SIT
Sordina IORT Technologies

LIAC

mobile IOeRT accelerator

"IntraOperative Radiation Therapy (IORT) in its broadest sense refers to the delivery of irradiation at the time of an operation.
IORT evolved as an attempt to achieve higher effective doses of irradiation while dose-limiting structures are surgically displaced".

"IntraOperative irradiation (IORT) refers to delivery of a single dose of irradiation to a surgically exposed tumor or tumor bed while the normal tissues are protected from the irradiation either by retracting the mobilized tissue or by shielding the anatomically fixed tissues. IORT has traditionally been performed by using an electron beam as the source of irradiation."

[Intraoperative Irradiation. Techniques and Results, Calvo F.A., Gunderson L.L. et al., Current Clinical Oncology, Second Edition, 2011.]

IntraOperative electron Radiation Therapy (IOeRT), which uses high energy electrons, is the most effective implementation of IORT.

Mobile Linear Accelerator

FLEXIBLE & EASY TO USE

Dimensions and weights are extremely limited and allow full and smooth operation in any operating room. The LIAC's flexible architecture also allows to easily perform hard-docking procedures in any position, as well as treatment of any district.

POWERFUL & SAFE

Adequate energy and applicator selection allows the target treatment with a thickness of up to 3.8 cm inside the 80% isodose (up to 3.2 cm inside the 90% isodose).

QUICK & EFFECTIVE

The accelerator's high mobility, together with the use of a high dose rate (IOeRT irradiation time is less than 2 minutes) ensures the implementation of faster and more reliable operating procedures.

BREAST & MULTI-CANCER APPLICATION

More than 20,000 patients diagnosed with neoplastic diseases have been treated worldwide.
Two protocols developed for the treatment of breast cancer are adopted internationally: the ELIOT protocol for single dose, and the HIOB protocol for the boost. The application of the former led to a local recurrence rate of 1.5% (at the 5-year follow-up), as it pertains to a selected group of patients.
Latest data relating to the boost technique show a local recurrence rate at 0.8% (at the 6-year follow-up), and, thus, a significant improvement of results obtained with external radiation therapy only.

FAST COMMISSIONING AND PLUG & PLAY INSTALLATION

Thanks to the possibility of performing a numerical commissioning already during the acceptance phase, as well as ease of installation (no work adjustment is required), LIAC permits to carry out the first IOeRT treatment only 5 days after delivery of the system to the hospital.

LIAC

The best way to perform IOeRT

FLEXIBLE & EASY TO USE

TRANSPORT INTO STRETCHER ELEVATOR:

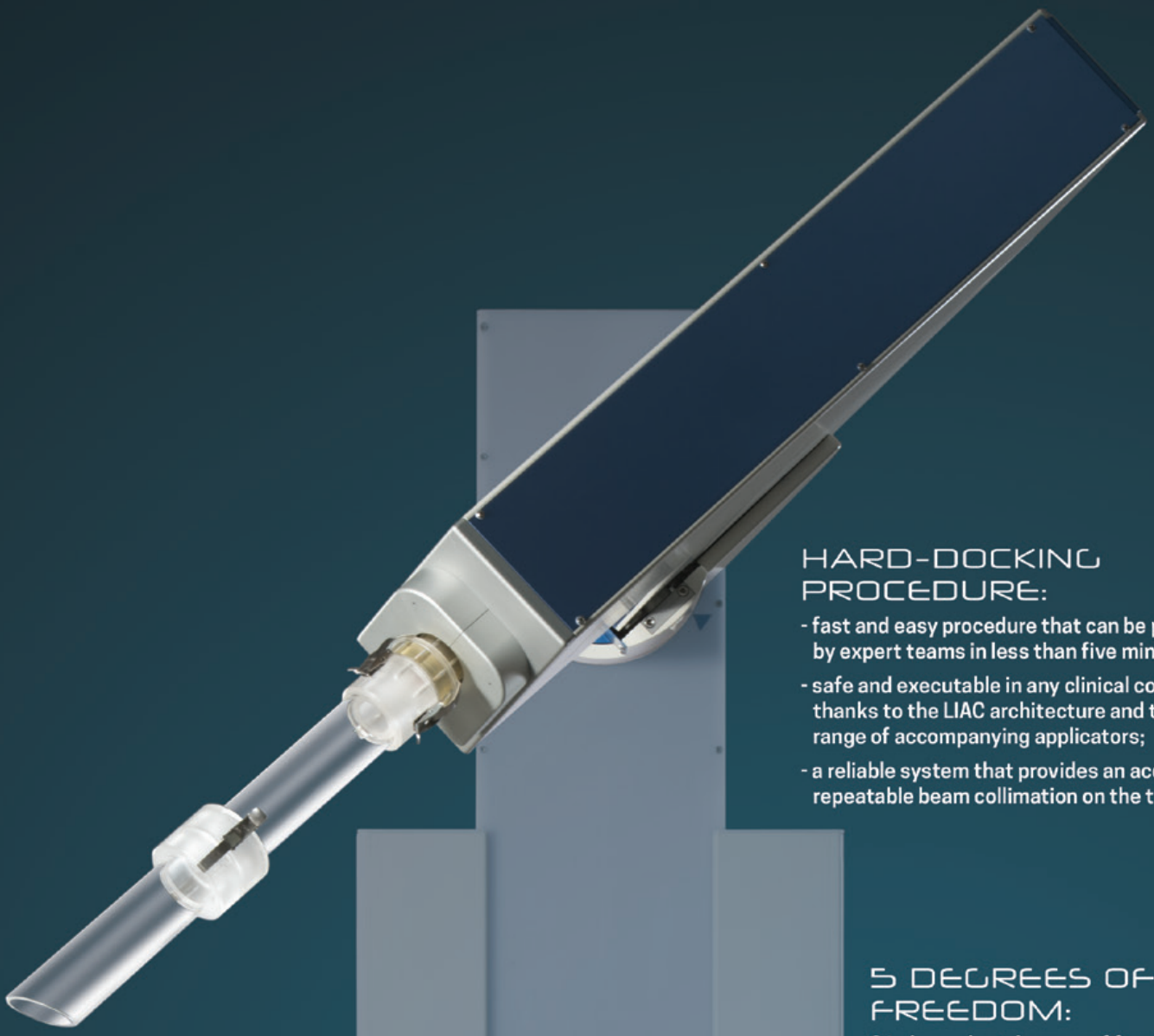
the dimensions are such that LIAC can be easily transported to the operating room through the use of any stretcher elevator.

