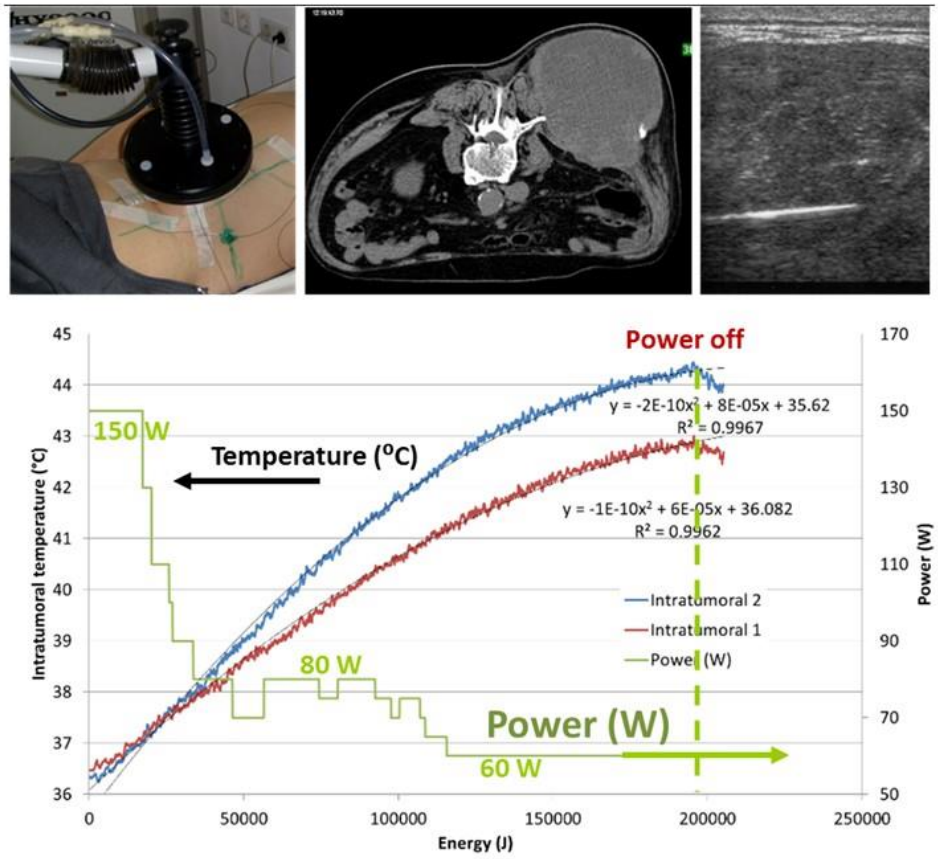
Temperature in ovary (Gronemayer Institute)



Mammary carcinoma measurement (Gronemayer Institute)



Temperature of sarcoma (Nurnberg University Hospital)



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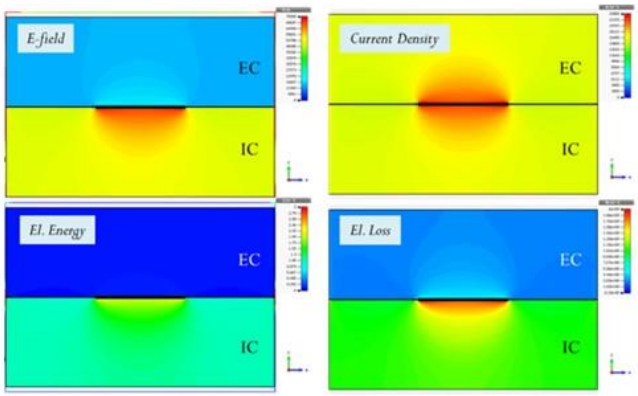
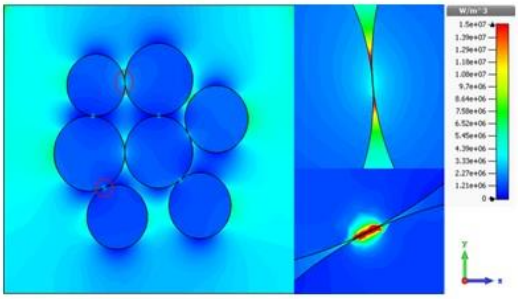
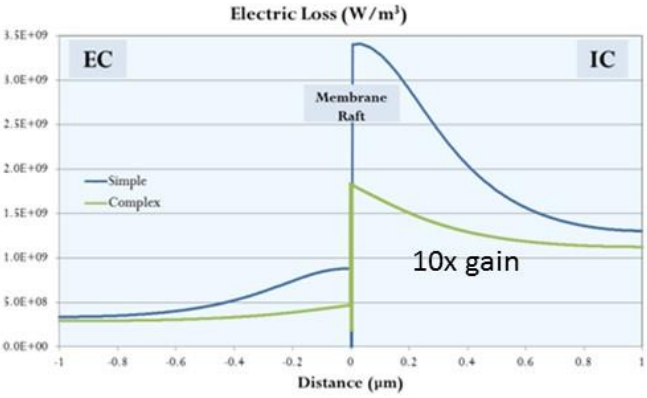
In silico model shows the raft-heating

