



The gentle power of hyperthermia

TCS – Tumor Cell Solution for
regional hyperthermia therapy


Partners in the fight against cancer.

Contents

- Who we are. 4
- One therapy. Three effects. 6
 - Hyperthermia to complement radiation therapy
 - Hyperthermia to complement chemotherapy
 - Hyperthermia to strengthen the body’s own immune system
- How hyperthermia works. 10
 - Mechanisms of action
- Hyperthermia brought to the point. 11
 - Innovative technology and therapeutic precision based on two electrodes
- One system. Variable therapy options. 12
 - Application
 - Intelligent electrode design
- Intuitive operation. Effective administration. 14
 - Safe treatment.
 - User interface
 - Treatment control
- Focus on the patient. 16
 - Focus on the patient
 - User safety
- Our responsibility: technology that works. 18
 - TCS – Tumor Cell Solution Dimensions
 - Technical performance data

Who we are.

The people working at Celsius42 have one shared goal – to be united in the fight against cancer. To pool knowledge. To leverage partners and resources. To explore increasingly intelligent pathways in medical technology to finally win the fight. Medicine has fought this battle for a long time. A battle against a clever opponent: cancer. Hyperthermia is the active principle of Celsius42 products. Targeted thermal energy that causes stress in cancer cells. It has many positive effects in chemotherapy or radiation therapy, but also strengthens the immune system. The people at Celsius42 know that they are on the right track. Their tenacity, energy and human experience make them a tight-knit team. With a single mission: to develop innovative hyperthermia products that help to fight cancer gently but effectively. **That is Celsius42. That is TCS – Tumor Cell Solution.**

A portrait of Christian Hartmann, a middle-aged man with short grey hair and a light beard, wearing a dark blue blazer over a dark blue button-down shirt. He is standing with his arms crossed against a background of large, white, stylized molecular or cellular structures.

„Our products are manufactured individually with care, diligence and expertise. We understand our responsibility – toward people and toward life.“

Christian Hartmann, Celsius42

One therapy. Three effects.

Deep-tissue hyperthermia increases the tumor temperature in a controlled way. This process gently enhances the impact of chemotherapy and radiation therapy, while supporting the immune system at the same time.

In this treatment process, the patient is part of the therapeutic effect. The body serves as a capacitor between the electrodes and therefore becomes part of a resonant oscillating action cycle. The system's capacitive, thermodynamic effects in the tissue generate heat. Based on this arrangement and the freely selectable energy input, the treatment can be adjusted to the patient, the tumor identity, and the tumor location.

The Celsius TCS – Tumor Cell Solution hyperthermia system includes 2 active therapy electrodes, which guarantee a high level of homogeneous overheating on the tumor tissue with an approved maximum output. Thanks to the various electrode sizes, the energy input can be specifically focused on the tumor.

01

Hyperthermia to complement radiation therapy

The proven effect of hyperthermia in combination with radiation therapy relies on various mechanisms. It has been documented in numerous comparative studies that hyperthermia reinforces radiation therapy. In-vivo studies have shown that the effectiveness of radiation therapy can be increased by a factor of 1.2 to 5 with hyperthermia.

(1) Hypoxia

The effectiveness of radiation therapy increases with a greater oxygen level in the target area. Hyperthermia can contribute to this by promoting higher blood circulation rates. The free oxygen radicals generated by the radiation cause damage to the DNA. This effect has been clearly documented in many tests.

Examples for treatments with the Celsius TCS – Tumor Cell Solution System

arm electrode 250 mm			session 1	session 2	session 3	session 4	session 5
tile electrode 250 mm							
cooling temperature			18°C	16°C	12°C	10°C	10°C
1. level	duration	[min]	20	20	20	20	20
	power	[W]	40	60	65	80	100
2. level	duration	[min]	10	10	10	10	10
	power	[W]	60	80	85	100	120
3. level	duration	[min]	10	10	10	10	10
	power	[W]	70	100	110	125	140
4. level	duration	[min]	10	10	10	10	10
	power	[W]	90	120	130	145	160
5. level	duration	[min]	10	10	10	10	10
	power	[W]	100	≥130	Max. tolerable power (> 130)	Max. tolerable power (> 150)	Max. tolerable power (> 160)
applied energy		[kJ]	~ 240	> 295	> 351	> 408	> 468
session time		[min]	60	60	60	60	60

Example: Therapy concept by Dr. med Hüseyin Shinbas, Praxis-Klinik Hyperthermie & Support Care.

