What is Deep Regional Hyperthermia?

The BSD-2000 provides deep regional therapeutic hyperthermia to solid tumors by applying radiofrequency (RF) energy at the frequency range of 75 to 120 MHz. The BSD-2000 delivers energy to a patient using a power source and an array of multiple antennae that surround the patient’s body. The BSD-2000 was designed to provide an optimized heating zone targeted to the tumor region by utilizing the adjustment of frequency, phase, and amplitude from multiple power sources. The energy can be focused electronically to the tumor region, thus providing dynamic control of the heating delivered to the tumor region.

Indication for Use

Humanitarian Use Device. In the U.S., the BSD-2000 has a Humanitarian Device Exemption (HDE) approval for use in conjunction with radiation therapy in the treatment of cervical carcinoma patients who would normally be treated with combined chemotherapy and radiation but are ineligible for chemotherapy due to patient related factors. The effectiveness of this device for this use has not been demonstrated.

What is Hyperthermia

The BSD-2000 Hyperthermia System (BSD-2000) is used to deliver therapeutic heating (hyperthermia) to cancerous tumors by the use of radiofrequency (RF) energy. During a treatment, the cancerous tumor is heated to 40 and 45°C (104 - 113 °F). Hyperthermia damages cells in solid tumors, without damaging normal tissues, because higher temperatures selectively damage cells that are hypoxic and have low pH, a condition of tumor cells and not a condition of normal cells. Hyperthermia has been shown to inhibit cellular repair mechanisms, induce heat-shock proteins, denature proteins, induce apoptosis, and inhibit angiogenesis.

Hyperthermia and Radiotherapy

Hyperthermia increases the effectiveness of radiation therapy due to the independent cytotoxic effects of hyperthermia combined with its radiosensitizing effects. Hyperthermia increases blood flow, resulting in improved tissue oxygenation and thus increased radiosensitivity. Hyperthermia also interferes with cellular repair of the DNA damage caused by radiation. Hyperthermia damages cells that are hypoxic, have a low pH, and are in the S-phase of division, which are all conditions that make cells resistant to radiation therapy. The addition of hyperthermia does not usually increase the toxicity of radiation therapy.
BSD-2000 Hyperthermia System

**BSD-2000 System Description**
The BSD-2000 consists of four major subsystems.

- RF power delivery subsystem.
- Proprietary, thermistor-based, thermometry subsystem.
- Computerized monitoring and control subsystem.
- 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 BSD-2000 comes in two configurations, a lower power basic system (BSD-2000B) that has a maximum power output of 1300 watts and an upgraded higher power system (BSD-2000U) that has a maximum power output of 1800 watts. The standard treatment usually involves the use of the 1300 watt BSD-2000B, while the 1800 watt BSD-2000U is reserved for larger patients.

**Power Delivery Subsystem**
- Solid-state amplifier with 4-channel independent phase and amplitude adjustment capability.
- Maximum power output of 0 to 500 watts per channel.
- Phase accuracy within a 10 degree tolerance.
- Computer automatically monitors and controls forward and reflected power, phase, and power on each channel.
- Optimized treatment settings are calculated through the use of treatment planning software tools provided with the system.

**Thermometry Subsystem**
- Non-perturbing, electromagnetically insensitive, temperature sensors with an accuracy of ±0.2°C over a range of 25 to 52°C.
- 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 reference sensor is accurate to ±0.05°C over a range of 0 to 60°C.
Sigma Treatment Base Unit
with Applicator

Applicator and Patient Support System

- Optimized power coupling.
- Optimized patient comfort.
- Water system automatically fills the bolus and controls the bolus water temperature.
- Fabric sling comfortably supports patient inside the applicator.
- Easy patient access and handling.
- Quick drain capability allows fast access to the patient - 15 seconds for patient access and 30 seconds for a complete drain.

Computer Control System

- User friendly, intuitive, color graphics interface.
- Step-by-step guide for setup and treatment procedure.
- Icon selectable adjustments of the treatment parameters.
- Tabs allow operator to easily switch between screen displays.
- Closed-loop feedback system provides automatic monitoring and control of treatment parameters, including power output, frequency, amplitude and phase, tissue temperatures, core temperature, and treatment time.
- System automatically records, displays, and prints patient treatment data.
- Control of power and tissue temperature to within ±0.1°C.
- Data regarding temperatures, RF power level, and RF power control updated every 2 seconds.
- Control algorithms smoothly adjust heating and cooling rates.
- The system controls the applied power level in accordance with operator inputs and automatically adjusts the level of power to maintain the operator selected temperatures throughout the treatment.
- The computer automatically performs numerous safety checks to ensure proper operation of the system and ensure safety for the patient and the operator.
Applicator Subsystem

The Sigma applicators (Sigma 60 and Sigma Ellipse) are annular phased array applicators that are comprised of a clear plastic shell, 8 radiating dipoles, and a bolus membrane. The Sigma 60 uses a cylindrical shaped plastic shell to support the 8 radiating dipoles. The Sigma Ellipse is an elliptically shaped plastic shell used to support the same components used in the Sigma 60. The Sigma Ellipse provides improved comfort for smaller size patients.