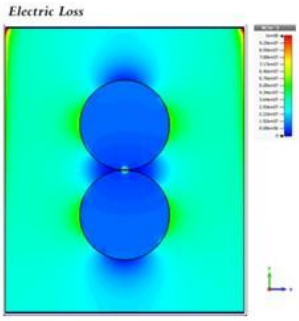


Additional extra energy loss by touching microdomains

12.5x gain



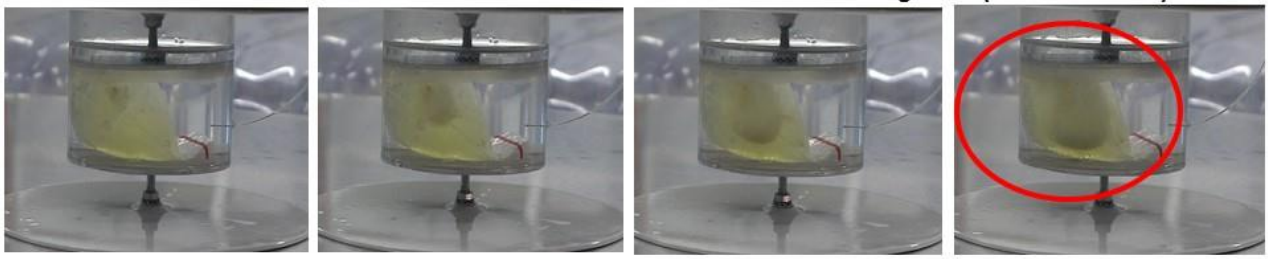




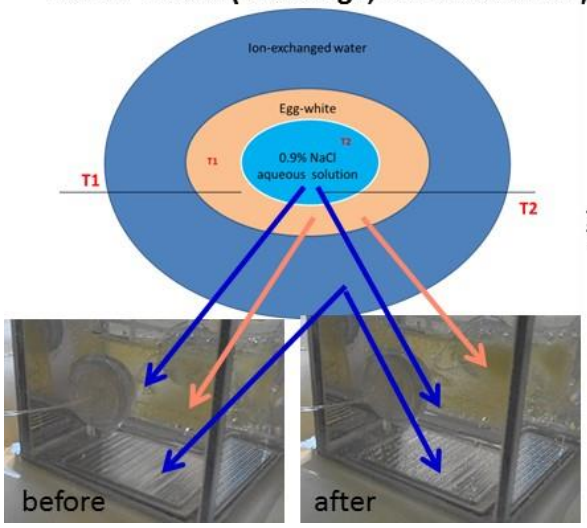
Egg-white in water-tank, heated by RF-current flow

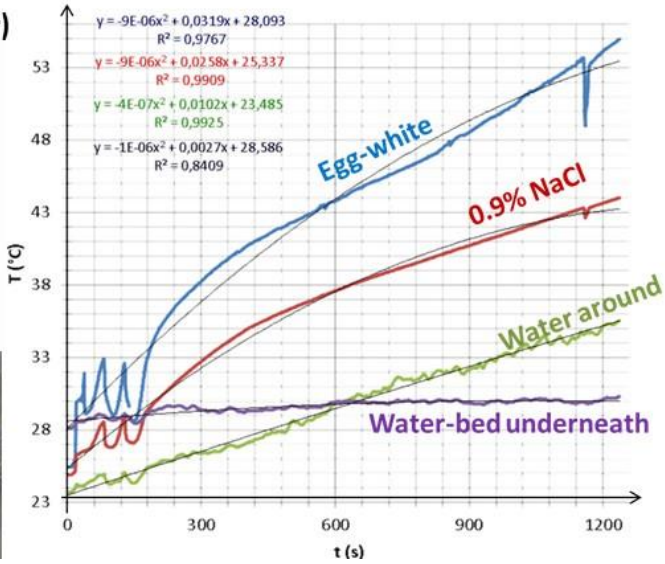
Tumor model (early stage)

The water was not heated-up, but the egg-white had been coagulated (from the center!)