FUNCTIONALITY IN MULTIPLE OPERATING ROOMS:

the system can be quickly moved via the dedicated remote control and utilized in any operating room, thus maximizing its employment.

NO LONGER MOVING THE PATIENT:

the system follows the treatment, thus avoids the need of moving patients from the surgical table.



HARD-DOCKING PROCEDURE:

- fast and easy procedure that can be performed by expert teams in less than five minutes;
- safe and executable in any clinical configuration, thanks to the LIAC architecture and the wide range of accompanying applicators;
- a reliable system that provides an accurate and repeatable beam collimation on the target.

5 DEGREES OF FREEDOM:

3 independent degrees of freedom of the radiant head (elevation, roll angle and pitch), and 2 degrees of freedom of the mobile unit (shift on the plane) permit to easily reach any district.

LIGHT WEIGHT OF MOBILE UNIT:

the impact in the operating room is minimal, and no structural changes are necessary.

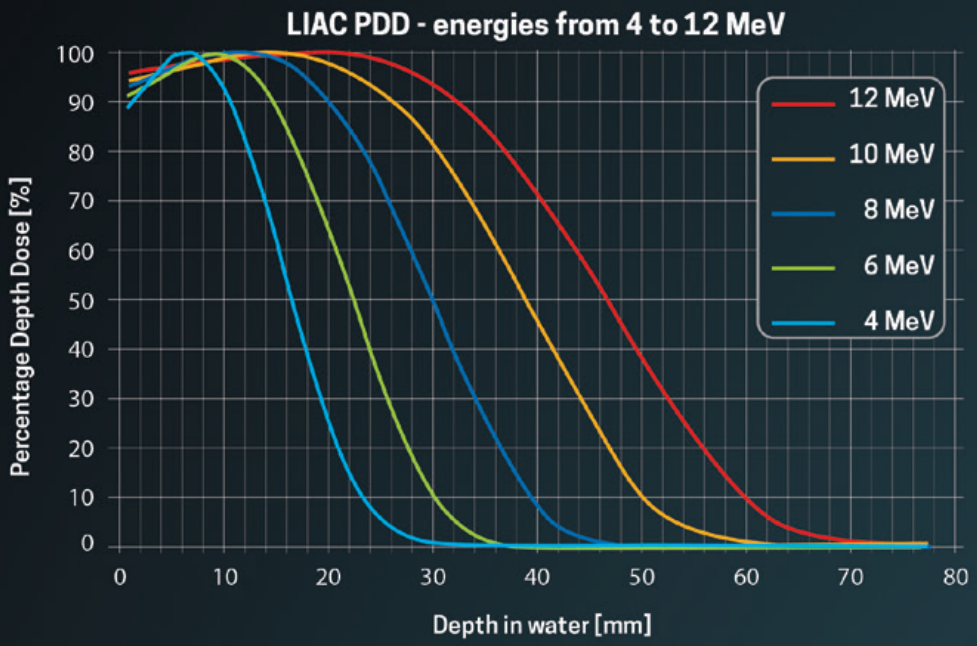
400 kg

LIAC is able to treat any clinical volume in the IOeRT environment.

By selecting the correct applicator/energy combination, it is possible to treat any neoplastic disease effectively and safely.

