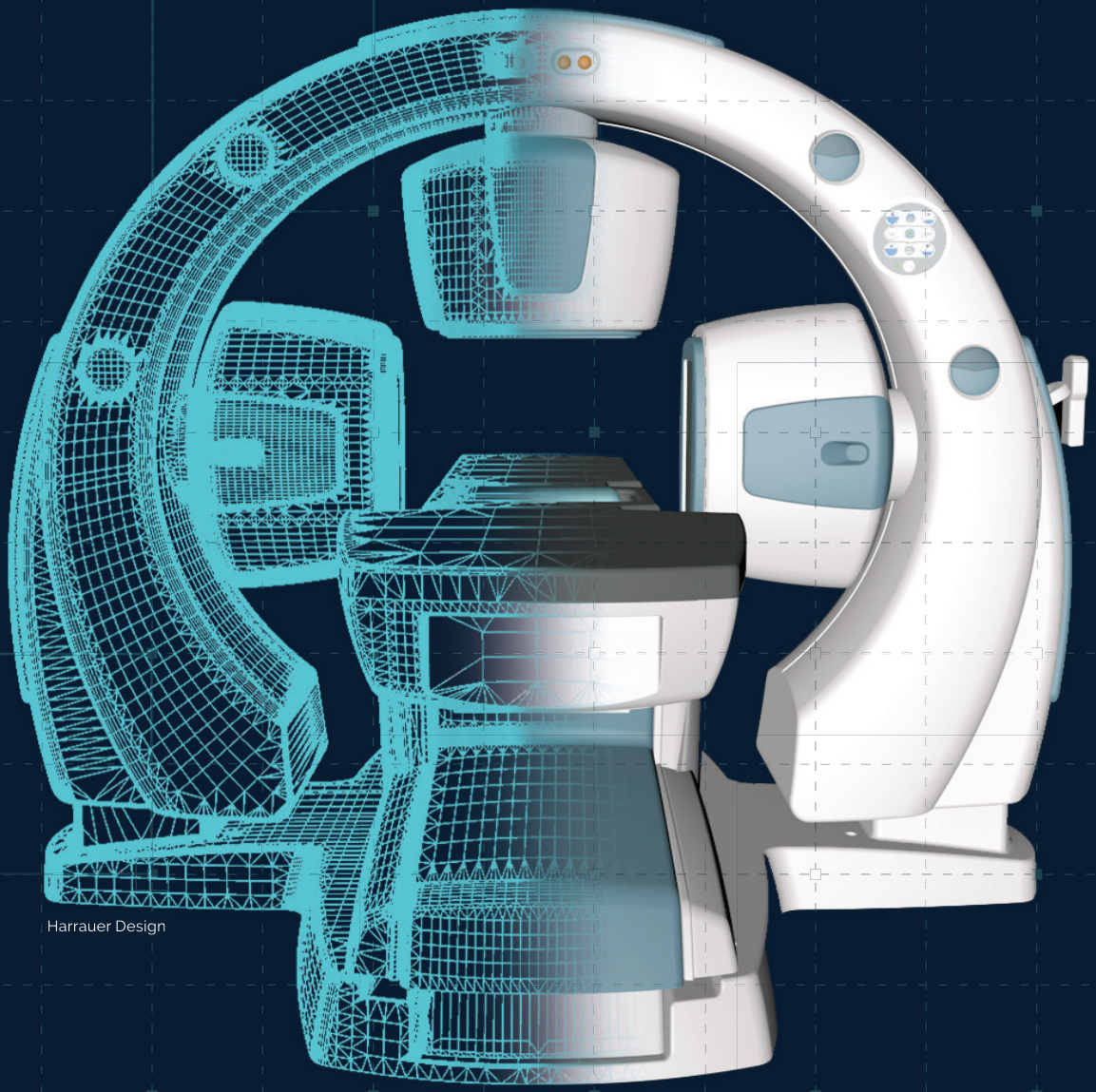
ALBA4D

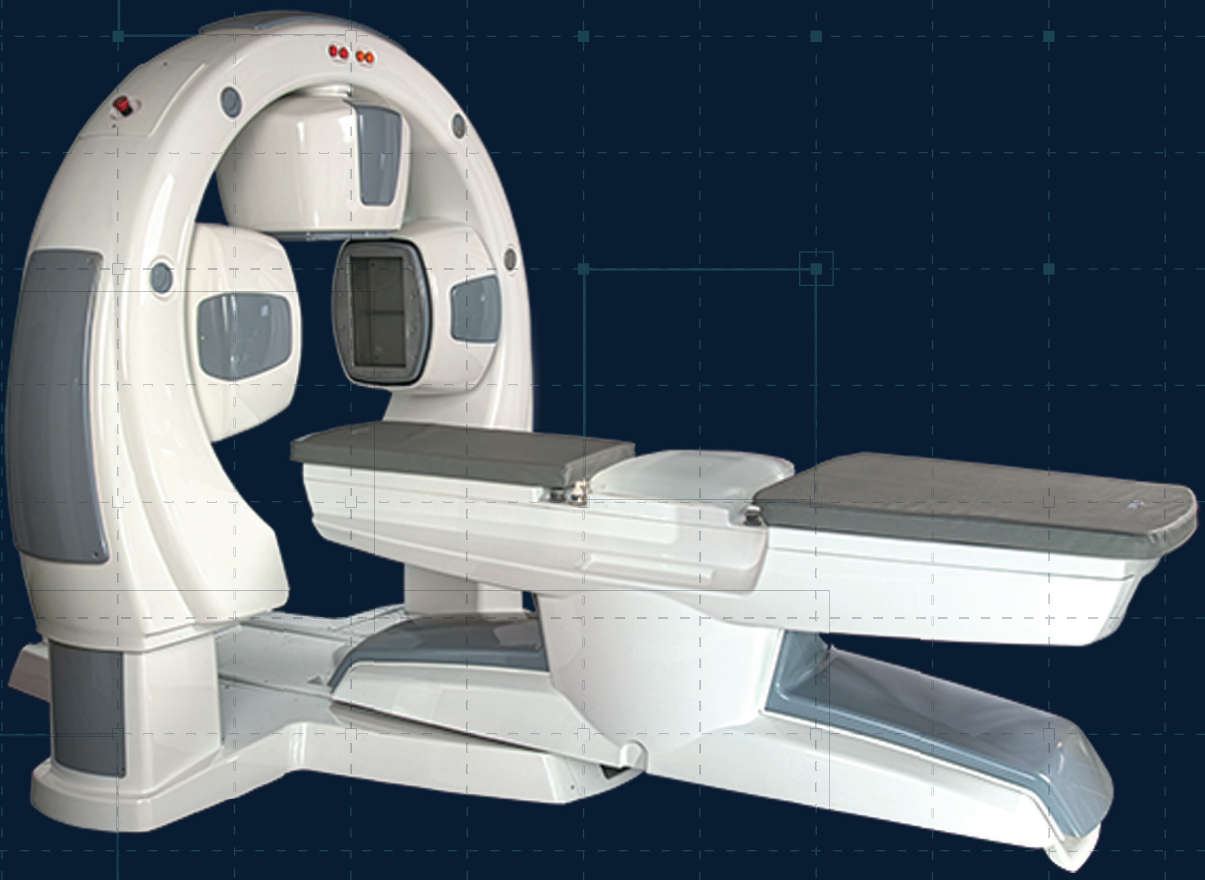
precision hyperthermia

PHASED ARRAY SYSTEM FOR DEEP HYPERTHERMIA



Harrauer Design

ALBA4D
precision hyperthermia



This brochure is intended for use by medical professionals

ALBA 4D is a phase control, loco regional deep hyperthermia system conceived and designed in full compliance with the Q.A. GUIDELINES of the ESHO - European Society for Oncological Hyperthermia and the latest radiotherapy standards.