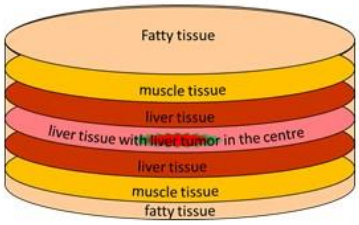


Tumor model (late stage, necrotic center)





Heterogeneous liver phantom

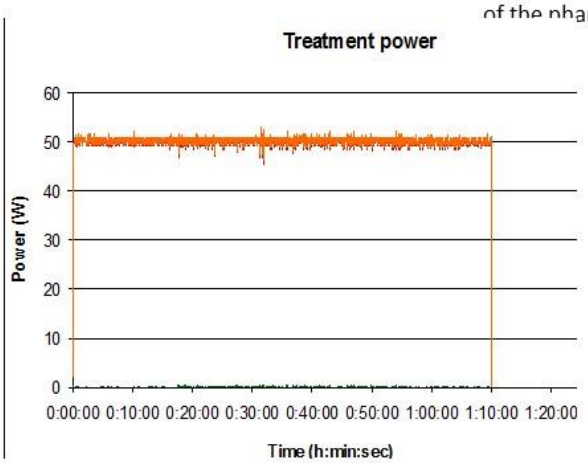


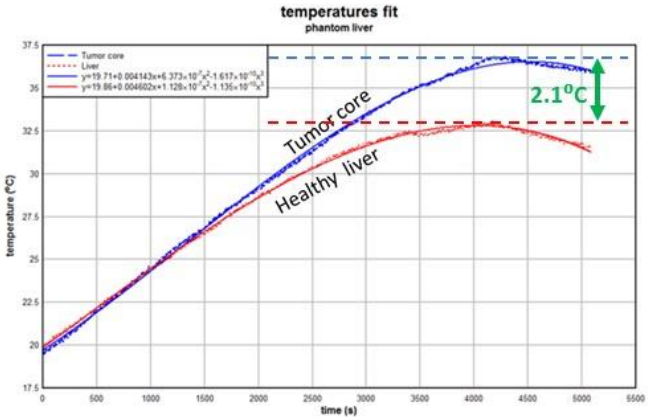
The structure of the phantom

Fat (down) and muscle layer (same on the top of the phantom)

Pig liver layer with cancer in the middle

Complete phantom with the electrode on its top





Oncothermia - cellular selectivity by active malignancies

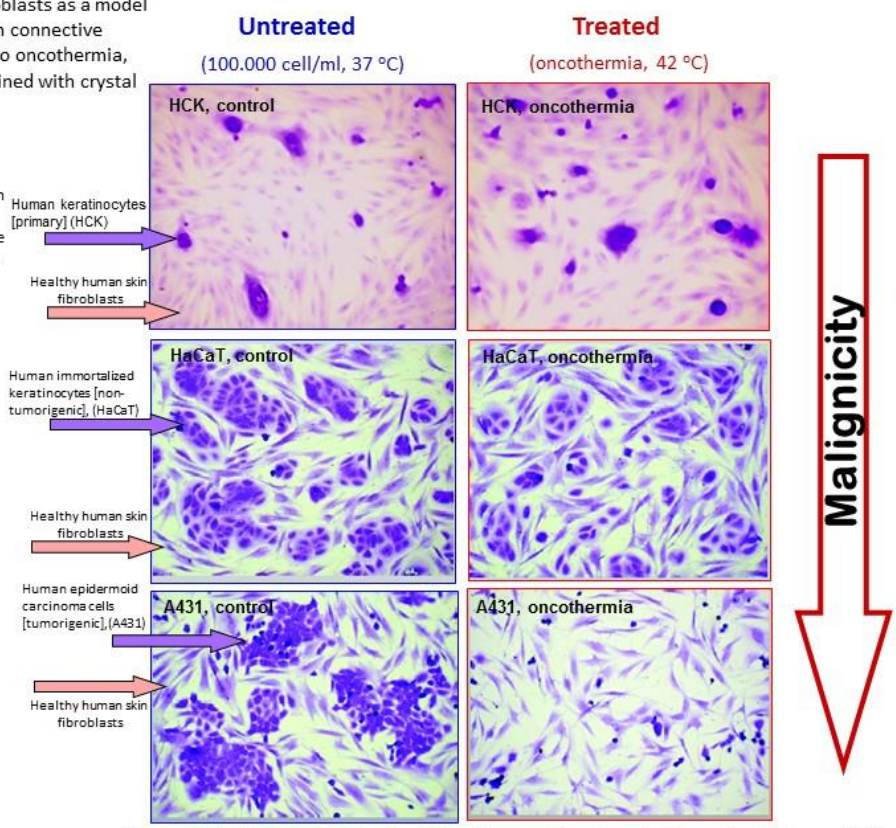
Co-culture with normal human skin fibroblasts as a model of a squamous carcinoma growing within connective tissue cells (100.000/ml) were exposed to oncothermia, incubated for 24 h at 37°C, fixed and stained with crystal violet

Cellular metabolic activity was measured using the MTT assay (standard colorimetric test) and quantitated at 630 nm. Data represent the mean value ± S.E.M. of 4-6 separate experiments assayed in triplicate, but some experiments were repeated up to 12 times to obtain reliable data.

