Temperature measurements during Oncothermia
(Collection of temperature measurements in loco regional hyperthermia)

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The temperature is a permanent question of the hyperthermia applications in oncology. There are numerous discussions and debates about its importance and problems of its rising deeply inside of the human body. There are intensive discussions about its role in the treatment, looking for controlling parameters and well defined treatment goals of clinical oncologic hyperthermia. The doubts about temperature have multiple origins.

The arguments are sharply differing. The temperature supporters base their opinion on the higher blood-flow by temperature, which delivers more oxygen for complementary radiotherapy and increases the drug concentration and its metabolism in the tumor. The opposition refers on the higher nutrition support and increased metabolic rate of the tumor by growing blood-flow, as well as the higher risk of the malignant dissemination by intensive blood-circulation. The pro-group refers on the control of the treatment by a measurable parameter, while the con-group notes the natural delocalization (smearing) of the temperature from a local volume in a well conductive environment.

Compare the different methods is not a simple task. The energy delivery does various changes in the complex living system, which makes the methods incomparable by an only single parameter. The identical energy exposition does not mean same heating efficacy. The heating efficacy depends on the actual conditions [1], [2], and on the organ to be heated [3] as well as the chosen frequency. The temperature is used in most of the cases as a “success parameter” in hyperthermia, trying to equalize it and declare as a measurement of the energy absorption. The temperature shows only the average kinetic energy of the particles and units in the measured target, but it tells nothing about the chemical and structural changes there. However, the aim of the therapy is to reach structural and chemical changes to stop the malignant processes. The temperature is not enough to compare the methods, [4].

Nevertheless, the temperature and energy distribution is very different [5], it is not possible to fit the specific absorption rate (SAR) and the developed temperature. The amount of the energy losses deviate by the actual conditions, and by the fundamental law of nature, the temperature smears in the environment. Any proper focus serves as a heat-source to heat up its surroundings. The debates are heated by increased interest for targeted therapies, for what the hyperthermia could be a potential candidate.

Oncothermia changes the paradigm. Oncothermia technology heats non-equally; concentrating the absorbed energy to the intercellular electrolytes [6]. This method creates inhomogeneous heating, microscopic temperature differences far from thermal equilibrium. The definitely large temperature gradient between the intra- and extracellular liquids changes the membrane processes, ignites signal pathways for natural programmed cell-death, avoiding the toxic effects of the simple necrosis. The synergy of electric field with the thermal effects potently and selectively does the job [7].

The applied power and the reached temperature are far not proportional. Despite of the longer time (by ~26%), larger forwarded power (by ~8%) the increased temperature is less (by ~12%) in the second time. It is not because the energy conservation is hurt, but due to the cooling which was applied (and not registered) during the treatment to prevent the skin from burn. We know it well, that the blistering threshold of heating power going through the human skin is ~0.45W when it is pumped during an hour [8], so the cooling was always fit for the safe use. The extra power was conducted away by the surface cooling. It is a patented technical trick of Oncotherm how to make...
the surface cooling well, and using most of the energy for the heating of the tumor without loosing it by the active cooling.

This is why oncothermia, (using the same blistering threshold) can reach higher temperatures. We recapitulate those results to clear the differences: oncothermia treatment had ~6°C temperature increase with ~70 W during 60 min in the human sarcoma [9] and reaching 44 °C with 120 W in case of mammary tumor [10]. In veterinarian application, where the blistering threshold was of course higher in the anesthetized animal and the heated volume was much smaller than in human cases, the temperature increase was ~14°C with ~25 W during 30 min [11].

The only point for these results is to keep the energy for the job, and not waste it for various energy factors in the electronic solution, in the filed emission (radiation), in the surface physiology or in the electrode construction. Despite of the fact, that Oncotherm is reaching his extremely good results by the electric field (which was directly shown clearly in “galvano” treatment), the temperature conditions are also present and necessary. This is well shown in the synergy of the temperature and field effects [12].

Below I will show our systematic proofs on the selective temperature developments, our high-scale temperature measurements and proofs of oncothermia as a definite improvement of oncologic hyperthermia. Oncothermia is such kind of oncologic hyperthermia, which together with the better efficacy, safer and controllable than other heating methods.

**Temperature measurement for BSD device**

This device is a radiative heating system, having antenna-array around the body. The published data show non-invasive temperature measurement (by MRI sensing and calculation from the T1 and T2 time-shifts). Results show a problematic focusing (having many hot-spots) as well as the smearing of the temperature by time.