- 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.
- Dipoles are covered by a thin dielectric layer to prevent contact with the bolus water.
- 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.
- 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.

BSD is sponsoring an FDA approved investigational study to evaluate the safety and efficacy of hyperthermia (using the BSD-2000 Hyperthermia System) combined with radiation therapy for the treatment of subjects suffering from locally advanced, persistent, or recurrent deep tumors of the pelvis; i.e., cervical, prostate, rectal, and bladder.
Site Planning

An enclosed RF shielded treatment area (not supplied by BSD as part of the BSD-2000) is required for use with the BSD-2000 in order to comply with FCC regulations. A standard hyperthermia treatment area consists of an RF shield enclosed treatment room (which contains the patient interface components), the operator room for installation of the RF power generator.

A standard hyperthermia suite consists of the treatment room, the operator room, and a small technical room. For convenient patient handling, the treatment room is equipped with electromagnetic shielding and typically requires floor space of 142.5 square feet. The adjoining operator room requires floor space of 78 square feet and an observation window looking into the treatment room. A small technical room of 34 square feet is required for installation of the amplifier.

Our site-planning specialists will be happy to assist you in finding the ideal layout for your environment. The installation manual includes specifications for building services, electricity, air conditioning, and other relevant factors.
Clinical Studies

A Phase III randomized study was conducted at Erasmus Medical Center – Daniel den Hoed Cancer Center (DHCC), Rotterdam, The Netherlands, to compare hyperthermia (HT) and radiation (RT) to RT only treatment of 65 advanced cervical cancer patients, referred to as the BSD Intent-to-Treat (“BSD ITT”) population. 33 patients were randomized into RT combined with HT and 32 were randomized into RT alone. All patients had prognostic indicators that are associated with a poorer outcome for cervical cancer. The study met its primary endpoint of a 20% increase in complete response rates for cervical cancer patients receiving HT and RT as compared to RT alone. (Complete response [CR] was defined as disappearance of all viable tumor in the irradiated volume.) These data were a subset of the Deep Dutch Hyperthermia Trial data that were published in The Lancet. (Van der Zee J, Gonzalez-Gonzalez D, Van Rhoon GC, et al. Comparison of radiotherapy alone with radiotherapy plus hyperthermia in locally advanced pelvic tumours: a prospective, randomised, multicentre trial. Lancet 2000;355:1119-1125.)

The addition of HT to RT demonstrated a statistically significant improvement (p=0.006, Fisher exact test, BSD ITT Population) in local tumor control for cervical cancer. The CR rate for RT+HT was 88%, whereas it was 56% for RT. In the BSD ITT population, 14/33 (42%) of the RT + HT patients and 18/32 (56%) of the RT patients died prior to three years.

For the BSD ITT population, 29/33 (88%) of the RT+HT arm had CR, as compared to 18/32 (56%) of the RT arm with a CR, for an odds ratio=0.1773 (95% confidence interval 0.0504, 0.6235) and the difference between treatments was statistically significant (p=0.006, Fisher exact test). This result corresponds to a much lower failure rate in the RT + HT subjects.

The median survival times were 31.7 months for the RT + HT group and 23.2 months for the RT group. The addition of the HT increased the survival time by 8.5 months. Even though there was a trend towards increased survival for the patients treated with the BSD-2000, the difference was not statistically significant (p=0.71, log rank survival) for the BSD ITT Population. However, this lack of significance may be due to relatively low patient numbers, together with the high long-term mortality rate generally seen in patients with advanced cervical carcinoma.

The side effects observed in the pivotal study were generally self-resolving or managed conservatively. There were no unanticipated safety considerations reported from the pivotal study. There was no difference between the RT arm and the RT+HT arm for side effects. Twelve year follow-up data demonstrated that side effects for HT were few and generally self-resolving and mild for the study patients. There were no severe or unexpected toxicities or late effects that were attributed to the BSD-2000 treatment from the pivotal study.

Restrictions

Federal (U.S.A.) law restricts this device to sale by or on the order of a physician trained in the use of this device.

The BSD-2000 System is to be used only by qualified operators upon the prescription and under the supervision of a physician who is experienced in clinical hyperthermia.

See BSD-2000 Essential Prescribing Information for complete information on the FDA approved indications for use and side effects.