UNIVERSITAT DE BARCELONA

Final Degree Project

Biomedical Engineering Degree

“ Comparative analysis of intraoperative radiotherapy technologies “

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Author: Yassir Hamdan BenKssouba
Director: Dr. Alberto Biete

Abstract

La radioteràpia intraoperatòria (RIO) és una tècnica en la qual la radiació s'administra directament en el llit tumoral immediatament després de l'extirpació quirúrgica, la qual cosa redueix la durada del tractament i limita el mal al teixit sa. Els hospitals que consideren la possibilitat d'aplicar la RIO s'enfronten a la decisió de triar entre sistemes d'electrons, unitats de raigs X de baix voltatge, braquiteràpia d'alta taxa de dosi o de feix extern convencional. En l'actualitat, no existeix cap guia comparativa dissenyada per a ajudar els gestors hospitalaris a seleccionar el sistema més adequat en funció dels seus contextos clínics, logístics i financers.

Aquesta tesi proporciona una anàlisi comparativa a partir d'informació procedent de revisió de literatura científica, observacions directes dels hospitals de Barcelona i entrevistes amb físics mèdics, oncòlegs radioteràpics, cirurgians i gestors sanitaris. S'han avaluat sistemàticament les indicacions clíniques, la complexitat tècnica, les exigències d'infraestructura, les necessitats de personal, els requisits de seguretat radiològica i els costos inicials i continuats de cada tecnologia. Els resultats revelen que els sistemes d'electrons ofereixen una àmplia versatilitat clínica i temps de tractament curts, encara que requereixen importants ajustos d'infraestructura. Els sistemes de baix voltatge ofereixen una configuració més senzilla amb un blindatge mínim, però es limiten a cavitats quirúrgiques específiques més petites. La braquiteràpia destaca per la precisió de la dosi en localitzacions anatòmiques irregulars, però afegeix complexitat operativa i costos continus de la font. La radioteràpia externa ofereix àmplies aplicacions clíniques, però exigeix inversió en infraestructures i tractaments prolongats.

En conclusió, aquesta tesi serveix com a recurs pràctic, dotant als responsables de la presa de decisions hospitalàries de criteris clars per a identificar i implantar la tecnologia de RIO òptima que millor s'ajusti a les seves capacitats institucionals i als objectius d'atenció al pacient.

Paraules clau: RIO, radioteràpia, baix voltatge, braquiteràpia, tecnologies intraoperatòries, càncer, raigs X, electrons, fotons.

Abstract

Intraoperative radiotherapy (IORT) is a specialized technique where radiation is delivered directly to a tumour bed immediately after surgical removal, significantly reducing treatment duration and limiting damage to healthy tissue. Today, hospitals considering IORT face a challenging decision among electron-based systems (IOeRT), low-voltage X-ray units, high-dose-rate (HDR) brachytherapy, or conventional external-beam IMRT. Currently, there is no practical comparative guideline tailored to help hospital administrators select the most suitable system based on their specific clinical, logistical, and financial contexts.

This thesis provides a comprehensive comparative analysis of these technologies by synthesizing information from an extensive review of the scientific literature, direct observations from leading hospitals in Barcelona, and structured interviews with medical physicists, radiation oncologists, surgeons, and healthcare managers. Each technology's clinical indications, technical complexity, infrastructure demands, staffing needs, radiation safety requirements, and both initial and ongoing costs were systematically assessed.

Findings reveal that IOeRT systems offer broad clinical versatility and short treatment times, though they require substantial infrastructure adjustments. Low-voltage systems offer simpler setup with minimal shielding but are restricted to specific, smaller surgical cavities. HDR brachytherapy excels in dose precision for irregular anatomical sites but adds operational complexity and ongoing source costs. IMRT provides extensive clinical applications but demands significant infrastructural investment and prolonged treatment schedules.

Ultimately, this thesis serves as a practical resource, equipping hospital decision-makers with clear criteria to identify and implement the optimal IORT technology that aligns best with their institutional capabilities and patient care goals.

Keywords: IORT, radiotherapy, low-voltage, brachytherapy, intra-operative tecnologies, càncer, X-Ray, electron, photon.