The ALBA 4D project is inspired by the AMC 4/8 systems developed by the hyperthermia team of the Academic Medical Center of Amsterdam. Since the early 80's the AMC Cancer Research Center has been one of the most active institutes in the use of hyperthermia with more than 2800 successfully treated patients. Numerous scientific studies have shown the efficacy of the AMC systems, such as, and in particular, the phase III randomized clinical trial (Van der Zee et al., The Lancet 2000).

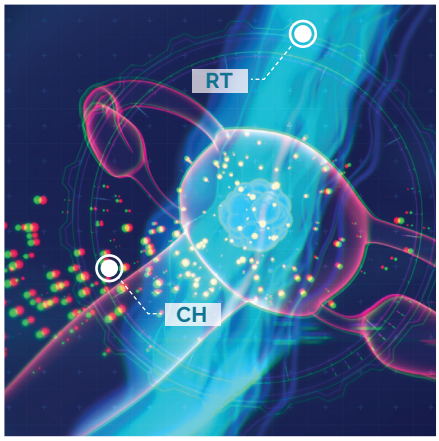
The ALBA 4D project, developed with the cooperation of AMC's hyperthermia team, is the product of the union between the most modern and efficient technologies specifically designed for hyperthermia and vast clinical and technical experience gained over 30 years of research and applications.

HYPERTHERMIA RADIO-BIOLOGICAL RATIONALE

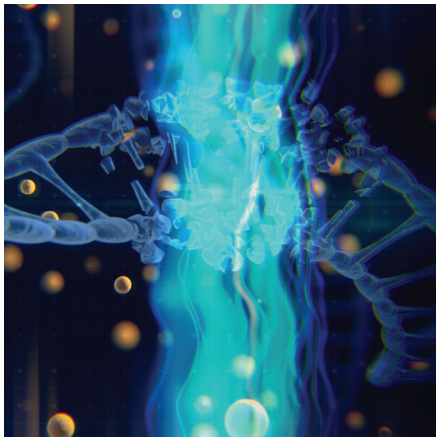
Hyperthermia (HT), heating tumors in the range 41-43°C, is a powerful radio and chemosensitizer.
HT effectiveness as well as safety in combination with radiotherapy and chemotherapy has already been proven in phase III clinical trials [1,3], especially in patients with very large or very advanced stages of cancer and recurrent tumors.
HT allows enhancing radiotherapy effect on the tumor, without additional toxicity for healthy tissues, by means of three synergistic mechanisms:

(1) Inhibition of DNA damage repair: HT enhances the effectiveness of radiotherapy by inhibiting repair of DNA damage [2,4,5,6].
(2) Direct cell killing: HT selectively kills radioresistant hypoxic tumor cells [2]
(3) Reoxygenation: HT increases tissue perfusion resulting in reoxygenation, thereby reducing hypoxia and increasing radiosensitivity [2,6,7]
With regards to chemotherapy, hyperthermia targets its action within the heated tumor region without affecting systemic toxicity[8]. It has also been shown that local hyperthermia has the capability of inducing systemic anti-tumor immune responses [1].

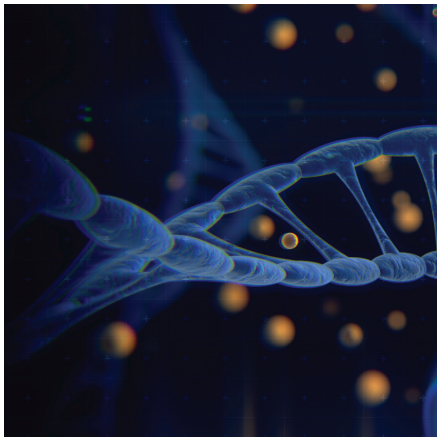
WITHOUT HT



Standard therapy

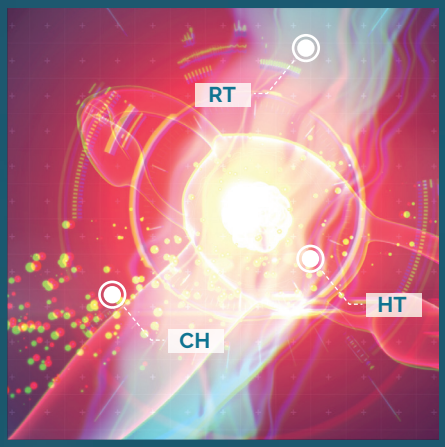


DNA damage



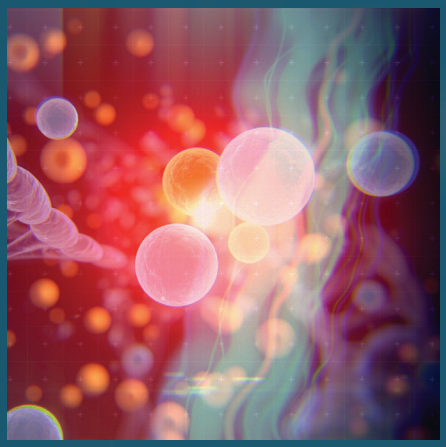
DNA repair

WITH HT



Standard therapy plus hyperthermia

HT induced re-oxygenation, direct cell killing, increased intratumoral drug uptake, enhanced tumor DNA damage

