Whole-Body Hyperthermia (WBH): Historical Aspects, Current Use, and Future Perspectives

11

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Abbreviations

DGHT	Deutsche Gesellschaft für Hyperthermie (German Society for Hyperthermia)
ECG	Electrocardiogram
ESHO	European Society for Hyperthermic Oncology
FRWBH	Fever-range whole-body hyperthermia
HR	Heart rate
IR	Infrared
NIBP	Non-invasive blood pressure
RESP	Respiration
sCMT	systemic cancer multistep therapy
SpO_2	Oxyhemoglobin (HbO_2) saturation (using peripheral pulse oximetry)
T	Temperature
WBH	Whole-body hyperthermia

11.1 History of Whole-Body Hyperthermia (WBH)

Numerous ancient cultures already knew the beneficial effects of physical heating of the organism, using hot water baths, hot sand, or hot steam. In the seventeenth century, the English physician Sir Thomas Sydenham emphasized: "Fever itself is Nature's instrument," making a claim in the controversial discussion whether fever is just a troublesome symptom to be suppressed or a mechanism of the organism to stimulate self-healing processes. Before the introduction of anti-inflammatory drugs

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and antibiotics, physicians deliberately triggered infections in patients suffering from incurable life-threatening diseases in order to induce a strong fever reaction. Julius Wagner-Jauregg was awarded the Nobel Prize in Physiology and Medicine in 1927 for the injection of malarial parasites in the treatment of dementia paralytica. He also reported improvements in depressive disorders [1]. An association between febrile response and tumor regression was noted as early as 1866 by Wilhelm Busch, and independently by Friedrich Fehleisen, who observed cancer remission in patients afflicted by severe erysipelas [2]. A similar case report on a complete remission of a sarcoma encouraged the American surgeon W.B. Coley to intravenously inject a mixture consisting of *Streptococcus erysipelas* and *Bacillus prodigiosus*. "Coley's toxins" achieved remissions in refractory progressing malignant diseases. Meanwhile, Coley is acknowledged as the "father of anti-cancer immunotherapy" [3]. Until the 1960s, "active fever therapy" using pyrogenic drugs (e.g., Pyrifer, Pyrexal, Vaccineurin) as well as whole-body hyperthermia, defined as physical warming of the organism, were widely accepted as a medical therapy. "Hot fever baths" were comprehensively described as a treatment for infectious and inflammatory diseases [4, 5]. In 1960, Martin Heckel [6] presented the first whole-body hyperthermia (WBH) device which used near-IR as an alternative to hot water baths. From 1965 onwards, Manfred von Ardenne [7] developed the concept of "systemic cancer multistep therapy" (sCMT), including extreme whole-body hyperthermia. Initially, using a special two-chamber water bath, he later changed to the application of wIRA and developed the first wIRA-WBH device. While interest in hyperthermia in oncology focused more and more on local forms of application, Klaus L. Schmidt [8] published a monograph on "Hyperthermia and Fever" in 1975 which included a comprehensive literature review on the therapeutic application of WBH in infections, allergic, and rheumatic diseases.

11.2 Three Levels of Whole-Body Irradiation (WBH)

WBH, defined as physically induced elevation of body core temperature, ranges from short, mild heat applications that can be performed at home, up to extreme WBH which must be performed in an intensive care unit environment. A classification of WBH into three levels has been published in the Guidelines of the "Deutsche Gesellschaft für Hyperthermie" (German Society for Hyperthermia) [9] (Table 11.1).

Notably, this classification is not applicable for local/regional hyperthermia, where "mild HT" includes temperature elevations from 39 °C to 43 °C. Even in the WBH literature, the term "mild" has frequently been used for temperature elevations that are classified here as moderate, resp. fever range.