Acknowledgements

I would like to express my sincere gratitude to Dr. Biete for his invaluable guidance throughout this work and for connecting me with various experts in the field. I am also deeply thankful to Antonio Herreros for providing essential materials that greatly enhanced my understanding of the subject. Finally, I wish to thank Dr. Guedea for all the information shared regarding the Catalan Institute of Oncology (ICO), which was relevant to this study.

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Glossary of abreviations

OS	Overall Survival
IMRT	Intensity-Modulated Radiotherapy
IOeRT	Intra-Operative Electron Radiotherapy
R0	Complete resection (no residual tumour)
CT	Chemotherapy
CRT	Chemoradiotherapy
RT	Radiotherapy
EBRT	External-beam radiotherapy
HDR-IORT	High-dose-rate intraoperative radiotherapy
OR	Operating room
SSD	Source–surface distance.
PMMA	Polymethyl methacrylate
LINAC	Linear accelerator QA Quality assurance
PDD	Percentage depth dose curve
R100	100% depth in water used as the beam quality index for electron beams
R90	90% depth in water used as the beam quality index for electron beams
R50	Half-value depth in water used as the beam quality index for electron beams
R10	10% depth in water used as the beam quality index for electron beams
Euratom	European Atomic Energy Community

Contents

1. Introduction

1.1. Context

Intra-operative radiotherapy (IORT) delivers a curative radiation dose directly to the tumour bed while the patient is still on the operating table. By targeting immediately after surgical excision, IORT can shorten or even eliminate the need for prolonged external-beam courses, spare surrounding organs, and streamline the entire cancer-care pathway. Three main modalities are now in use: electron-based IORT (IOeRT), low-kilovoltage X-ray IORT, and high-dose-rate (HDR) brachy-IORT with ^{192}Ir.

Each employs a distinct physical principle, demands a different hospital infrastructure, and carries its own clinical evidence base. As a result, the choice of platform has far-reaching implications for patient outcomes, workflow, staffing, shielding, and long-term cost.

Despite the growing number of IORT systems entering the market, hospital managers and clinical directors lack a consolidated, decision-oriented comparison. Published studies tend to focus on narrow clinical endpoints or on the physics of a single device rather than on the broader operational questions a hospital must answer before investing in an IORT programme

Early-stage breast cancer trials have validated both electron and low-kV techniques, pelvic and pancreatic surgeons are exploring HDR-IORT for locally advanced disease, and manufacturers continue to refine mobile linacs, miniaturised X-ray tubes, and adaptive brachytherapy applicators. In short, the technology is advancing faster than the practical guidance available to those who must purchase, install, and run it.

1.2. Objectives

The goal of this project is to deliver a comprehensive comparison of different IORT technologies from multiple perspectives, ultimately providing a practical guide for hospital managers and decision-makers who are considering the acquisition of an IORT system. The intention is for this work to serve as a clear, accessible reference to support strategic decisions in a field that is growing rapidly but still lacks consolidated guidance.

What makes this project original and unique is that, to date, there are no published papers or studies offering a structured comparison for hospital administrators and managers. While clinical research on IORT continues to expand, little attention has been given to practical, management-focused evaluations. As the use of IORT grows globally, a resource like this could become highly valuable, helping hospitals efficiently plan and invest in establishing or expanding their intraoperative radiotherapy divisions. By bridging the gap between technical, clinical, and administrative perspectives, this work aims to make a meaningful contribution to the future development of IORT programs.

1.3. Methodology and Scope

This project was developed through a combination of deep research, real-world observation, and expert interviews. To build a strong foundation, an extensive review of scientific literature was conducted, analyzing dozens of research papers focused on cancer treatment, intraoperative radiotherapy (IORT), and the physical principles behind these technologies. This helped create a clear understanding of how IORT works both clinically and technically.

Alongside the literature review, fieldwork was carried out in several hospitals in Barcelona. These visits made it possible to observe how IORT technologies are used in practice and to better understand the hospital infrastructure needed to support them. Also, interviews were held with medical physicists, hospital managers, and doctors specializing in radiation oncology and related fields. These conversations provided direct feedback, real-world opinions, and a deeper understanding of how different professionals view and experience IORT in their day-to-day work.