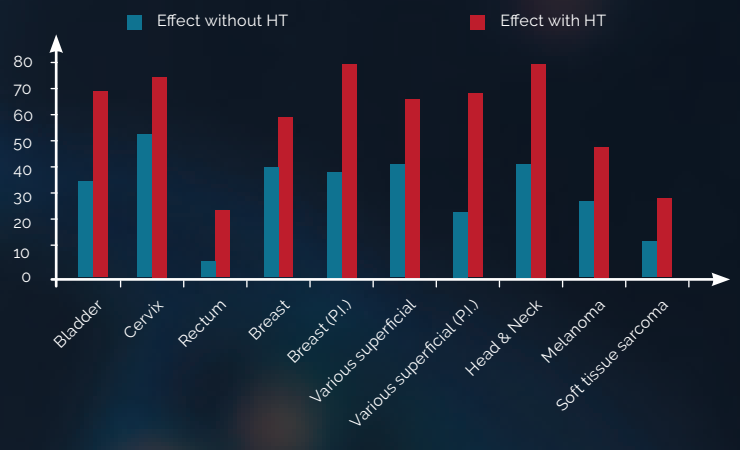


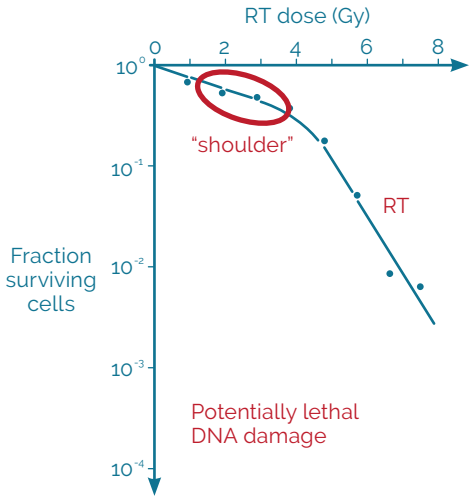
DNA repair inhibition

HYPERTHERMIA CLINICAL EVIDENCE

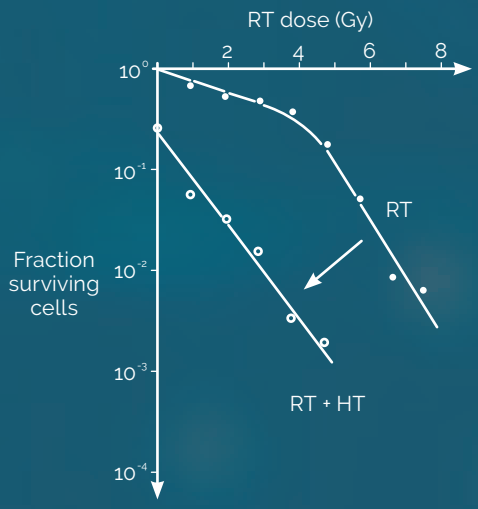
Several phase III randomized clinical studies have already shown the benefits of adding hyperthermia to standard therapies (chemo-radiotherapy).
Response rates, local control and overall survival are often 1.5 times higher than with radiotherapy or chemotherapy alone, without inducing additional side effects [1,3].

COMPLETE RESPONSE





Sub-lethal DNA damage



Sub-lethal DNA damage becomes lethal

ALBA 4D CLINICAL INDICATIONS

ALBA 4D is certified to treat:

- Cervical cancer
- Vaginal cancer
- Vulva cancer
- Ovarian cancer
- Rectal cancer
- Bladder cancer NMI
- Bladder cancer MI
- Soft tissue sarcoma
- Prostate cancer
- Esophageal cancer
- Pancreatic cancer
- Pediatric tumors
- Peritoneal Carcinomatosis

ALBA 4D TECHNOLOGY

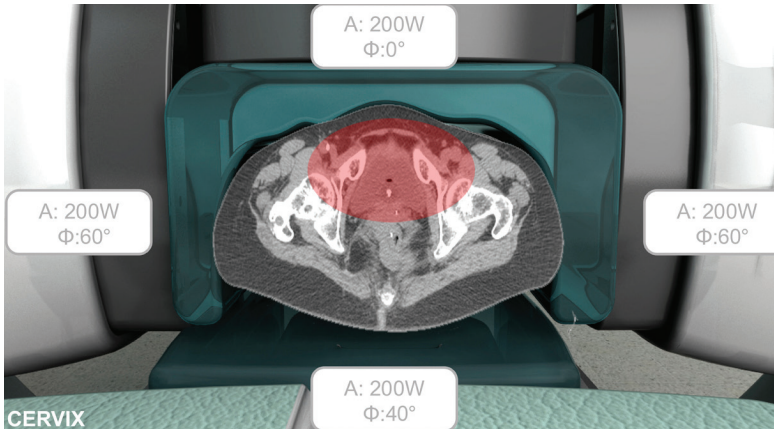
ALBA 4D is a radiative technology unit consisting of a phased array of 4 waveguide applicators working at 70 MHz. ALBA 4D generates 4 RF digitally synthesized phase coherent signals independently controlled both in amplitude and phase. Varying these parameters allows a dynamic constructive interference of the 4 radiated electromagnetic fields to focus the energy at depth in the target area inside the patient.

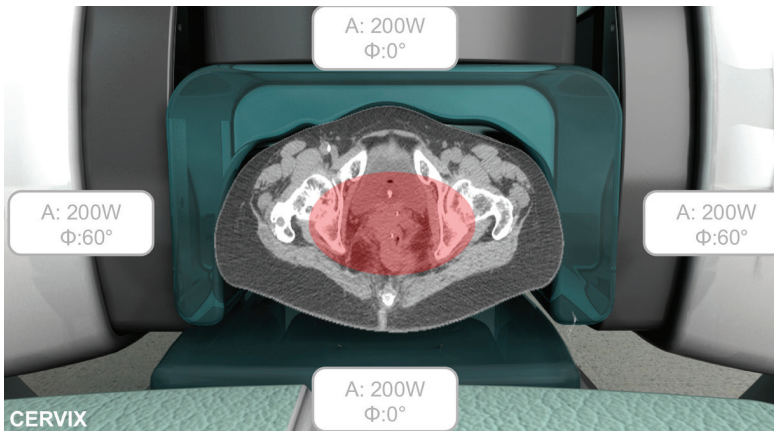
The focusing of the field in the target volume allows to reach therapeutic temperatures which must be maintained for 60 minutes. Clinical response is correlated with temperatures. Therefore it is of extreme importance to use equipment able to reach therapeutic temperatures at target locations.

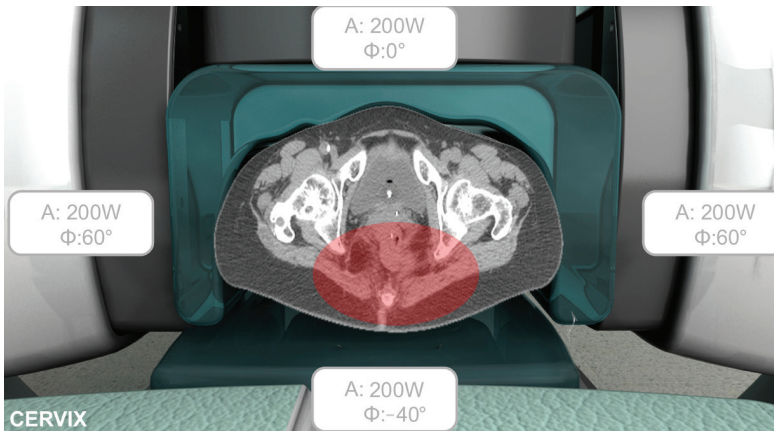
Among available techniques, radiative phased array hyperthermia has been found to generally yield much more favorable heating patterns for deep-seated pelvic tumors and it is considered also by ESHO guidelines most suitable for deep hyperthermia treatments [9,10].

