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Workshop, local hyperthermia

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Workshop, local hyperthermia

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Outline

- ❑ Decisional points
- ❑ Possible solution
- ❑ Future points

- ○ Take-home messages

The task

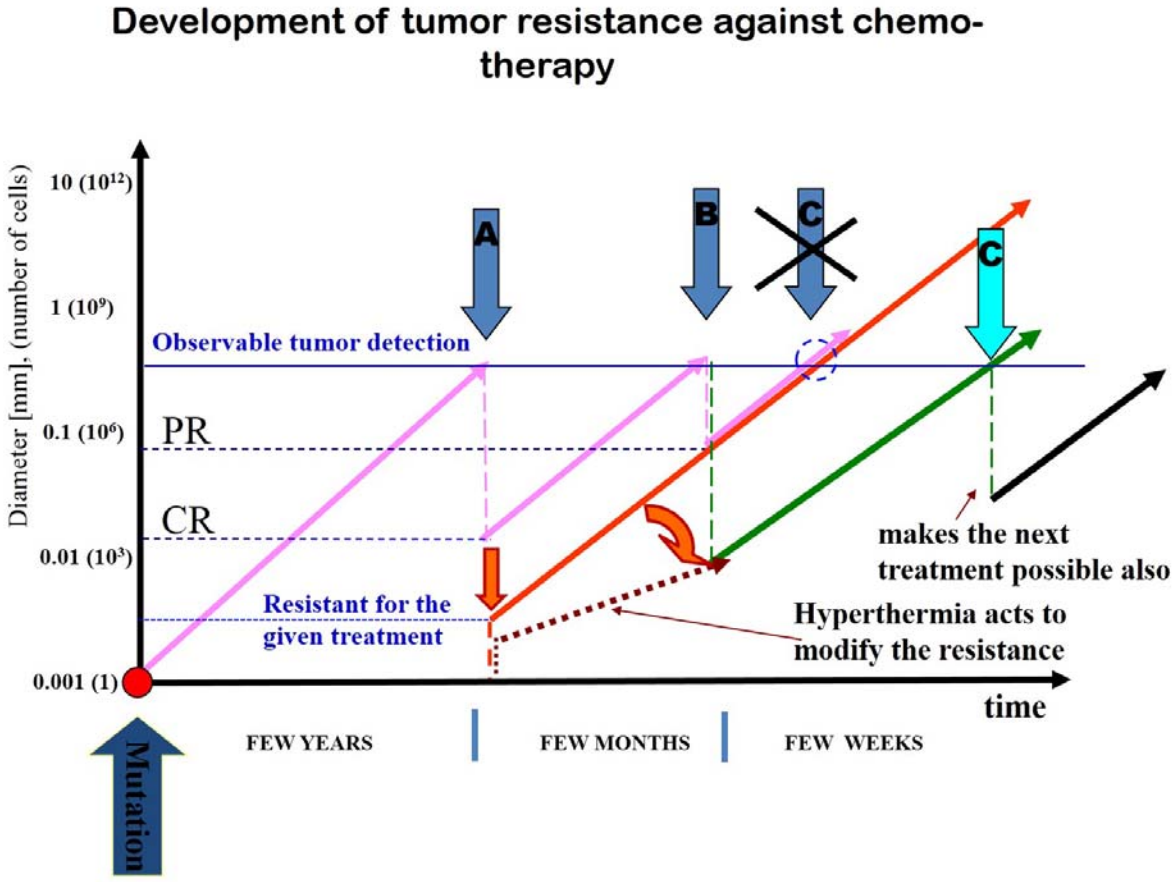
Hyperthermia is a perfect, capable method in oncology

However, we need further development
and think about the decisional points

The task

Decisional point 1

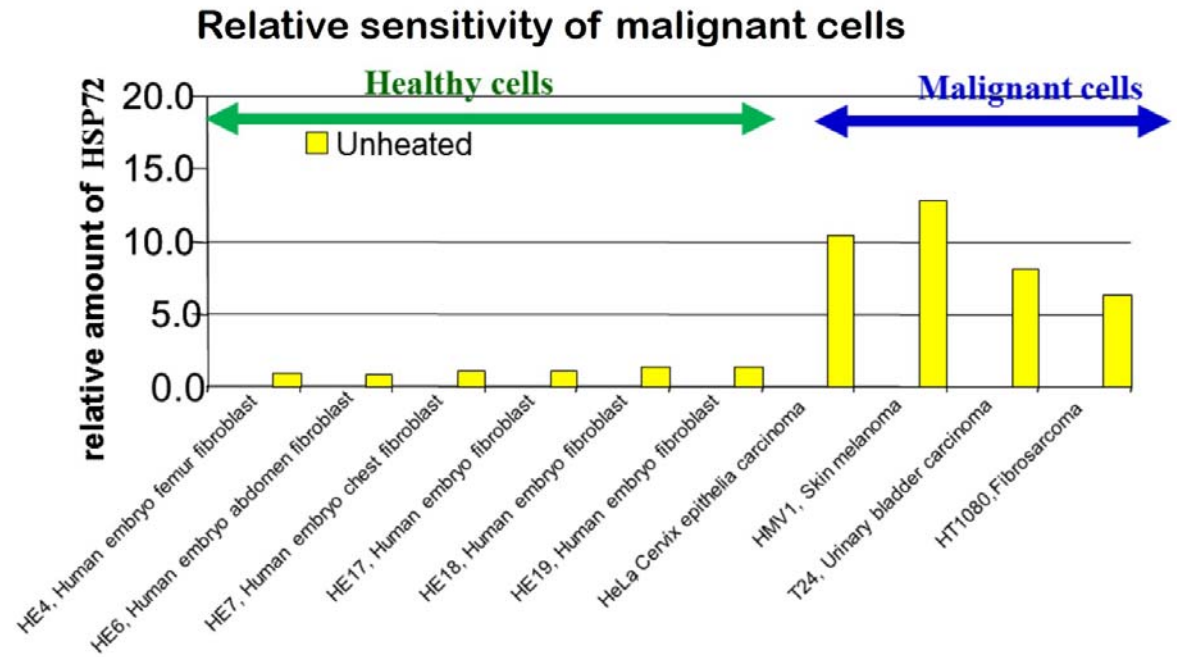
Development of tumor resistance against chemo-therapy



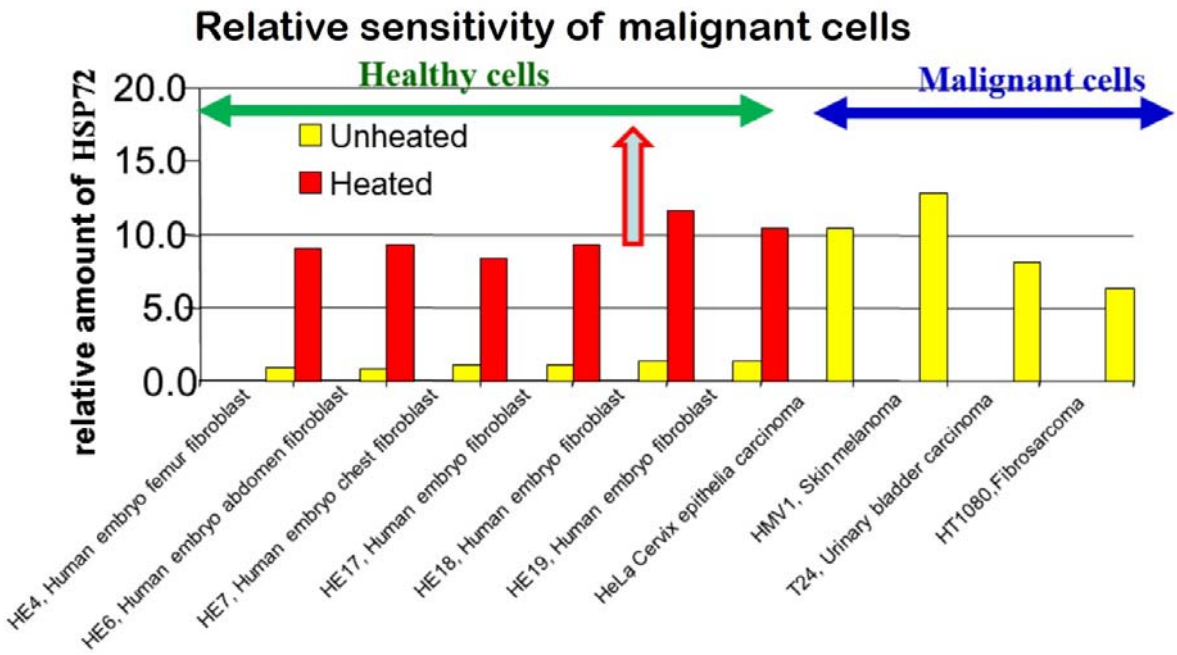
The task

Decisional point 2

Selective protection



M. Watanabe et al.: Normal human cells at confluence get heat...
Carcinogenesis vol. 16. no. 10 pp. 2373-2380, 1995



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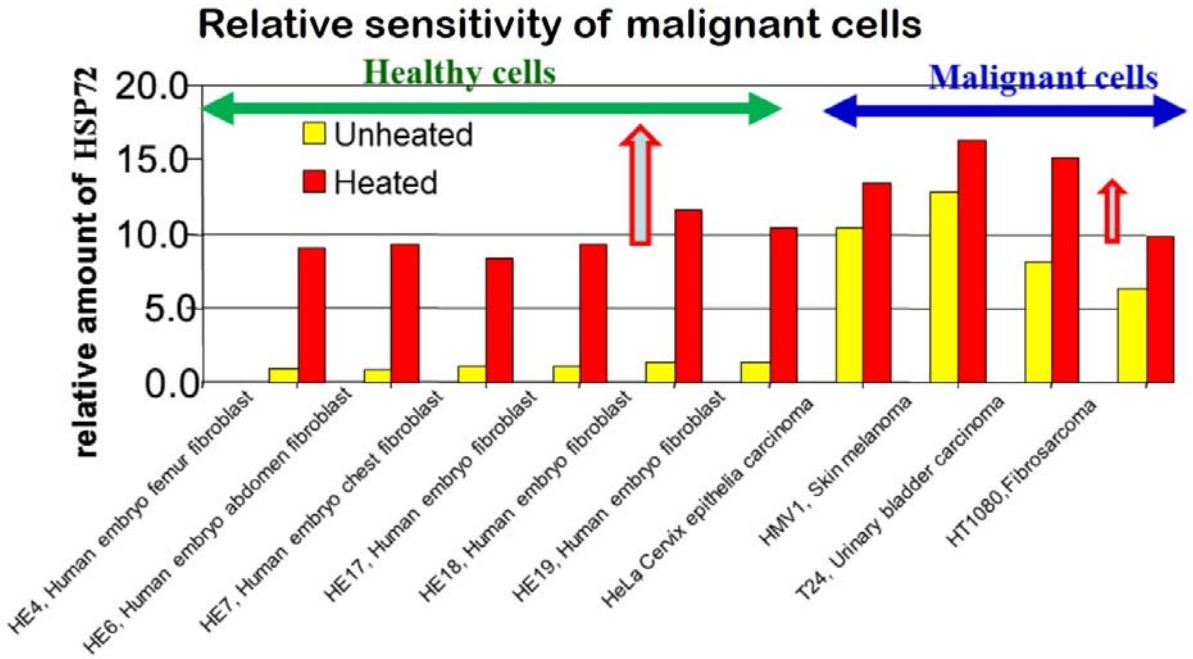
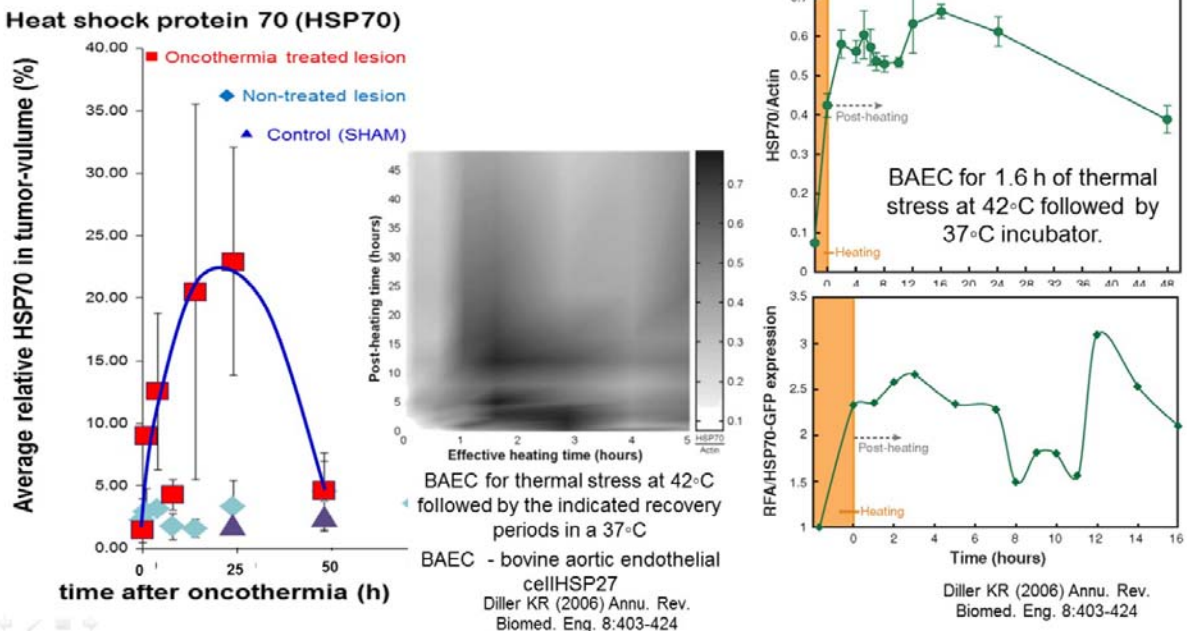


M. Watanabe et al.: Normal human cells at confluence get heat...
Carcinogenesis vol. 16. no. 10 pp. 2373-2380. 1995

Relative sensitivity of malignant cells



The task

Decisional point 3

The threshold challenge

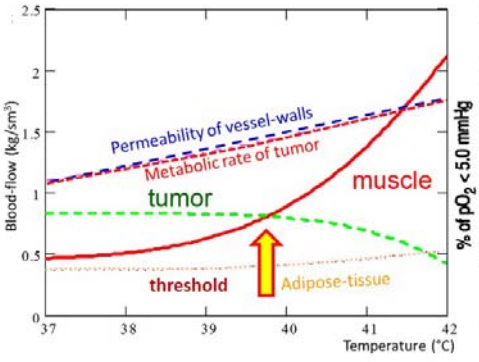
Threshold challenges

Hyperthermia is mostly complementary treatment

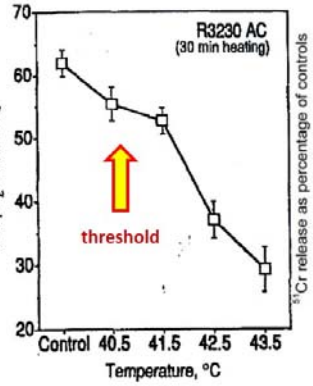
- **Chemotherapy needs high blood-flow to deliver the drug**
- **Radiotherapy needs high blood-flow for proper oxygen content**
- **Immuno-simulation needs higher blood-flow and fever**

Hyperthermia sensitizes all the "gold-standards", it looks perfect sensitizer

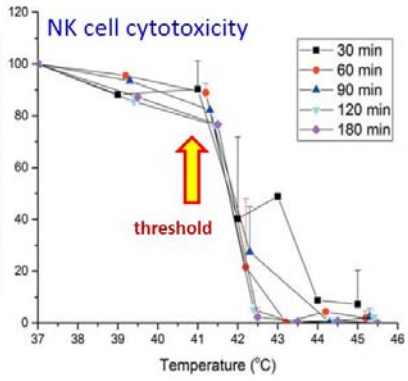
However, as usually, the overdosing of the therapy turns the usefulness



Erdmann B., Lang J. Seebass M.: Optimization of temperature distributions for regional hyperthermia based on a nonlinear heat transfer model, Annals of NYAS, 858, 36-46, September 1998



Song CW et.al: (2009) Tumor oxygenation is increased by hyperthermia at mild temperatures, Int.J. Hyperthermia, 25:91-95

