
BSD-2000

DEEP REGIONAL HYPERTHERMIA



DR. SENNEWALD MEDIZINTECHNIK GMBH

Dr. Sennewald Medizintechnik was founded with the aim of discovering innovative and beneficial cancer therapies and we have since amassed over 30 years of experience in regional and superficial hyperthermia. Our aim is to help improve the range of products on offer, to support the growth of this proven technology and so increase the survival rate among cancer patients.

To help us achieve this goal, we have entered into a long-term partnership with the pioneers and world leaders, Pyrexar Medical, to further develop the manufacture of hyperthermia systems. These high-quality medical devices are designed for maximum efficacy combined with minimum risk for greater patient comfort and are installed in oncology departments, research organizations and leading universities throughout Europe.

Our unrivaled links to the scientific community have led to the acceptance of hyperthermia, the development of dedicated software, the reimbursement of hyperthermia and its use in the treatment of children. Strategic partnerships with medical centers have resulted in phase III clinical studies demonstrating that Pyrexar systems offer a significant increase in cancer response rates, and are the only ones to have received FDA approval.

The success of Dr. Sennewald Medizintechnik GmbH is a result of continuity. We are able to draw on our many years of experience for our in-depth knowledge of customers' clinical requirements and of the precise technical specifications for all the hyperthermia systems we offer. In addition, our teams of engineers, technicians and software developers remain as close to customers as possible, offering support in the planning, installation and set-up of the systems, as well as after-sales service.

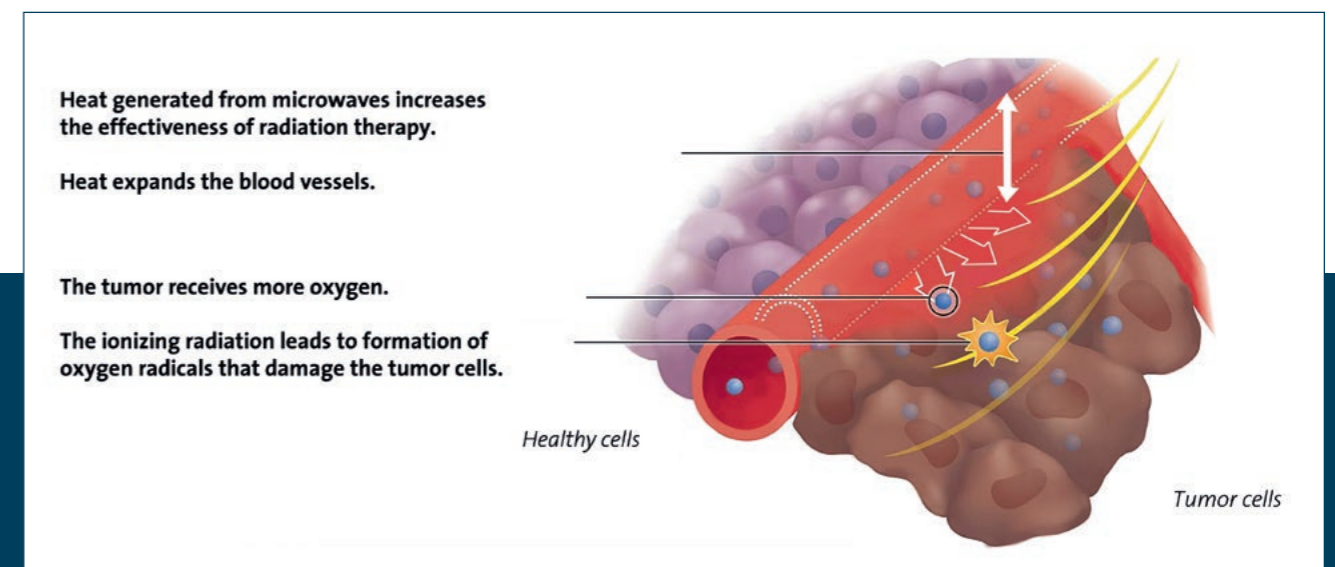
WHAT IS HYPERTHERMIA?

Hyperthermia is a treatment method in cancer therapy that has proved effective in combination with the classic standard therapies, namely radiation therapy and/or chemotherapy. It involves heating the tumor to 42°C, using focused electromagnetic waves, without damaging the surrounding tissue.