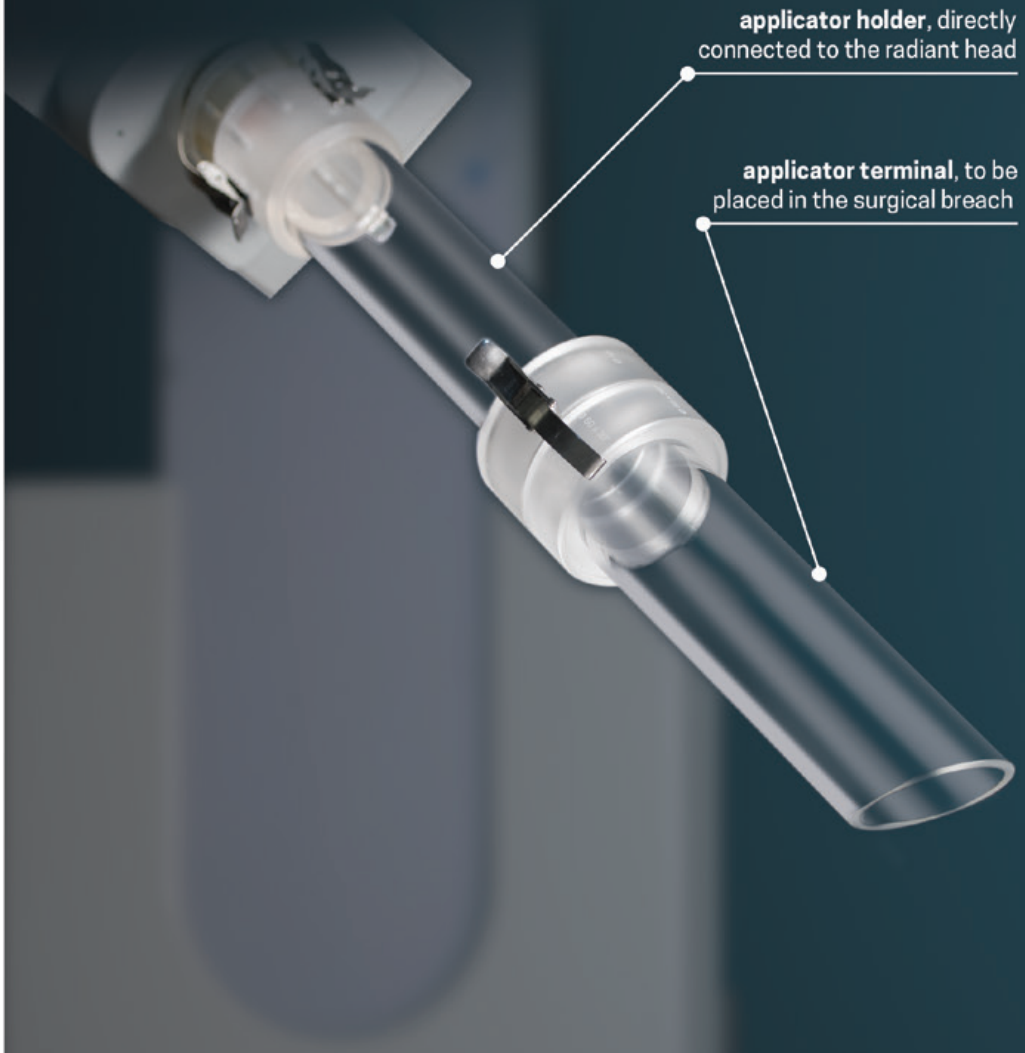
The 100% PMMA (polymethylmethacrylate) applicator allows:

- implementation of the safest and fastest hard-docking technique;
- direct visualization of the surgical breach, thanks to the transparency of the material and the length of the terminal applicator;
- full compatibility with x-rays imaging;
- increase of the surface dose by more than 90%, thus avoiding the need of any bolus.

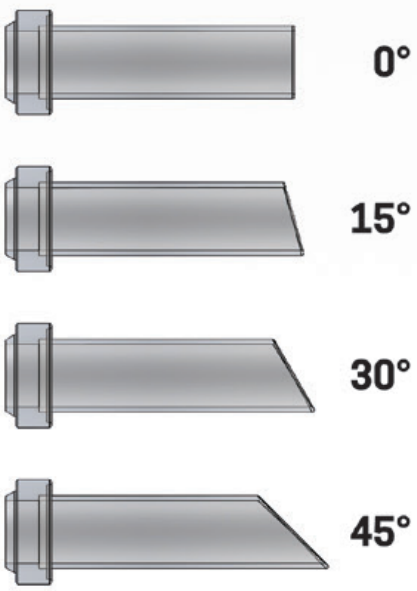


The appropriate energy and applicator selection allow to treat the target with a thickness of up to 3.8 cm inside the 80% isodose (up to 3.2 cm inside the 90% isodose).

The applicator is made of two parts that are connected during the hard-docking phase:



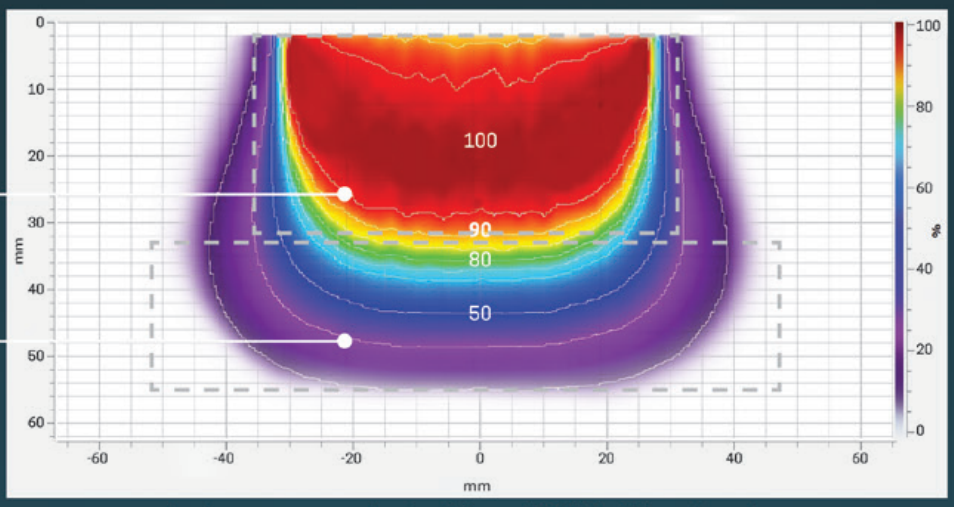
Applicators are available in diameters from 3 to 12 cm, and bevel angles of 0°, 15°, 30° and 45°.