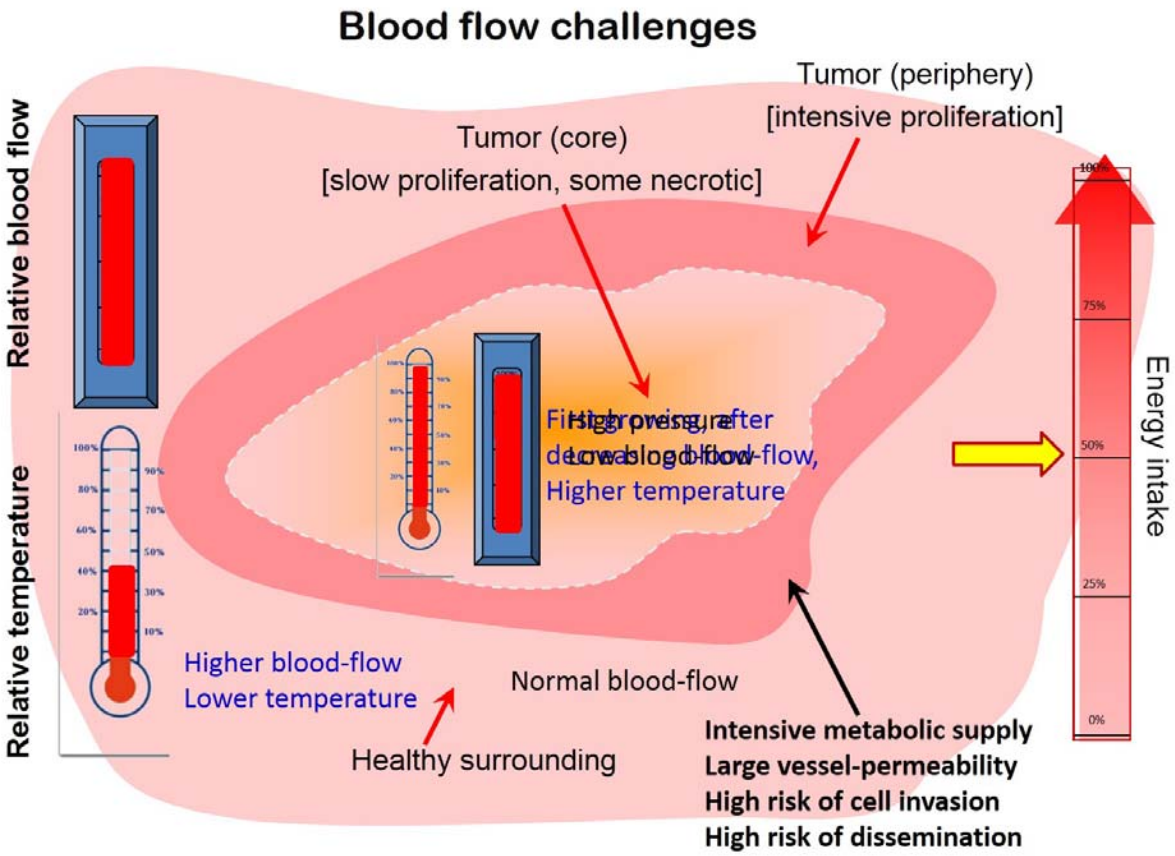


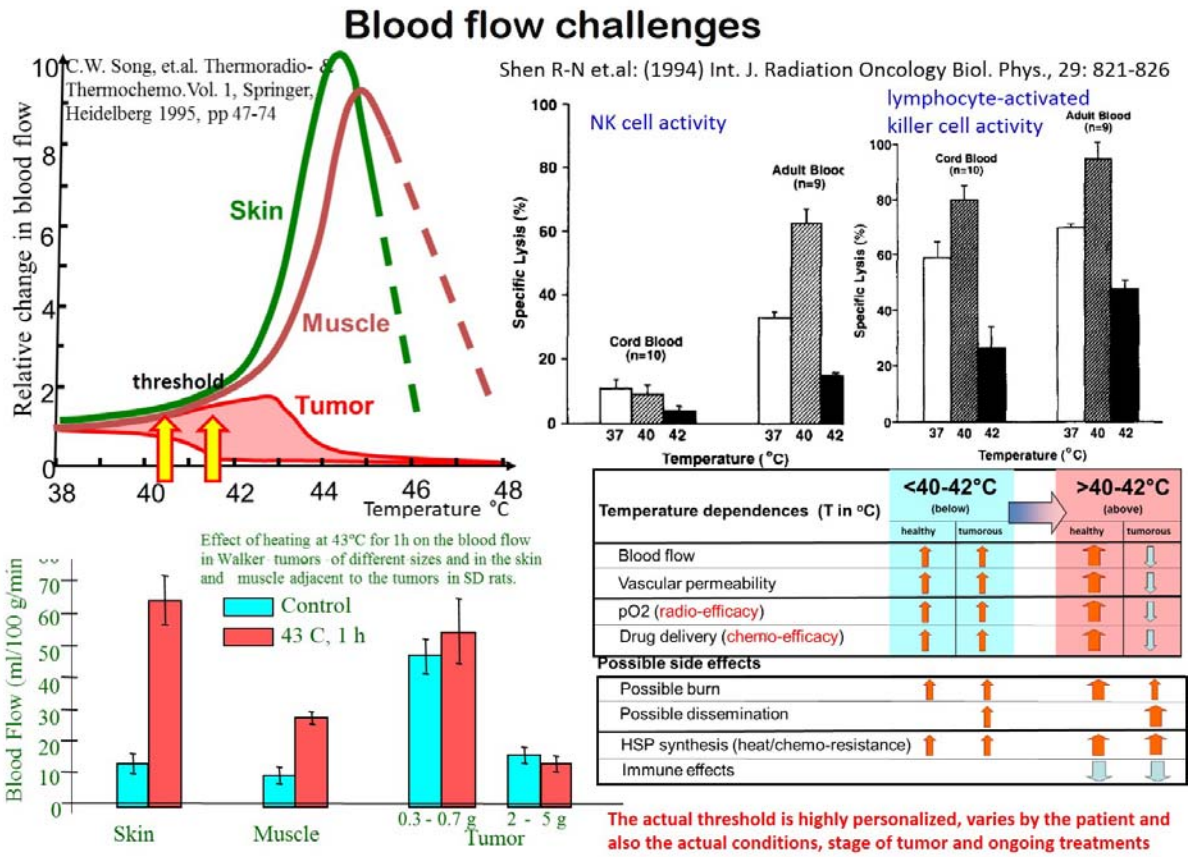
Hietanen T et al. Restoring Natural Killer Cell Cytotoxicity After Hyperthermia Alone or Combined with Radiotherapy, ANTICANCER RESEARCH *36*: 555-564 (2016)

The task

Decisional point 4

The blood-flow challenge



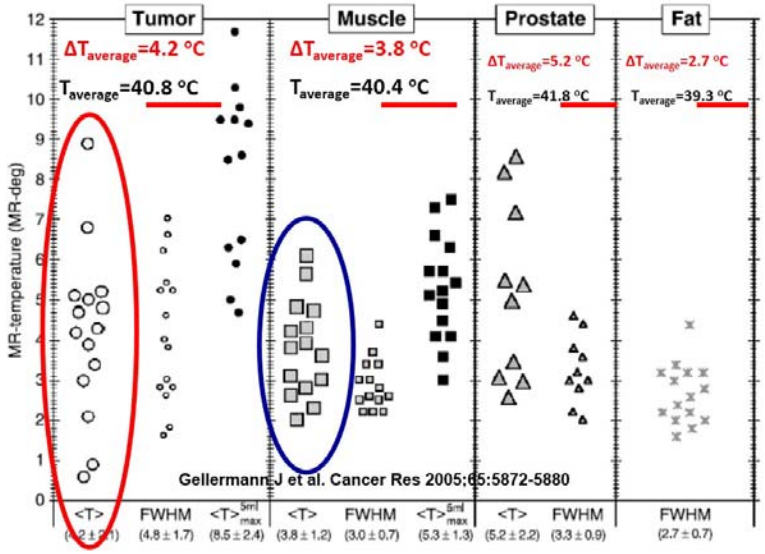


The task

Decisional point 5

The heterogeneity challenge

Heterogeneity of temperature

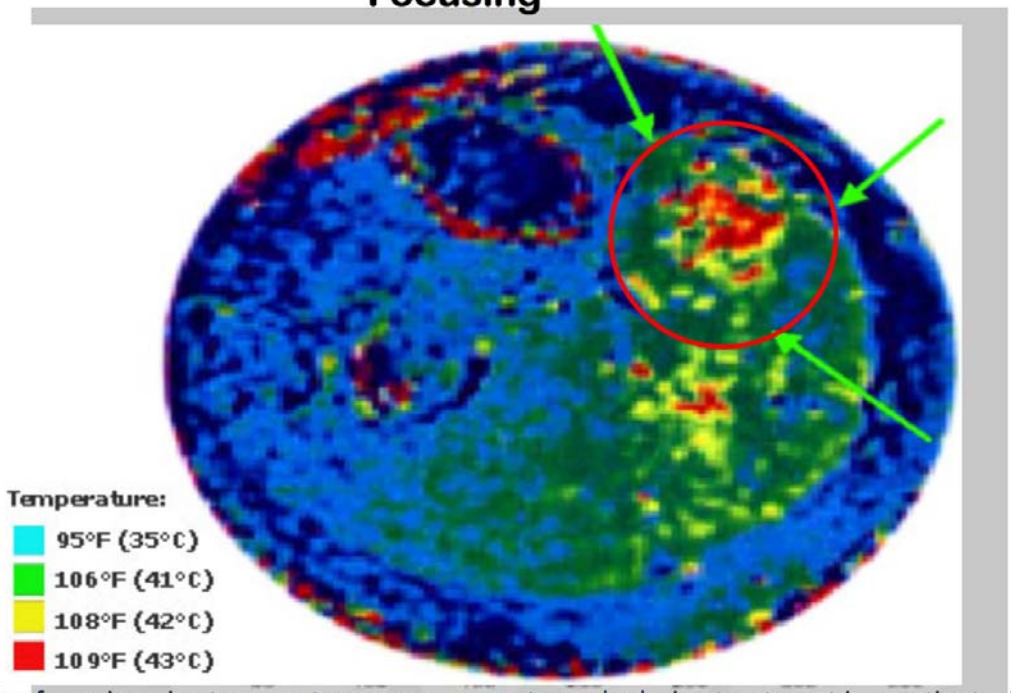


The task

Decisional point 6

The focusing challenge

Focusing



Example of non-invasive temperature measurements made during treatment in a patient with a soft tissue sarcoma of the lower leg (arrows). The colors indicate the temperatures reached during this part of the treatment, which range from 95-109°F (35-42.7°C).

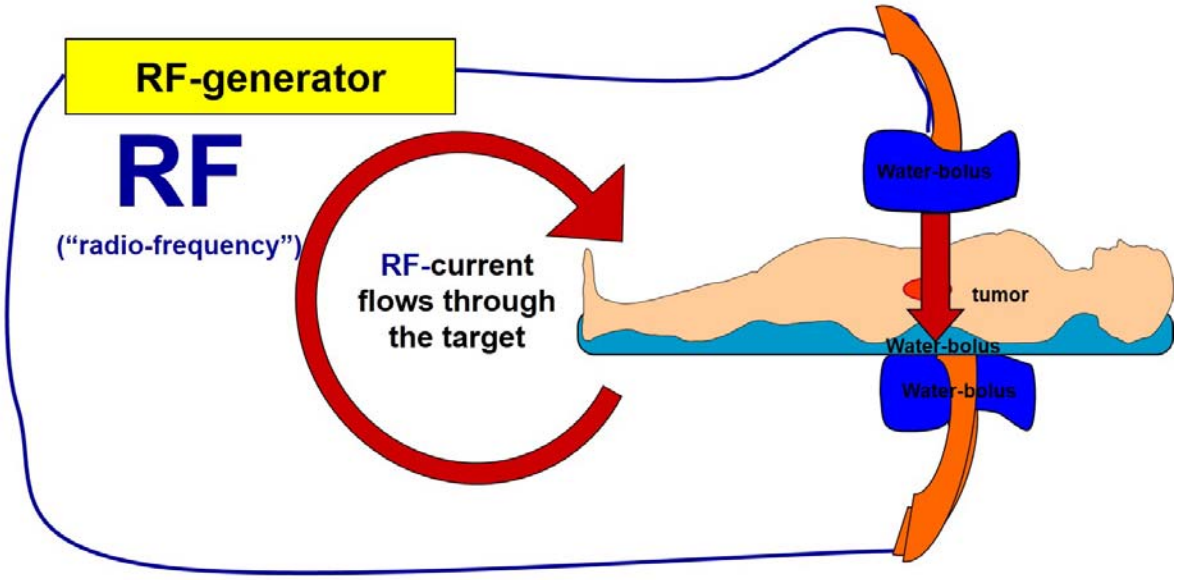
http://hyperthermia.mc.duke.edu/sp_research.htm

The task

Decisional point 7

The matching challenge

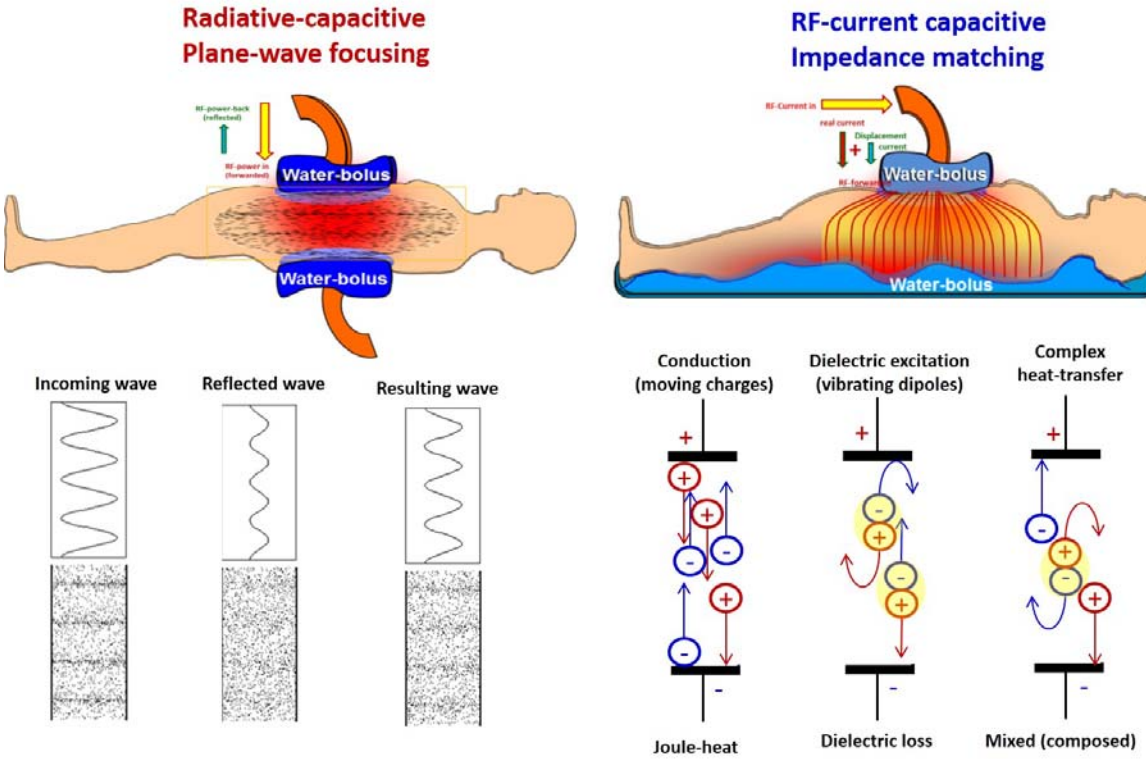
Type of treatment



Energy is carried by RF-current, targeting the absorbers

Patient is a part of the RF electric circuit

Principles of capacitive electric targeting



The task

Decisional point 8

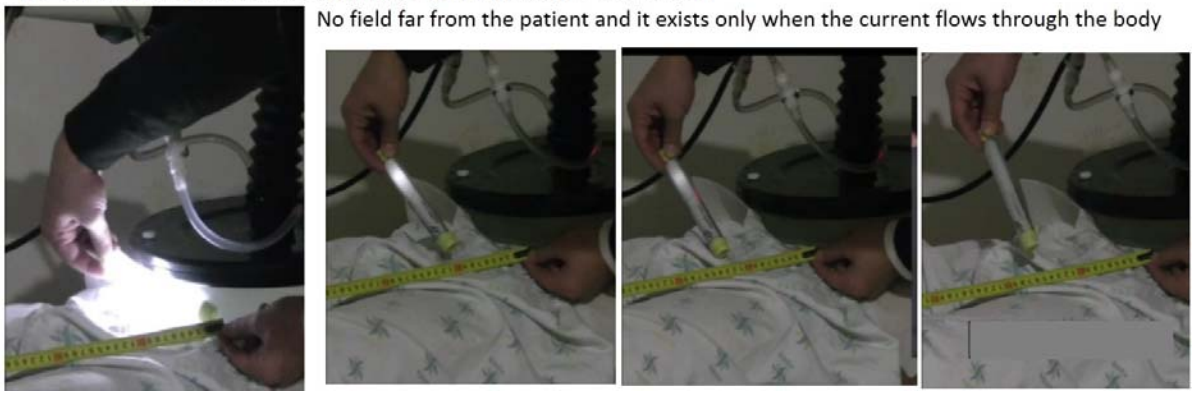
Targeting (safety) challenge

Differences between the capacitive couplings

Radiative capacitive coupling: long distance radiation, even without patient

RF-current capacitive coupling: short distance radiation

No field far from the patient and it exists only when the current flows through the body