DYNAMIC STEERING

Varying the power acts on the intensity of the emitted radiation and, consequently, on the temperatures reached: as the power increases, the temperature increases. Varying the phase of each applicator acts on the position of the focus, which is changed according to target location. The heart of the technological innovation of the ALBA 4D system is the RF power supply and control system designed specifically for deep oncological hyperthermia applications to guarantee high performance in terms of reliability and stability of the focus position during the entire treatment session.







DOSIMETRY

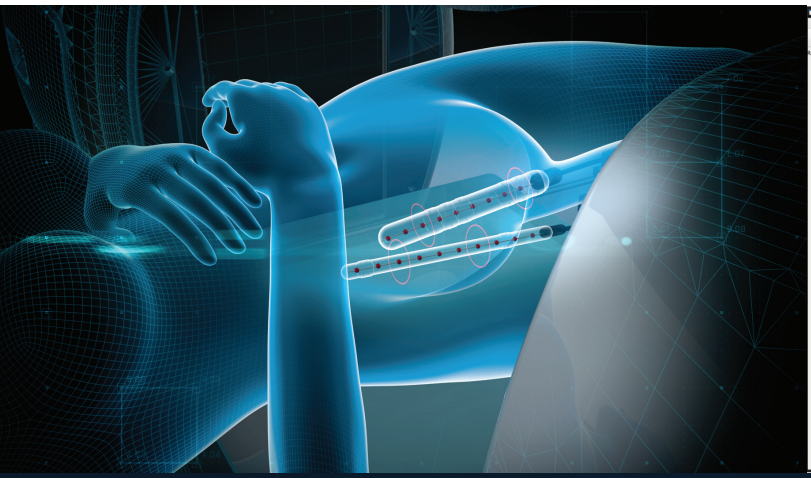
According to ESHO (European Society for Hyperthermic Oncology) guidelines dosimetry must be based only on temperature measurements during the treatment, that is by means of thermometric probes positioned in the patient.
ALBA 4D is equipped with a real-time dosimetry system, which is positioned in the natural cavities of the pelvic region:

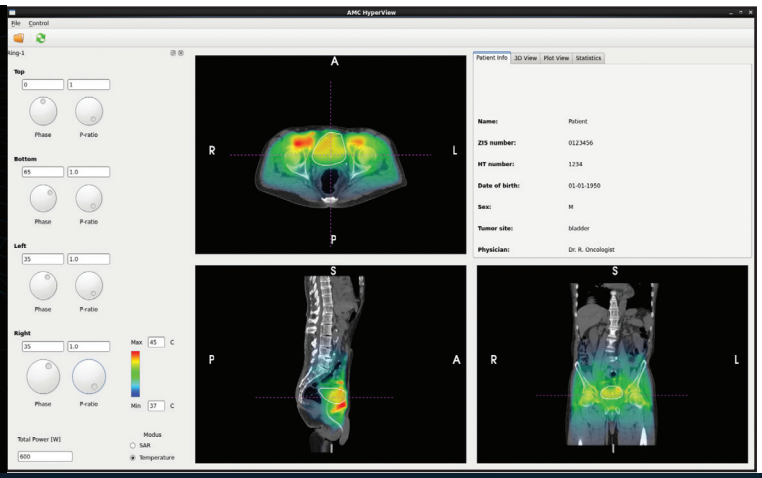
- Numerous multi-point temperature probes;

- Miniature optical E-field sensor for an in-vivo optimization of the treatment setting (optional).

HTPS

ALBA 4D can be provided with a hyperthermia treatment planning software **PLAN2HEAT** in continuous development in collaboration with AMC [11]. The goal is to find the optimal setting to maximize the power deposition in the target area while preserving the surrounding healthy tissue. PLAN2HEAT is able to calculate the power absorption, the consequent temperature distribution and the optimized setting in a 3D patient-specific anatomy model generated from CT/MRI DICOM patient images.



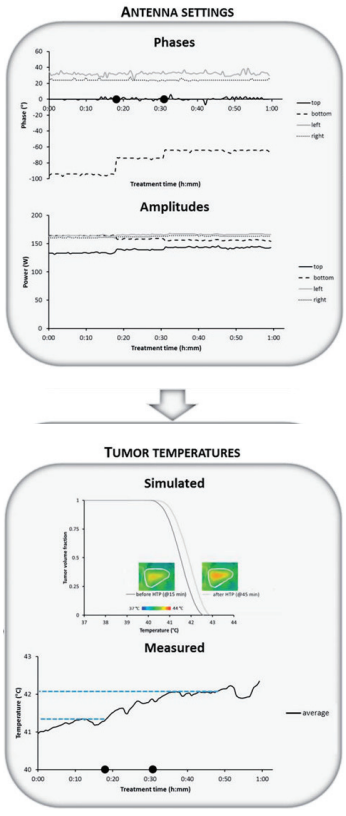


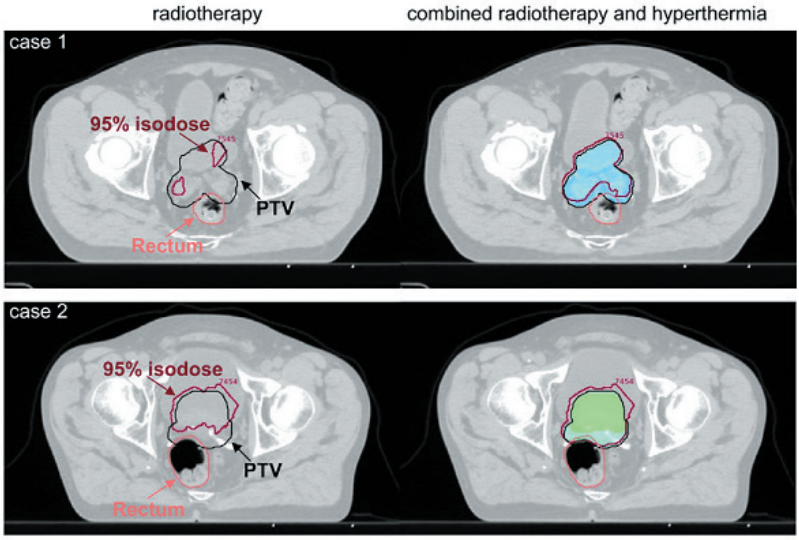
ADAPTIVE HTPS

PLAN2HEAT can also be used for on-line temperature-based hyperthermia treatment to assist in effective phase-amplitude steering to improve tumor temperature, without inducing treatment-limiting hot spots in normal tissue [12].

RT+HT EQUIVALENT DOSE

An extension of PLAN2HEAT quantifies the effect of combined radiation therapy and hyperthermia in terms of equivalent dose distributions [13,14].
(Tool development in progress)





isotemperature levels
- 44°C
- 43°C
- 42°C
- 41°C
- 40°C
- 39°C
- 38°C

ALBA 4D

The ALBA 4D is composed of a phased array of four antennas and a mechanically removable bed for patient positioning during treatment. One of the four antennas of the array is embedded directly into the table and is fixed. The other three antennas are positioned on the arched gantry around the bed and can move toward the patient. The arch as a whole can move vertically.