POWERFUL & SAFE

PLANNING TARGET VOLUME

HEALTHY TISSUE



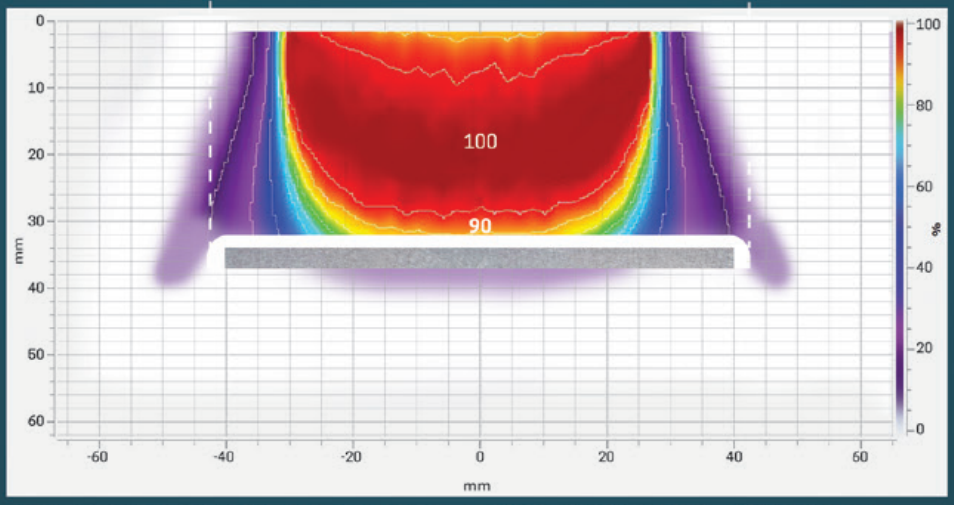
Isodose curve, applicator Ø 6 cm, 12 MeV, 0° bevel angle.

The IOeRT technique ensures reduction of dose exposure of the healthy tissue during the irradiation.

In breast cancer treatment, the use of a radioprotection disc **(Italian Patent no. 1392099)** temporarily inserted between the target and the chest wall fully protects the healthy tissue underneath.

The disc is a medical device made of steel and PTFE (polytetrafluoroethylene), biocompatible and sterilizable materials; is available in the following diameters: 6, 7, 8, 9, 10 and 11 cm.

The disc has 4 holes placed along the crown, which allow adhesion to underlying tissues, thus ensuring their protection.



Isodose curve modified by RP disc Ø 8 cm, applicator Ø 6 cm, 12 MeV, 0° bevel angle.

IOeRT can be performed either as a single treatment (SINGLE DOSE), which replaces the entire external radiotherapy cycle, or as a BOOST, followed by a reduced external radiotherapy cycle. More than 20,000 patients have been treated worldwide.

MULTI CANCER APPLICATION

	INDICATION Stage / Locally advanced	INSTITUTION reference	RESULTS
PANCREAS	Unresected	MGH (1)	16% 2 y OS (survivors > 5 y)
	Bordeline	Mayo Clinic (2)	84% LC; 40% vs 0% 3 y OS
	Resected	HGUGM (3)	58% 5 y LC
ESOPHAGO-GASTRIC	Resected	HGUGM (4)	85% 5 y LC
GASTRIC	Resected	Systematic review (5)	St III IOeRT promoted OS
RECTAL	cT2-4 N+	HGUGM (6)	96% LC 5 y
	Primary and recurrent	Systematic review (7)	IOeRT improved LC and OS
PROSTATE	Metastatic D1 and D2	Saitama Cancer C (8)	5-10 y OS 75/52%
RENAL	Recurrent/Primary resected	US-Europe Pooled-analysis (9)	OS 5y 37% (p) vs 55% (r)
PEDIATRIC	Ewing/Rhabdomyosarcoma	Pooled-European (10)	5-10 y OS 74% - 68%
	Neuroblastoma + sarcoma incomplete resection	Heidelberg Univ (11)	1/18 local recurrences
SARCOMAS	Retroperitoneal	Heidelberg Univ (12)	5 y LC 72%
		Mayo Clinic (13)	5 y LC 89%
	Extremity soft tissue	Pooled- European (14)	5 y LC 82%
	Osteosarcomas	Pooled- European (15)	10 y 82% LC, 73% OS
OLIGO-RECURRENCES	Gynaecologic, rectal	HGUGM (16)	5 y LC 53%, 46% OS

MGH = Massachusetts General Hospital
LC = Local Control
OS = Overall Survival
y = years
(p) = primary locally advanced disease
(r) = recurrent disease
St = stage
IMRT = Intensity Modulated RadioTherapy
IOeRT = IntraOperative electron RadioTherapy
R1 = microscopic residual disease
C = Centre
S = Surgery
RT = Radiation Therapy
D1 = cancer spread to the lymph nodes only
D2 = cancer spread to the distant lymph nodes and or to bones or internal organs
HGUGM = Hospital General Universitario Gregorio Marañon
cT2-4 N+ = clinical stage transmural or metastatic nodes