The task

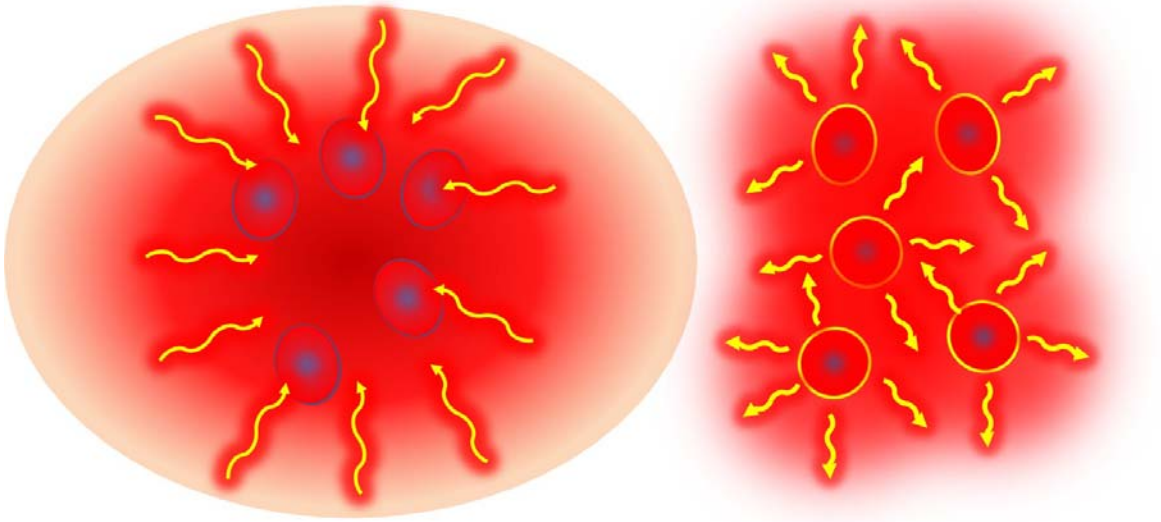
Decisional point 9

The heat-flow challenge

Concept of homogenic and heterogenic heating

Conventional homogeneous heating
(radiation + conduction + convection)

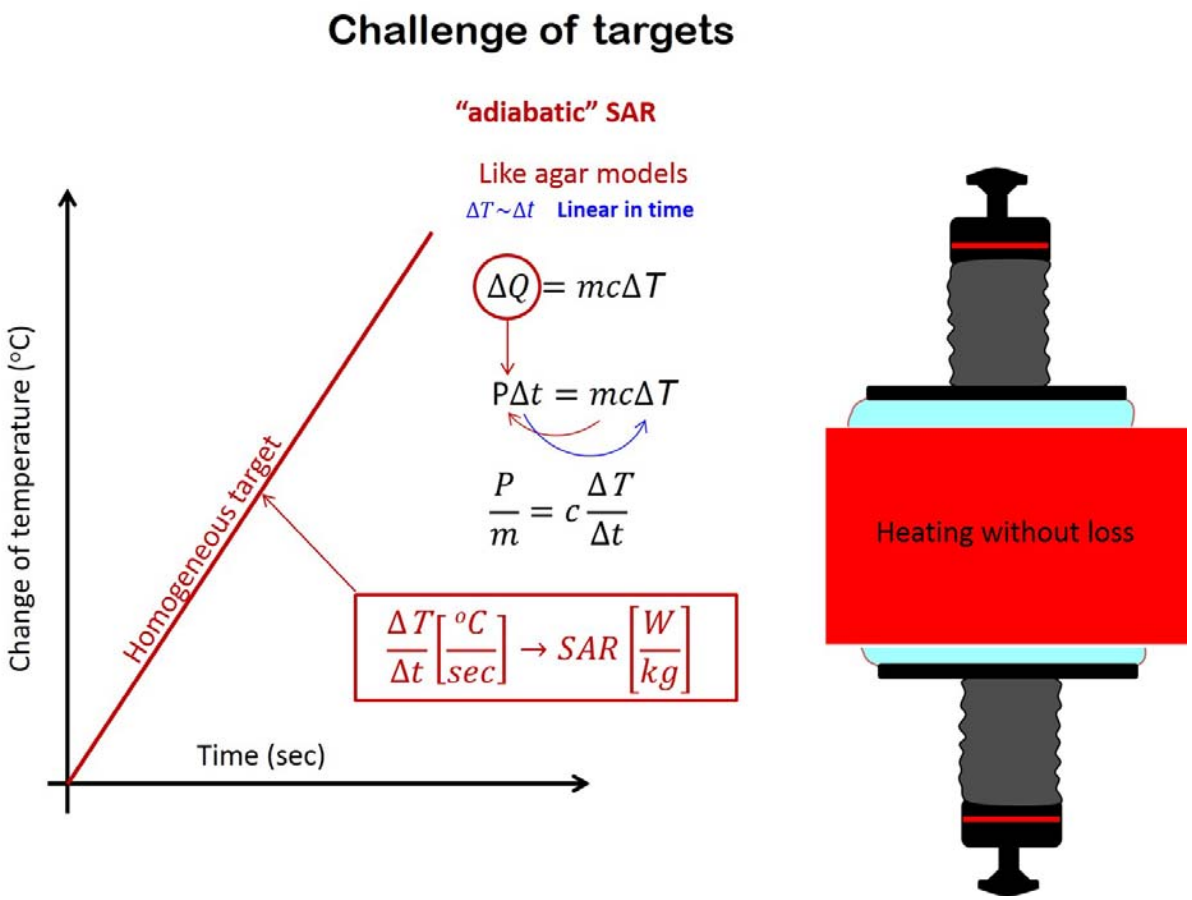
Selective heterogeneous heating
(targeting tissues, groups of molecules, etc.)



The task

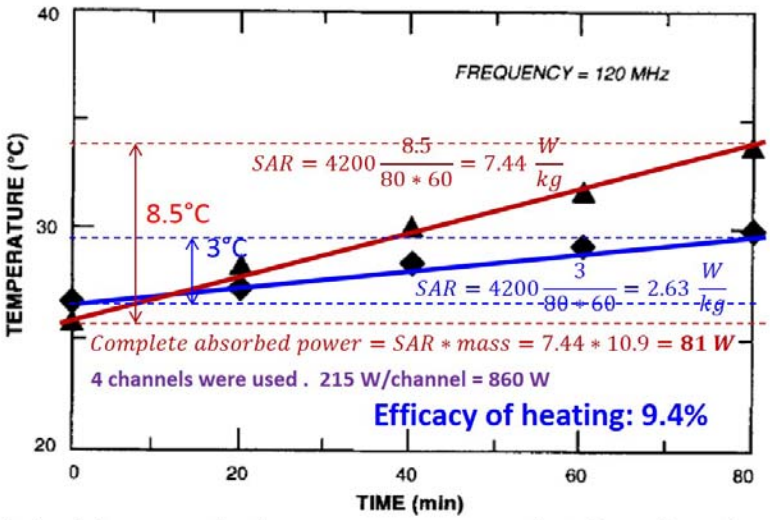
Decisional point 10

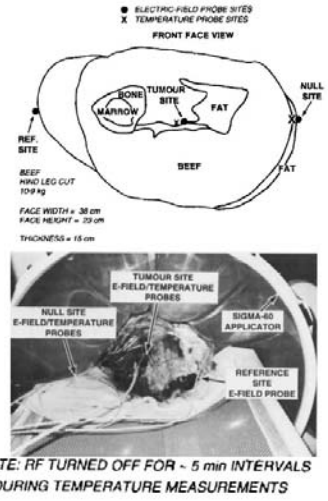
The dosing challenge



Challenge of unknown losses: BSD2000

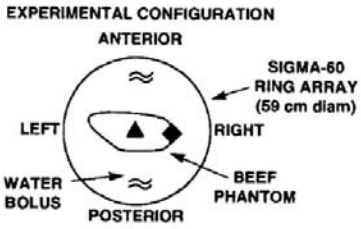
Temperature Measured temperatures in the beef phantom. Eighty minutes after the start of the experiment. **a 4°C** higher temperature exists at the tumor site (Δ) compared to the null site (◆).





NOTE: RF TURNED OFF FOR ~ 5 min INTERVALS DURING TEMPERATURE MEASUREMENTS

The beef phantom used in these experiments is a tapered cut obtained from the hind leg just above the knee. The front face of the beef has a horizontal width of 38 cm and a vertical height of **23** cm. The thickness of the beef is 15 cm and the weight is **10.9 kg.**

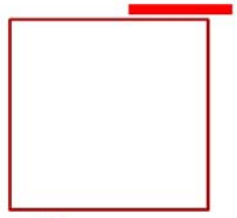


Fenn AJ. King GA. Adaptive radiofrequency hyperthermia-phased array system for improved cancer therapy: phantom target measurements. Int. J. Hyperthermia. 10:189-208 (1994)

Challenge of the unknown losses: Thermotron

Agar gel mass density is 0.999 ± 0.004 kg/liter
Liliana Aranda-Lara. Eugenio Torres-García. Rigoberto Oros-Pantoja. Biological Tissue Modeling with Agar Gel Phantom for Radiation Dosimetry of 99mTc. Open Journal of Radiology. 2014. 4. 44-52

The changes in temperature at varying depths along the central axis of cylindrical agar phantom of 25 cm diameter and 14 cm thick. The phantom was heated with a pair of electrodes of 25 cm and 10 cm diameters. The electrodes were cooled with 20°C saline bolus and the power applied was 700 W.



$M = \frac{\pi h \rho}{3}(r^2 + R^2 + rR)$
$M \cong 1.4\ kg$

$SAR = 4200\frac{9}{7*60} = 90\ \frac{W}{kg}$

$SAR = 70\ \frac{W}{kg}$

$SAR_{average} = 70\ \frac{W}{kg}$

$SAR = 40\ \frac{W}{kg}$

$SAR = 35\ \frac{W}{kg}$

$Complete\ power = SAR * mass = 70 * 1.4 = 98\ W$

700 W was used, efficacy is 14%

Song CW. Rhee JG. Lee CKK. Levitt SH. Capacitive heating of phantom and human tumors with an 8 MHz radiofrequency applicator (Thermotron rf-8) Int. J. Radiation Oncology Biol. Phys . 12:365-372 (1986)

Deep-temperature measurements

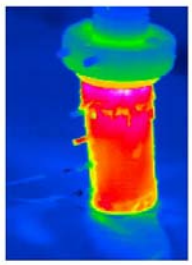
$V = 25 * 3.14 * 31 = 2434\ cm^3$

Mass = $2.3\ kg$

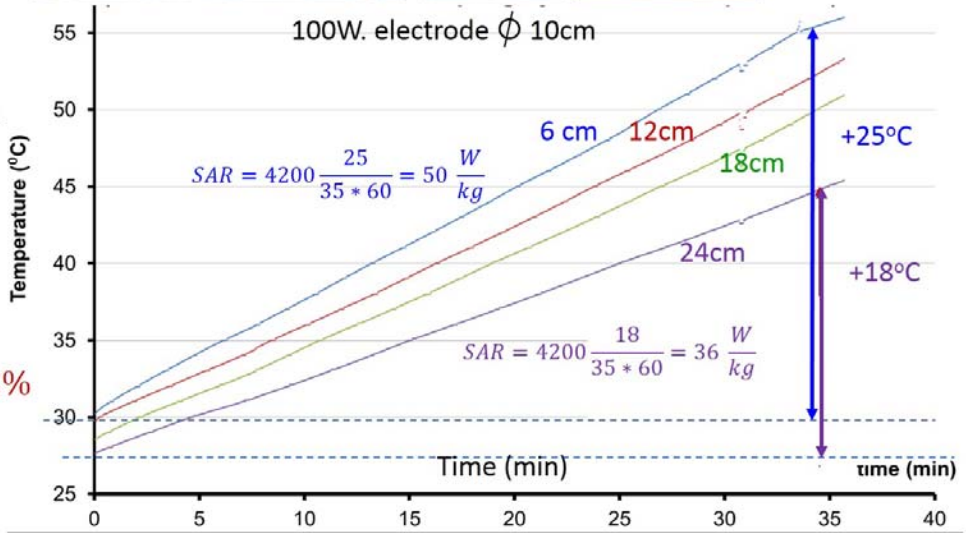
Mean-energy =

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

Efficacy = 92%



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

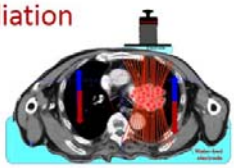


Dose for thermal effect

The normal dose of thermal effect depends on the energy absorption of the target.

When the absorption efficacy is low (like BSD < 10%. Thermotron < 15%) then the only way to measure the absorbed energy is the temperature because the forwarded power veer weekly depends on the useful energy absorption.

When the absorption efficacy is high (like oncothermia > 90%) then the classical measurement of the absorbed energy is the dose like in the ionizing radiation therapies.



Open Journal of Biophysics, 2015, 5, 97-114
Published Online October 2015 in SciRes. http://www.scirp.org/journal/ojbiphy
http://dx.doi.org/10.4236/ojbiphy.2015.54009