The limitations in comparative technology analyses arises from variability in data availability and consistency. Often, different technologies or manufacturers report their outcomes using diverse methods and standards, complicating direct comparisons and potentially introducing biases. Additionally, studies and sources included in the analysis might inherently favour certain technologies, either because those technologies are better studied or due to publication bias towards positive findings. Expert consultations, while valuable, may also introduce subjective judgments shaped by personal experiences or institutional preferences.
Recognizing these limitations is essential for accurately interpreting results and making informed decisions based on the analysis.

2. Background

Intraoperative radiotherapy (IORT) is a technique that involves precise delivery of a large dose of ionising radiation to the tumour or tumour bed during surgery.

2.1. History

European pioneers in the field of IORT are Spain, Italy, Austria, and Germany. Although it is true that most of the scientific information generated before 1980 was of little practical influence in the oncology community. The first known treatment of IORT was documented by Comas and Prio in 1905 [1], in a case of endometrial cancer. The modern approach to IORT began with studies by Abe at the University of Kyoto [1] in the 1960s by using high doses (25–30 Gy) of gamma rays from cobalt unit and betatron electrons. In the 1970s, special facilities dedicated to performing IORT procedures with conventional linear accelerators were set up at Howard University Hospital and Massachusetts General Hospital. In the early 1990s, mobile linear electron accelerators and low-energy miniature x-ray machines were introduced into clinical practice in a series of radiation therapy centers worldwide.

2.2 . IORT Techniques

Electrons, low-kV X-rays and HDR brachytherapy are all different methods of IORT in current clinical use. Each method has its own unique set of advantages and disadvantages and its own set of indications where one may be better suited than the other

2.2.1 Electron IORT

The introduction of electron IORT (IOeRT) marked the beginning of the IORT era in the early 1960s [2, 3]. IOeRT is a technique where a concentrated dose of electron radiation is delivered directly to the tumor bed during surgery, immediately after the tumor is removed. This approach allows high-dose treatment to be focused precisely where it is needed, minimizing exposure to surrounding healthy tissues. IOeRT is typically completed in a few minutes and helps reduce the need for additional external radiation sessions after surgery.

2.2.2. Low voltage (50kv)

Low-voltage intraoperative radiotherapy uses low-energy X-rays, typically around 50 kilovolts, to deliver a precise dose of radiation directly to the surgical cavity immediately after tumor removal. A small, spherical applicator is placed in the cavity, and the X-rays radiate outward, treating the surrounding tissue while limiting penetration beyond a few centimeters. This method concentrates the dose at the area most at risk for recurrence, preserving healthy tissue and reducing the need for external radiotherapy. The procedure is performed in the same surgical act, so the added time is minimal.[3]

2.2.3. HDR Brachytherapy

High-dose-rate (HDR) brachytherapy for intraoperative radiotherapy (IORT) involves placing a balloon or catheter applicator directly into the surgical cavity after tumor removal. A small radioactive source, usually ^{192}Ir, travels through the applicator and delivers a high dose of radiation from inside the cavity. The dose is carefully controlled by adjusting the position and time the source spends at each point. This allows precise treatment of the area at highest risk for recurrence while limiting radiation to surrounding healthy tissues. The entire process typically takes 5 to 20 minutes and is performed during the same surgery.[3]

2.3. Biological Mechanism

The biological action of IORT follows the same principles as other forms of radiation therapy. When radiation interacts with tissue, it ionizes DNA and molecules, leading to the creation of free radicals. These free radicals can then damage the DNA of cancer cells, causing cell death or preventing them from dividing and growing.

2.3.1. Biological effect. [4]

When the single IORT dose strikes the fresh tumour cavity it kills residual tumour and stromal cells outright and sprays the area with damage-associated molecular patterns (DAMPs). These danger signals, together with local chemokines, draw in professional antigen-presenting cells (APCs) and natural killer (NK) cells, while helping APCs load tumour antigens for presentation in the nearby lymph-node chain. The result is fresh priming and re-priming of cytotoxic T cells that can return to the cavity or seek out remaining disease elsewhere. Regulatory T cells (Treg) and myeloid-derived suppressor cells (MDSC) may blunt this response, but immune-checkpoint blockade (ICB) antibodies given systemically can lift that brake and amplify the tumour-directed attack. In short, the physical sterilisation of the tumour bed by IORT also sets off a brief, self-contained inflammatory burst that can act as a built-in adjuvant for systemic anti-tumour immunity. [4][5]