(1) Cancer. 2013; 119:4196-204.
(2) J Gastrointest Oncol. 2013;4:352-60
(3) Pancreatology. 2013;13:576-82
(4) Ann Surg Oncol. 2013;20:1962-9
(5) Mol Clin Oncol. 2015; 3:185-189
(6) Radiother Oncol. 2014;112:52-8
(7) Surg Oncol. 2013;22:22-35
(8) Int J Clin Oncol. 2016
(9) Int J Radiat Oncol Biol Phys. 2014;88:618-23
(10) Int J Radiat Oncol Biol Phys. 2015;92:1069-76
(11) Int J Radiat Oncol Biol Phys. 2006;64:235-41
(12) BMC Cancer. 2014;14:617
(13) J Surg Oncol. 2014;109:798-803
(14) Strahlenther Onkol. 2014;190:891-8
(15) Radiother Oncol. 2016
(16) Ann Surg Oncol. 2015 Suppl 3:1247-55

Additional references:
- Pancreas: Semin Radiat Oncol. 2014; 24:126-31
- Extremity recurrent sarcomas: Sarcoma. 2015; 91:3565
- Rectal cancer: Am J Clin Oncol. 2015; 38:11-6
- Pediatric sarcomas: Int J Radiat Oncol Biol Phys. 2014; 90:172-80

BREAST & MULTI-CANCER APPLICATION

REMARKS / IOERT effects
IORT (applicator ≤ 8cm), Charlson comorbidity index ≤ 3 and chemotherapy improve OS
Median survival: 23 m R0 vs 10 m R2/unresectable
98% local control with IOeRT boost
IOeRT significant improvement of local control
Any stage IOeRT promoted local control
Prognostic index for risk-adapted treatment.
No toxicity increment by IOeRT
In D2 IORT significantly cancer-specific survival
Survival affected by nodal involvement, sarcomatoid features and IORT dose
R1 and recurrent influence outcome
6 clinical significant late toxicity
preoperative IMRT for external RT escalation
89% vs 46% S+RT vs S alone (p=0.003)
In-field LC promoted by IOeRT dose ≥12.5 Gy
R1 adverse for local control
External beam radiotherapy + IOeRT compensate adverse factors fragmentation

BREAST APPLICATION

IOeRT as **SINGLE DOSE**: the ELIOT Protocol [17]

The 5-year rate of ipsilateral breast recurrence according to 2009 ASTRO APBI guidelines [18] for a selected patients group is **1.5%** [22].
The Update of ASTRO guidelines, published in September 2016, confirms the validity of the IOeRT technique as APBI, and broadens the patients selection criteria [19].

IOeRT as **BOOST**: the HIOB Protocol [23]

The reference study [24] about IOeRT as boost, published by Fastner at al. in 2013, reports that the rate of local recurrences at the 6-year follow-up is **0.8%**, compared to a rate of local recurrences at 5-year follow-up of 3.3% for standard external radiotherapy treatments and 1.9% for hypofractionated external radiation therapy [25].

(17) Intraoperative radiotherapy versus external radiotherapy for early breast cancer (ELIOT): a randomised controlled equivalence trial, Veronesi U., Orecchia R. et al., Lancet Oncology, 2013.

(18) Accelerated Partial Breast Irradiation Consensus Statement From The American Society For Radiation Oncology (ASTRO), Buchholz T. A., et al., Int. J. Radiation Oncology Biol. Phys., Vol. 74, No. 4, pp. 987–1001, 2009.

(19) Accelerated Partial Breast Irradiation: Executive Summary for the Update of an ASTRO Evidence-Based Consensus Statement, Correa C, Harris, E.E. et al., Pract Radiat Oncol (PRO), 2016.

(20) Patient selection for accelerated partial-breast irradiation (APBI) after breast-conserving surgery: Recommendations of the Groupe Européen de Curiethérapie- European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) breast cancer working group based on clinical evidence (2009), Polgár C., et al., Radiotherapy and Oncology 94, pp. 264–273, 2010.

(21) Accelerated partial breast irradiation with intraoperative electrons: Using GEC–ESTRO recommendations as guidance for patient selection, Leonardi M. C., et al., Radiotherapy and Oncology 106, pp. 21–27, 2013.

(22) How Do the ASTRO Consensus Statement Guidelines for the Application of Accelerated Partial Breast Irradiation Fit Intraoperative Radiotherapy? A Retrospective Analysis of Patients Treated at the European Institute of Oncology, Leonardi M. C., Orecchia R., et al., Int. J. Radiation Oncol. Biol. Phys., Vol. 83, No. 3, pp. 806-813, 2012.

(23) http://www.clinicaltrials.gov/ct2/show/NCT01343459?term=hiob&rank=1

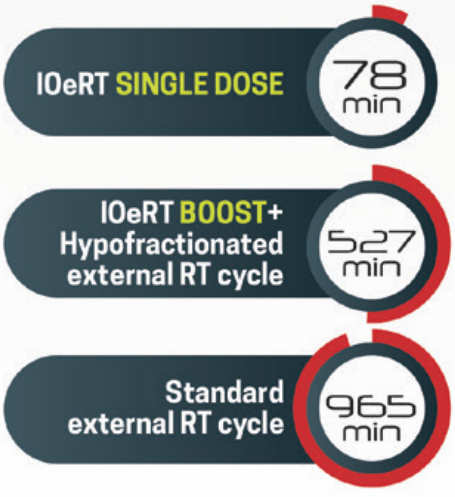
(24) IORT with electrons as boost strategy during breast conserving therapy in limited stage breast cancer: Long term results of an ISIORT pooled analysis, Fastner G. etal., Sedlmayer F., et al., Radiotherapy and Oncology, Vol. 108, Issue 2, pp. 279-286, 2013.