Scientific Research Publishing

Generalization of the Thermal Dose of Hyperthermia in Oncology

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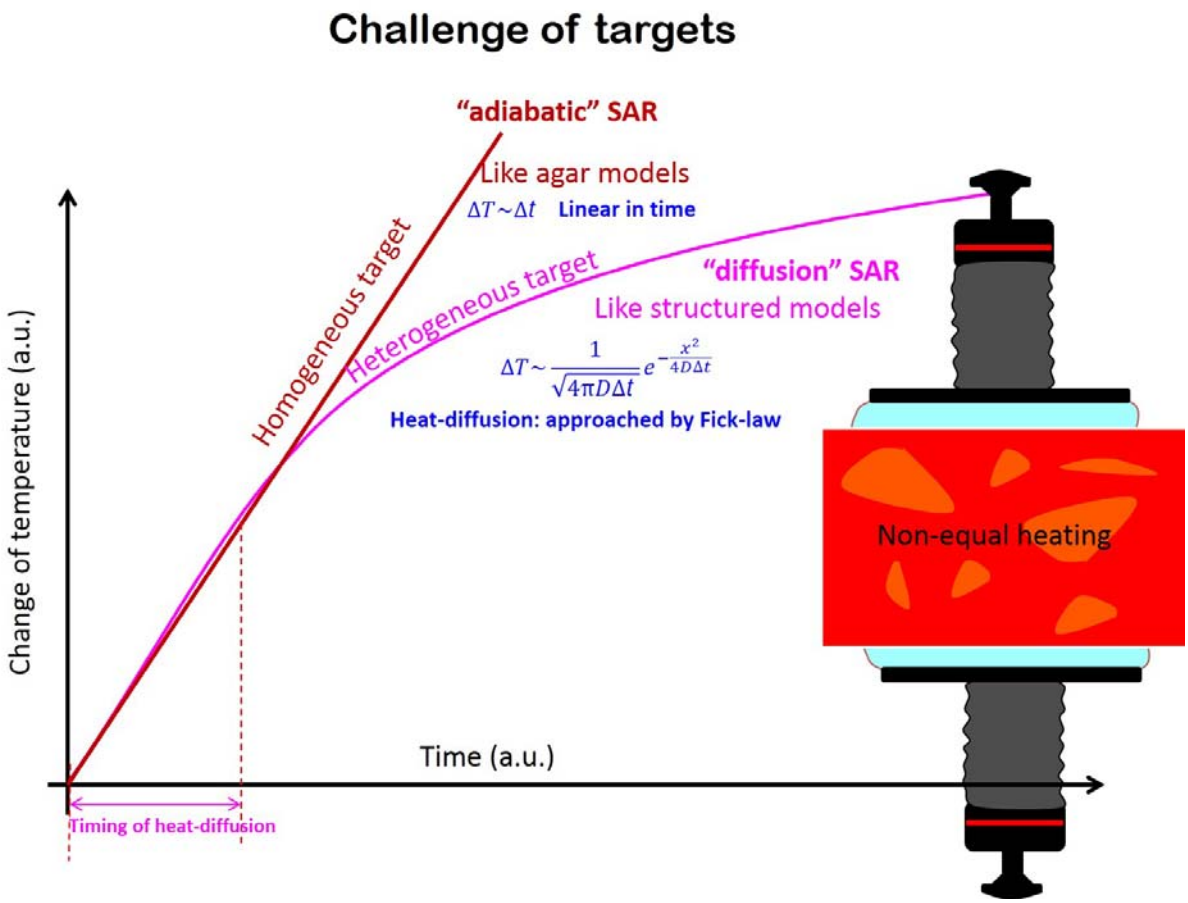
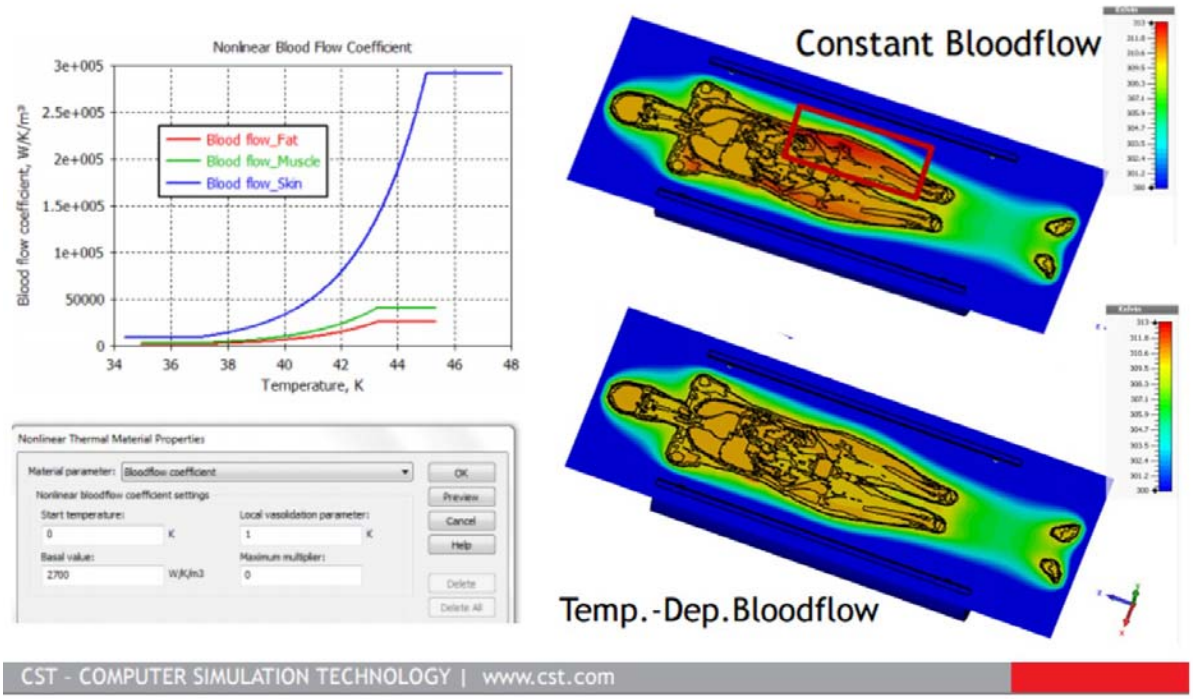


The task

Decisional point 11

The physio-feedback challenge

Challenge of the model-construction



https://www.cst.com/Content/Events/Downloads/euc2014/4.2.3.pdf

The task

Decisional point 12

The principle challenge and its consequences

Comparison of the basic principles, the mechanism of action, the technical realization and its biological effects of Thermotron and Oncothermia method

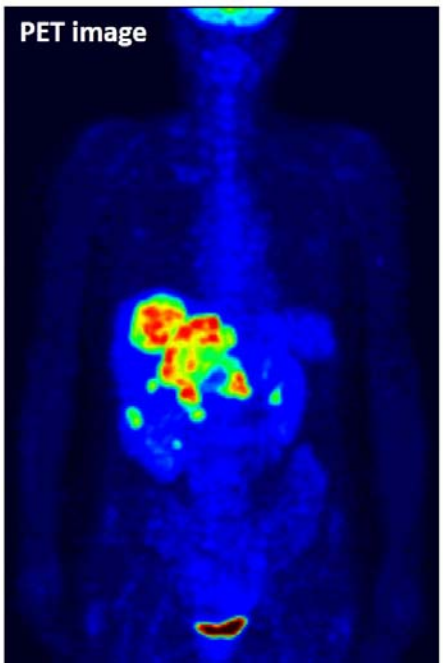
RF-hyperthermia
Thermotron RF-8

Vs.

Oncothermia
EHY-2000

The similarity

Both methods take advantage on the same principle:
Tumor tissue has higher RF absorption than the healthy tissue



Malignant tissue has much higher glucose influx and higher metabolic rate than healthy tissue (FDG-PET is based on this phenomenon)

↓

Increased concentration of metabolites in the extracellular electrolyte in the malignant tissue

↓

High ionic concentration

↓

High electrical conductivity

The higher electrical conductivity can be directly measured!

INSTITUTE OF PHYSICS PUBLISHING
PHYSIOLOGICAL MEASUREMENT
Physiol. Meas. 24 (2003) 251–260
PII: S0967-3334(03)56535-2

In vivo electrical conductivity of hepatic tumours

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[3] Department of Electronics Engineering, King Mongkut's Institute of Technology Ladkrabang, Chulongkrung Road, Ladkrubang, Bangkok, 10520, Thailand
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E-mail: haemmeri@surgery.wisc.edu

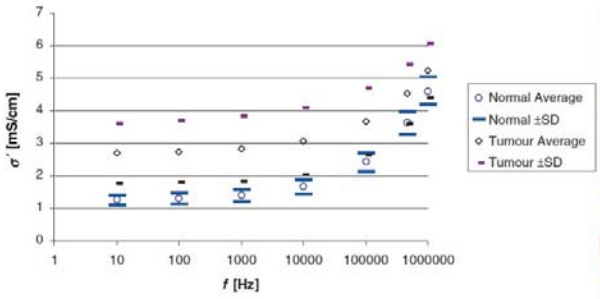

Figure 4. Mean ± SD. Electrical conductivity of tumour and normal liver tissue.

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In Vivo MRI Electrical Impedance Tomography (MREIT) of Tumors

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A significant increase in electrical conductivity of neoplasticities compared to healthy tissues and benign formations has been reported in several studies. We previously reported preliminary results with MR based Electrical Impedance Tomography (MREIT) on several phantoms and a single animal. In the presented study, we applied the technique on ten tumor-bearing rats and collected MREIT images to investigate the potential of MREIT for characterizing malignant tumors. Results show that the tumors had significantly higher mean conductivity compared to the mean of conductivity in the rest of the body. Although heterogeneity of conductivity was observed in the tumor, the mean was still higher than the background.

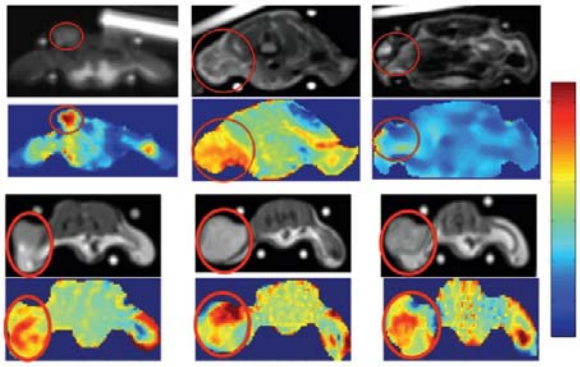


Figure 4: Structural and MREIT images of six animals are illustrated. Anatomic (T2 weighted) scans are displayed in gray levels and corresponding impedance (MREIT) images are depicted in color right below the T2 weighted images. Each image pair shows axial images from different animals. Tumor areas are circled with red lines. Bright objects outside the animals' body were markers to identify exact location of electrodes.

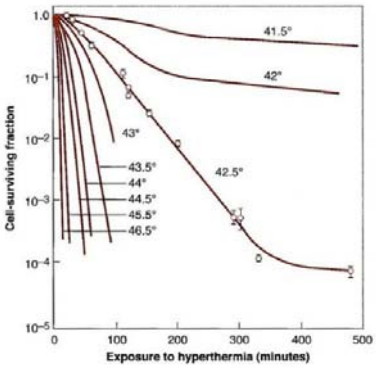
The difference : basic principle in tumor cell destruction

RF-hyperthermia
Thermotron RF-8

Oncothermia
EHY-2000

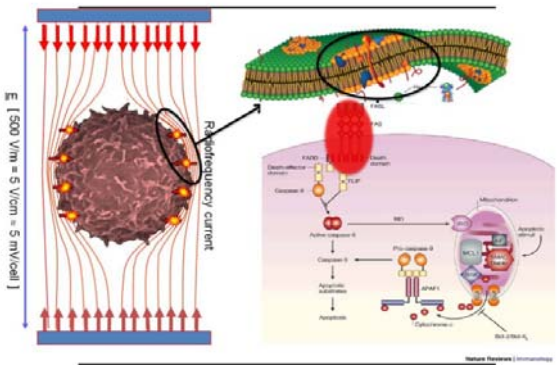
Classic hyperthermia concept:
Reach the cytotoxic level temperature range (>43°C) quickly and keep the tumor on this temperature range as necessary

Homogenous, equilibrium heating – the **tumor temperature is very important**



New hyperthermia concept:
Keep the tumor temperature below the cytotoxic range (<42°C) but induce continuous temperature gradient on the tumor cell membrane

Inhomogenous, non-equilibrium heating – **the temperature gradient is important**



Consequences of the different basic principles

RF-hyperthermia
Thermotron RF-8

Oncothermia
EHY-2000

Classic hyperthermia concept:
Homogenous, equilibrium heating at cytotoxic temperature range

↓

Necrotic cancer cell death, the tumor destruction rate is highly temperature dependent

↓

Significant protein denaturation, tumor antigens also destroyed

↓

Inflammation

↓

Limited possibility for immunotherapy combinations

New hyperthermia concept:
Inhomogenous, non-equilibrium heating below cytotoxic temperature range

↓

Temperature gradient on the membrane induce signal transduction pathways resulting programmed cancer cell death

↓

No protein denaturation occur, tumor antigens became recognizable, DAMP is generated

↓

Immunogenic cancer cell death

↓

Good basis for immunotherapy combinations

Experimental proofs of the new hyperthermia concept

Tsang *et al. BMC Cancer* (2015) 15:708
DOI 10.1186/s12885-015-1690-2

BMC Cancer

RESEARCH ARTICLE Open Access

Improving immunological tumor microenvironment using electro-hyperthermia followed by dendritic cell immunotherapy

Yuk-Wah Tsang[1,2], Cheng-Chung Huang[3], Kai-Lin Yang[3], Mau-Shin Chi[3], Hsin-Chien Chiang[3], Yu-Shan Wang[3], Gabor Andocs[4], Andras Szasz[5], Wen-Tyng Li[3*] and Kwan-Hwa Chi[3,6*]

Abstract

Background: The treatment of intratumoral dentritic cells (DCs) commonly fails because it cannot evoke immunity in a poor tumor microenvironment (TME). Modulated electro-hyperthermia (mEHT, trade-name: oncothermia) represents a significant technological advancement in the hyperthermia field, allowing the autofocusing of electromagnetic power on a cell membrane to generate massive apoptosis. This approach turns local immunogenic cancer cell death (apoptosis) into a systemic anti-tumor immune response and may be implemented by treatment with intratumoral DCs.

Methods: The CT26 murine colorectal cancer model was used in this investigation. The inhibition of growth of the tumor and the systemic anti-tumor immune response were measured. The tumor was heated to a core temperature of 42 °C for 30 min. The matured synergetic DCs were intratumorally injected 24 h following mEHT was applied.

Results: mEHT induced significant apoptosis and enhanced the release of heat shock protein70 (Hsp70) in CT26 tumors. Treatment with mEHT-DCs significantly inhibited CT26 tumor growth, relative to DCs alone or mEHT alone. The secondary tumor protection effect upon rechallenging was observed in mice that were treated with mEHT-DCs. Immunohistochemical staining of CD45 and F4/80 revealed that mEHT-DC treatment increased the number of leuko-cytes and macrophages. Most interestingly, mEHT also induced infiltrations of eosinophil, which has recently been reported to be an orchestrator of a specific T cell response. Cytotoxic T cell assay and ELISpot assay revealed a tumor-specific T cell activity.

Conclusions: This study demonstrated that mEHT induces tumor cell apoptosis and enhances the release of Hsp70 from heated tumor cells, unlike conventional hyperthermia. mEHT can create a favorable tumor microenvironment for an immunological chain reaction that improves the success rate of intratumoral DC immunotherapy.

Keywords: Dendritic cells, Modulated electro-hyperthermia, Immunotherapy, Tumor microenvironment

d the promotion
n signals in a colorectal
erthermia

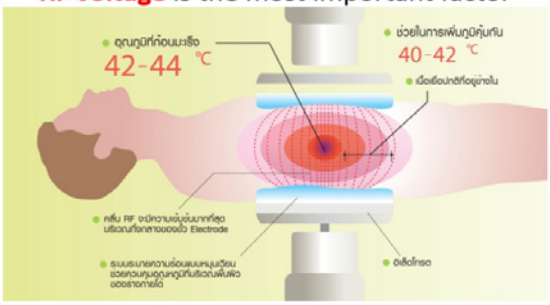
cant cell death response upon mEHT treatment
companied by the early upregulation (4-h post-
nt) of heat shock protein (Hsp70 and Hsp90)
levels. In situ, the treatment resulted in spatio-
al occurrence of a DAMP protein signal sequence
d by the significant cytoplasmic to cell membrane
cation of calreticulin at 4 h, Hsp70 between 14
h and Hsp90 between 24- and 216-h post-
nt. The release of high-mobility group box1 pro-
(MGB1) from tumor cell nuclei from 24-h post-
nt and its clearance from tumor cells by 48 h
so detected. Our results suggest that mEHT treat-
can induce a DAMP-related signal sequence in

Method of RF coupling

RF-hyperthermia
Thermotron RF-8

capacitive planewave coupling

RF voltage is the most important factor

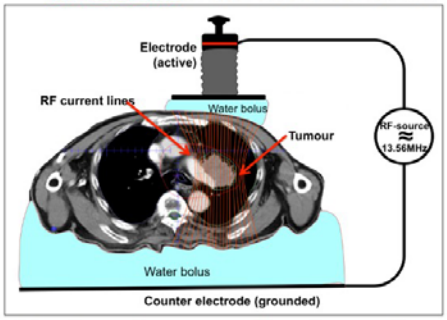


The electrodes in this case like antennas are sources of RF waves. Air layers or bubbles can not block the wave propagation in this concept.

Oncothermia
EHY-2000

capacitive impedance coupling

RF-current is the effective factor



In capacitive impedance coupling the applicators are real electrodes that need as tight connection to the target as possible, because the RF-current must flow through the target that makes the effect. The impedance is the treated body, and the biological effect is expected from the current-flow through it, so no air or unproven isolation could be applied.