BED MOVEMENT

Manual positioning of the bed allows for an easy and comfortable patient preparation and fast emergency patient removal.

VENTILATION

The ventilation system is composed of 4 fans which can be regulated for the comfort of the patient during treatment.

WATER BOLUS

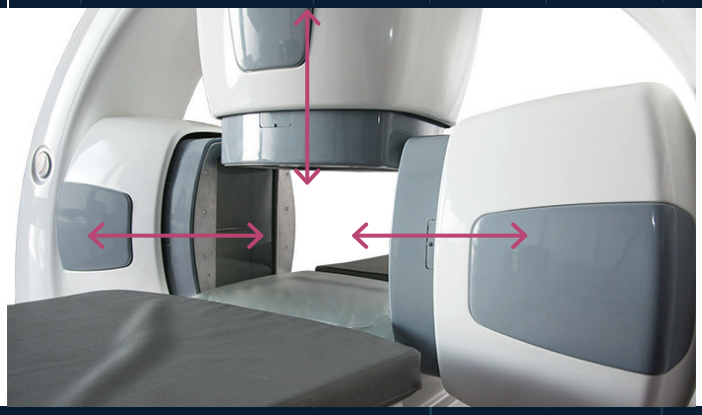
2 water boli filled with circulating distilled water are independently and remotely thermo-regulated. They lie between the patient and the antennas both for signal coupling and superficial cooling.

POWER DELIVERY AND CONTROL SYSTEM

The 4 radio frequency signals are generated through a Direct Digital Synthesizer (DDS) RF generator and amplified to 500W/channel.
An embedded and robust feedback system for phase/amplitude control allows for focus stability in the ROI.

ANTENNA MOVEMENT

The vertical movement of the gantry and the conversion of the antennae towards the patient allow the system to easily adapt to different patient sizes.



THERMOMETRIC SYSTEM

The multichannel thermometric system consists in multi-point probes containing 0.5/1 cm spaced thermocouples. The signals generated by the thermocouples are acquired and digitalized in a compact thermometer integrated in the bed structure allowing a ergonomic and functional management of the probes before, during and after treatment.

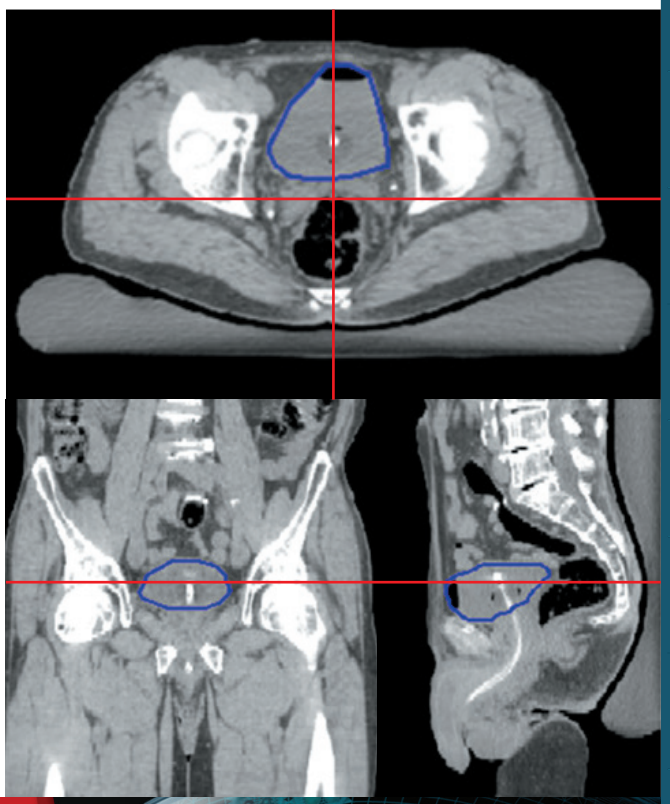
QUICK DISCONNECTING COUPLINGS

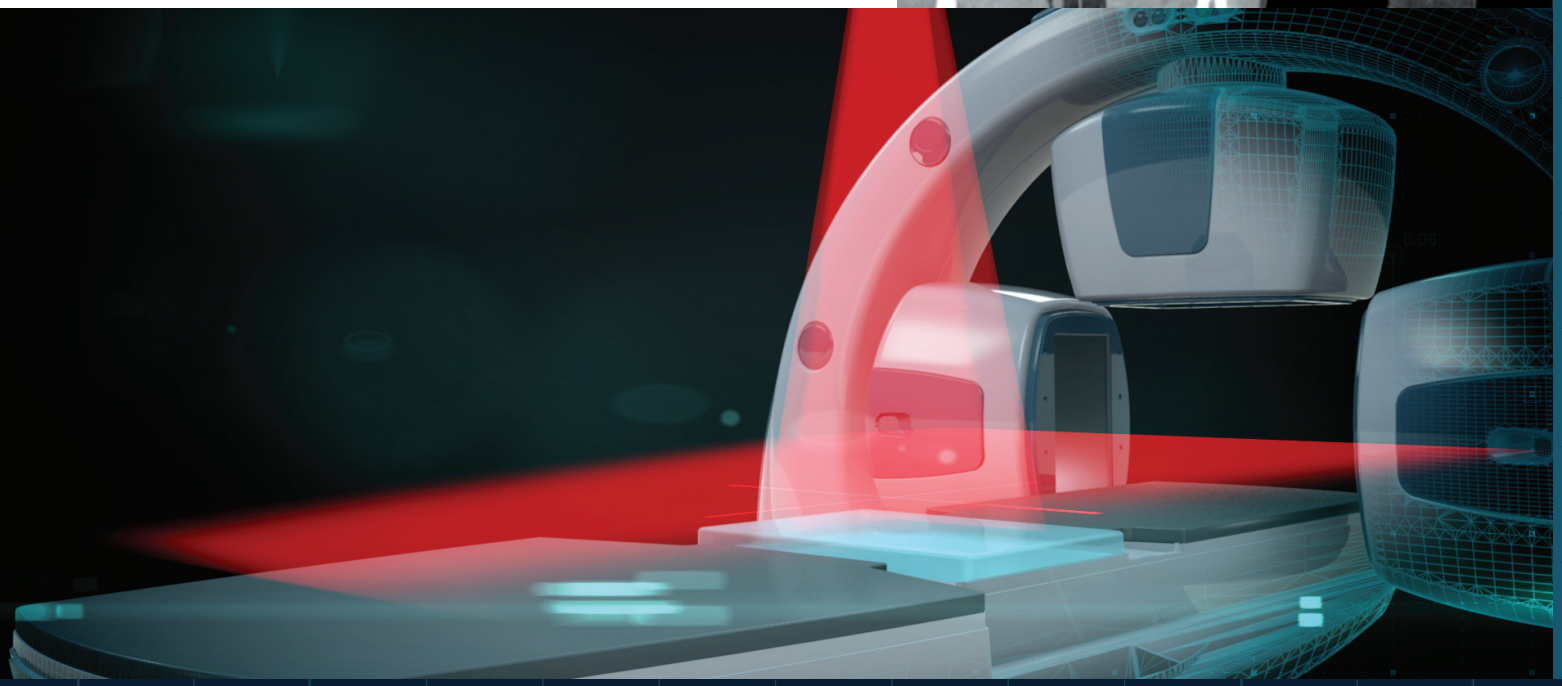
Quick disconnecting couplings, directly located on the patient bed eliminate accidental misconnections and create cleaner, faster, safer bolus connection.