Moderate hyperthermia is ideally suited to achieve a higher oxygen saturation level in the tumor area by promoting blood circulation if it is administered shortly before the radiation therapy.

(2) Inhibition of DNA repair mechanisms

Every living cell includes automatic mechanisms to repair breaks in DNA double strands. If a cell is exposed to additional stress after the damage described above, these repair mechanisms are significantly disrupted. Heat is one possible stress factor for this purpose. As a consequence, the desired cell killing effect of radiation therapy is reinforced in the target area ("fix the damage").

(3) Complementary sensitivities

Cells in the hypoxic and low pH range as well as the cells in the S-phase are less likely to be affected by radiation therapy – but respond to the above-described effects of hyperthermia even more strongly. This results in a complementary effect. In summary, hyperthermia is probably the most effective radiosensitizer currently known.



The TCS – Tumor Cell Solution System is designed to treat various body regions with ergonomic precision. This is made possible by the flexibility of the hydraulic arm and the versatile positioning options for the electrodes.

02 Hyperthermia to complement chemotherapy

The interactions of hyperthermia and cytostatic drugs can be independent, additive and synergistic.

The most important mechanism leading to an interactive effect with cytostatic drugs include an increased intratumoral drug concentration, which is associated with higher blood circulation and optimized permeability of the membrane with higher intracellular uptake. In addition, studies have proven an increased intracellular drug metabolism and accelerated response

rate in an elevated temperature environment. To date it has been demonstrated for a wide range of chemotherapy drugs that the combination of chemotherapy with hyperthermia helps to prevent chemo-resistance. Supra-additive cytotoxic effects were particularly observed in combination with alkylating antineoplastic agents and platinum derivatives.

03 Hyperthermia to strengthen the body's own immune system

Hypothermia increases both the effectiveness of the two above-mentioned methods, while supporting the body's own immune system as an additional benefit. After all, responding to certain situations with a fever is a natural reaction of the body, which in effect creates hyperthermia conditions on its own.

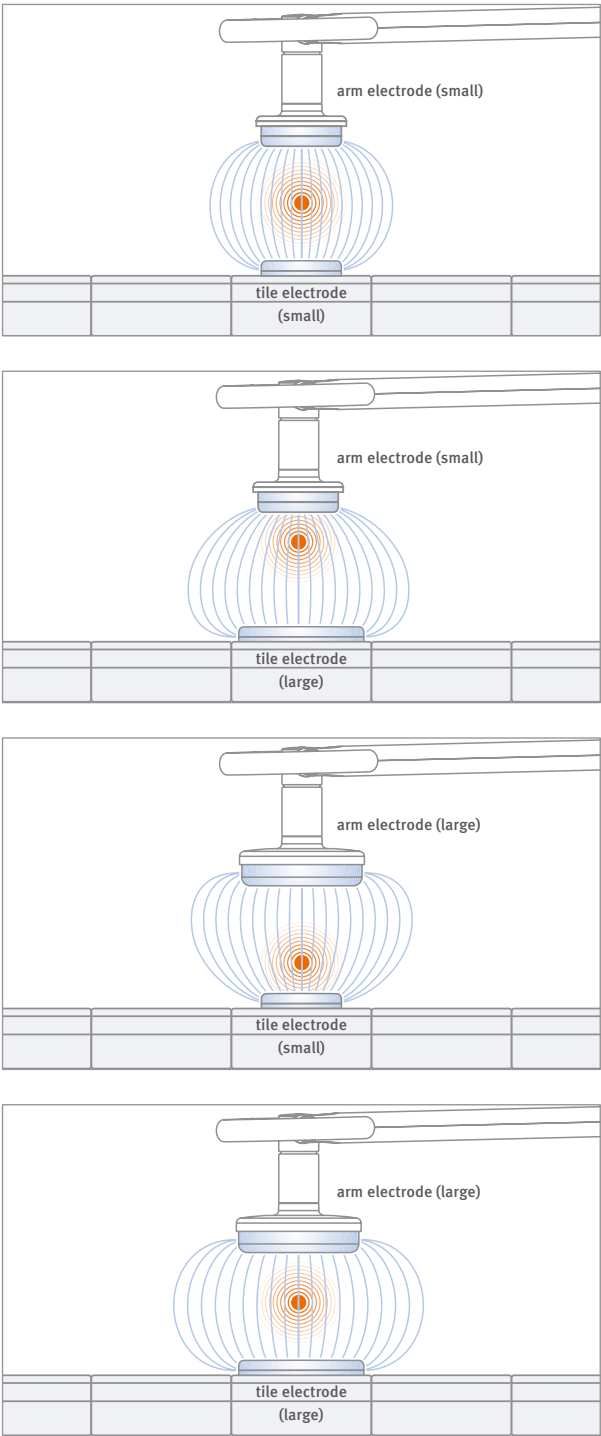
Current studies in this area will hopefully generate further interesting insights. It is already obvious that natural killer cells are more effective in an elevated temperature environment.