Temperature limits between the three WBH levels are given just for orientation since they are subject to individual variations. The initial body core temperatures of patients differ significantly (reference range: 36.0 °C–37.5 °C), and it is not known whether the absolute value of the body core temperature achieved, or the relative

Table 11.1 Three levels of WBH [9]

	Mild WBH		Fever-range (moderate) WBH		Extreme WBH
Target temperature of body core, T (rectal)	<38.5 °C		38.5 °C – 40.5 °C		>40.5 °C
Application time in the specified temperature range	≤30 min	>30 min	≤ 180 min	>180 min	≥ 60 min
Patient stress	Perspiration, no thermoregulatory stress	Perspiration, no thermoregulatory stress	Thermoregulatory stress, non-sedated/lightly sedated	Thermoregulatory stress, lightly/heavily sedated	Thermoregulatory stress, deep intravenous anesthesia
Patient monitoring	Without nursing care	Nursing care T (axillary) or T (rectal) or T (sublingual) or T (tympanic)	Nursing care under medical supervision Continuous T (rectal/vaginal) ± T (axill/tymp) + HR/SpO_2 ± ECG Periodic ± NIBP ("+" means mandatory, "±" means optional)	Nursing care under medical supervision Continuous T (rectal/vaginal/vesical) + T (axill) + HR/SpO_2 + ECG/RESP Periodic + NIBP	Medically supervised treatment Intensive care monitoring
Indications (selection)	Relaxation, wellness	Rehabilitation, physical therapy, rheumatology, orthopedics	Rheumatology, dermatology, oncology, psychiatry, immunology, environmental medicine	Oncology, chronic infections	Oncology, chronic infections

value of the temperature increase compared to the baseline temperature is more important for the therapeutic effect.

11.3 Practical Implementation, Mechanisms of Action, Indications

11.3.1 Mild WBH

During the first phase of WBH, the temperature of the body shell is elevated up to the level of the core temperature which is a temperature increase of several degrees in the extremities (Fig. 11.1). The duration of this phase is individually most heterogeneous, generally ranging between 10 and 20 min, in rare cases even up to 30 min. The same goes for the speed of the following increase in body core temperature. For mild WBH, the heating of the body can be stopped as soon as the patient feels uncomfortable due to the initiation of thermoregulatory stress. The duration of the following heat-retention phase—with activation of the parasympathetic system—ranges from 30 to 120 min. Data on duration–efficacy relationships are currently not

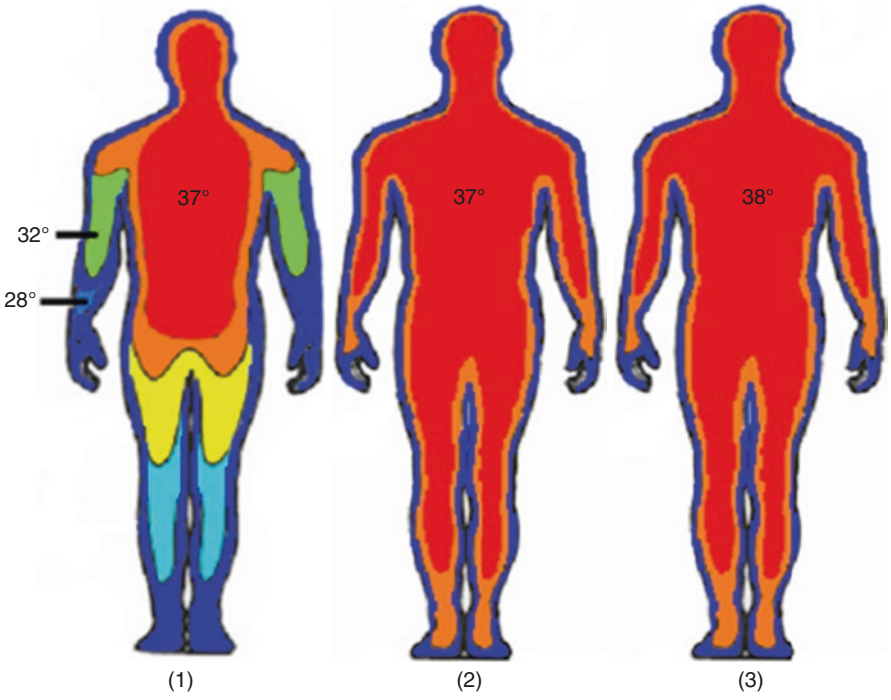


Fig. 11.1 (1) Temperature fields of body shell (skin, extremities) and of body core (with radial and axial temperature gradients in a 20 °C environment, (2) expansion of the core temperature in a 35 °C environment, (3) mild whole-body hyperthermia. Modified from [10]

available. A total treatment duration of 90 min is recommended as this allows for a new assignment of the treatment station every 2 h.