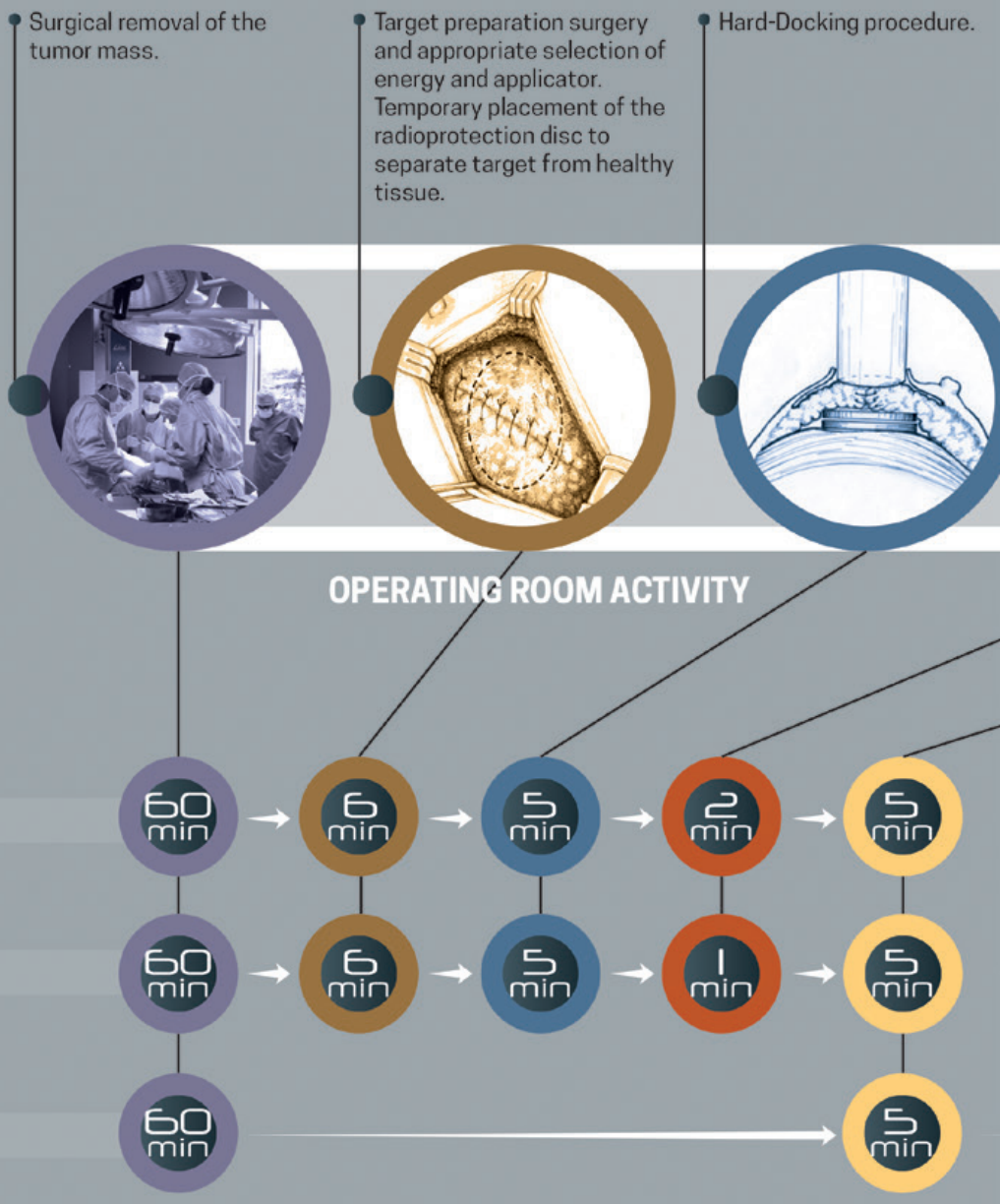
(25) The UK Standardization of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials, Haviland J. S., et al., Lancet Oncol, Vol. 14, pp. 1086–1094, 2013.

ADVANTAGES OF THE IOeRT TECHNIQUE:

- improvement of local control;
- reduction (in the case of boost) and elimination (in case of single dose) of the external radiotherapy cycle;
- time zero between surgery and radiation, resulting in inhibition of the repopulation of neoplastic cells;
- precision, thanks to direct visualization of the target;
- significant reduction dose to healthy tissues;
- minimization of side effects;
- feasibility of the treatment as the only solution when external radiation therapy is not possible.

TREATMENT TIMES





QUICK & EFFECTIVE

IOeRT irradiation.

Surgical suture.

EXTERNAL RADIATION THERAPY CYCLE

Hypofractionated external radiation therapy cycle

15 days

Standard external radiation therapy cycle

30 days

ADVANTAGES FOR THE PATIENT:

- reduction of the entire cycle to a single day!
- elimination of side effects caused by conventional therapy.
- decrease in costs to undergo treatment.

ADVANTAGE FOR SOCIETY:

decrease of social costs associated to the need for care and lack of patient productivity.

ADVANTAGE FOR THE MEDICAL FACILITY:

substantial reductions in waiting lists for radiotherapy centers.