II. Applied power and electrode cooling

RF-hyperthermia
Thermotron RF-8

Relatively weak coupling +necessity of high temperature range to reach the cytotoxic level

1500 W

The very high RF power needs extreme surface cooling to prevent the skin burn

⬇

The cooling water temperature is around +4 °C

⬇

Skin surface temperature is below the physiologycal range

Oncothermia
EHY-2000

Strong impedance coupling + mild hyperthermia range

150 W

The low RF power needs only moderate cooling

⬇

The cooling water temperature is around +25 °C

⬇

Skin surface temperature is in the physiologycal range

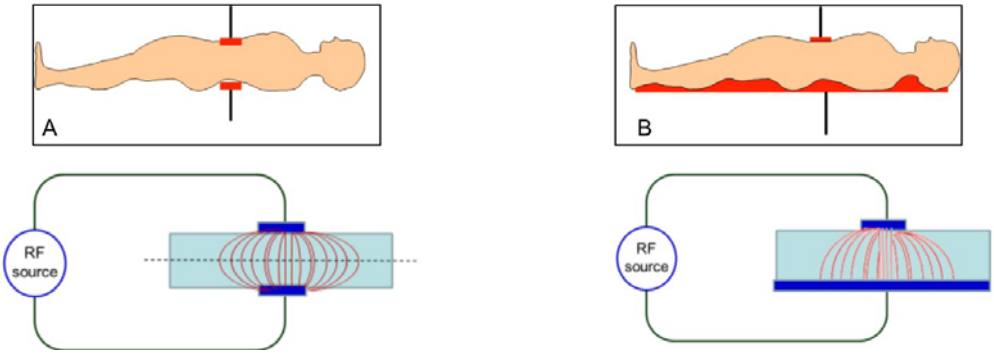
RF-hyperthermia
Thermotron RF-8

III. Electrode configuration

Oncothermia
EHY-2000

Double symmetric electrode configuration:
In geometry: two equal size and shape electrodes
In electronics: both electrodes are equal

Double assymmetric electrode configuration:
In geometry: one large and one small electrode
In electronics: the large electrode is directly grounded (reference point), the smaller electrode is the active electrode



IV. Operation frequency

RF-hyperthermia
Thermotron RF-8

Oncothermia
EHY-2000

8 MHz

⬇

Not a free frequency

⬇

Can not be used freely

⬇

The operation of the RF-8 system needs a special, very expensive RF shielded room

13.56 MHz

⬇

ISM band - free frequency

⬇

Can be used without a limitation

⬇

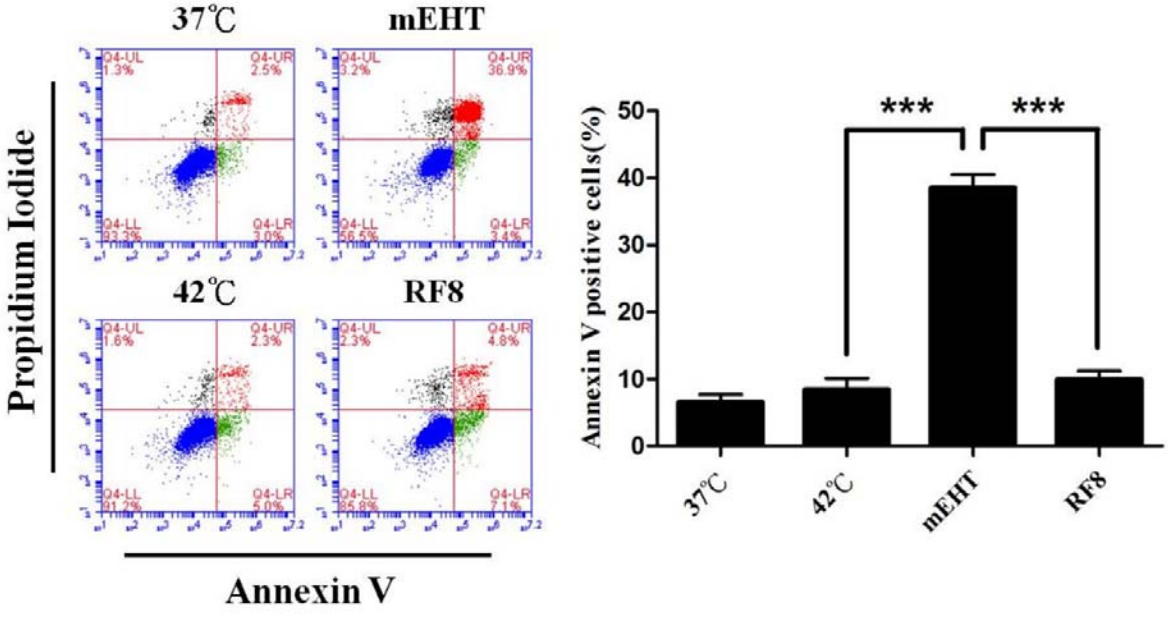
The EHY-2000 device can be operated anywhere without a shielded room

Are these challenges real?

Different basic principles of operation result different technical solutions in the device!

Experimental comparison of the induced biological effect of RF-8 and mEHT

Results

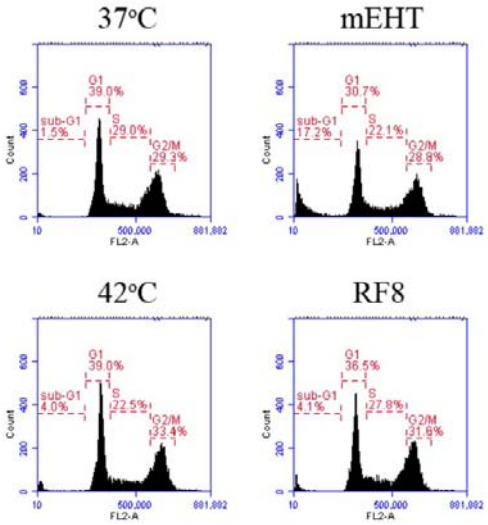


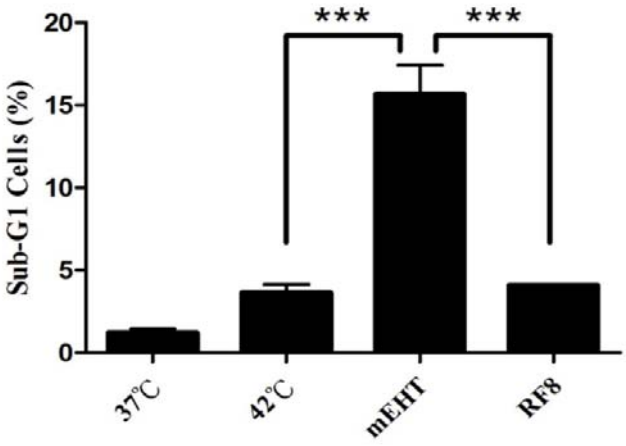
Experimental comparison of the induced biological effect of RF-8 and mEHT

Dr. Wang et al.
Taiwan National Univ.

Results

Cell death analysis: Cell cycle distribution analysis



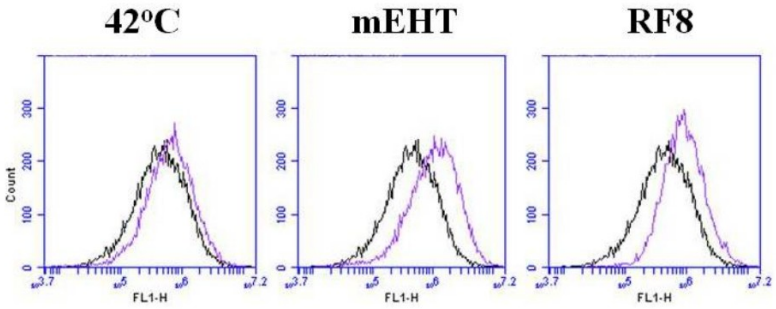


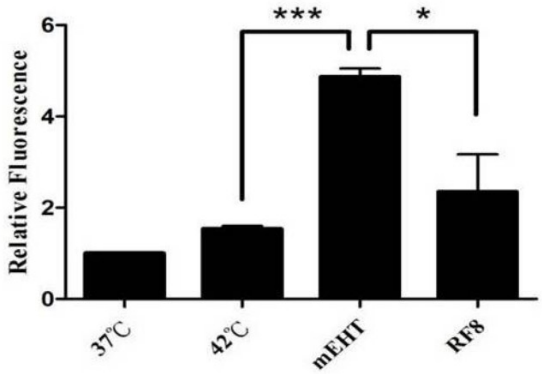
Experimental comparison of the induced biological effect of RF-8 and mEHT

Dr. Wang et al.
Taiwan National Univ.

Results

Cell death analysis: Total cellular ROS level



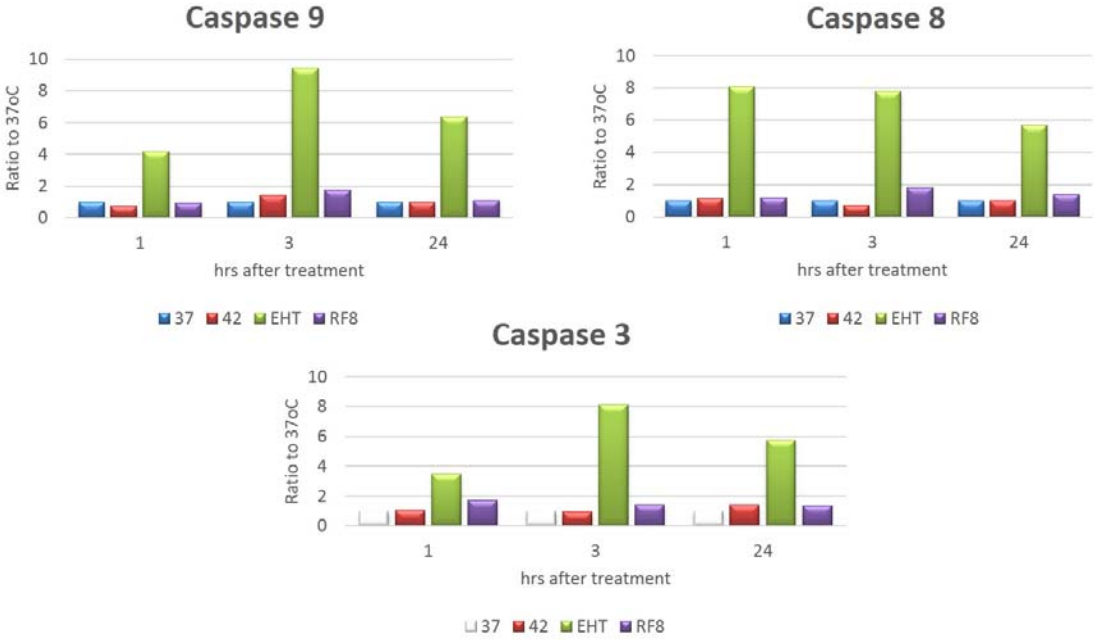


Experimental comparison of the induced biological effect of RF-8 and mEHT

Dr. Wang et al.
Taiwan National Univ.

Results

Cell death analysis: The caspase signaling pathway

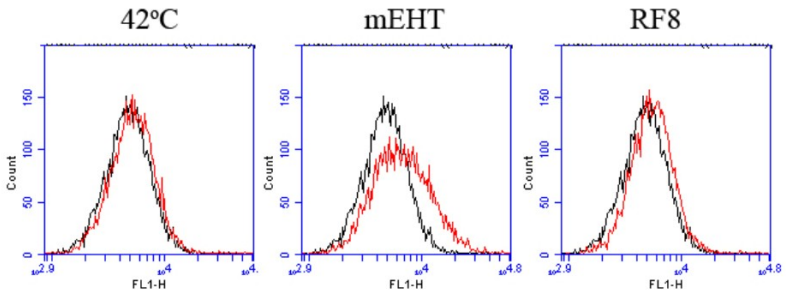


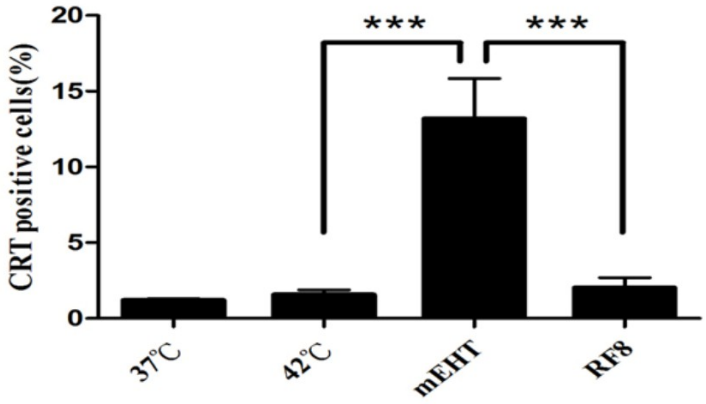
Experimental comparison of the induced biological effect of RF-8 and mEHT

Dr. Wang et al.
Taiwan National Univ.

Results

Stress protein analysis: CRT expression assay



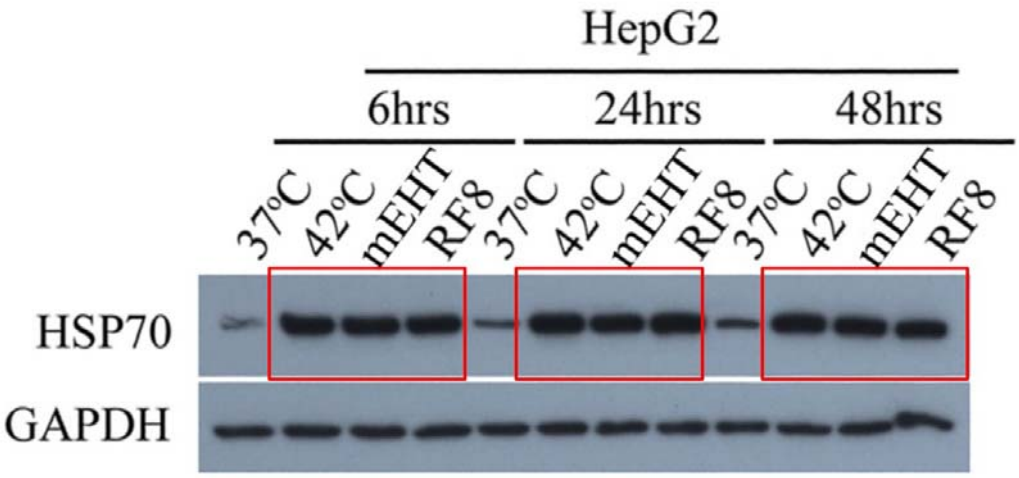


Experimental comparison of the induced biological effect of RF-8 and mEHT

Dr. Wang et al.
Taiwan National Univ.

Results

Stress protein analysis: Intracellular level of HSP70 expression



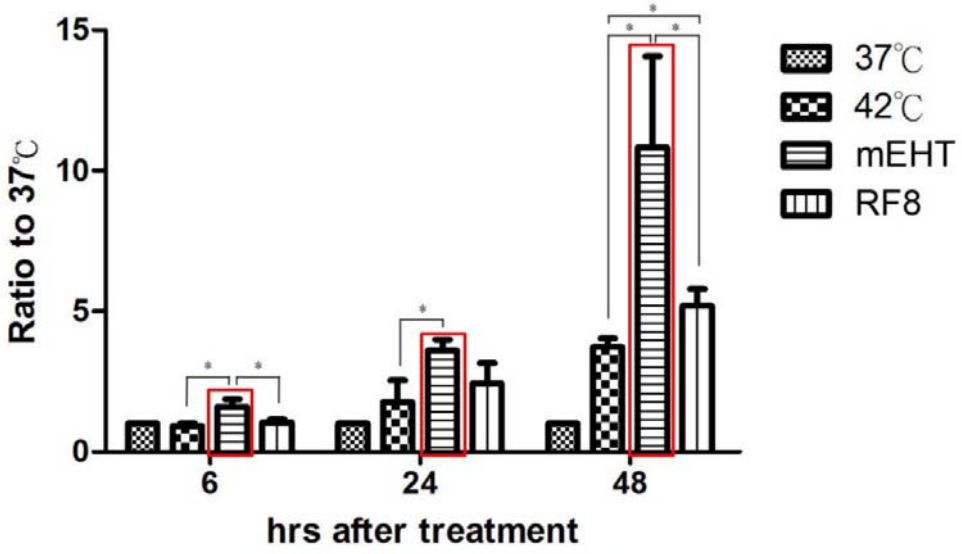
All kinds of hyperthermia could induce intracellular HSP70 expression.

Experimental comparison of the induced biological effect of RF-8 and mEHT

Dr. Wang et al.
Taiwan National Univ.

Results

Stress protein analysis: HSP70 release from the cells



Oncothermia triggered a significantly secretion of HSP70 from cancer cells.