Hyperthermia is mainly used for tumors that have so far been resistant to treatment or that have relapsed. Clinical studies have proven* that hyperthermia in combination with conventional therapies clearly improves the prognosis of patients with certain types of tumor.

Primarily inoperable tumors are another indication. Hyperthermia treatment in combination with radiation therapy can reduce the size of the tumor and/or separate the tumor from surrounding tissue and thus enable its successful surgical removal.

* References to clinical studies can be found on our website under Clinical Evidence.



HYPERTHERMIA TREATMENT

EFFICACY

HOW DOES HYPERTHERMIA WORK?

Malignant tumors receive insufficient oxygenation due to poor blood circulation. The poor circulation also leads to metabolites accumulating in the tumor, causing it to over-acidify and damaging the tumor cells. This makes the tumor heat sensitive. Over-heating leads to a denaturation of proteins, death of some tumor cells, cell necrosis and the release of cell components. Special proteins end up in the extra cellular space, where they can activate cells belonging to the immune system. The details of these biological processes are currently the subject of intensive research.

Today scientists consider the activation of the immune system the most important contribution that hyperthermia makes in fighting tumors. Tumors can only survive if they are able to effectively trick or paralyze the immune system and thus prevent the immune system from attacking the tumor. Targeted heating of the tumor shuts down several of the mechanisms that cancer cells have developed for this purpose. Once the immune system is activated, it can neutralize cancer cells in the entire organism. This could also reduce the risk of metastasis.

HOW DOES HYPERTHERMIA WORK IN CONJUNCTION WITH RADIATION AND/OR CHEMOTHERAPY?

Hyperthermia treatment is extremely effective in combination with radiation therapy. Ionizing radiation destroys cancer cells by a number of biological mechanisms, including generating oxygen radicals that attack the DNA of the cancer cell. In tumor tissue, which has poor perfusion, oxygen is deficient, thus limiting the efficiency of radiation therapy. Since hyperthermia increases perfusion, and thus improves oxygenation, cancer cells can be destroyed more effectively by radiation therapy.

Hyperthermia also increases the sensitivity of cancer cells to chemotherapy. Oxygen radicals play an important role here, too. An additional factor is the effect of the heat on the metabolism, which increases the reaction capability of the cytostatic remedies and thus significantly increases the efficiency of the treatment.

With the aid of hyperthermia and thermo-sensitive liposomes filled with cytostatic drugs, the toxicity of chemotherapy can be targeted to the tumor area. The liposomes release the agents in the area of the tumor, thus reducing the systemic toxicity.

COMBINED TREATMENTS

COMBINED TREATMENTS WITH HYPERTHERMIA

HYPERTHERMIA AND RADIOTHERAPY

Clinical studies* have revealed that the addition of hyperthermia to radiotherapy can almost double the efficacy of the treatment. This is because the temperatures attained through hyperthermia increase blood flow to the tumor, accentuating the formation of the oxygen radicals required to attack cancer cell DNA through radiotherapy. Heat shock through hyperthermia is also an effective agent in inhibiting DNA repair in cancer cells after double-strand breaks occur from ionizing radiation. Further, hyperthermia kills radiation-resistant hypoxic cancer cells by forcing a rise in their anaerobic metabolism, causing them to weaken as they deplete their energy supply and become toxically acidic as their consumption exceeds their ability to expel waste.

HYPERTHERMIA AND CHEMOTHERAPY

Hyperthermia used in combination with chemotherapy increases the drug concentration in the tumor region due to increased blood flow, thus raising the effectiveness of cytostatic drugs. In addition, hyperthermia has been proven* to enhance drug toxicity in cells resistant to many drugs. Hyperthermia can, therefore, be employed synergistically with chemotherapy in strategies to treat high-risk tumors with a view towards total tumor eradication.

* References to clinical studies can be found on our website under Clinical Evidence.