The primary physiological effects of mild WBH are a decrease in the tone of skeletal and smooth musculature, and an increased perfusion in the periphery including the extremities. This might be especially important for bradytrophic tissue which has been damaged by degenerative diseases.

Indications of mild WBH include diseases of the musculoskeletal system (e.g., chronically raised skeletal muscle tone, especially chronic back pain, post-accident care, degenerative osteoarthritis, fibromyalgia (see Chap. 19, this book), arterial hypertension [11]), systemic scleroderma [11], and Raynaud's syndrome [12].

11.3.2 Fever-Range Whole-Body Hyperthermia (FRWBH)

After reaching a core temperature in the fever range, most patients find the treatment exhausting, but nevertheless an "interesting" body experience. The nurse will assist this situation by empathic communication, application of cold cloths on the forehead, and similar procedures. Patients can listen to music and even watch videos for distraction. Interestingly, the development of thermoregulatory stress is not directly correlated to the rise of core temperature and may suddenly increase and decrease in spite of steadily increasing temperature. After reaching the target temperature level, the wIRA radiators can be switched off and the patient be covered by a blanket and remaining in the tent or wrapped into the tent fabric allowing for a half-sitting position (Heckel device) or the intensity of wIRA irradiation is decreased while the patient keeps lying on the net (Iratherm device). During this plateau phase, body core temperature in most patients rises for another 0.2–1 °C without further increase in stress. The duration of this phase is often 60 min, but can be prolonged as long as it is tolerable for the patient.

Clinical protocols of long-duration fever-range WBH (FRWBH, 4–6 hours above 39 °C) require sedation of the patients. These protocols have demonstrated safety and suggested efficacy in combination with chemo- and immunotherapy [13–15]. In the latter cases, "WBH may have the great advantage of allowing treatment of widely disseminated tumors in metastatic patients, with the same HT" [16].

At the end of heat retention, when all insulation or further energy supply is terminated and the thermoregulatory cooling mechanisms are no longer counteracted, most patients feel immediately well and free of stress, even if the temperature has not yet started to decline. The stress is obviously not caused by the increased temperature itself, but by the impeded thermoregulation.

The requirements for monitoring of vital parameters and the staff specifications are listed in Table 11.1 and are comprehensively described in the WBH guidelines of DGHT [9] (Fig. 11.2).

The concept of fever-range WBH (FRWBH) is mainly based on the assessment of elevated body core temperature as an essential trigger for initiating a strongly activated immune response. While in cold-blooded animals, elevation of body core temperature occurs by movement to warmer environments, warm-blooded creatures

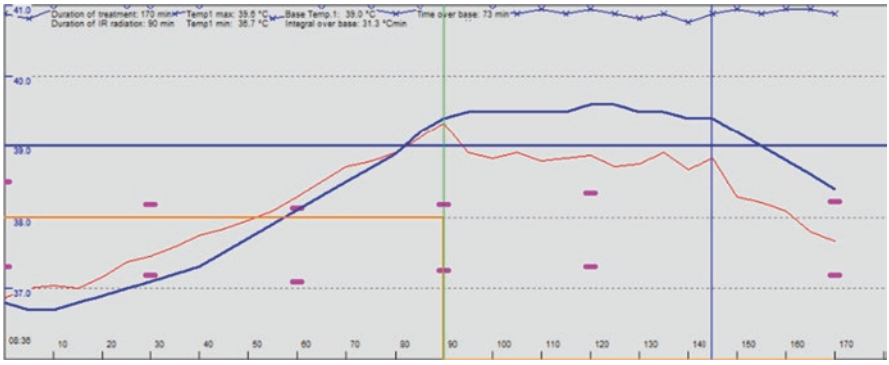


Fig. 11.2 FRWBH treatment, documented in the software Febrodata®, Heckel Medizintechnik (Esslingen, Germany). Blue curve: T rectal, starting at 36.8 °C and reaching 39.4 °C after 90 min. Heat-retention phase (90th to 145th min). Cool-down phase (145th–170th min). Red curve: heart rate (min. 65/minute, max. 120/minute). Pink spots indicate sporadically measured blood pressure (min. 110/78 mmHg, max. 115/82 mmHg)

develop a fever. Even if fever, as a response to infection, cannot be equated with hyperthermia as a physical heating of the body, FRWBH can strongly activate innate and adaptive immune responses. Interestingly, fever temperatures can also promote anti-inflammatory effects in case of chronic inflammation and autoimmune diseases [17]. To simplify, it could be considered as a "reset of the immune system" to overcome chronic pathologic dysfunctions correlating with too high or too low immune activity. Numerous preclinical studies have confirmed the therapeutic potential of controlled increases in body core temperature and have gradually examined the underlying biological mechanisms [18, 19].