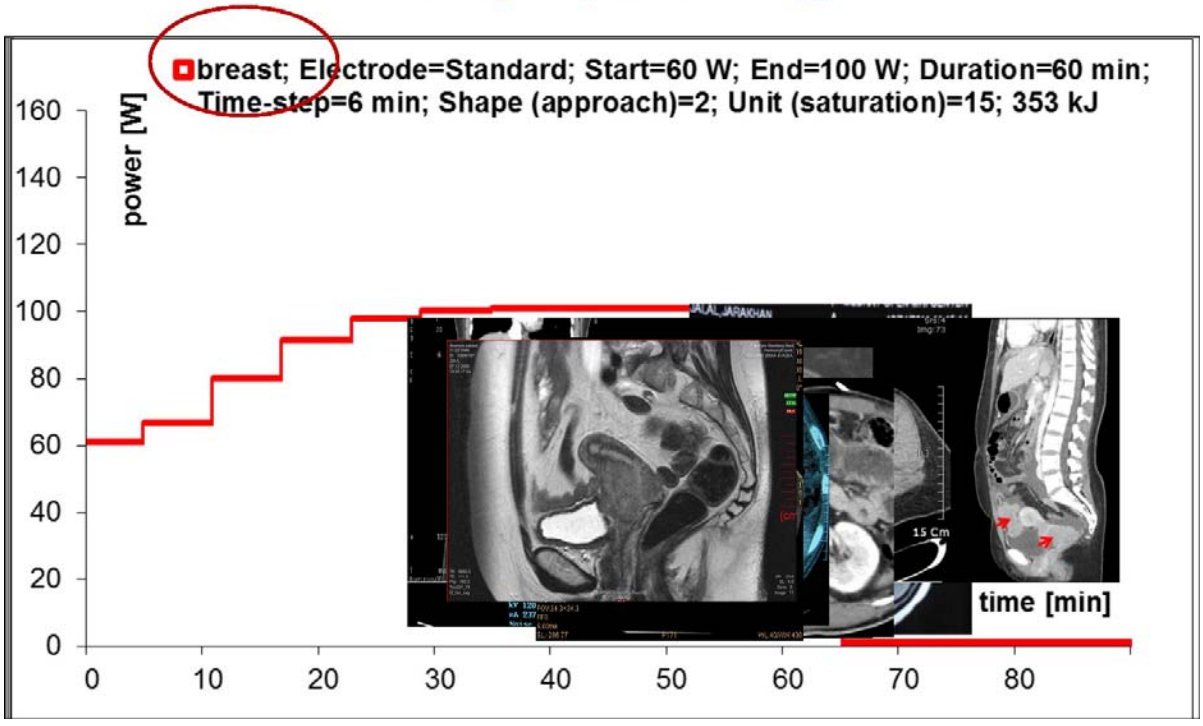
Outline

- ❑ Decisional points
- ❑ Possible solution
- ❑ Future points

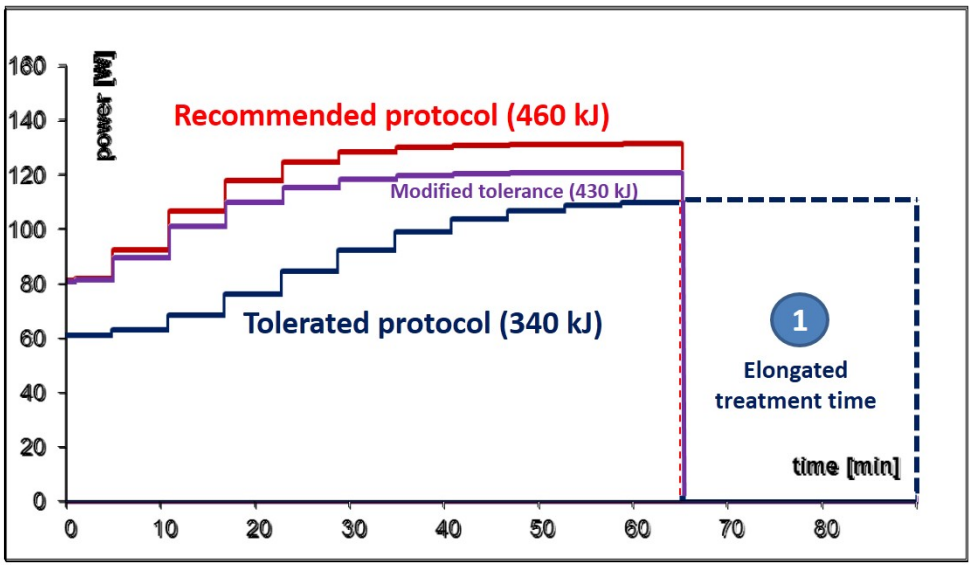
- ○ Take-home messages

Protocol examples with chemotherapy

Step-up heating!



Considering the personal tolerance with chemotherapy



The difference is 120 kJ

However, it could approach the recommended by increasing tolerance

2

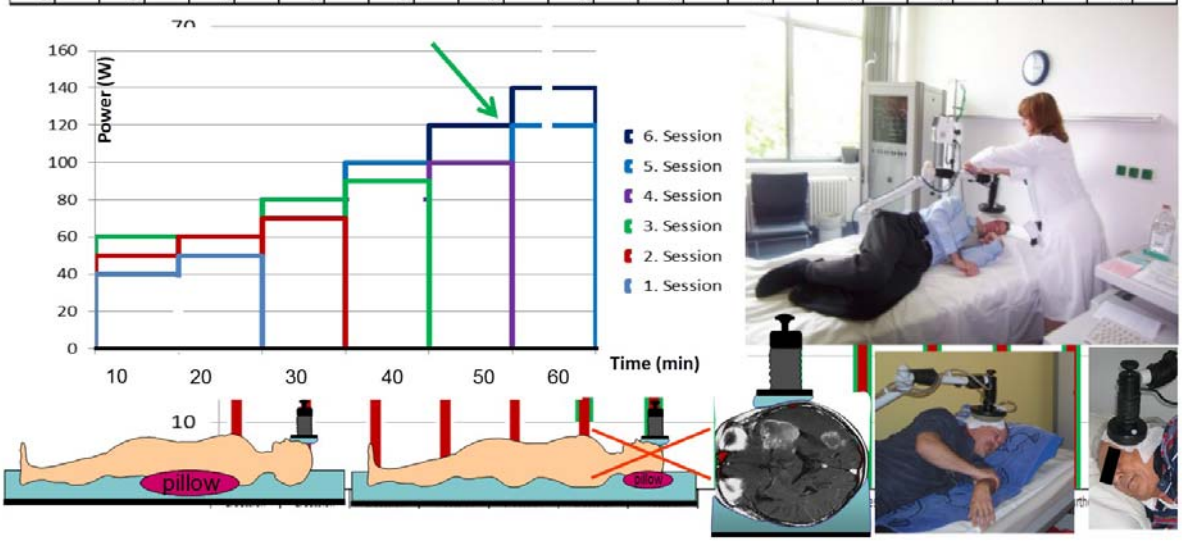
Collect the differences and correct the number of sessions with their sum!

Oncothermia for central nervous system with chemotherapy

It needs special care and protocol

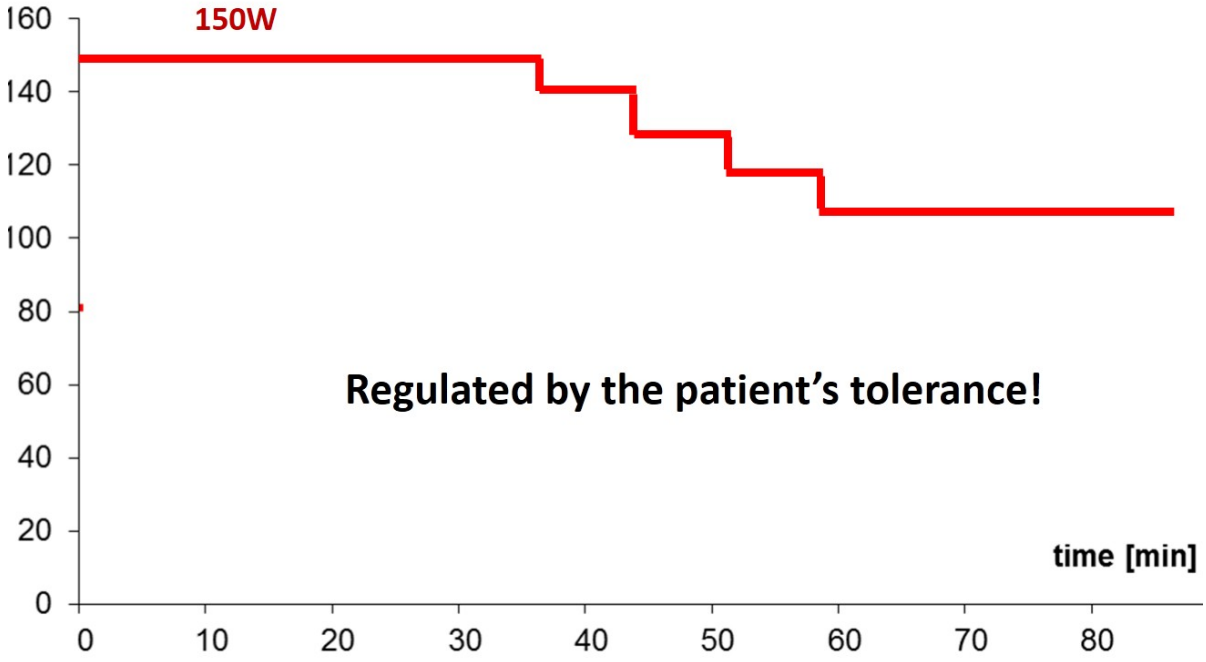
Protocol of Neurology Clinic of Medical School of Regensburg University, Germany

1. Session		2. Session		3. Session		4. Session		5. Session		6. Session		7. Session		8. Session		9. Session		10. Session		11. Session		12. Session		Further	
min	Watt	min	Watt	min	Watt	min	Watt	min	Watt	min	Watt	min	Watt	min	Watt	min	Watt	min	Watt	min	Watt	min	Watt	min	Watt
10	40	10	50	20	60	20	60	20	60	20	60	20	60	20	60	20	60	20	60	20	60	20	60	20	60
10	50	10	60	10	80	20	80	10	80	10	80	10	80	10	80	10	80	10	80	10	80	10	80	10	80
		10	70	10	90	10	100	20	100	10	100	10	100	10	100	10	100	10	100	10	100	10	100	10	100
								10	120	10	120	10	120	10	120	10	120	10	120	10	120	10	120	10	120
										10	140	10	140	10	140	10	140	10	140	10	140	10	140	10	140
20		30		40		50		60		60		60		60		60		60		60		60		60	



Protocol examples in monotherapy

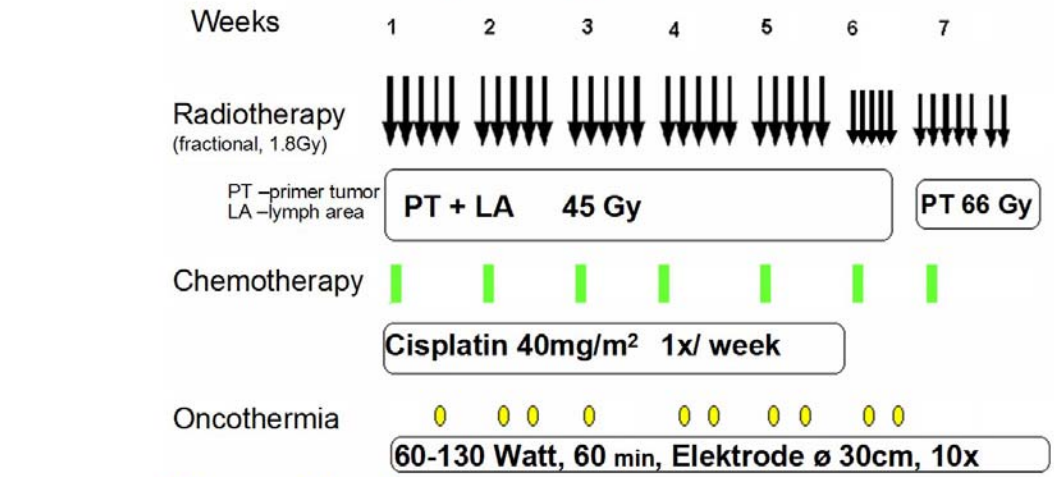
Step-down heating!

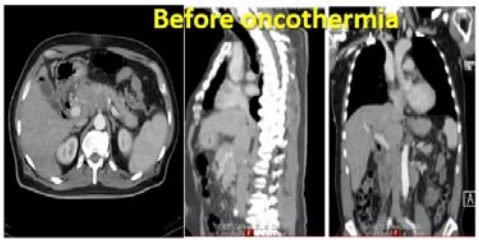


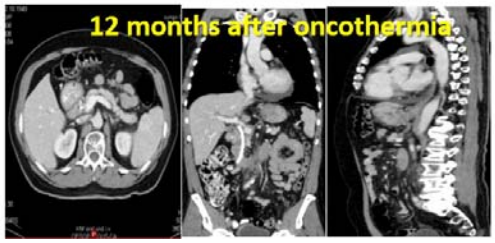
Trimodal protocol –personalized (esophagus) (2)

Investigator: Prof.H.Renner, **Institute:** Klinikum Nord, Nürnberg, Germany, **Patient:** G.U., 50 y, male, **Primer-tumor:** Esophagus carcinoma, inoperable; **Histology:** Squamous cell carcinoma G3; **Metastases:** in mediastinum & celiac ganglia

Tumor-classification: cT2 cN1 M1a G3 R2; **Result:** Complete remission (CR) **Follow-up:** after 12 month tumor-free

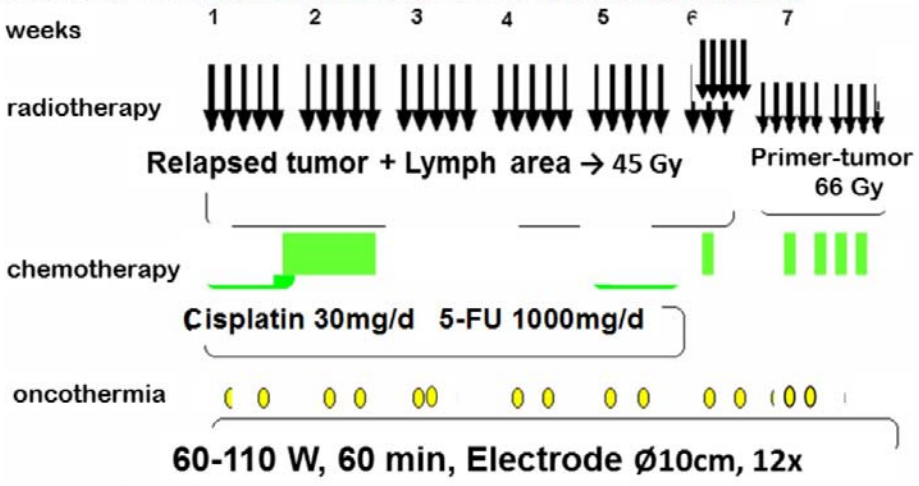




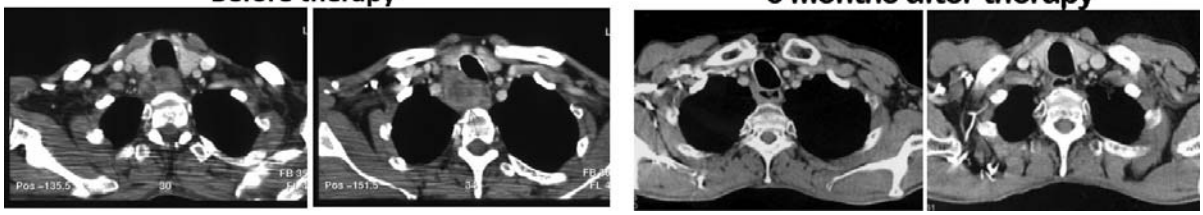


Trimodal protocol –personalized (esophagus)

Investigator: Prof.H.Renner, **Instutute:** Klinikum Nord, Nürnberg, Germany, **Patient:** H.K., 49 y, male,**Primer-tumor:** esophagus, diagn.02/03; **Histology:** Squamous cell carcinoma G3, **Resection** – **Relapse:** 06/05, inoperable **Metastases:** multilocal lymph node; **Result:** Complete remission (CR) **Follow-up:** after 30 month tumor-free,



Before therapy **6 months after therapy**



Colorectal cancer liver metastasis, (n=15)

Investigator: Prof.H.Kirchner & Dr.P.Panagiotou; **Department:** Department of Hematology & Oncology, Hospital Siloah, Hannover, Germany, **Published**: Panagiotou P, Sosada M, Schering S, Kirchner H: Irinotecan plus Capecitabine with regional electrohyperthermia of the liver as second line therapy in patients with metastatic colorectal cancer; **ESHO**, 2005, Graz, Austria,