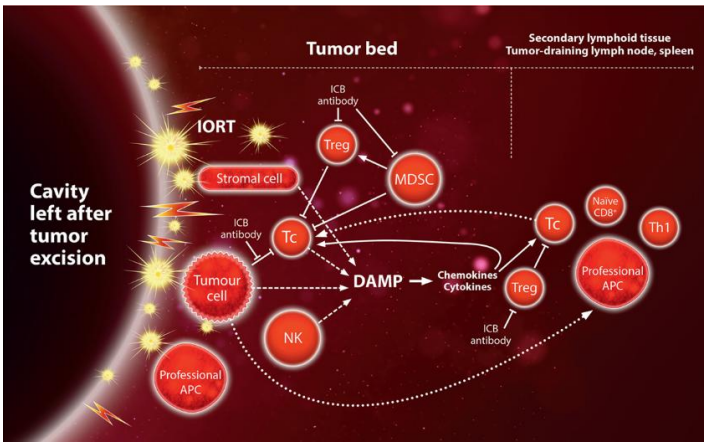


Fig.10 Hypothetical immune activation by IORT to the tumor bed after tumor excision of the metàstasis [5]

2.4. Regulations

IORT is governed by strict legal and regulatory standards to protect both patients and healthcare workers. In Europe, it follows the EURATOM Basic Safety Standards, which require proper justification of radiation use, dose optimisation, and established quality assurance programmes. National regulations, such as Spain's Real Decreto 601/2019, further specify rules on equipment authorisation, shielding requirements, staff qualifications, and regular inspections. All IORT devices must carry CE marking (in Europe) or FDA approval (in the United States) to certify safety and performance. Hospitals are also required to maintain detailed documentation, including calibration records, staff training certificates, and radiation protection plans. These regulations ensure that IORT procedures are performed safely, minimising risks while maximising clinical benefits.

3. Results

3.1. Clinical Analysis

In clinical practice, the three main modalities of intraoperative radiotherapy (IORT), electron, low kilovoltage X-ray and ^{192}Ir HDR brachytherapy, offer distinct advantages and limitations that determine their suitability for different tumour sites.

Electron IORT (IOeRT) is the most versatile platform. By selecting energies between 4 and 12 MeV, clinicians can match the therapeutic depth to cavities ranging from a few millimetres to almost four centimetres. Beyond the classic boost for breast-conserving surgery, electrons are used in extremity sarcomas, pelvic recurrences, pancreatic tumours, retroperitoneal disease and gynaecologic sites. Their flat beam profile and cones up to ten centimetres in diameter facilitate coverage of irregular or large surgical beds. The main drawbacks are the need to place an aluminium-lead shielding disc under the field and the logistical demands of bringing a mobile linear accelerator into the operating room. [6]

Low-kilovoltage systems, such as INTRABEAM or Xoft Axxent, stand out for their ultra compact design and the fact that they do not require structural shielding. They fit in any standard operating theatre and are covered like ordinary surgical instruments. Their dosimetric profile is ideal for spherical cavities of three to five centimetres in diameter, which explains why more than ninety-five percent of the published experience relates to breast reinforcement or definitive partial breast irradiation in early stages of disease. Since the 50 kilovolt are rapidly attenuated, organs such as the heart and lungs receive negligible doses. However, the sharp drop in dose makes the technique less suitable for deep beds or wide margins, and the beam application time of 25 to 40 minutes lengthens the surgical procedure. [7]

HDR brachy-IORT with a balloon or multilumen catheters. A ^{192}Ir source passing through dozens of dwell positions allows dose sculpting with great precision, so the method has become established for irregular cavities in rectal, cervical and head-and-neck recurrences, as well as pelvic tumours where nearby critical structures make hot spots unacceptable. Immediate CT-based planning enhances precision, but at the cost of a more complex workflow, the need for mobile lead panels and the recurring expense of replacing the radioactive source four times per year. In breast cancer it is mainly chosen by centres that already run an HDR unit and want a single system adaptable to many indications.[8,9]

In summary, anatomical considerations usually guide the choice. Electrons for wide or deep fields, low-kV for small surface cavities and HDR when the highest three-dimensional compliance is required. Scientific maturity also plays a role: IOeRT has the broadest multicentre evidence, low-kV shows solid but almost exclusively breast-based results, and HDR offers smaller series but excels in hard-to-reach sites. Finally, institutional resources are decisive: operating theatres without additional shielding favour low-kV units, facilities equipped with mobile accelerators favour electrons, and departments already using HDR brachytherapy naturally extend it to the intraoperative setting.