These studies describe the migration of natural killer cells (NK), their effectiveness and aggressiveness at temperatures ranging from 39 to 40.5°Celsius. In contrast, the activity levels of NK appeared to be inhibited again at temperatures above 41 to 42°Celsius.

Conventional therapies generate necrotic cells, which can trigger another valuable adaptive immune reaction under thermal reinforcement.

How hyperthermia works.

Schematic representation of the TCS – Tumor Cell Solution targeting mechanism.



Capacitive radiofrequency hyperthermia takes advantage of the absorption behavior of extracellular fluids on the tumor tissue.

Mechanisms of action

This method uses electromagnetic waves with a frequency of 13.56 MHz (radio waves) for energy transfer in accordance with the principle of capacitive coupling.

The body tissue located between the two electrodes becomes the dielectric and heats up due to the adapting orientation of the ions in the cells and in the intercellular space. Depending on the region and output, significant temperature gradients can be reached. Based on this technology and the underlying base frequency, the system is able to reach deeper regions in the body tissue.

Regional warming also has an impact on the micro-environment. Additionally, the slight local dilation of the vessels in the target area caused by the increased temperature also results in higher permeability for cytostatic drugs and the body's own immune cells.

Hyperthermia has been shown to have a stimulating effect on the immune system. It not only facilitates the above-mentioned exchange, but also enhances the activity of natural killer cells in an elevated temperature environment for greater effectiveness. That is most likely one of the reasons why our body responds to infections with a natural fever, i.e. by elevating the body temperature.



Therapy brought to the point.

The TCS – Tumor Cell Solution system by Celsius42 takes effect where it is needed.

Innovative technology and therapeutic precision based on two active electrodes

The Celsius TCS – Tumor Cell Solution system is equipped with two active electrodes, which sets it apart from other systems currently on the market. Our technical innovation ensures that the tumor is subject to a more homogeneous temperature development. Thanks to the various electrode sizes, the target area in the patient's body can be heated up precisely. The various levels of impedance ("sensitivity") in the diseased

and healthy tissue therefore further support the treatment focus. Tumors located deeper within the body can be treated as well. This is accomplished by a carrier frequency of 13.56 MHz, which is generally able to reach even deeper-lying regions. At the same time, the powerful high capacity generated by the intelligent technical impact and a particularly sustainable water cooling system ensure a significant penetration depth.

One system. Variable therapy options.

The TCS - Tumor Cell Solution system features adjustable tile electrodes, a movable hydraulic arm and dual-action electrodes to quickly and easily create the best possible individual treatment situation for every patient.

Application

The hyperthermia system Celsius TCS – Tumor Cell Solution is designed for optimal operation in every-day patient situations.

The treatment of tumors in various points of the body can be realized with the help of the easily movable electrodes of the hydraulic arm and the flexibly adjustable tile electrodes in the treatment bed.

Most thermal receptors are located close to the skin surface. The water bolus in the electrodes is part of a powerful cooling system that enables better dissipation of the heat developing on the skin surface.

The high level of operator convenience of the TCS - Tumor Cell Solution system enables the swift and easy conversion to each patient's particular needs.

This allows achieving a higher and more efficient energy input for the deeper target areas the treatment is aimed at.

This results in effective treatment of deeper body regions without any risk of overheating the skin. The cooling of the electrodes significantly reduces any possible burning risk.