Healthy tissue is unaffected

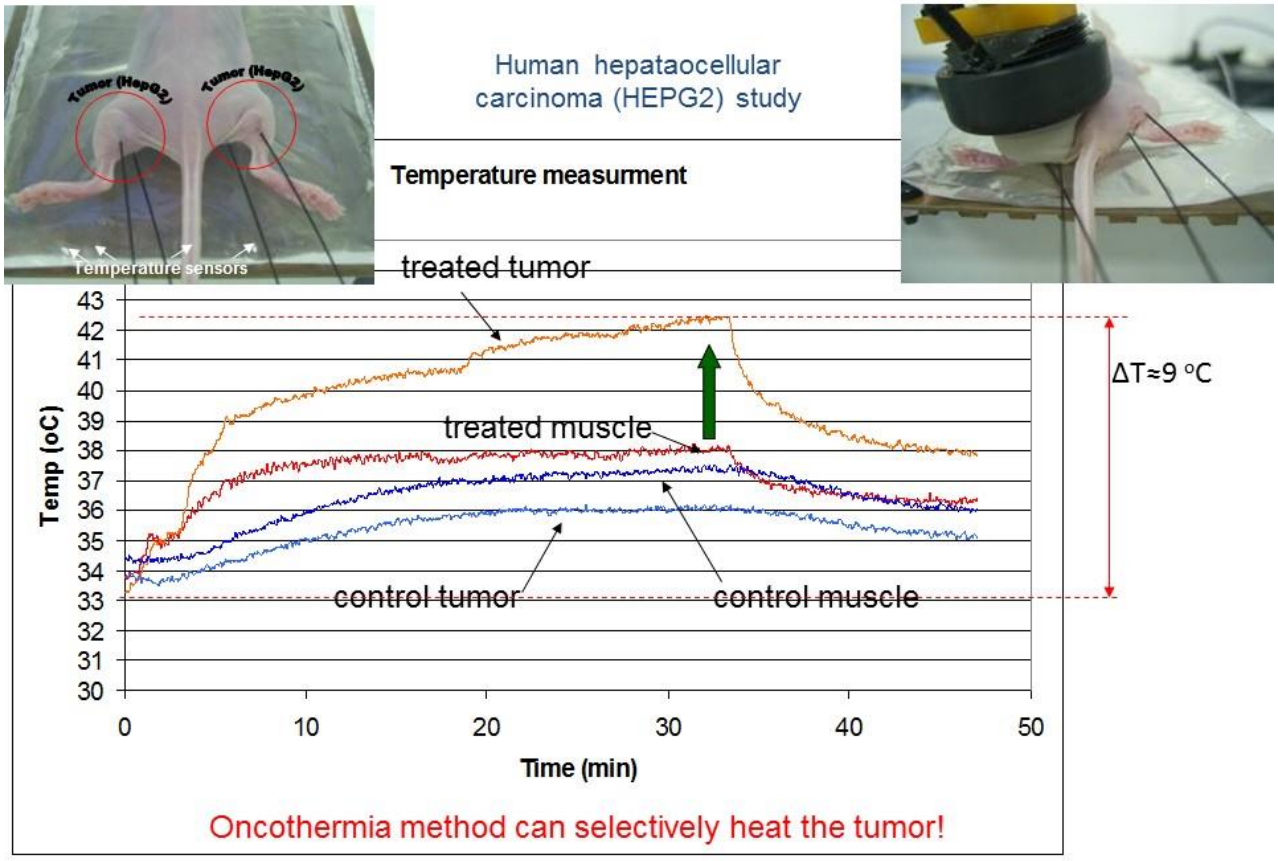
Highly proliferating tissue is slightly affected, but the healthy cells are intact

Malignant tissue is selectively treated, the malignance is destroyed, the healthy cells are intact