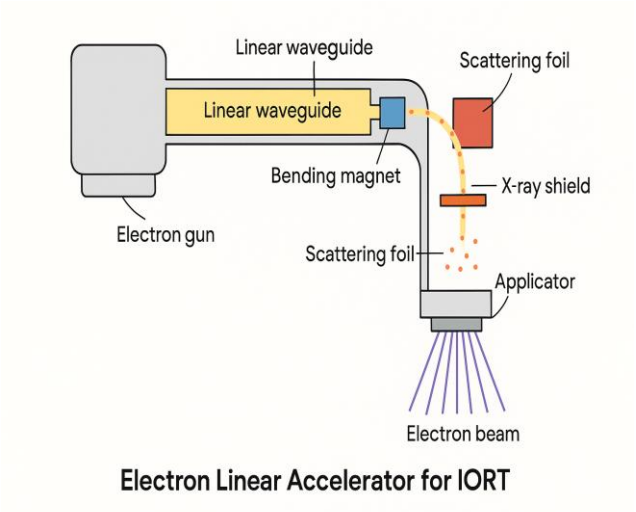
3.2. Technical Analysis

Selecting one technology over another depends largely on the hospital's clinical priorities and logistical capacity. Development across this sector remains relatively limited because each system is technically intricate and costly to produce.

3.2.1. IOERT

A. Radiation source

The source is electron beams at nominal energies of 4, 6, 8 and 10 MeV and a high dose rate of 4-31 Gy/minute depending on beam energy and applicator size [10], with the purpose to deliver a high, precise radiation dose during surgery while protecting surrounding tissue.



Electron Gun: Produces electrons.
Linear Waveguide: Accelerates electrons using electromagnetic waves.
Bending Magnet: Redirects the beam downward.
Scattering Foil: Spreads the beam for even dose distribution.
X-ray Shield: Blocks stray radiation.
Applicator: Directs the electron beam to the surgical site.

Fig. 11 Simplified diagram of a mobile linear accelerator for IOeRT done by IA

B. Shielding requierements [11]

Wall and Ceiling Shielding

Beam Energy	Concrete (density ≈ 2.35 g/cm³)	Lead
6 MeV	60–80 cm	4–5 mm
9 MeV	80–100 cm	6–8 mm
12 MeV	100–120 cm	8–10 mm

Table 8 Information on radiation protection requirements.

Primary walls (those in beam direction): require thicker shielding.
Secondary walls (for scatter radiation): need about 50–75% of the primary wall thickness.
Ceiling: Same thickness as walls if areas above are occupied.

Beam Stopper
These shields are typically manufactured from high-density plastic or metal, for example 10 to 12 cm of high-density polyethylene or 5 to 7 cm of a tungsten–steel composite, and must be thick enough to stop the full energy of the electron beam

Floor Shielding
If there are occupied rooms beneath the treatment area, floor shielding similar to primary wall specifications is required; for 9 to 12 MeV beams, concrete slabs approximately 10 to 12 cm thick may be needed.

Mobile Lead Shields
The standard barrier consists of 2 mm lead, stands roughly 180 to 200 cm tall, and is intended to shield staff from scattered radiation rather than the direct beam.

C. Workflow [12]

Operating-room set-up
Surgeon performs standard resection and confirms clear margins.
Cavity dimensions are measured
If deeper than planned, the team may switch to a higher energy or larger cone.

Shield placement and cone docking
A sterile aluminium-lead disc is first placed beneath the target area to shield underlying organs such as the lung, heart and bowel. The chosen cone, typically 3 to 10 cm in diameter and either flat or bevelled, is then mounted on the LINAC pivot arm and pressed flush against the tissue, making sure no air gaps remain.

Final dosimetric check
Physicist verifies SSD (source-to-surface distance), gantry angle (usually 0°), selected energy and prescribed dose.

Beam delivery
After the staff move behind the mobile shielding barriers, the radiation oncologist activates the beam, and the electron pulse runs for approximately two minutes.