In case of radiative applications the situation is not better. The temperature elevation in the tumor after 57 min was 4.2 °C; reached by as high power as 1300 W [13]. The overall heating is obviously shown with some characteristic (unwanted) hot-spots. The elapsed time smears the relative focused temperature. The temperature increase in the tumor was in average 4.2 °C, while in the surrounding muscle 3.8 °C [13]. Is this the focus, which we expected?
Temperature by BSD devices


ANATOMY
(GRE, TE = 4 ms) before start

UNCORRECTED PHASE IMAGES
at 57 min

MR-TEMPERATURE DISTRIBUTIONS
after fat correction (57 min)

4 cm below symphysis

central plane (symphysis)

4 cm above symphysis

presacral recurrence

17 min

29 min

presacral recurrence

43 min

57 min

Heating the bolus

Unwanted hot spots

 Desired heated area
(naturally spread in large volume)

Power=1300 W

Selectivity < 0.5°C
The few centigrade increase of the temperature by 1300 W energy shows how much mass is heated instead to concentrate on the tumor. To see the power capacity, we compare the electric heating for tea-making. A standard speedy Electric Tea Kettle uses 1500 W to boil two cups of water within two minutes. The increase of the temperature for the ~ 0.5 liter water is ~75 ºC. The electric power is very effective to change the temperature when it is focused to do so. The electromagnetic radiation increases the tumor temperature by 3.2 ºC, while the intensively cooled, large volume water-bolus had a higher increasing (5.8 ºC) with pretty linear growth slope.

**Thermotron device**

The Thermotron is a capacitive coupled device, using the electro-hyperthermia technique (no modulation is applied). The same problems as for BSD (except the hot-spots) could be realized in this case as well. A typical capacitive coupling solution pumps enormous energy, exceeding 1 kW. The rise of temperature after 45 min was 4.8 ºC but the reached focus does not differ greatly in its temperature from its overall neighborhood [14]. The focus, however, is not effective. The temperature is distributed by time.
Capacitive (electro) hyperthermia: Themotron

Heating by 1200 W

Source: brochure of Thermotron
The physiological feedback regulates the local temperature, which acts also against the local heating.

Dutch device (Rotterdam)

Dr. van der Zee had shown clearly the problem of the difference between the absorbed energy and the developed temperature. When the blood-flow is high, the temperature remains low despite of the extreme energy absorption, and vice versa, the low energy can heat the volume where the blood does not cools intensively. Nevertheless, the temperature and energy distribution is very different [15], it is not possible to fit the specific absorption rate (SAR) and the developed temperature. The amount of the energy losses deviate by the actual conditions, and by the
fundamental law of nature, the temperature smears in the environment. Any proper focus serves as a heat-source to heat up its surroundings.

Energy and temperature are not the same!

CT scan

Energy distribution

Temperature distribution

Oncotherm measurements

I would like to show various experimental and clinical temperature measurements without comments, only for the documentation.

Model systems

Comparison of bolus and textile electrodes on saline (100W)
Presentation of the capacitive heat delivery

Egg experiment

\[ \Delta T = 30 \, ^\circ C \]

![Graph showing temperature changes over time with different sensor readings.]

RF-off
Sensor out
Early experiment with bolus in that time (~1993)

Meat temperature

Sensors in depth

$\Delta T = 6 \, ^\circ\text{C}$

Celsius

Time

Piglet experiment power on/off (~2001)

$\Delta T = 16 \, ^\circ\text{C}$

$\Delta T = 8 \, ^\circ\text{C}$

Power (W)

Temperature (°C)

Time (min)
Deep heating of the rib/liver model (Prof. Herzog, Fachklinik Dr. Herzog, Published in Forum Hyperthermie)
Zusammenfassung: Messungen mittlerer Applikator (20 cm); 15 min mit 100 W

\[ \Delta T \text{ Haut} \quad 5,4^\circ \text{C} (2,8^\circ - 7,1^\circ \text{C}) \]
\[ \Delta T \text{ Leber-Oberfläche} \quad 4,1^\circ \text{C} (2,6^\circ - 3,9^\circ \text{C}) \]
\[ \Delta T \text{ Lebertiefe} \quad 2,4 - 3,9^\circ \text{C} \]

Lokale Hyperthermie am Modell

Messwerte: Leberoberfläche; \( \Delta T = \text{Temperaturanstieg} \degree \text{C} / 15 \text{ min} \)

Bedingungen:
20 cm Applikator
100 W Leistungsaufnahme 15 min
(Leistungsaufnahme 100 W)

Altitude:
Gute Kopplung
Hirnareale Reflexion

Thermo-camera control

Thermo-control (non-invasive)

Tumorenum s. Pleuralmetas. Carcinoma pleuropulmonale interstital
chemotherapy, radiotherapy.
Selective macroscopic energy deposition

Human hepatocellular carcinoma (HEPG2) study

Temperature measurement

Oncothermia method can selectively heat the tumor!

Invasive optical temperature measurement

ΔT=6 °C

ΔT=10 °C

ΔT=9 °C

7W/1.4W, 42 min (SWR=1.5)

17.5 kJ / 3.5 kJ

6 kJ / 1.4 kJ

Liver temp. — Rectal temp.
Invasive optical temperature measurement

[Images of invasive temperature measurement setup and a healthy female Beagle dog, 3 years old, 10kg bodyweight, with graphs showing temperature changes.]