INDICATIONS

HYPERTHERMIA IS USED FOR THE FOLLOWING TYPES OF TUMOR:

- ▶ cancer of the colon (i.e. the large bowel or intestine), which is locally advanced or recurring
- ▶ recurring breast cancer on the chest wall
- ▶ cancer of the uterine cervix (cervical carcinoma)
- ▶ soft-tissue sarcomas
- ▶ recurring skin cancer (malignant melanoma)
- ▶ locally advanced head-neck tumors
- ▶ locally advanced or recurring bladder cancer
- ▶ cancer of the pancreas (pancreatic carcinoma)
- ▶ locally advanced or recurring anal carcinoma (cancer of the anus)

HYPERTHERMIA IS NOT SUITABLE FOR:

- ▶ patients with serious heart disease or with a heart pacemaker
- ▶ when there are artificial joints in the area of treatment
- ▶ pregnant patients

HYPERTHERMIA

PROVEN TREATMENT FOR MALIGNANT TUMORS

Hyperthermia has now been established as the fourth column in oncology in the fight against cancer. Numerous studies at renowned university hospitals have impressively proven its effectiveness in combination with the standard procedures of radiation therapy and/or chemotherapy, including an improved quality of life and an increased survival rate among many patients. On our website you can find clinical studies from the past three decades on the effectiveness of adding superficial and regional hyperthermia to radiation therapy and/or chemotherapy.

SUMMARY OF EVIDENCE-BASED HYPERTHERMIA TREATMENT RESULTS:

- ▶ increased remission rates, as well as improved, long-term palliation
- ▶ improvement and extension of local tumor control
- ▶ clear improvement of survival rates and quality of life
- ▶ direct destruction of heat-susceptible tumor cells, especially of chemo-radiation resistant cells
- ▶ reduction in tumor size to enable resection
- ▶ increased effectiveness of other forms of treatment without increased toxicity
- ▶ improved effectiveness and results when combined with radiation therapy and chemotherapy (thermo-radio-chemotherapy)
- ▶ improved response to and acceptance of cytostatic drugs
- ▶ reduced disfiguration due to surgical tumor resection

THERAPY

THERAPY

REGIONAL DEEP HYPERTHERMIA

With the help of regional deep hyperthermia, deep seated tumors or large tumor areas are treated in combination with radiation, chemotherapy, or radiochemotherapy. These include, for example, rectal cancer, bladder cancer, high-risk soft tissue sarcomas, cervical cancer or pancreatic cancer.

With regional deep hyperthermia, the patients lie in a ring applicator. A water bolus and antennas that radiate high-frequency electromagnetic waves are integrated into this applicator. These waves can be focused on the tumor via the independent control of individual antennas and lead to a regional heating. The treatment region can be heated to targeted therapeutic temperatures of 41°C through 43°C. To achieve the therapeutic temperatures while protecting the surrounding tissue, it is necessary to use special applicators with suitable control systems.

THERAPY SYSTEM BSD-2000

The BSD-2000 therapy system consists of a ring applicator with integrated water bolus, a control unit and a patient-positioning system. The ring applicator has four antennas that can be individually activated in both power and phase. The energy is regulated by the control unit. The water bolus guarantees the continuous transfer of electromagnetic waves into the body and also helps to cool the skin surface.

The patient-positioning system ensures a comfortable position during the entire therapy session. Optimal positioning within the ring applicator is facilitated by way of a hydraulic lifting device. The applicators are available in various sizes for use in different application areas, for example for children and adults.