Applicator removal and surgical closure
After automatic beam shut-off, the cone and disc are removed.

D. IOeRT Technology supplier comparison [13-15]

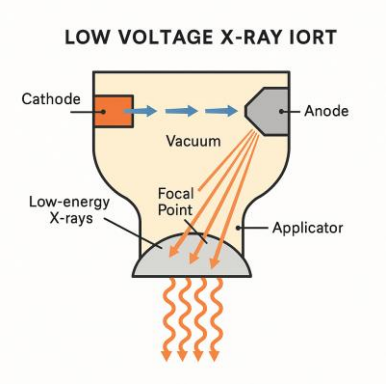
Features	Liac	Mobetron	Novac 11
Nominal energies (model 12 MeV)	6, 8, 10, 12 MeV	6,9,12 MeV	—
Nominal energies (model 10 MeV)	4, 6, 8, 10 MeV	—	4, 6, 8, 10 MeV
Surface dose	≥ 85 % (model 10 MeV) / ≥ 87 % (model 12 MeV)	>85%	≥ 85 %
Beam current	< 1.5 mA	No access to data	< 1.5 mA
Field dimensions	Ø (cm): 3, 4, 5, 6, 7, 8, 10 (12 cm on request) Angles (°): 0, 15, 30, 45	Circular applicators Ø 3 – 10 cm in 0.5 cm	Ø (cm): 3, 4, 5, 6, 7, 8, 10 Angles (°): 0, 15, 22.5, 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	No access to data	≤ 5 % — Ø 10, 8, 7 cm ≤ 9 % — Ø 4, 5 cm ≤ 11 % — Ø 3 cm
Symmetry (maximum-energy value)	≤ 3 %	No access to data	≤ 3 %
Source–surface distance (SSD)	60 [cm] 71.3 cm	50cm	65 cm — Ø 3, 4, 5, 6, 7, 8 cm 80 cm — Ø 10 cm
Dose rate (applicator Ø 10 cm)	3 – 20 Gy / min	10 Gy/min	4 – 30 Gy / min
E-gun pulse duration	< 4 µs	0.5 – 4.0 µs	< 4 µs
Long-term stability	≤ 3 %	No access to data	≤ 3 %
Short-term stability	≤ 1 %	No access to data	≤ 1 %
Linearity	≤ 1 %	1%	< 1 %
Stray X-Radiation	< 0.7 %	< 0.5 %	≤ 0,2 %
Indications	Breast Cancer Pancreatic Cancer Colorectal Cancer Gynecological Cancer Head and Neck Cancer Sarcomas Skin Cancer	Breast Cancer Pancreatic Cancer Colorectal Cancer Gynecological Cancer Head and Neck Cancer Sarcomas Skin Cancer	Breast and Multi-cancer application.

Table 9 Comparison of the main suppliers of the IORT technology

3.2.2. Low Voltage

A. Radiation source

Low-voltage IORT uses a specialized, compact X-ray source to deliver radiation to the tumor bed during surgery, typically at a 50 kV energy level. This approach offers a localized dose with minimal impact on surrounding healthy tissues, making it a viable option for certain cancers, especially breast cancer. [37] [38]



Cathode emits electrons.
Electrons travel in vacuum to the anode.
Anode converts them into low-energy X-rays.
X-rays exit through a **spherical applicator** and treat the surgical site.
Uses 30–50 kV, ideal for shallow targets like early breast cancer. Requires minimal shielding and can be used directly in the OR.

Fig. 12 Simplified diagram of Low voltage for IORT done by IA

B. Shielding requirements [11]

The IAEA document *"Radiation Protection in Intraoperative Radiotherapy"* [16] explains that systems operating at 50 kV or below generates very little scatter, so most operating rooms need no structural shielding and only minimal protective measures.

Lead Shielding (Walls, Doors)

Standard operating room walls usually need no additional shielding, but if the unit is positioned close to sensitive areas such as an adjacent office or corridor, it is advisable to install one to two millimeters of lead equivalent, either as mobile panels or fixed inserts; some centres also deploy 0.5 to 1 mm lead mobile shields to protect staff during treatment.