POSITIONING SYSTEM

ALBA 4D is the only device equipped with an embedded laser pointing system for optimal **CRANIO-CAUDAL, DORSO-VENTRAL and LATERAL** patient positioning.

This allows for both the reproducibility of the antennas/patient positioning throughout all the treatments, as well as the collimation of the antennas/patient block with the PLAN2HEAT simulation software.

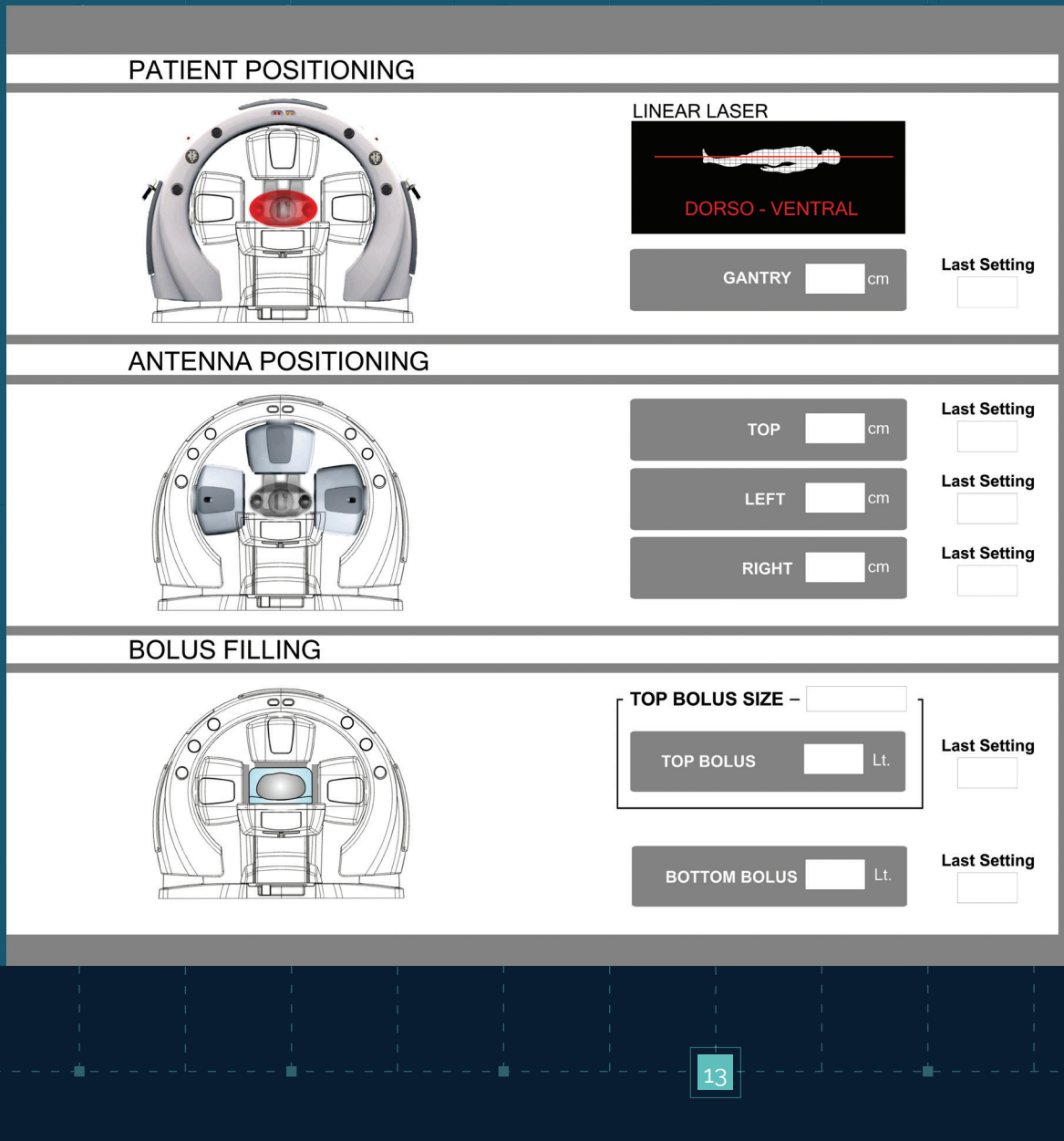




SOFTWARE POSITIONING

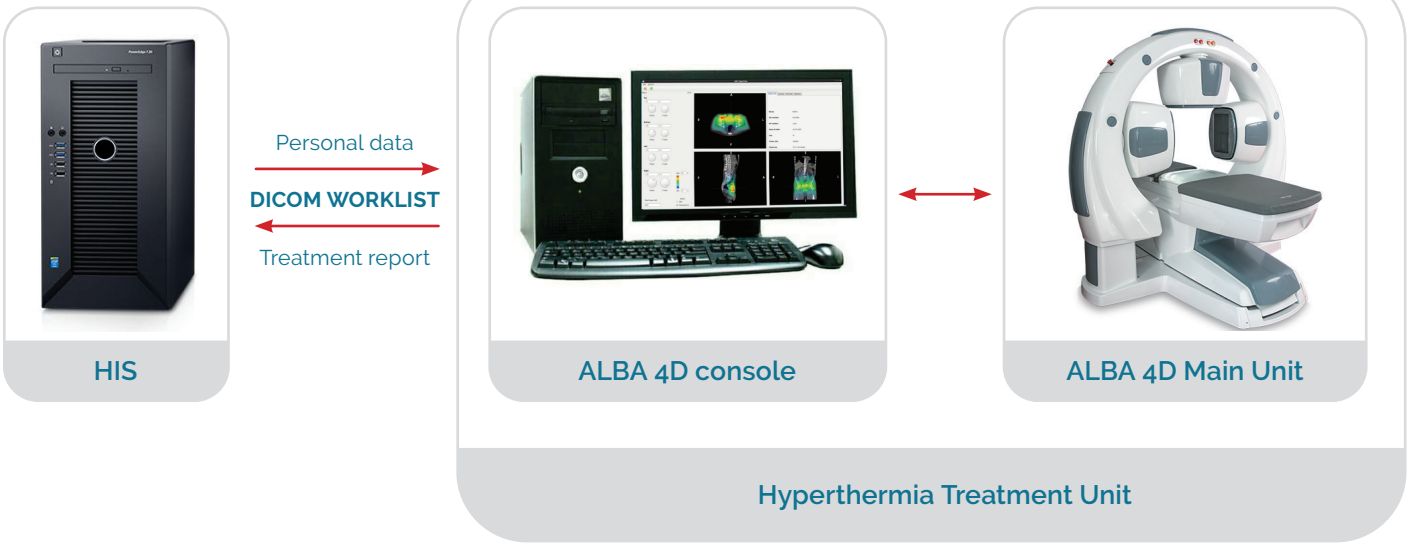
ALBA 4D is equipped with sensors which automatically detect and record the position of the gantry and antennas.