Incident 50W (150 kJ), absorbed: 36 W (138 kJ), 50 min (SWR=1.6)

Invasive remote temperature tests

Test animal: healthy Beagle dog
Power: 20W 16W (SWR=1.5)
Energy: 36 kJ 28.5 kJ
Treatment duration: 30 minutes
Temperature sensor: placed subcutaneously under the electrode
Temperature measurement: every 5 minutes (RF switched off)

[Graph showing temperature changes over time with ΔT=14 °C]
Aim of the study: investigating the effect of hyperthermia to bone tissue — monitoring the radiopharmacon ($^{99m}$Tc-MDP) uptake of the hyperthermized knee joint

Test animal: healthy Beagle dog
Power: 30W (SWR: 1.5) [54 kJ]
Treatment duration: 30 min
Radiopharmaceutical: 400 MBq $^{99m}$Tc-MDP

Scintigraphy: 1 hour after the intravenous injection of radiopharmacon at the end of 30 min hyperthermia treatment

Oncothermia raised the bone-specific radiopharmacon uptake in the treated knee-joint by 17%.
OSTEOSARCOMA (DOG, dorka, 2007.01.18-29.)

Diagnosis: osteosarcoma

Before oncothermia 2007.01.09

ROI (total count):
Healthy femur: 26612
Tumoral femur: 238246
Tumor/healthy ratio: 8.95

After oncothermia 2007.02.05

ROI (total count):
Healthy femur: 33433
Tumoral femur: 183625
Tumor/healthy ratio: 5.49

Oncothermia decreased the intake of the radiopharmacon by 40%!

Preparation of temperature measurement in bull-terrier
Human measurements (by chronology)
Thermo-control (invasive)

St. Georg Klinik, Bad Aibling, 2000

Thermothermiesystem ETHY 2000 der Onco-Therm GmbH
Invasive Temperaturmessung der Firma Onco-Therm GmbH; Messgenauigkeit < 0,1 °C

Temperaturverläufsprotokoll

- Leistungsabgabe - Leistungsaufnahme - Temperaturanzeige - Kanal 1 nicht im Tumor
- Kanal 2 im Tumor - Kanal 3 Oberflächenmessung - Kanal 4 Oberflächenmessung

Anmerkung:
Die Leistungsabgabe und die Leistungsaufnahme wurden in Watt gemessen und für die graphische Darstellung jeweils durch 2 dividiert.

Thermo-control (invasive)

St. Georg Klinik, Bad Aibling, 2001

Temperaturverläufsprotokoll

- Leistungsabgabe - Leistungsaufnahme - Temperaturanzeige - Kanal 1 nicht im Tumor
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Thermo-control (invasive)

St. Georg Klinik, Bad Aibling, 2001

**Patient:**
Cervix-Ca.

**Diagnose:**
Tiefen-Hyperthermie

**Therapiekombination:**
Oberflächen-Hyperthermie und Chemotherapie (Cisplatin)

**Messung vom:**
05.01.2001

**Therapiegerät:**
Hyperthermiesystem EHY 2000 der Onco-Therm GmbH

**Messanrichtung:**
Invasive Temperaturmessung der Fa. Onco-Therm GmbH; Messgenauigkeit < 0,1 °C

**Anmerkung:**
Die Leistungsabgabe und die Leistungsaufnahme wurden in Watt gemessen und für die graphische Darstellung jeweils durch 2 dividiert.
**Invasive Temperaturmessung**

Diagnose: Cervix-Ca.
Therapiekombination: Tiefe-Tumorexstirpation
Messung vom: 08.01.2001
Therapiegerät: Hyperthermiesystem EHY 2000 der Onco-Therm GmbH
Messeinrichtung: Invasive Temperaturmessung der Firma Onco-Therm GmbH; Messgenauigkeit < 0,1°C

St. Georg Klinik, Bad Aibling, 2001

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**Thermo-control (invasive)**

Patientin: K., geb. 29.12.1940
Therapiekombination: Oberflächen-Hyperthermie und Chemotherapie (Cisplatin)
Messung vom: 04.01.2001
Therapiegerät: Hyperthermiesystem EHY 2000 der Onco-Therm GmbH
Messeinrichtung: Invasive Temperaturmessung der Firma Onco-Therm GmbH; Messgenauigkeit < 0,1°C

St. Georg Klinik, Bad Aibling, 2001

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Anmerkung: Die Leistungsabgabe und die Leistungsaufnahme wurden in Watt gemessen und für die graphische Darstellung jeweils durch 2 dividiert.
Oncothermia Mammary CA

Investigator: Prof. D. Gronemeyer & Dr. H. Sahinbas (2002)
Department: Department of Radiology and Microtherapy, University of Witten-Herdecke, Bochum, Germany

![Graph showing temperature and power variation with time.]

321 kJ → 44 °C

EXPERIMENTAL SETUP: WITH OPEN MRI TOSHIBA 0.062T
CT guided invasive thermometry

Abdomen measurement, 12 cm depth. Bochum, Dr. H. Sahinbas (2004)
Invasive thermometry

Investigator: Prof. D. Gronemeyer & Dr. I. Sahinbas (2005)
Department: Department of Radiology and Microtherapy. University of Witten-Herdecke, Bochum, Germany

INVASIVE THERMOMETRY

TUMOR

Surface sensor
Intratumoral sensor 1
Extratumoral sensor
Intratumoral sensor 2
MRI-monitoring


[14] Brochure of Thermotron RF 8. (Yamamoto Vinita, Osaka, Japan)