Intelligent electrode design

The water bolus in the electrodes closely fits the body's anatomy and tolerates minor movements such as those occurring during the course of a typical treatment session. The polyurethane material of the electrode membrane is skin-compatible, sturdy and easy to clean. The electrode

itself is designed to safely rule out any direct contact of the electrode plate with the patient's skin to optimally minimize the treatment risk.

The TCS – Tumor Cell Solution hyperthermia system stands out for its dual-action electrodes. The system automatically detects which electrode size is connected and checks the plausibility of the settings. This prevents an overly high output setting for small electrode sizes, resulting in a high level of safety for users and patients alike. Various electrode formats and the option to use two selective electrodes help to make the energy input more targeted.

Intuitive operation. Effective administration. Safe treatment.

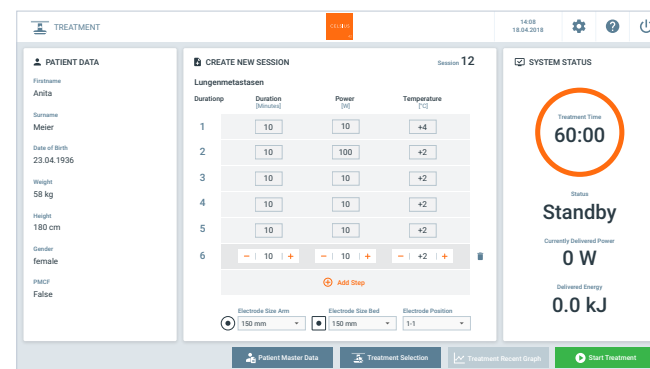
The easier the handling and the more intuitive the user interface, the safer the therapy process. Two monitors allow for entering new data with simultaneous therapy control.

User interface

A well-thought-out workflow saves valuable time for treatments and guarantees safe therapy even during busy clinic hours. The software includes a patient database that offers a simple search tool to quickly and safely locate current or past patient data. The Celsius TCS - Tumor Cell Solution user software is easy to handle. All recorded data, both medical and economic, as well as all relevant performance parameters are saved in the device and can be quickly and easily summarized and evaluated (statistics).

The therapy session data management and the input of session parameters occur centrally via the computer unit of the Celsius TCS - Tumor Cell Solution. The dual-monitor operation enables data input at the second monitor, while the ongoing treatment is recorded on the first monitor. This ensures a uniform treatment course.

At the Celsius TCS - Tumor Cell Solution system, a small control panel as well as the monitor permanently display the most relevant parameters of the treatment.



The treatment plan provides information on the therapy course and the planned treatments.*