Gantry and antenna positions are also shown on screen to guide the operator in the patient positioning phase.



ALBA DATA MANAGEMENT SYSTEM

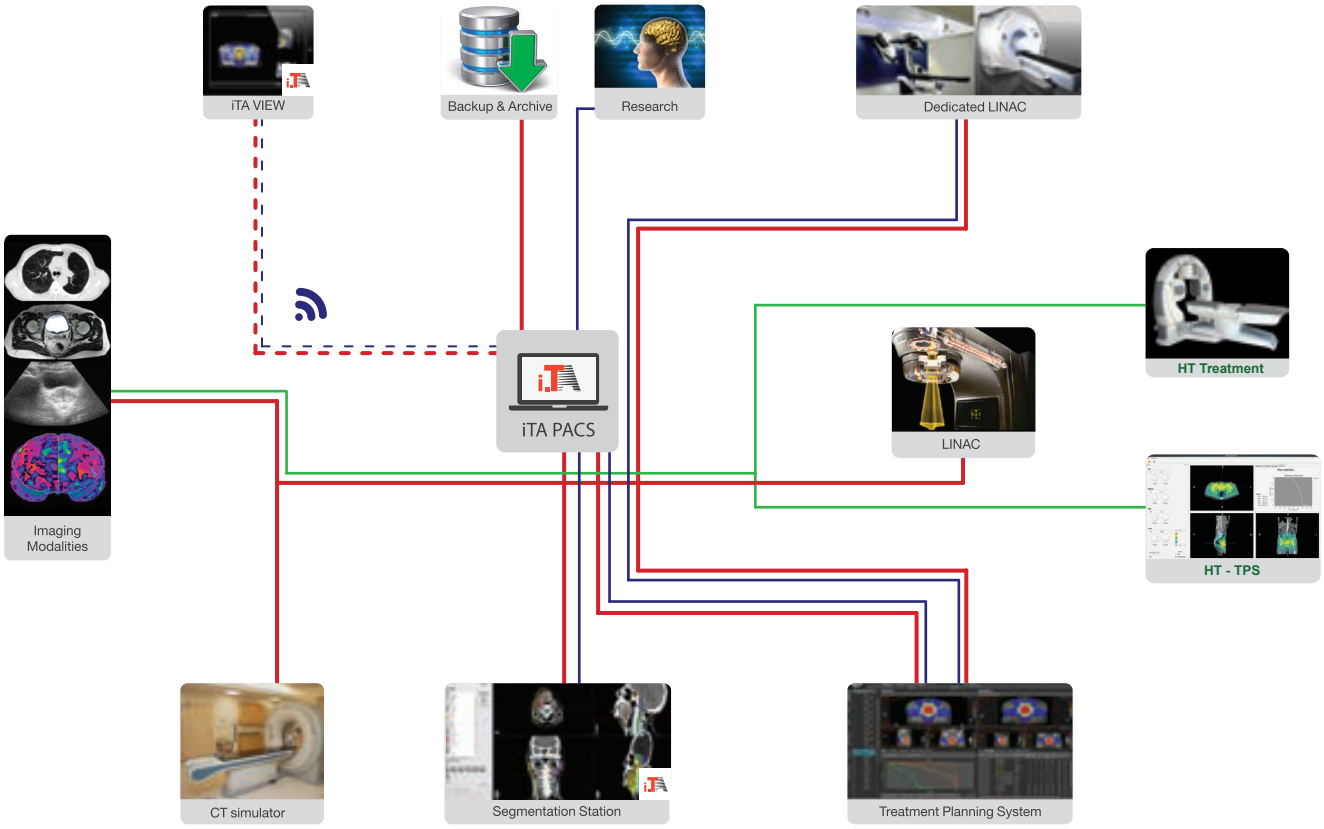
The ALBA Data Management system offers an integrated data management solution wich allows the import of patient personal data as DICOM Worklist and the export of treatment reports in PDF to Hospital Information System (HIS). Treatment raw-data is stored in standard xml files which allows for post-processing and to simplify data sharing which is useful for data analysis within clinical trials.



INTEGRATION WITH RADIOTHERAPY PACS SYSTEM

The ALBA 4D software is designed to be fully integrated with the radiotherapy PACS systems in order to introduce hyperthermia into the radiotherapy workflow from treatment planning to treatment more easily.

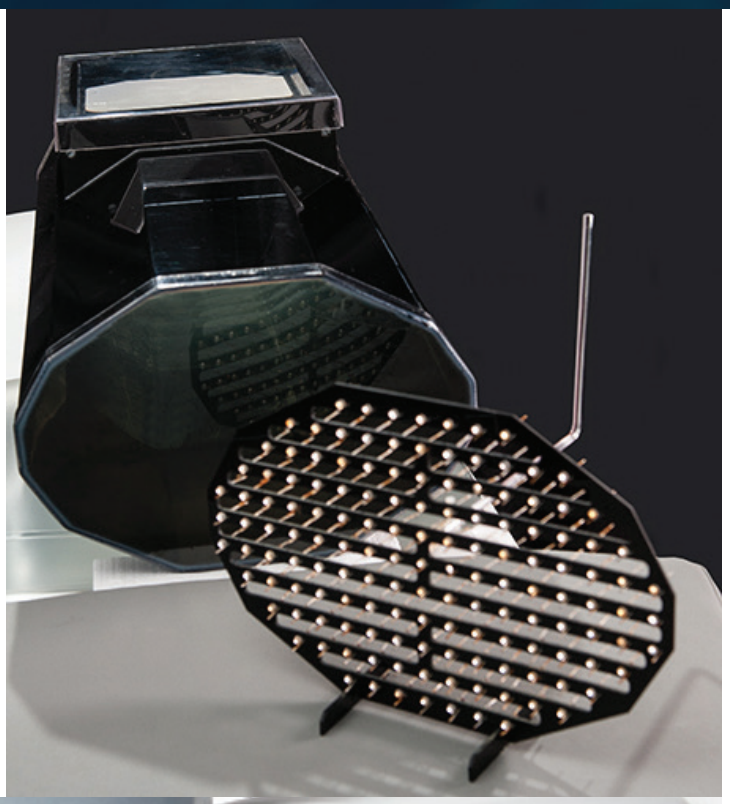
Image courtesy of Tecnologie Avanzate SpA