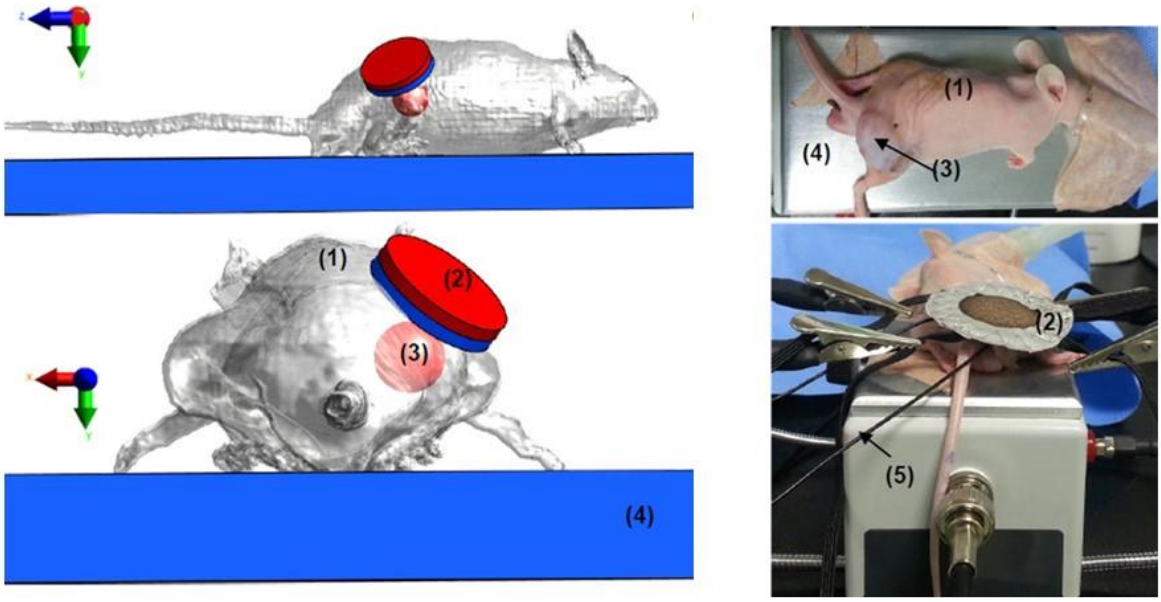
Brunner G, Klinik Hornheide, Munster Univ., Germany, Hyperthermia Symposium, Cologne, 2006

Selective macroscopic energy deposition



Temperature mapping

Jung Kyung Kim, Bibin Prasad, Suzy Kim; (2017) **Temperature mapping and thermal dose calculation in combined radiation therapy and 13.56 MHz radiofrequency hyperthermia for tumor treatment,** Proc. of SPIE Vol. 10047 1004718-1; Optical Methods for Tumor Treatment and Detection: Mechanisms and Techniques in Photodynamic Therapy XXVI, edited by David H. Kessel, Tayyaba Hasan, Proc. of SPIE Vol. 10047, 1004718 © 2017 SPIE · CCC code: 1605-7422/17/$18 · doi: 10.1117/12.2253163



(1) Mouse (2) RF electrode (3) Tumor (4) Constant temperature bed (5) Fiber Optic Sensor

Temperature mapping

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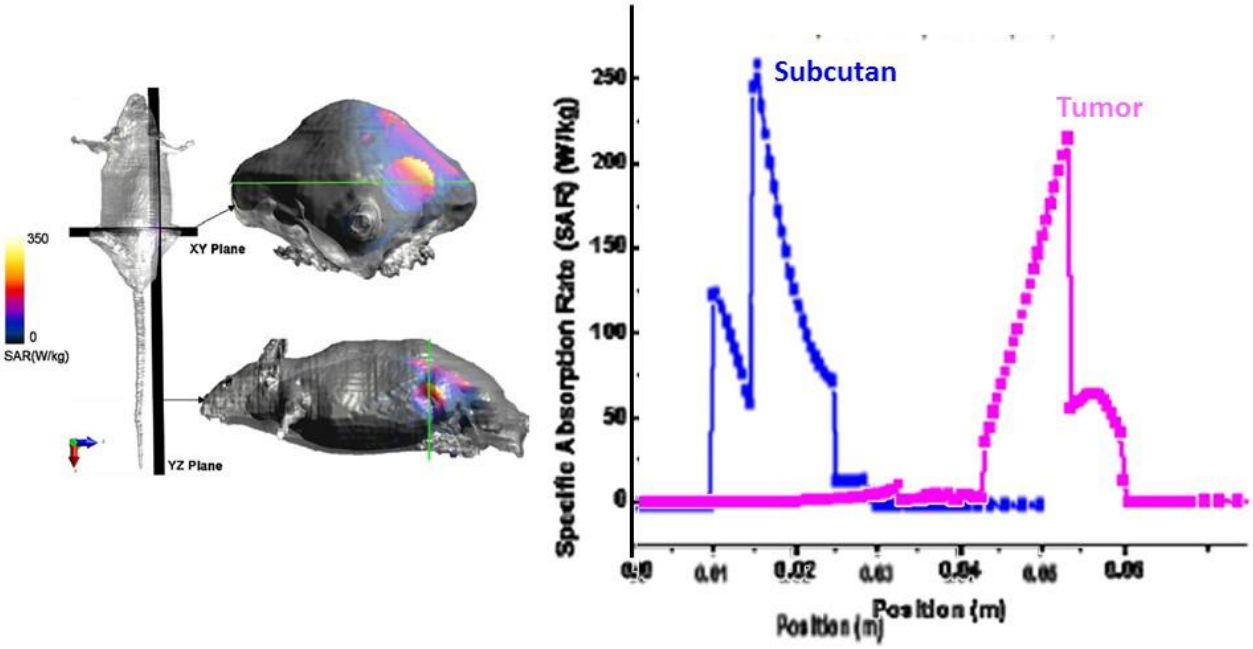