THE HYPERTHERMIA DEVICE



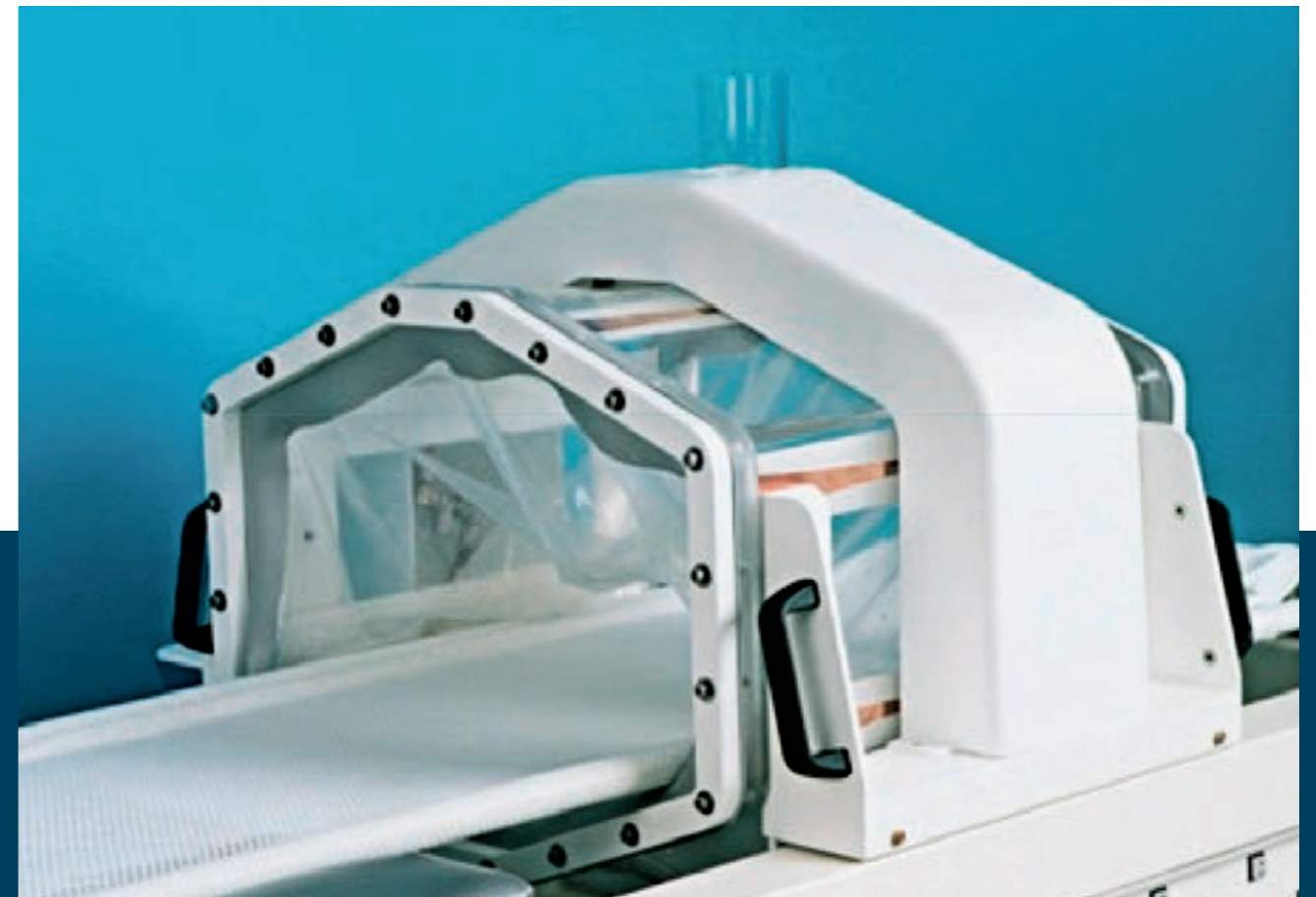
KEY FEATURES

The Sigma 60 and Sigma Ellipse annular-phased array applicators are composed of a clear plastic shell, eight radiating dipoles, and a bolus membrane. The former makes use of a cylindrical shape to support the dipoles, while the latter has an elliptically shaped shell to support these components. Additionally, the Sigma Ellipse provides improved comfort for smaller patients.

OVERVIEW:

- ▶ advanced annular phased array principles create a central focusing of energy, which significantly overcomes the penetration losses of the energy radiated into the body
- ▶ phased array applicators allow the operator to shape the heating pattern to the targeted treatment area and achieve selective power targeting at depth for treatment of deep tumors
- ▶ water filled bolus dielectrically loads the individual antennas and provides an energy-confining medium that directs the RF energy into the body
- ▶ quick and easy patient setup

- ▶ the plastic shell provides a clear view of the patient's surface to allow visual verification of the applicator positioning and to facilitate monitoring of any skin color changes, which would be indicative of surface hot spots adapted to the tumor region
- ▶ the BSD-2000 Deep Regional Hyperthermia System is FDA approved under HDE exemption



BSD-2000 DEEP REGIONAL HYPERTHERMIA

The deep regional system uses an annular phased array configuration to shape and focus thermal energy on the targeted treatment area deep inside the limbs, pelvis or abdomen.

1. THE SIGMA TREATMENT BASE UNIT

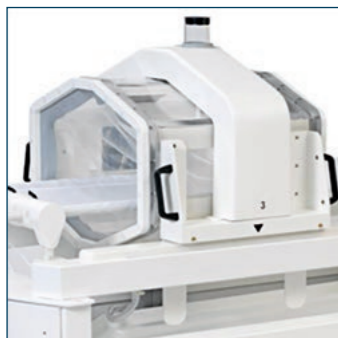
- ▶ RF power delivery subsystem
- ▶ proprietary, thermistor-based, thermometry subsystems
- ▶ computerized monitoring and control subsystems
- ▶ applicator subsystem that includes an applicator and patient support system
- ▶ various accessories, including a tissue equivalent QA lamp phantom that provides verification of the energy focus, pattern steering, and system operations

The standard BSD-2000 has a maximum power output of 1300 watts.