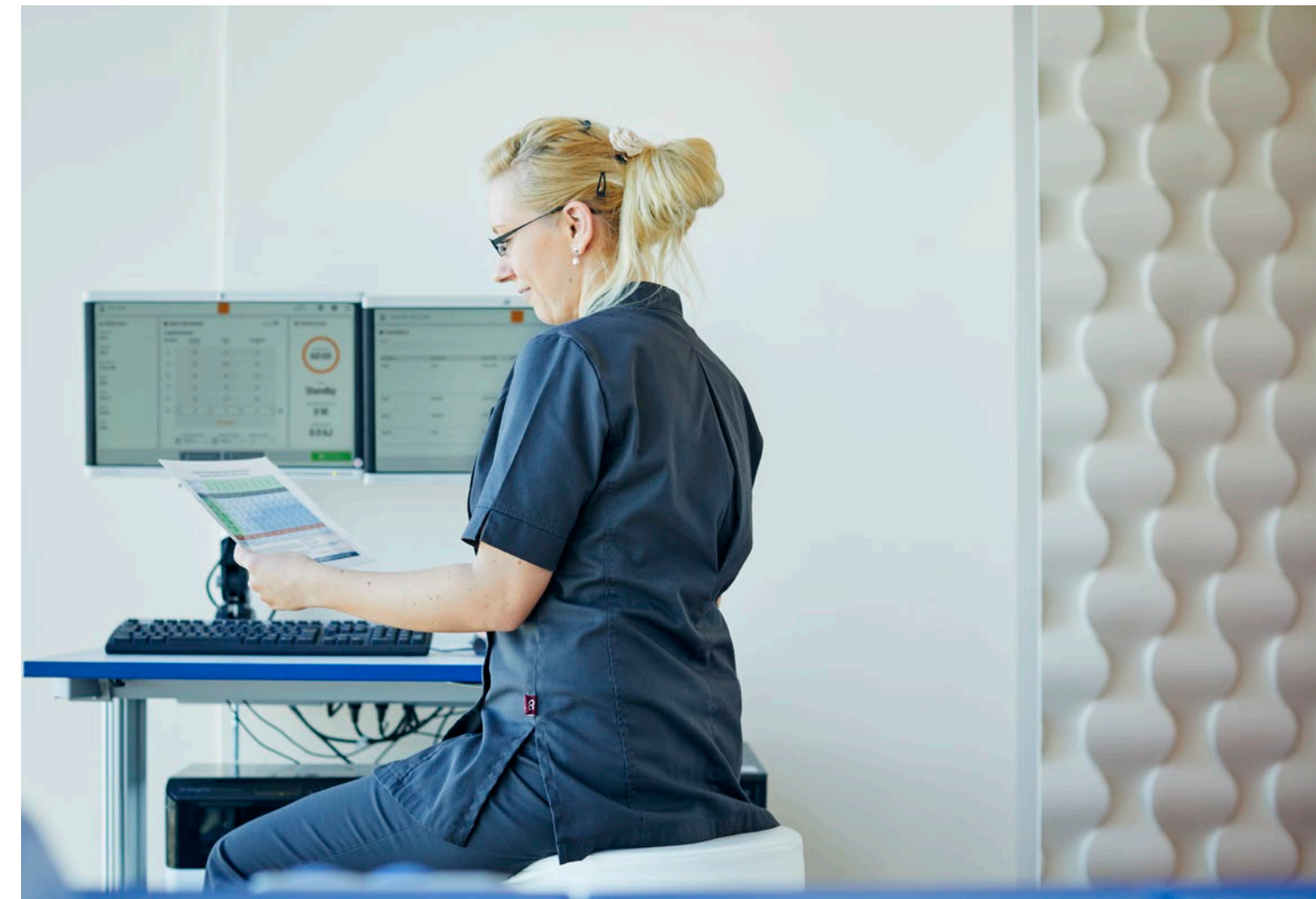


Current bio-values can be viewed at any time in the ongoing therapy.

*Legal information: The software shown will be available by late 2018.

Treatment control

Patient data is managed safely and easily. All treatment data is accessible throughout the therapy, including for long-term treatment. Individually programmable treatment protocols guarantee an up-to-date, and above all, consistent therapy course.



Patient data and the course of therapy are visible at all times. Legal information: The software shown will be available by late 2018.

In everyday clinical practice, patient and treatment information and data must be accessible quickly and easily. That not only saves time, but also guarantees the proper therapy settings.

Focus on the patient.

We not only care about the optimal treatment success of our hyperthermia system, but also its delivery method. It should be gentle and free of stress and pain.



Control panel and emergency shut-off button Easily accessible. Convenient to use.

Focus on the patient

The well-being of the patient during hyperthermia treatment is continuously monitored. Patients can independently cancel the session at any time at the push of a button. The hydraulic

arm automatically allows the patient to get up right away. In addition, the Celsius TCS – Tumor Cell Solution system prompts the patient to regularly actuate a confirmation hand switch in all phases associated with high power output. When the patient fails to give the confirmation signal, the auto-stop function is activated immediately.

User safety

The safety level of our Celsius TCS – Tumor Cell Solution is continuously adapted to the state of the art with further development efforts. Thus, we continuously measure and monitor the applied power output to enable subsequent evaluation if needed. This is clearly shown on the monitor and recorded. The system software permanently reviews the power output and directly switches off the system in case of abnormalities. As an additional protection, all treatment steps are shown on the control panel and must be confirmed by the operator prior to starting treatment in each case to properly identify the patient and the allocated therapy.