Temperature mapping

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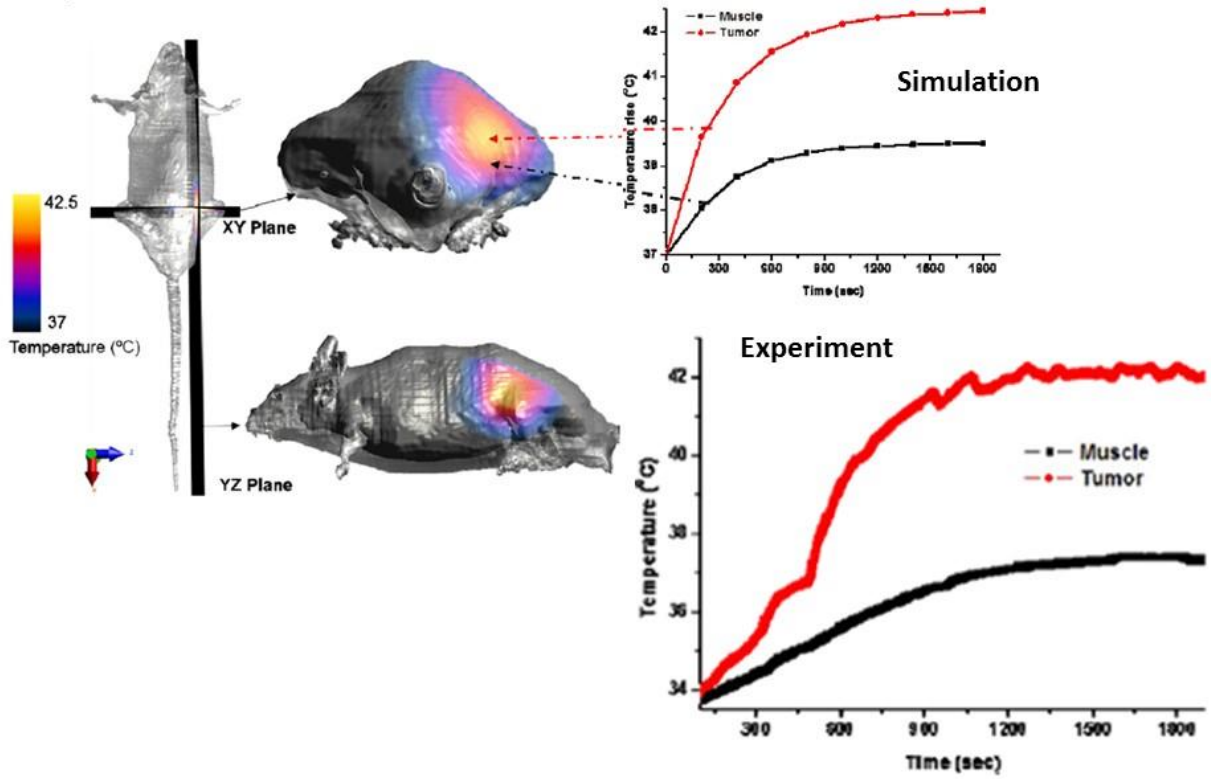
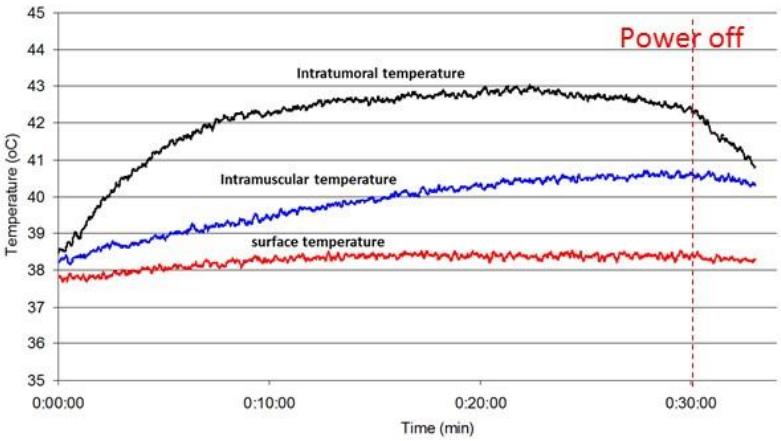