Indications for FRWBH include major depression (see Chap. 12, this book), chronic inflammatory diseases of the muscolo-skeletal system such as ankylosing spondylitis and psoriasis arthritis (see Chap. 20, this book), and additive use in oncology (see Chap. 8, this book). FRWBH may increase the efficacy of antibiotic drugs in the treatment of chronic Lyme disease [20] and stimulate anti-bacterial immune responses.

11.3.3 Extreme Whole-Body Hyperthermia (WBH)

Extreme WBH is an intensive care application under deep intravenous anesthesia and requires comprehensive preparation, extensive monitoring of vital parameters, and a careful follow-up directly upon treatment [9, 21]. Risks of side effects are considerably higher than in FRWBH, since the set body core temperature is far beyond the range of fever which is developed in humans regarding immune reactions to common infections. Moreover, specific skills and experience in visual monitoring of the skin and in positioning of the patient are required to minimize the risk of thermal skin damage. Extreme WBH has been used to directly damage malignant

cells in the oncological setting and to fight bacteria and viruses in chronic infection. In 1965, M. von Ardenne introduced extreme WBH as a key element of his "systemic cancer multistep therapy (sCMT)," consisting of the three main steps: (a) extreme whole-body hyperthermia (maximum temperature of at least 42 °C), (b) induced hyperglycemia, and (c) respiratory hyperoxemia. Hyperglycemia was applied in order to render cancer cells selectively more heat sensitive, by lowering the pH values in the cancer tissues. In 1974, the concept was extended by including a chemotherapy protocol adapted to the respective tumor entity [7, 22, 23]. Since hyperglycemia may stimulate cancer growth [24], it must be carefully considered whether this growth-promoting effect is fully excluded if applied in the framework of sCMT.

From the mid-1990s until 2005, numerous phase I and II trials with extreme WBH were published, most of them with target temperatures between 41.5 °C and 41.8 °C, combined with chemotherapy. Interest in this therapeutic schedule rapidly declined thereafter. A recently published review presents an excellent overview on these publications, concluding that "as modern oncology offers many less invasive treatment options, it is unlikely WBH will ever find its way in routine clinical care" [25]. On the other side, promising results in the above-mentioned trials may justify further research in this field, and extreme WBH should not completely be excluded as a therapy option for patients not satisfyingly responding to modern standard therapies.

In 2018, Douwes [26] published the concept of "antibiotically augmented thermal eradication of chronic Lyme disease," combining extreme WBH up to 41.6 °C and antibiotics, based on the heat sensitivity of *Borrelia* and the temperature-dependent efficacy of antibiotics [20]. Results in 601 of 809 patients treated in the past 3 years were "very good" or "good" (data presented at the ESHO Annual Meeting, Berlin 2018) [27].

11.4 Contrary Effects of WBH on Blood Flow of Inner Organs and Body Periphery

Regarding the impact of all WBH levels on blood flow, a widespread misunderstanding needs to be addressed. Contrary to general assumptions, WBH does not necessarily increase perfusion in the whole organism. In contrast, the thermoregulatory response on passive heating of the body includes a shift of large blood volumes into the periphery in order to cool the body by increased heat transfer and subsequent heat release to the environment supported by evaporation/perspiration. Consequently, blood flow through inner organs can be decreased. Deja et al. [28] reported a significant decrease in liver perfusion during extreme WBH in approximately 50% of the treatments. In a self-experiment conducted in 2009 (S. Heckel-Reusser), these basic mechanisms were tested during FRWBH. Liver blood flow was measured directly before and immediately after WBH when the rectally measured body core temperature reached 39 °C. In this experiment, liver perfusion immediately after WBH was 70% of the baseline value measured before WBH