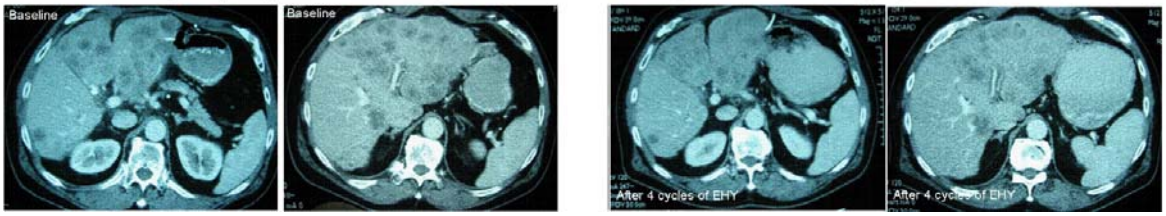
Treatment protocol in 2nd line

Drug	Day1	Day8	Day15	22
Irinotecan 80 mg/m²	X	X		Repetition
Capecitabine 2 g/m²	O O O O O O O	O O O O O O O		
Oncothermia	↓ ↓ ↓	↓ ↓ ↓	↓ ↓	

(“first line” was: Oxalyplatin & folic-acid&5-FU)

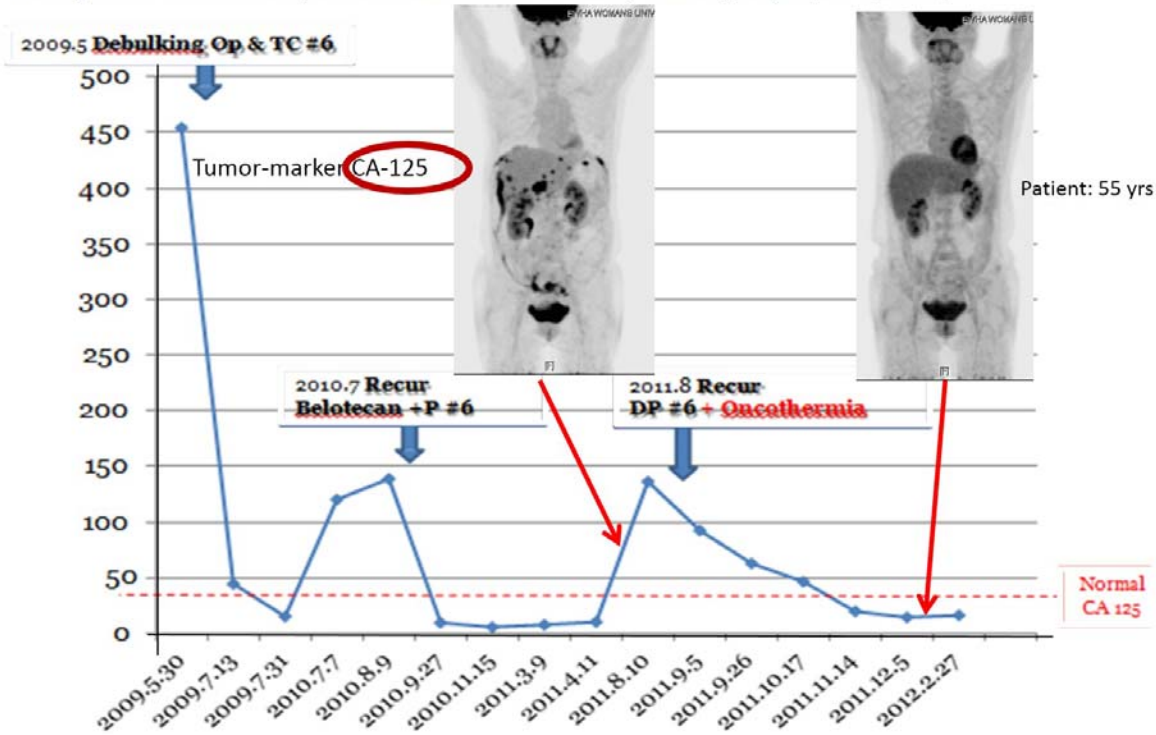
80% local control in 2nd line [with oncothermia combination] (1st line was 51%, without oncothermia)

Case example (PR) This patient died after a stable phase of 26 months (lung and brain mets.)



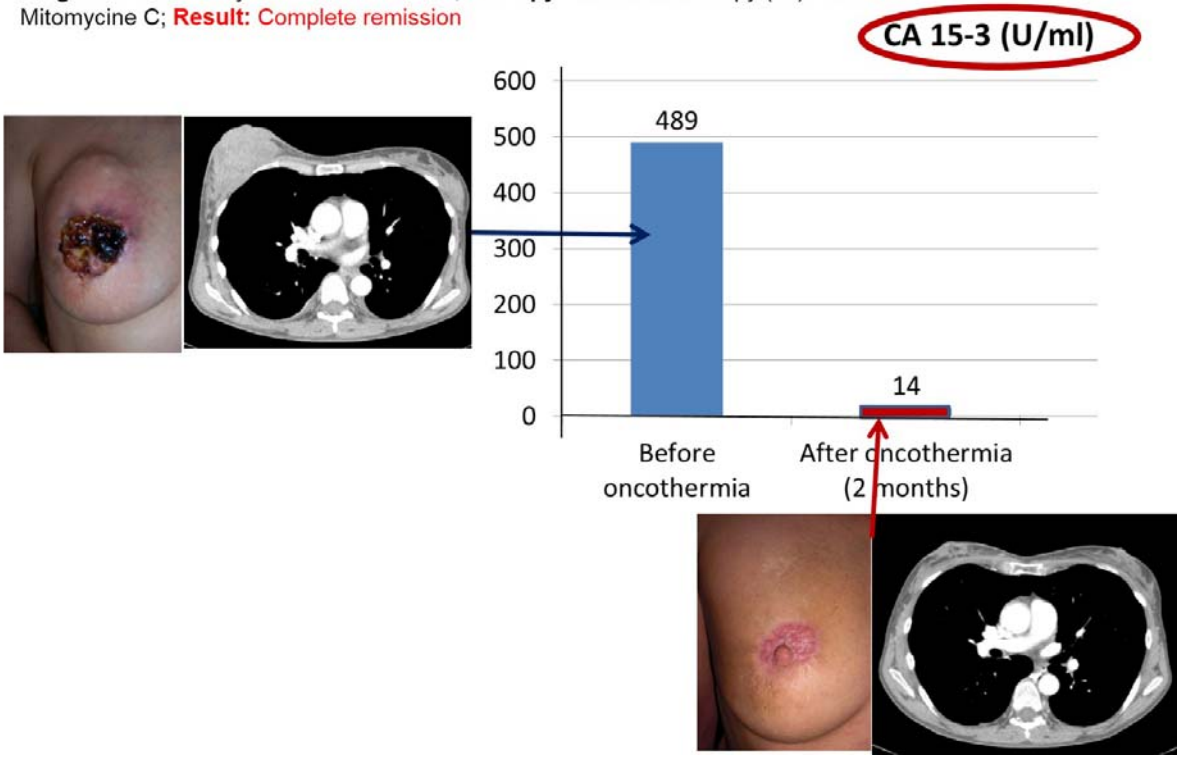
Recurrent, refractive progressive ovarian cancer

Investigator: Prof.YunHwan Kim; **Institute:**Ewha Womans University Mokdong Hospital, Seoul, Korea,



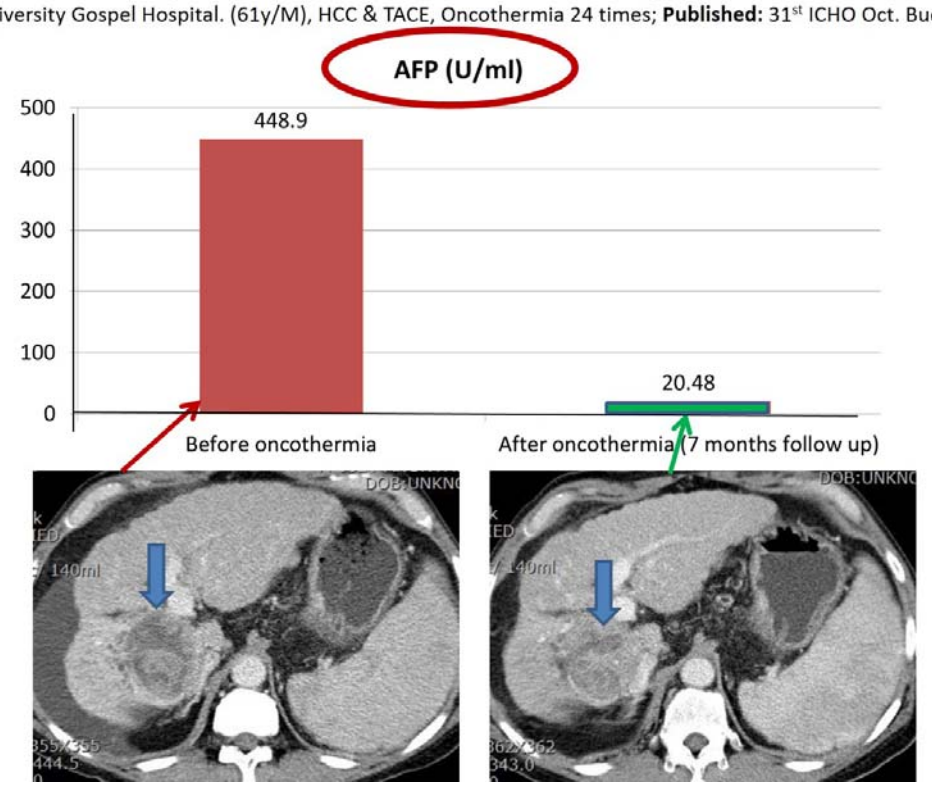
Metastsic mammary cacinoma

Investigator: Dr. W-P. Brockmann, **Institute:** Institute OncoLight Hamburg, Germany; **Patient:** 51 y, (M.S., ♀)
Diagnosis: Mammary Carcinoma >10 cm, **Therapy :** Radiation therapy (2x) + oncothermia + WBH + Mitomycine C; **Result:** Complete remission



Hepatocellular carcinoma

Investigator: Prof.Dr.Taesing Jeung; **Institute:** Department of Radiotion Oncology, Kosin University, College of Medicine & Kosin University Gospel Hospital. (61y/M), HCC & TACE, Oncothermia 24 times; **Published:** 31st ICHO Oct. Budapest; 2012



Outline

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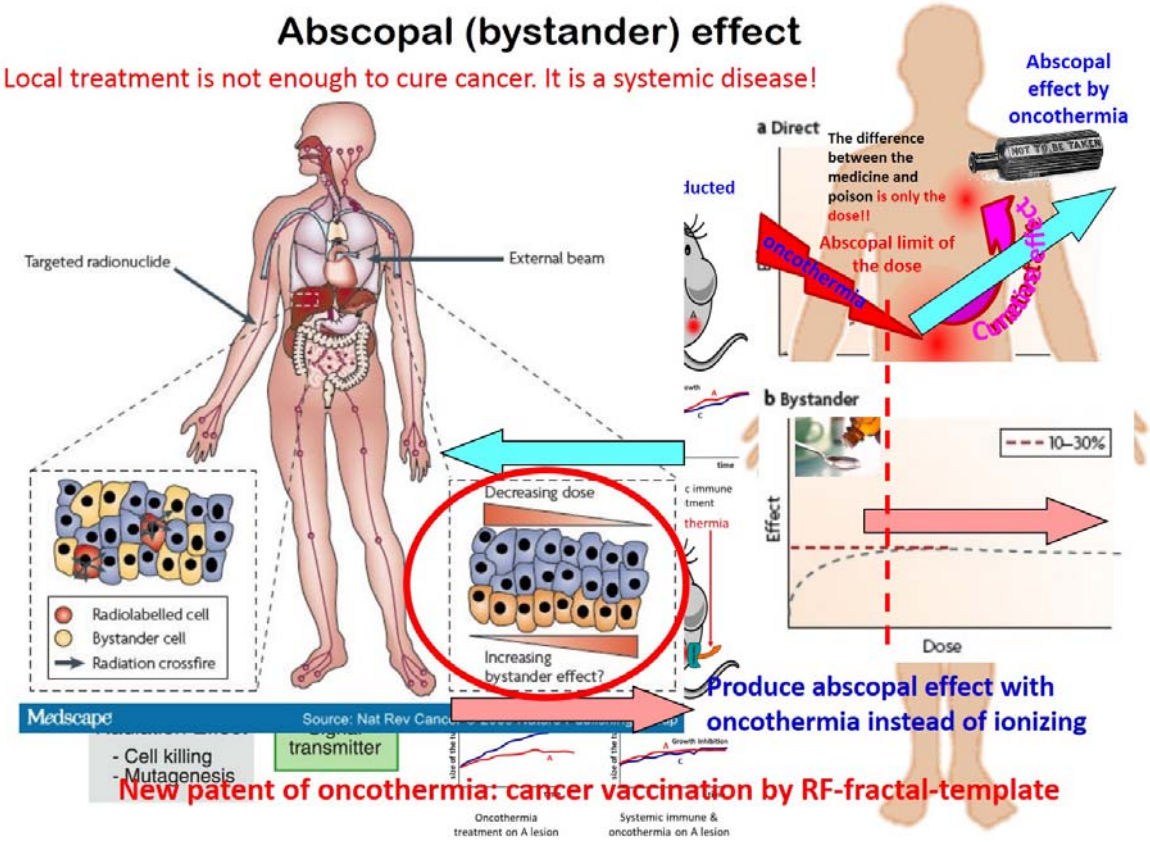
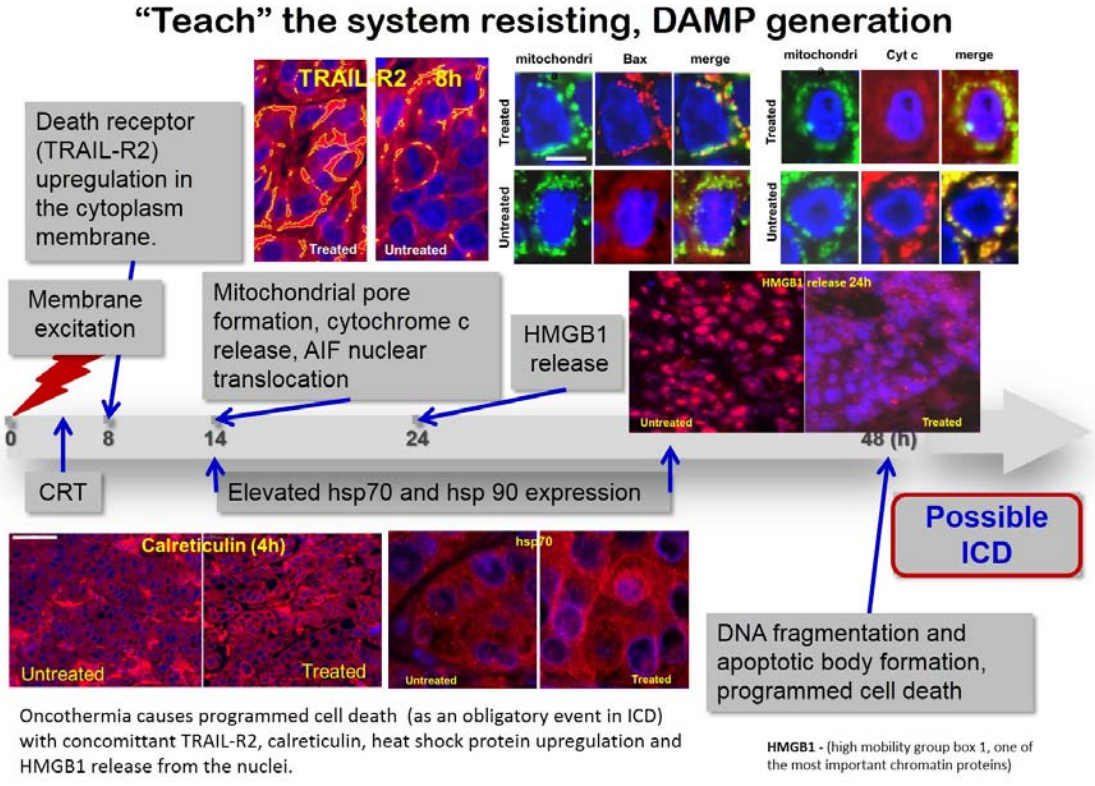
- ❑ Possible solution
- ❑ Future points