Mobile Lead Screens

Although optional, a 2 mm lead-equivalent barrier with an integrated viewing window is recommended to shield staff from scattered radiation and should be placed between the radiation source and the clinical team

Floor/Ceiling

No special shielding is required because 50 kV X-rays have low penetration, and their scatter diminishes quickly through a combination of inverse-square fall-off and material absorption.

Beam Containment
The spherical applicator naturally confines stray radiation, and the emitted X-rays are absorbed within a few centimeters of the surrounding tissue or the applicator itself

C. Workflow [12]

Preparation
The medical physicist performs equipment checks outside the operating room, installs radiation warning signs and places area dosimeters while the surgical team begins tumour excision.

Eligibility confirmation and applicator selection
After the cavity is exposed, the surgeon and radiation oncologist confirm that IORT is appropriate, choose the correct applicator size and prepare the target area; meanwhile the physicist enters patient and dose data at the console.

Device setup and sterile coupling
The radiation oncologist drapes the X-ray source stand, attaches the sterile applicator, and together with the surgeon positions it flush inside the surgical cavity.

Prescription and dose delivery
From the console the radiation oncologist finalises the treatment parameters, then the team steps behind protective barriers and monitors the automated delivery of the prescribed dose.

Applicator removal and closure
Once the beam stops, the applicator is withdrawn, the surgeon completes wound closure, and the physicist secures the equipment, retrieves dosimeters and records the delivered dose.

D. Low-voltage Technology supplier comparison [17]

Feature	Xoft Axxent® highlight	Intrabeam Highlight
Radiation source	Miniaturised disposable 50 kV X-ray tube (2.25 mm Ø, 5.4 mm assembly; lengths 25 & 50 cm)	Miniaturized X-ray tube 30–50 kV / ≤ 40 µA
Dose-rate / treatment time	High-dose-rate: typical delivery 4 – 15 min depending on applicator and Rx	To deliver 20 Gy at the surface: ≈ 20–48 min, depending on applicator size
Dose fall-off & shielding	Very steep fall-off; minimal room shielding. taff may remain inside the OR during exposure	50 kV photons with a very steep fall-off (< 5–10 mm); minimal room shielding required, often allowing staff to stay in the OR.
Mobility	Cart-mounted controller weighs 92 kg (202 lb)	Mobile cart 105 kg (full workstation up to 155 kg
Power & cooling	50 kV / 300 µA, 15 W source power; controller draws 150 VA from 100-240 V mains; integral cooling sheath around tube	Connected load 300 VA, 110–240 V, 50–60 Hz; internal water/glycol cooling for the tube; insulated transformer in base.
Applicator portfolio	Balloon (intracavitary & extended), surface cones, vaginal/cervical, rigid shields – all connect via flexible HV cable	Reusable spherical applicators 1.5–5 cm, flat/surface applicators, needle applicator; SMART single-use applicators with RFID and colour coding.
Clinical indications (regulatory)	FDA-cleared & CE-marked “anywhere in the body”; routinely used for early-stage breast IORT, APBI, NMSC (skin), GYN; clinical trials in brain & pancreas.	CE- and FDA-cleared for intracavitary intraoperative RT (e.g., breast, vertebra, brain); spheres for tumour bed, needle for intracranial lesions; may be used “anywhere in the body” at the physician’s discretion.

Table 10 Comparison of the main suppliers of the Low.kv IORT technology

3.2.3. HDR Brachytherapy

A. Radiation Source

The radiation source is ^{192}Ir. HDR brachytherapy delivers a concentrated dose of radiation to the tumor bed using a flexible applicator that allows precise placement of the ^{192}Ir source. This technique is particularly useful in situations where electron beam therapy might be difficult to access, such as in the pelvis or for pediatric patients.

How HDR IORT Works

A small ^{192}Ir source is sent into a balloon applicator or a multi-channel catheter at the surgical site.
It emits high-dose radiation to the surrounding tissue.
Shielding protects staff and healthy areas.
After treatment, the source is retracted and the applicator is removed.

Treatment is precise, fast, and done during surgery.