(personal communication, Dr. J. Gellermann, Charité University Hospital, Berlin). A few weeks later, the same measurements were repeated before injection of a pyrogenic drug (Coley's toxin), and 3 h later, when fever temperature had reached 39 °C. As expected, there was no difference in liver perfusion. By administration of Coley's toxin, the temperature setpoint was shifted to >39 °C and body core temperature thus increased in order to achieve this elevated setpoint. Consequently, thermoregulation did not aim at any cooling of the organism and no blood redistribution from the core to the periphery was observed. In contrast, the perfusion of inner organs might decrease during WBH. This must be taken into account for the timing of medication, e.g., in case of combined thermochemotherapy in the treatment of liver metastasis.

11.5 Currently Applied WBH Techniques

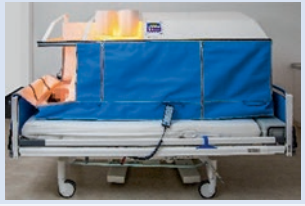
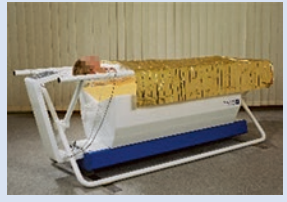
Techniques applied for therapeutic WBH include extracorporeal blood heating, water immersion, 27 MHz short waves, long-wave IR irradiation in a chamber with almost 100% humidity, IR A/B ("near IR"), and wIRA irradiation [29, 30].

In 2010, Jia et al. [29] listed four commercially available medical WBH devices "for high-performance whole-body hyperthermia therapy": ET Space (Energy Technology, Shenzhen, China), IRATHERM1000 (von Ardenne Institute of Applied Medical Research, Dresden, Germany), heckel-HT3000 (Hydrosun Medizintechnik, Müllheim, Germany), and Oncotherm WBH2000 (Oncotherm, Budaörs, Hungary). Currently, only the heckel-HT3000 and IRATHERM1000 (in addition, a slightly modified model IRATHERM800 just for mild WBH) are commercially available. wIRA irradiation penetrates deeply into the subcutis, followed by (mainly) convective transport of the absorbed heat energy to all regions of the body by blood flow. At the same time, heat dissipation to the environment is impeded by a tent tempered with IR-C (heckel-HT3000) or by an insulating blanket (IRATHERM). Both techniques have proven high treatment tolerability and patient compliance. The main features of these two devices and of heckel-HT2000 (which was available until 2006 and is still in use in many clinics) are listed in Table 11.2.

11.6 Contraindications and Side Effects

There are no general contraindications for mild hyperthermia as long as body core temperature is only slightly increased. However, a good general health condition is absolutely required for fever-range and extreme WBH. Contraindications of fever-range WBH depend on the level of temperature increase and are primarily based on cardiovascular stress and the possibility of unwanted activation of inflammatory processes and destabilization of unbalanced hormonal and metabolic constellations. Most important absolute contraindications are cardiac insufficiency (>grade 2), major internal organ insufficiencies, and peripheral artery diseases. Relative contraindications, which must be individually assessed and may require prior treatment,

Table 11.2 Features of three different WBH devices

Products	heckel-HT3000	heckel-HT2000(M)	IRATHERM 1000
			
WBH levels (intended use)	Mild, fever range, extreme	Mild, fever range	
Energy input	wIRA from above to the upper part of the body	Diffuse-reflected IR-A/-B from chest to knees	wIRA from below
wIRA irradiance	Max. 100 mW/cm² to the uncovered skin	Max. 100 mW/cm² to the skin covered by cotton fabric	Max. 140 mW/cm² to the uncovered skin
Prevention of heat dissipation	Tent tempered by IR-C	Tent tempered by IR-A/-B	Insulating blanket from above
Patient positioning	Supine or prone position on a mattress Possibility of half-sitting position in the heat-retention phase		Supine position on a knotless net
Maintenance of temperature plateau	wIRA switched OFF, tent still lightly tempered or heat-retention package allowing for a half-sitting position 		Decreased power of wIRA radiators
Power consumption, total	3000 W	1250 W	5500 W
Rated voltage	230 V		3 phase 230/400 V

include cardiac arrhythmias, acute infections, major lymphedemas, high risk of thrombosis, and erratically progressive diseases (e.g., multiple sclerosis). In case of inflammatory diseases manifesting in exacerbations, such as progressive primary chronic polyarthritis, WBH is generally applied in the subacute phase, based on the concern of an unintended stimulation of acute inflammatory activities. This paradigm may be controversially discussed in view of new findings on direct anti-inflammatory effects of FRWBH, as described by Lee [17].