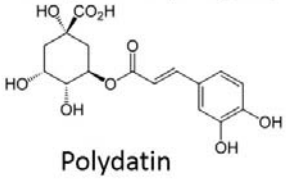
- ○ Take-home messages


Abscopal (bystander) effect
Local treatment is not enough to cure cancer. It is a systemic disease!
Abscopal effect by oncothermia
a Direct
The difference between the medicine and poison is only the dose!!
Abscopal limit of the dose
oncothermia
Curative effect
Targeted radionuclide
External beam
b Bystander
10–30%
Effect
Dose
Decreasing dose
Increasing bystander effect?
Radiolabelled cell
Bystander cell
Radiation crossfire
Medscape
transmitter
- Cell killing
- Mutagenesis
Produce abscopal effect with oncothermia instead of ionizing
New patent of oncothermia: cancer vaccination by RF-fractal-template
Oncothermia treatment on A lesion
Systemic immune & oncothermia on A lesion

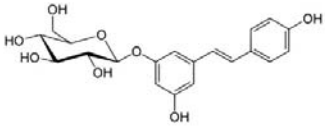

"Teach" the system resisting, DAMP generation
Death receptor (TRAIL-R2) upregulation in the cytoplasm membrane.
TRAIL-R2 8h
Treated
Untreated
mitochondri
Bax
merge
Cyt c
Membrane excitation
Mitochondrial pore formation, cytochrome c release, AIF nuclear translocation
HMGB1 release
HMGB1 release 24h
0
8
14
24
48 (h)
CRT
Elevated hsp70 and hsp 90 expression
Possible ICD
Calreticulin (4h)
hsp70
DNA fragmentation and apoptotic body formation, programmed cell death
Oncothermia causes programmed cell death (as an obligatory event in ICD) with concomittant TRAIL-R2, calreticulin, heat shock protein upregulation and HMGB1 release from the nuclei.
HMGB1 - (high mobility group box 1, one of the most important chromatin proteins)

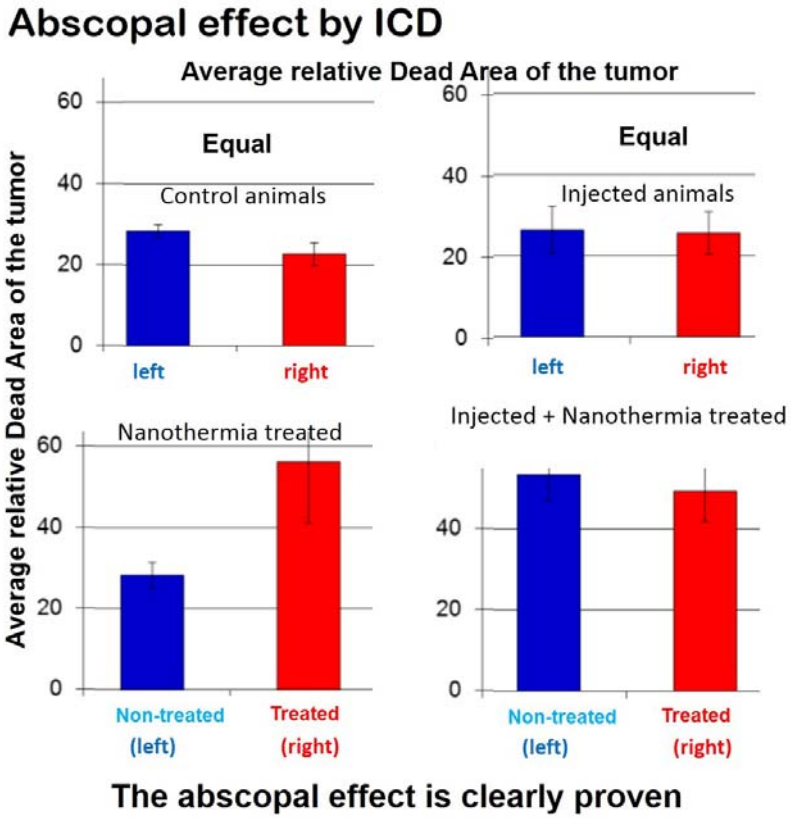
Marsdenia tenacissima (Tongguanteng) decoctum Injection before nanothermia

Chlorogenic-acid (11 mg/ml)



Polydatin

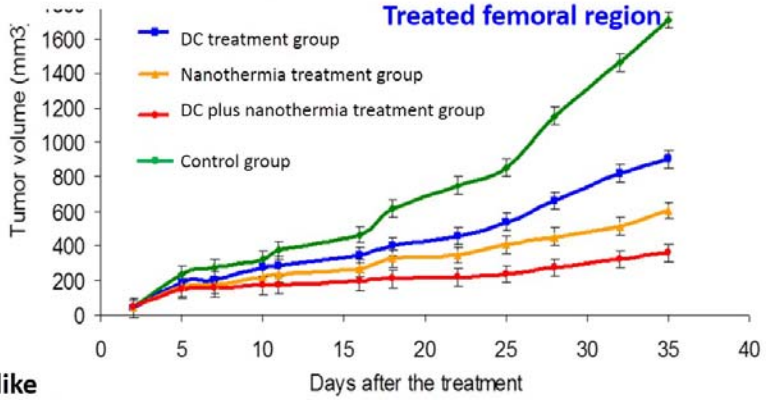




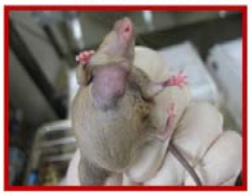
The abscopal effect is clearly proven

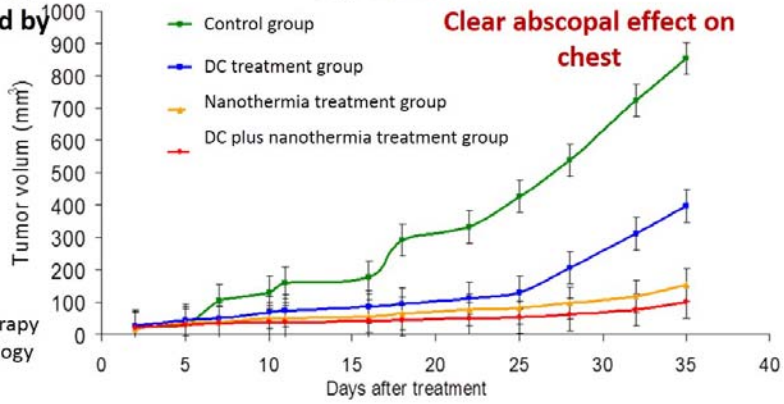
Nanothermia + DC therapy combination

Tumor induced on femoral region (treated by nanothermia)



Tumor induced on chest region like model of metastasis, not treated by nanothermia



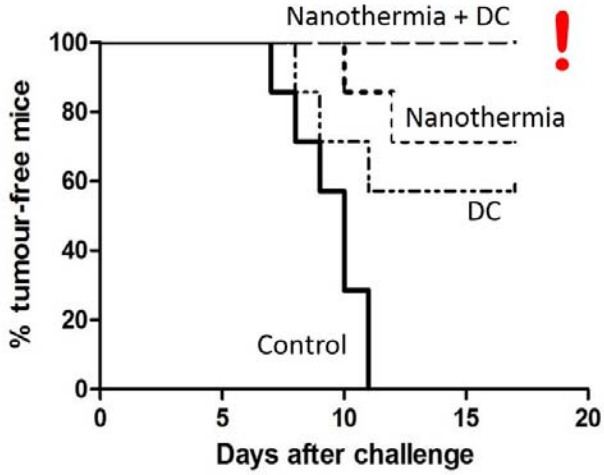


Wei Quin et.al; Modulated electro-hyperthermia enhances dendritic cell therapy through an abscopal effect in mice; Oncology Reports 32: 2373-2379, 2014

Tumor growth inhibition and rechallenge inoculation

Mice were injected with 5 × 105 CT26 tumor cells s.c. in the right femoral area on the starting day and treated with nanothermia on day 14, followed by DC injection on day 15 in different groups. The data from each mouse was plotted after tumor-cell inoculation.

A secondary rechallenge with CT26 tumor cells was administered to mice 30 days after first injection as a result of either DC alone, nanothermia+DC therapy. Mice from therapy groups and untreated control BALB/c mice were inoculated subcutaneously in the left (105 parental CT26 cells) flank. (n = 7 mice per group.).



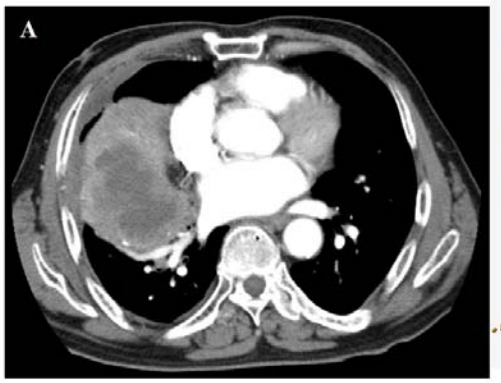
Yuk-Wah Tsang, Cheng-Chung Huang, Kai-Lin Yang, Mau-Shin Chi, Hsin-Chien Chiang, Yu-Shan Wang, Gabor Andocs, Andras Szasz, Wen-Tyng Li Kwan-Hwa Chi, Improved Immunological Tumor Microenvironment by Combined Electro-Hyperthermia followed by Dendritic Cell Immunotherapy; Cancer Immunology, Immunotherapy (submitted (2015))

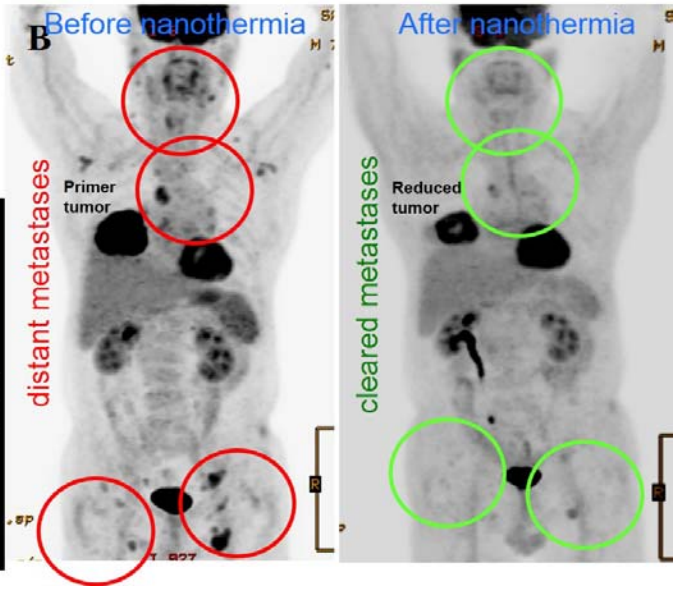
Abscopal effect

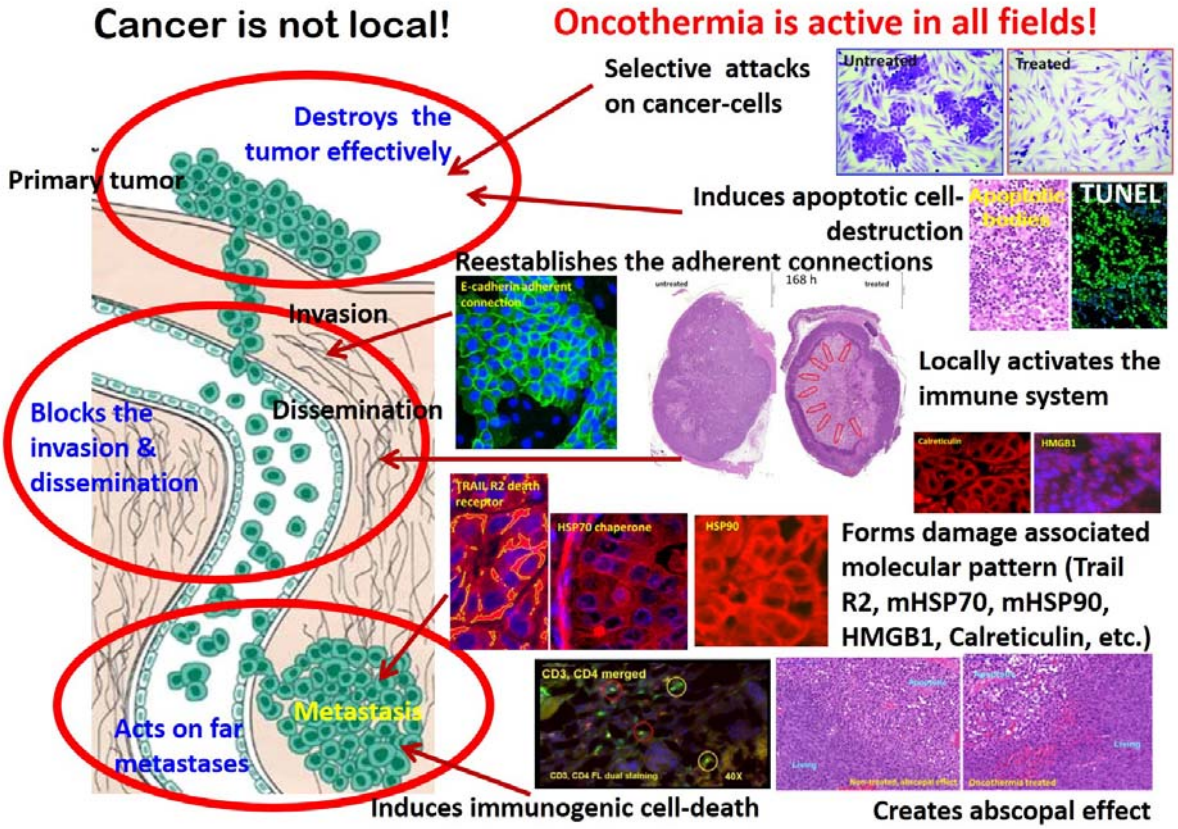
Investigator: Prof. Dr. Seong Min Yoon,
Institute: Division of Hematology-Oncology, Department of Internal Medicine, Samsung Changwon Hospital, Sungkyunkwan University, Korea
Patient: SAsc, 72 y, male,
Primer-tumor: Non-small cell lung cancer; Size: 9.5 cm right middle lobe
Metastases: in sentinel and distant lymph-nodes
Tumor-classification: cT2 cN2 M0, stage IIIB
Treatment: trimodal protocol: 28x1.7 Gy; support: 250 microgram Leukine and Nanothermia 6x

Only the primer tumor was treated

Result: Good partial remission (PR)
Abscopal effect: complete remission (CR)
in the non treated metastaic lesions also







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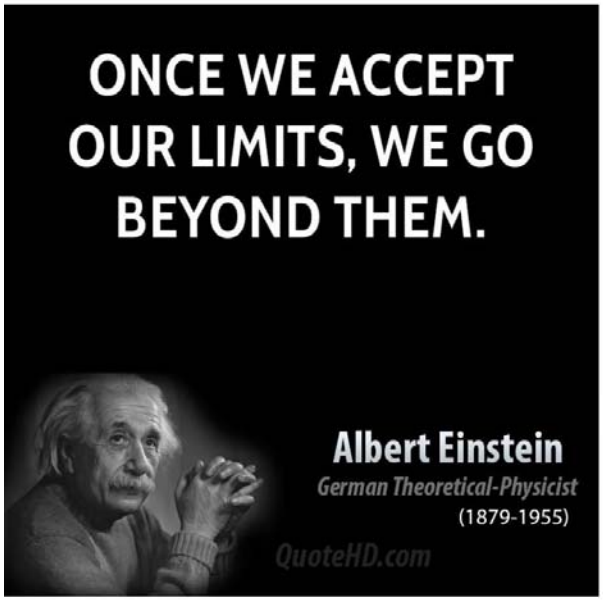
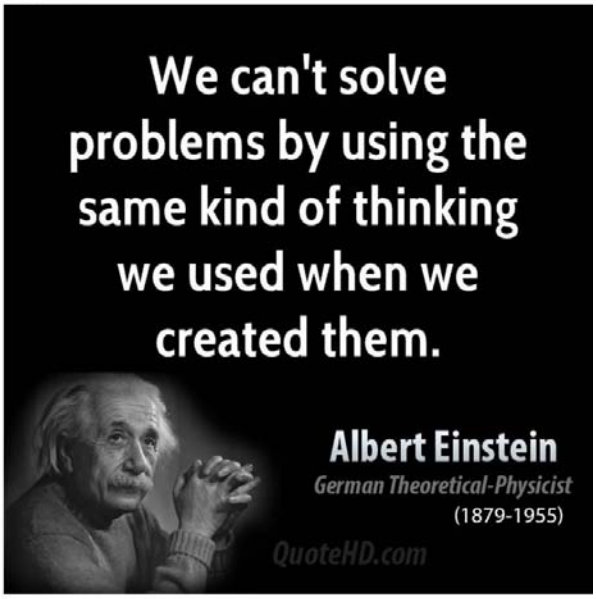
Messages





Have we recognized our limits? **Do we think differently?**

Thank you for your attention

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