LIAC COMMISSIONING

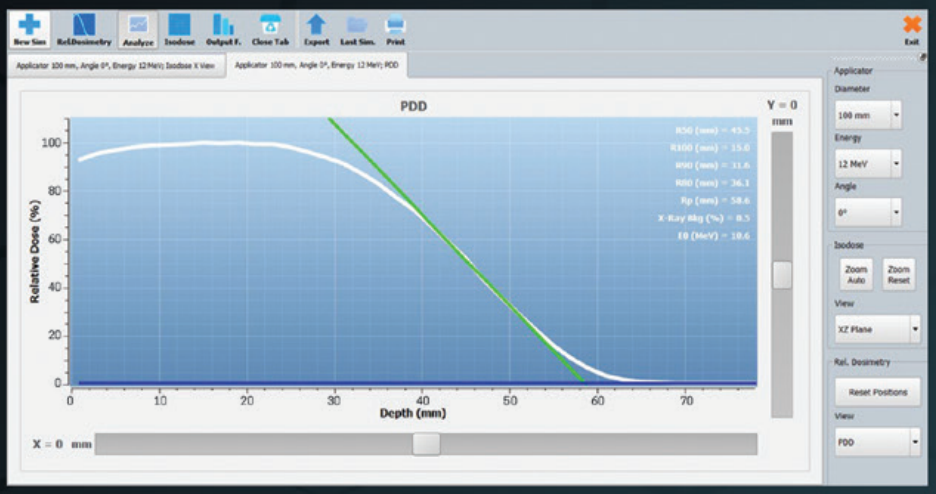
The LIAC commissioning is performed in accordance with primary international protocols through the use of standard dosimetric instrumentation, as well as use of the LIAC Monte Carlo Simulation proprietary software.

The use of the Monte Carlo software allows to dramatically reduce (3 working days) the dosimetric characterization of the accelerator already during its acceptance test performed at the main factory.

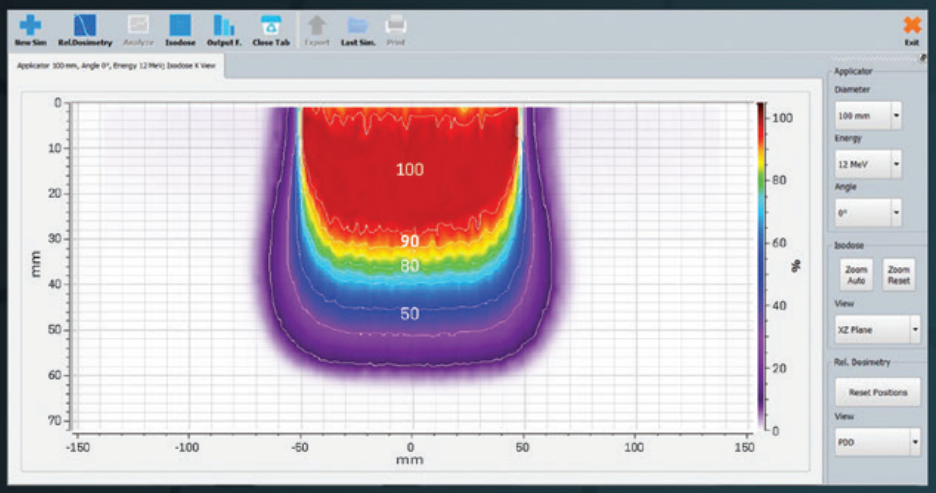
The clinical dosimetry of the totality of combinations (4 energies x 8 diameters of the applicator x 4 bevel angles) is immediately available, thus allowing to overcome the need for execution of the whole experimental characterization.

The software results are generated starting from a simple set of experimental measurements and using an Monte Carlo library of simulated monochromatic beams across the whole spectral region.

Thanks to the user-friendly interface, these results are easy and quick to use. During the clinical phase, the display of real-time isodose curves guides the correct choice of applicator and energy.



PDD analysis, applicator Ø 10 cm, 12 MeV energy, 0° bevel angle.



Isodose curve, applicator Ø 10 cm, 12 MeV energy, 0° bevel angle.

PLUG & PLAY INSTALLATION

LIAC is a plug & play device.

It is not necessary to conduct any upgrading in operating rooms.

It is sufficient to connect the mobile unit and the control unit by a dedicated cable.

The LIAC installation only requires availability of:

- socket (230 mono-phase + ground [V] 50 Hz);
- acoustic and optical signaling system, where required.

After just 5 days after delivery at its destination site, the system is ready for the first IOeRT treatment.

Thanks to the experience honed over the years, SIT is able to run an ad hoc preliminary proteximetric studies based upon the hospital's operational needs and the selected operating room.

day 1 — **LIAC delivery to hospital and transport to operating room. Installation check; LIAC is connected to the alarm and signal system of the operating room in order to verify proper functioning.**