A most common side effect of fever-range WBH in almost all patients is a feeling of restlessness due to the strain on the central thermoregulatory system. Headache may indicate a minor dehydration.

IR-WBH, and especially wIRA-WBH, decreases the thermal load to the skin surface compared with conductive HT techniques and, thus, can significantly improve treatment tolerability and patient compliance. Paradoxically, this intended effect of energy absorption in deeper skin layers increases the risk of thermal skin damage in areas with circulatory impediments [23]. The technical design and procedure of wIRA-WBH deliberately prevent heat dissipation to the surroundings. At the same time, disturbed blood perfusion can diminish the intended convective heat transfer from the periphery to the core, in rare cases leading to thermal skin damage. The heckel-HT3000 is designed in a way that the area irradiated with wIRA is free of any compression and fully accessible for visual inspection and countermeasures in case of the development of hot spots.

In detail, contraindications and side effects are listed in the WBH guidelines of DGHT [9]. It has to be emphasized that the performance of extreme WBH treatments requires a comprehensive training in experienced centers in order to decrease the rate of side effects, the latter decreasing significantly with experience [31].

11.7 Conclusion and Outlook

Given the growing importance of immunotherapies in oncology, rheumatology, and other indications of chronic inflammation, it is worth considering the concept of WBH. Modern WBH techniques using wIRA have been proven to be safe, feasible, and well tolerated. Nevertheless, there is a general need to enhance the level of evidence by documenting treatment outcome data of routine use and by conducting controlled clinical trials.

References

1. Wagner-Jauregg J. The history of the malaria treatment of general paralysis. 1946. Am J Psychiatry. 1994;151:231–5. https://doi.org/10.1176/ajp.151.6.231.
2. Dobosz P, Dzieciątkowski T. The intriguing history of cancer immunotherapy. Front Immunol. 2019;10:2965. https://doi.org/10.3389/fimmu.2019.02965.
3. Bickels J, Kollender Y, Merinsky O, et al. Coley's toxin: historical perspective. Isr Med Assoc J. 2002;6:471–2.
4. Lampert H. Überwärmung als Heilmittel. Stuttgart: Hippokrates; 1948.