APPLICATORS

ANNULAR PHASE ARRAY

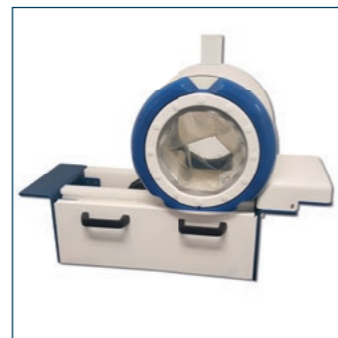
The Sigma applicators are annular phased array applicators that comprise a clear plastic shell, 8 radiating dipoles, and a bolus membrane. The Sigma Ellipse provides improved comfort for smaller sized patients.



SIGMA ELLIPSE



SIGMA 60



SIGMA 30

PATIENT SUPPORT SYSTEM

- ▶ **COOLING SYSTEM** – Water system automatically fills the bolus and controls the bolus water temperature. This keeps patient exterior within a comfortable temperature range.
- ▶ **FABRIC SLING** – Fabric sling comfortably supports patient inside the applicator for optimized patient comfort. Hydraulic lift system used for an optimal positioning.
- ▶ **QUICK DRAIN BOLUS** – Quick drain capability allows fast access to the patient – 15 seconds for patient access and 30 seconds for a complete drain.
- ▶ **SIGMA SYSTEM** – Three interchangeable phased array applicators support different patient sizes and indication-specific applications.

CONTROL SYSTEM

- ▶ **INTUITIVE INTERFACE** – Provides a fully featured, user friendly, intuitive, graphical user interface and touch screen with step-by-step guide for setup and treatment procedure. Primary user features are presented on main screen.
- ▶ **MONITORING** – Closed-loop feedback system is equipped with automatic monitoring and control of treatment parameters, including power output, frequency, amplitude and phase, tissue and core temperature, and treatment time.
- ▶ **TEMPERATURE CONTROL** – The control of power and tissue temperature is performed within steps of ± 0.1 °C in compliance with ESHO guidelines.
- ▶ **SAFETY CHECKS** – The computer automatically performs safety checks to ensure correct operation of the system and ensure patient protection with auto shutdown features.

POWER GENERATOR

- ▶ **PHASE & AMPLITUDE** – Solid-state amplifier provides four-channel independent phase and amplitude adjustment.
- ▶ **325 W PER CHANNEL** – Outputs of 0 to 325 watts per channel and phase accuracies within a tolerance of 10 degrees can be achieved.
- ▶ **PHASE OFFSET** – Computer automatically monitors and controls forward and reflected power, phase, and power on each channel.
- ▶ **TREATMENT PLAN** – Treatment settings are calculated through the use of treatment planning software tools provided with the system.

THERMOMETRY

- ▶ **HIGH ACCURACY** – Non-perturbing, electromagnetically insensitive, temperature sensors operate with an accuracy of ± 0.2 °C over a range of 25 to 52 °C.
- ▶ **AUTO POSITIONING** – Automated positioning system allows the operator to map the sensor along the length of the catheter in order to determine the temperature profile.
- ▶ **PRECISE CALIBRATION** – Precise calibration reference sensor is accurate to ± 0.05 °C over a range of 0 to 60 °C. New thermal well for easy pre-treatment calibration.
- ▶ **PROBE MAPPING** – Motorized probe mapping allows for the mapping of temperature in 0.5 cm increments along catheter path.

2. RF ISOLATION CAGE FOR THE BSD-2000

The BSD-2000 generates non-ionizing radiation, in the form of radio frequency (RF), during deep regional hyperthermia treatments. Phased array RF energy excites cells in the body, producing cell friction, which generates localized heat. Stray RF field emissions can interfere with communication products, like FM radio. As with the EMF shielding required for MRI systems, the German Bundesnetzagentur requires the prevention of these competing frequencies from leaking out of the treatment room.

Shielding can be an expensive and disruptive process for any cancer treatment center. There is a high quality, lower cost, alternative solution, that can be installed without affecting the existing lighting, air handling, fire monitoring and fire suppression systems.

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