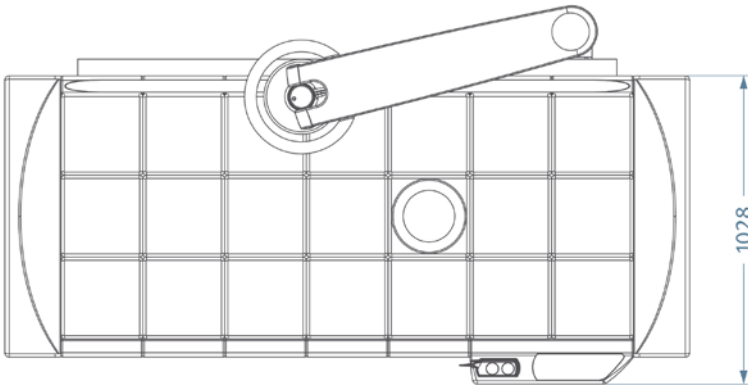
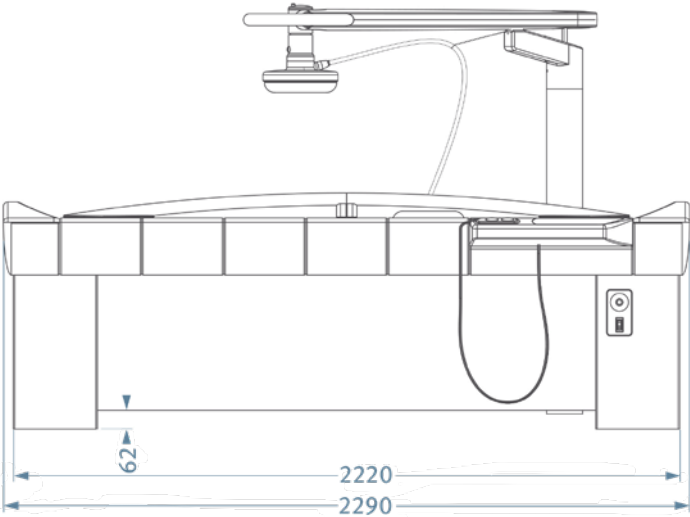
*In focus at any time
of the therapy: the
patient's well-being*



Our responsibility. Technology that works.

The Celsius42 developers and engineers
will not rest until all product features form
a perfect synergy.

TCS – Tumor Cell Solution Dimensions



All medical technology must prove useful in everyday applications. That is particularly true for the hyperthermia products of Celsius42. We treat cancer. Sensitive and successfully. That's the claim of our research. And that's the objective of our product development.

The TCS - Tumor Cell Solution system must work. It must be safe and easy to operate. In addition to intuitive operation, that also means convenient management of patient data.

The robust, low-maintenance technology guarantees long, trouble-free operating times and continuous patient care.

Along with guaranteed sustainability and economic reason based on the durability of our products.

The TCS - Tumor Cell Solution system from Celsius42 can be installed in any medical office or clinic room. No special shielding measures are required.

Of course, Celsius42 offers courses to learn skilled and professional handling of the TCS - Tumor Cell Solution system. That also includes smaller regular maintenance work for maximum autonomy.

Would you like more information?
We will be glad to assist you.

Technical performance data

Article no.	2070
Operating temperature	+15°C to +35°C
Air pressure	860 hPa to 1060 hPa
Relative humidity	20% to 70%, non-condensing
Line voltage	230 V AC, 50/60 Hz
Line frequency	50/60 Hz
Load resistance	10 to 100 ohms
Rated mode of operation	S1 continuous operation
Power consumption	2500 W
Ingress protection	IP X0
Protection class	Class I, BF
Electromagnetic compatibility	EN 60601-1
Cooling	Water circuit with adjustable water temperature
Cooling medium	Ultra-pure water, fully deionized, degassed and sterilized
Weight	about 600 kg
Service life	10 years
Maintenance interval	1 year
Noise	<60 db(A)
Filter insert	Pocket filter, duration of use 1 per maintenance interval
MDD class	II b

RF generation

Carrier frequency	13.56 MHz
RF output before matchbox	6 to 600 W, duty cycle 100%
Potential maximum RF output	500 W
RF output to patient	Arm electrode 150 mm: max. 250 W, Safety mode 130–250 W Arm electrode 250 mm: max. 350 W, Safety mode 180–350 W
Modulation	none
Impedance range	10 ohms to 100 ohms
Coordination speed	<3 S

Patient bed

Dimensions L x W x H (mm)	2290 X 940 X 785
Material	Polyurethane, viscoelastic

Electrodes

Variants	Tile and arm, diameter of 150 mm and 250 mm, respectively, replaceable
Electrode surface	Polyurethane
Weight	approx. 5 kg (water-filled)

Technical Cancer Treatment

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