Tumor temperature in bull-terrier

Intratumoral temperature measurement using invasive fluoroptic temperature measurement sensors, 12 years old bullterrier, recidival epithelial cell carcinoma in the lower neck region, Oncothermia (10W)

Tottori University
Japan



Cases not possible with conventional heating

Investigator: Prof.Dr. A. Herzog,

Institute: Fachklinik Dr.Herzog, Nidda, (Bad Salzhausen), Germany;

Patient: 38 y, female

Diagnosis: Non-Hodgkin lymphoma, **Stage:** WHO IV,

Treatment: Oncothermia + Bendamustin,

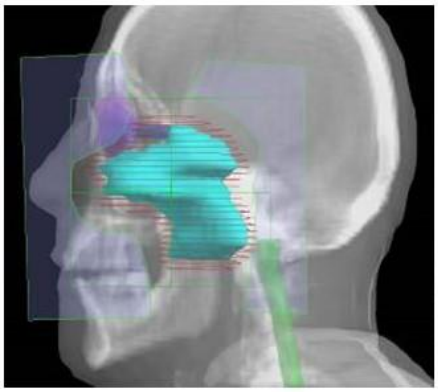
Results: Complete Remission, (CR),

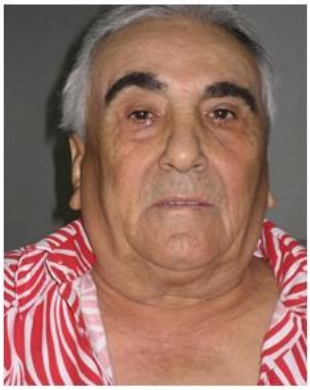
Cases not possible with conventional heating

Investigator: Prof.Dr.H. Renner,
Department: Klinikum Nord, Nürnberg, Germany,
Patient: REN1. 67 y, male.
Diagnosis: Sinus sphenoidalis, inoperable.
Histology: Squamous epithelium carcinoma.
Development: Complete right opthalmoplegy

Therapy: Radiotherapy, 54 Gy, fractional,
Oncothermia: 6 sessions, after radiotherapy

Result: complete remove of opthalmoplegy





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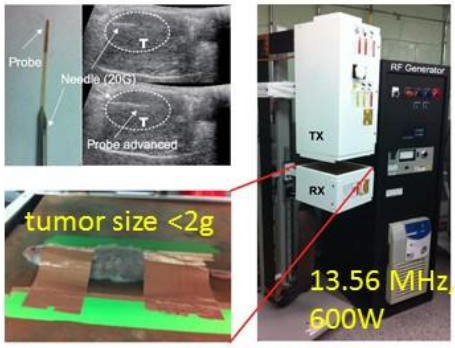
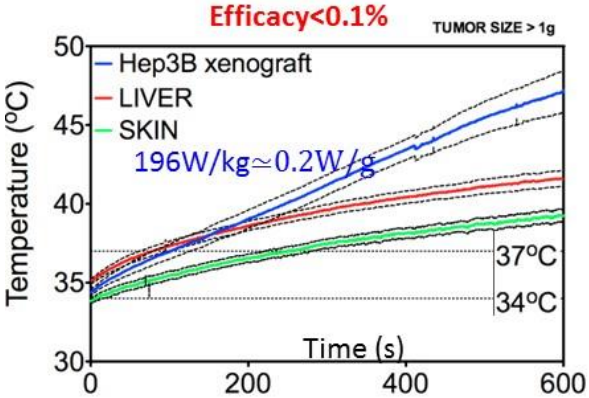
Experiments (energy cannot be the dose)

ThermMed, (LLC, Erie, PA, USA) [Kanzius generator]