days 2-3 — **LIAC dosimetric check.**

day 4 — **Training for IOeRT staff.**

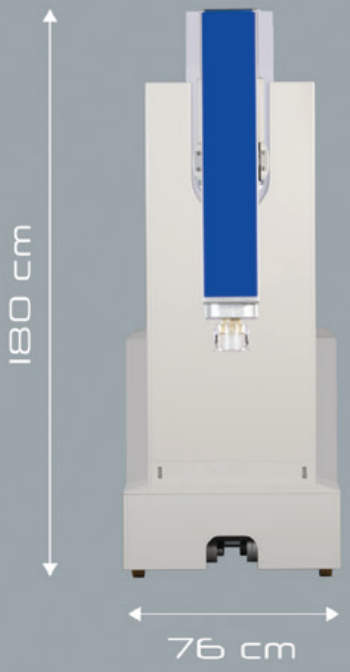
day 5 — **First patient treatment.**

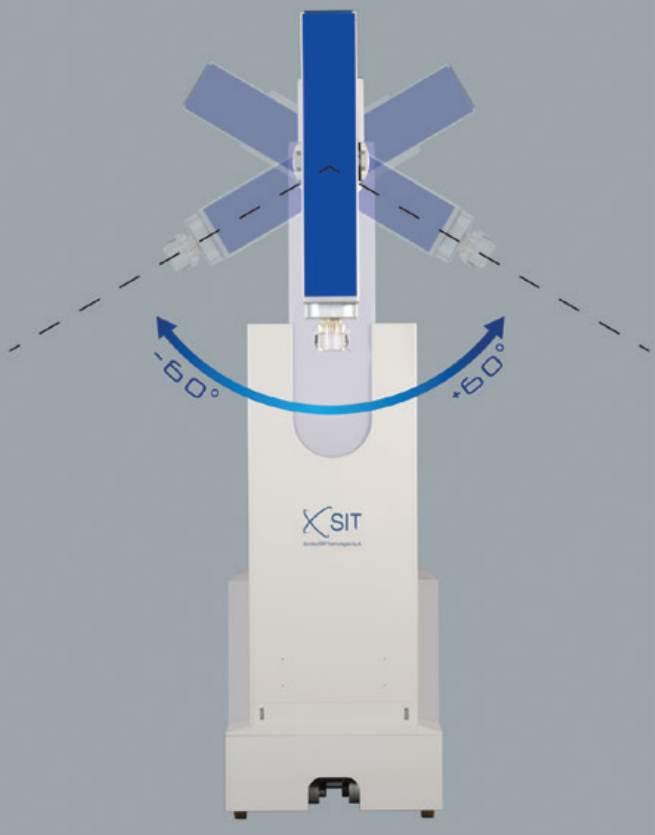
FAST COMMISSIONING AND PLUG & PLAY INSTALLATION

WORLD WIDE DIFFUSION

Italy
Austria
Belgium
Chile
Costa Rica
Cuba
Ecuador
Georgia
Germany
Greece
Iran
Kazakhstan
Kuwait
Mexico
Poland
Russia
Saudi Arabia
Spain
Switzerland
Thailand
Turkey
USA - Florida
USA - Illinois
USA - Oklahoma
USA - Pennsylvania
Venezuela

FEATURE	VALUE
Nominal Energies (model 12 MeV)	6, 8 ,10, 12 [MeV]
Nominal Energies (model 10 MeV)	4, 6 ,8, 10 [MeV]
Surface Dose	≥ 85 % model 10 MeV ≥ 87 % model 12 MeV
Beam Current	≤ 1.5 [mA]
Field Dimensions	Ø: 3, 4, 5, 6, 7, 8, 10 [cm] (12 [cm] on request) Angles: 0°, 15°, 30°, 45°
Flatness (maximum energy value)	≤ 12 % Ø 12 [cm] ≤ 3 % Ø 10, 8, 7, 6 [cm] ≤ 9 % Ø 4, 5 [cm] ≤ 12 % Ø 3 [cm]
Symmetry (maximum energy value)	≤ 3 %
Applicator length	60 [cm]
Source Surface Distance (SSD)	71.3 [cm]
Dose rate (applicator Ø 10 cm)	3 ÷ 20 [Gy/min]
E-gun pulse duration	≤ 4 [µs]
Long term stability	≤ 3 %
Short term stability	≤ 1 %
Linearity	≤ 1 %
Stray X-radiation (PDD Bremsstrahlung tail)	≤ 0.7 %
MOBILE UNIT	
Length	210 [cm] | 83 [inch]
Width	76 [cm] | 30 [inch]
Height	180 [cm] | 71[inch]
Weight	400 [kg] | 882 [lb]
CONTROL UNIT	
Length	80 [cm]| 32 inch]
Width	60 [cm]| 24 [inch]
Height	120 [cm]| 47 [inch]
Weight	120 [kg]| 265 [lb]
ELECTRICAL SPECIFICATIONS	
Temperature	18 ÷ 25 [°C] | 64.4 ÷ 77 [°F]
Relative humidity	30 ÷ 75 % (not condensing)
Voltage	230 mono-phase + ground [V]
Voltage variation	± 10%
Frequency	50 [Hz]
Nominal capacity	2 [kVA]
Environment power dissipation	1.8 [kW]
ACCESSORIES	
Mobile radioprotection barrier	HVL, TVL (lateral) Be beam absorber (horizontal)
Patient Radioprotection Disc PATENTED	Ø: 6, 7, 8, 9, 10 and 11 [cm]
Software	MU Calculation Dose View





Roll angle ± 60°

TECHNICAL FEATURES

Elevation 90 cm

Pitch angle + 30° - 15°

For more information about scientific and clinical evidences related to IOeRT technique:
ISIORT web
www.isiort.org

SIT Patents:

RADIATION DOSE CONTROL DEVICE FOR CONTROLLING AN ELECTRON BEAM PULSE DELIVERED DURING IORT

ABSORBER DEVICE

DEVICE FOR SHAPING AN ELECTRON BEAM OF A MACHINE FOR INTRAOPERATIVE RADIATION THERAPY

IORT MEDICAL ACCELERATOR WITH A PARTICLES BEAM ENERGY MEASURING DEVICE

SHIELDING DEVICE, IN PARTICULAR FROM RADIATION EMITTED BY AN ELECTRON ACCELERATOR

MACHINE FOR INTRAOPERATIVE RADIATION THERAPY

A IONIZING RADIATION BEAM DETECTOR

LIAC HWL

TREATMENT PLANNING SYSTEM (TPS) FOR IOeRT (PATENT PENDING)

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900050001_2 BR Rev. E_EN, February 2019