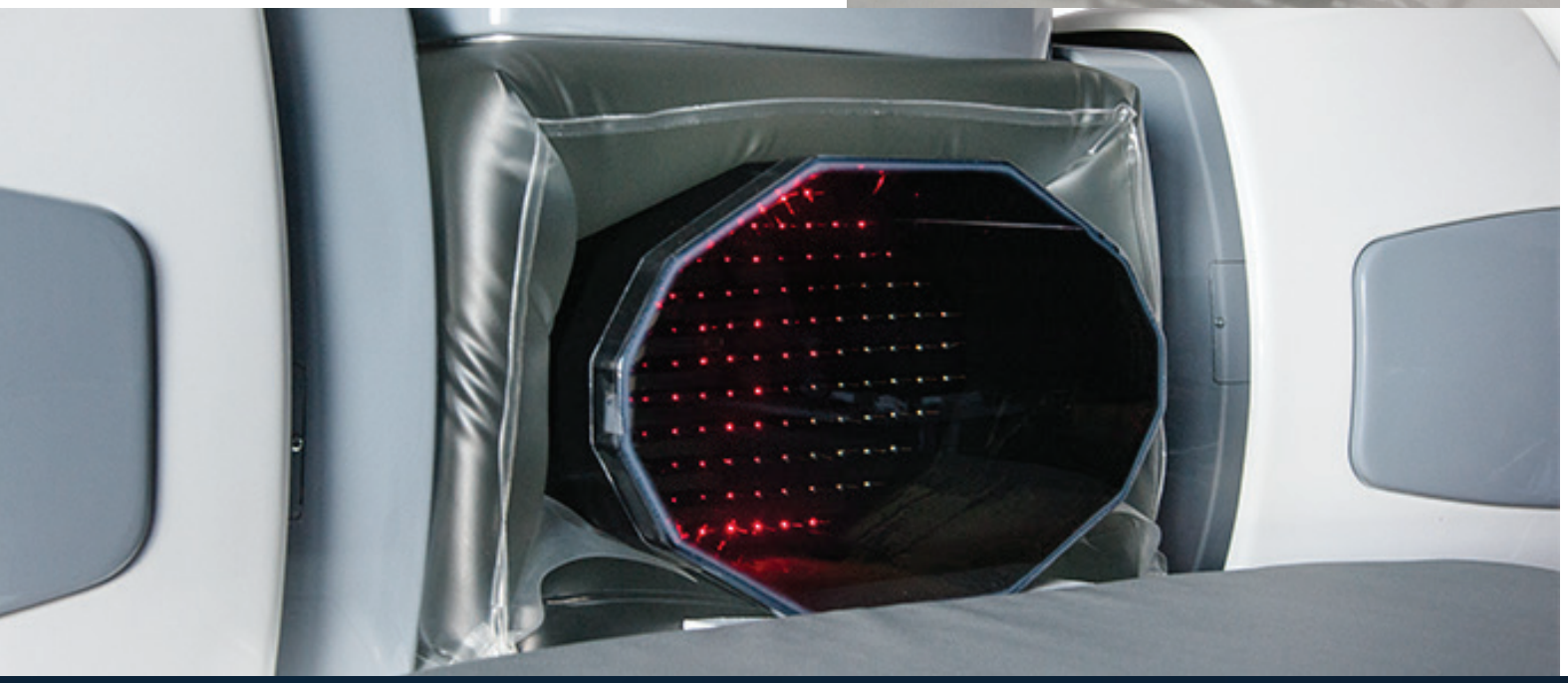


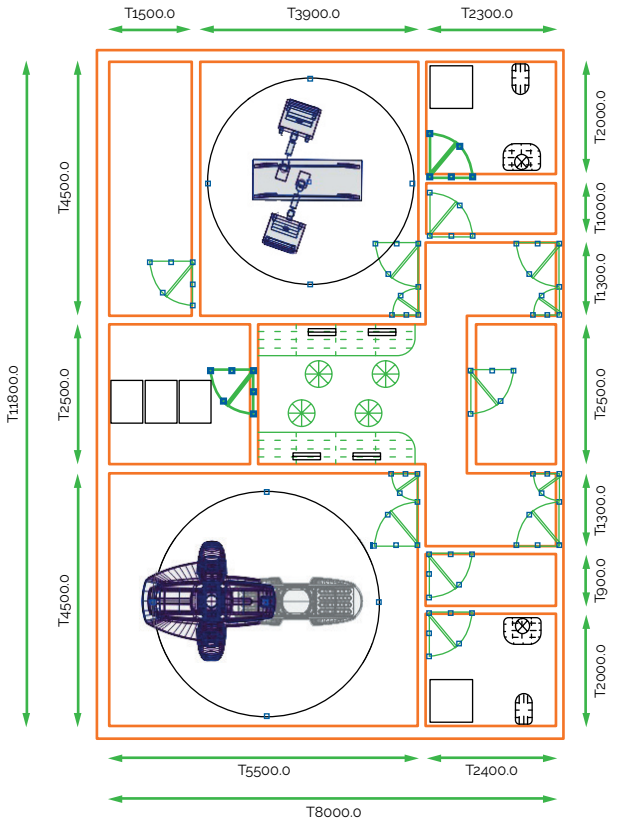
QUALITY ASSURANCE

The ALBA 4D system is equipped with an AMC ESHO-approved quality assurance kit consisting in a tissue equivalent phantom and a LED matrix to control the deposition of the system's electromagnetic power and the focus steering capability.

These will ultimately guarantee an optimal system performance over time.



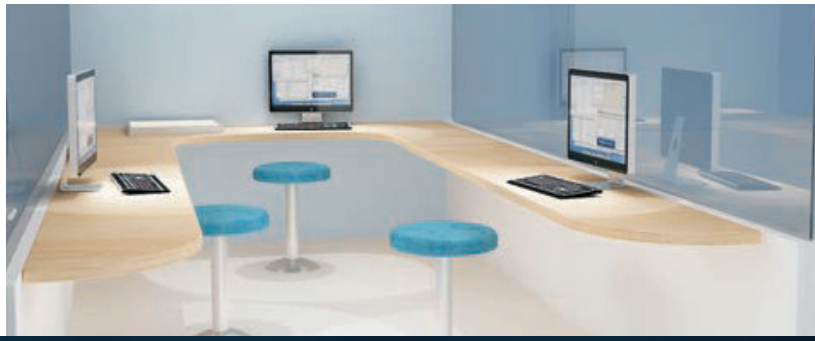




SITE PLANNING

A standard ALBA 4D treatment unit consists of a RF shielded treatment room an operator console, a technical room and a changing room.

A site planning guide is provided to help with the layout of the environment which will host ALBA 4D. Our designers are available to optimize the space in order to guarantee both the respect of safety rules for patients and operators and the compliance with hyperthermia unit workflow within the RT department.



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