5. Schlenz M. Wie kann man unheilbar scheinende Krankheiten mit Erfolg behandeln? Innsbruck: Inn-Verlag; 1951.
6. Heckel M. Beliebig langdauernde und gezielt dosierbare Erhöhung der Körpertemperatur durch eine Infrarotbestrahlungsanordnung. Strahlentherapie. 1960;111(1):149–53.
7. von Ardenne M. Principles and concept 1993 of the Systemic Cancer Multistep Therapy (sCMT). Extreme whole-body hyperthermia using the infrared-A technique IRATHERM 2000--selective thermosensitisation by hyperglycemia--circulatory back-up by adapted hyperoxemia. Strahlenther Onkol. 1994;170(10):581–9.
8. Schmidt KL. Hyperthermie und Fieber. Stuttgart: Hippokrates; 1987. p. 2.
9. Deutsche Gesellschaft für Hyperthermie (DGHT). Leitlinie zur Ganzkörperhyperthermie - Version 1.0. Forum Hyperthermie. 2018;1:5–24.
10. Aschoff J, Wever R. Kern und Schale im Wärmehaushalt des Menschen. Naturwissenschaften. 1958;45(20):477–85.
11. Meffert H, Scherf HP, Meffert B. Milde Infrarot-A-Hyperthermie: Auswirkungen von Serienbestrahlungen mit wassergefilterter Infrarotstrahlung auf Gesunde und Kranke mit arterieller Hypertonie bzw. systemischer Sklerodermie. Akt Dermatol. 1993;19:142–8.
12. Förster J, Fleischanderl S, Wittstock S, et al. Letter to the editor: infrared-mediated hyperthermia is effective in the treatment of scleroderma-associated Raynaud's phenomenon. J Investig Dermatol. 2005;6:1313–6.
13. Kraybill WG, Olenki T, Evans SS, et al. A phase I study of fever-range whole body hyperthermia (FR-WBH) in patients with advanced solid tumours: correlation with mouse models. Int J Hyperthermia. 2002;18(3):253–66.
14. Bull JM, Scott GL, Strebel FR, et al. Fever-range whole-body thermal therapy combined with cisplatin, gemcitabine, and daily interferon-alpha: a description of a phase I-II protocol. Int J Hyperthermia. 2008;24(8):649–62.
15. Kleef R, Nagy R, Baierl A, et al. Low-dose Ipilimumab plus Nivolumab combined with IL-2 and hyperthermia in cancer patients with advanced disease: exploratory findings of a case series of 131 stage IV cancers - a retrospective study of a single institution. Cancer Immunol Immunother. 2021;70:1393–403.
16. Hall EJ, Giaccia AJ. Hyperthermia. In: Radiobiology for the radiologist. 8th ed. Philadelphia: Wolters Kluwer; 2019.
17. Lee CT, Kokolus KM, Leigh ND, et al. Defining immunological impact and therapeutic benefit of mild heating in a murine model of arthritis. PLoS One. 2015;10:e0120327.
18. Evans SS, Repasky EA, Fisher DT. Fever and the thermal regulation of immunity: the immune system feels the heat. Nat Rev Immunol. 2015;15(6):335–49.
19. Repasky EA, Evans SS, Dewhirst MW. Temperature matters! And why it should matter to tumor immunologists. Cancer Immunol Res. 2013;1(4):210–6.
20. Reisinger E, Wendelin I, Gasser R, et al. Antibiotics and increased temperature against Borrelia burgdorferi in vitro. Scand J Infect Dis. 1996;2:155–7.
21. Hildebrandt B, Hegewisch-Becker S, Kerner T, et al. Current status of radiant whole-body hyperthermia at temperatures >41.5°C and practical guidelines for the treatment of adults. The German 'Interdisciplinary working group on Hyperthermia'. Int J Hyperthermia. 2005;21(2):169–83.
22. von Ardenne A, Wehner H. Extreme whole-body hyperthermia with water-filtered infrared-A radiation. In: Baronzio GF, Hager ED, editors. Hyperthermia in cancer treatment: a primer. Boston: Springer; 2006. p. 237–46.
23. Wehner H, von Ardenne A, Kaltofen S. Whole-body hyperthermia with water-filtered infrared radiation: technical-physical aspects and clinical experiences. Int J Hyperthermia. 2001;17(1):19–30.
24. Koobotse MO, Schmidt D, Holly JMP, et al. Glucose concentration in cell culture medium influences the BRCA1-mediated regulation of the lipogenic action of IGF-I in breast cancer cells. Int J Mol Sci. 2020;21(22):8674.
25. Lassche G, Crezee J, van Herpen CML. Whole-body hyperthermia in combination with systemic therapy in advanced solid malignancies. Crit Rev Oncol Hematol. 2019;139:67–74.

26. Douwes F. Komplextherapie der chronischen Borreliose (Lyme disease) - Ein neuer Therapieansatz: die Antibiotika augmentierte Thermoeradikation (AAT). OM & Ernährung. 2018;164:F10.
27. Douwes F. The successful antibiotic augmented thermal eradication of chronic lyme disease. Paper presented at the 32nd ESHO Meeting, Berlin, 16–19 May 2018.
28. Deja M, Ahlers O, Macguill M, et al. Changes in hepatic blood flow during whole body hyperthermia. Int J Hyperthermia. 2010;26(2):95–100.
29. Jia D, Liu J. Current devices for high-performance whole-body hyperthermia therapy. Expert Rev Med Devices. 2010;7(3):407–23.
30. Rowe-Horwege RW. Hyperthermia, systemic. In: Webster JG, editor. Encyclopedia of medical devices and instrumentation. 2nd ed. New York: John Wiley & Sons; 2006. p. 42–62.
31. Wust P, Riess H, Hildebrandt B, et al. Feasibility and analysis of thermal parameters for the whole-body-hyperthermia system IRATHERM-2000. Int J Hyperthermia. 2000;16(4):325–39.