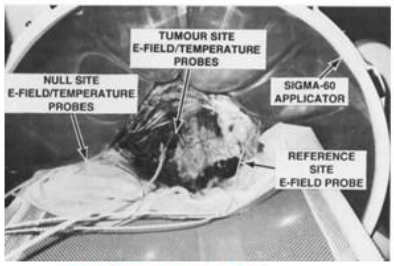
Efficacy<0.1%



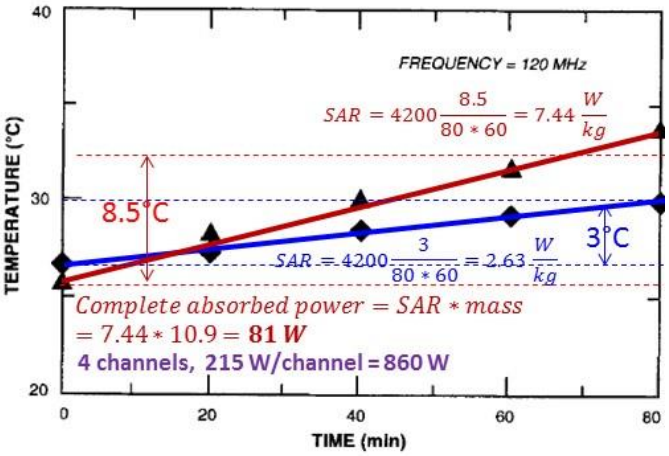
Raoof M, et al; (2013) Tumor Selective Hyperthermia Induced by Short-Wave Capacitively-Coupled RF Electric-Fields; Plos One 8:e68506 pp.9.

BSD Medical Phase-array calibration

Beef phantom, weight is **10.9 kg**

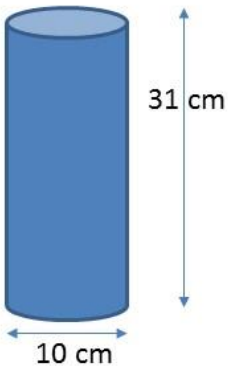


Efficacy <10%



Fenn AJ, King GA, Adaptive radiofrequency hyperthermia-phased array system for improved cancer therapy: phantom target measurements, Int. J. Hyperthermia, 10:189-208 (1994)

Energy is appropriate for the dose



Nagy G. Meggyeshazi N. Szasz O (2013) Deep temperature measurements in oncothermia processes. Hindawi ;Conference Papers in Medicine. Volume 2013. Article ID 685264

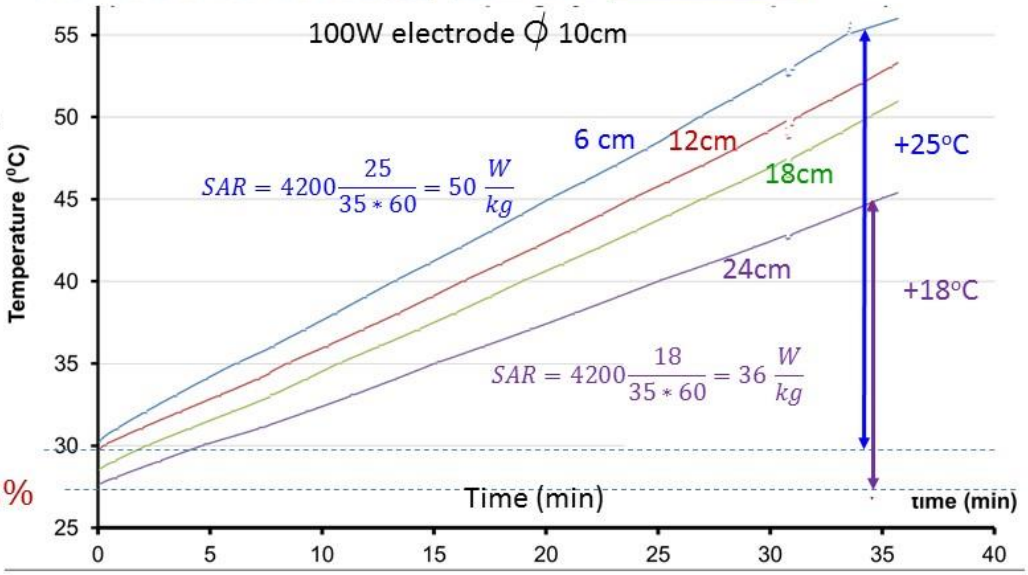
$V = 25 * 3.14 * 31$
$= 2434\ cm^3$

Mass $= 2.3\ kg$

Mean-energy $=$
$\mathbf{2.4\ kg * 40\frac{W}{kg} =}$
$\mathbf{= 92W}$

Reflected power is a couple of W.

Efficacy = 92%



Thank you for your attention.
Dr. Minnaar will continue with the clinical results.