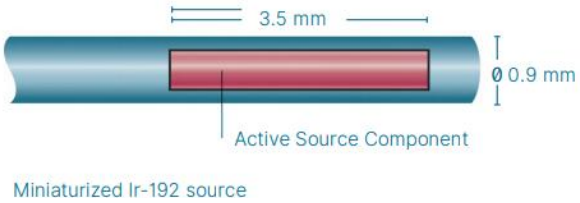


Fig. 13 Simplified diagram of a HDR Brachytherapy source for IORT [18]

B. Radiological protection [11]

Shielding Element	Recommendation
Mobile Lead Screens	5–10 mm Pb equivalent
Wall	30–40 cm concrete or 10–15 mm Pb
Source Housing	Built-in shielding in afterloader
Room Access	Restricted with signage and barriers

Table 11 Information on radiation protection requirements.

Shielded Operating Room [11]

Ideally, IORT with ^{192}Ir is done in a dedicated shielded OR or HDR suite.

Mobile Shielding

Lead screens should be positioned between the patient and staff, constructed with roughly 5 to 10 mm lead equivalent, standing about 2 m tall, and often fitted with a viewing window.

Wall/Floor/Ceiling Shielding

Permanent shielding is needed only in a dedicated HDR room, where walls typically contain thirty to forty centimeters of concrete or ten to fifteen millimeters of lead, and floors or ceilings require similar protection if adjoining spaces are occupied; however, most IORT programmes rely on mobile shielding rather than full structural barriers.

Source Containment (Afterloader)

The ^{192}Ir source is housed in a remote afterloader with integral shielding, and it is fully retracted into this shielded housing between treatments.

Controlled Area and Access
No one is permitted to enter the room during radiation delivery; warning signs, door interlocks, and real-time dose monitoring are required, and the room is classified as a controlled radiation area during exposure.

C. Workflow [12]
Preoperative Planning
A multidisciplinary team reviews imaging to confirm the patient's suitability for IORT, the applicator type and dose are selected in advance, and the patient provides informed consent for HDR brachytherapy.

Tumor Resection
The surgeon removes the tumour, whether gynecologic, rectal, or breast, and the surgical cavity is then assessed to determine if it is suitable for IORT.

Applicator Placement
The radiation oncologist inserts a balloon or catheter-based applicator into the surgical cavity and positions it carefully to conform to the target volume.

Treatment Setup
The applicator is connected to the HDR afterloader through transfer tubes, and staff either exit the room or move behind lead shielding before radiation delivery begins.

Radiation Delivery
The ^{192}Ir source advances through the applicator, pausing at pre-programmed dwell positions to deliver high-dose radiation over a period typically lasting 5 to 20 minutes, with the entire process monitored from outside the room.

Source Retraction & Applicator Removal
The source retracts back into its shielded housing, the applicator is removed, and the surgical procedure then resumes.

D. HDR Brachytherapy Technology supplier comparison [18,19]

Feature	Varian Bravos™	BEBIG Medical SagiNova®
Radiation-source options	Miniaturised ^{192}Ir	Choice of ^{192}Ir *or* long-life ^{60}Co mini-sources (same 3.5 mm active length)
Maximum installable activity	555 GBq (15 Ci) ^{192}Ir	Not specified; Co-60's 5-year half-life minimises exchanges
Typical source working life	^{192}Ir replacement every 3–4 months	^{192}Ir ≈ 4–6 months ; Co-60 ≈ 60 months
Treatment channels / dwell range	30 channels, up to 100 dwells per channel; 1 mm programmable steps	Multi-channel support
Wire drive – speed & positioning	100 cm s^{-1}; ± 1 mm positional accuracy	System relies on Automatic Length Measurement check before each run
Afterloader shielding / leakage	Tungsten safe; ≤ 1 µSv h^{-1} at 1 m with max activity	Complies with IEC 60601-2-17
Typical room shielding	~ 4 cm Pb / 35 cm concrete	Determined case-by-case via BEBIG pre-install consulting
Weight & footprint	143 kg 113.8 × 53.8 × 68.8 cm	-
Power & UPS	100–240 VAC	50–60 Hz; 100 VA max; UPS + onboard batteries for safe retract
Integrated QA & safety tools	CamScale™ source-position test, LED tube status, custom checklists with e-signature	QAssist™ digital QA suite, Automatic Length Measurement, colour-coded channel indexing for mix-up prevention
Control interface	Back-panel touchscreen lets staff run dummy/length checks at patient side	Graphical, step-guided GUI designed with usability engineers for streamlined workflow
Treatment-planning ecosystem	Full DICOM RT; seamless with ARIA® OIS + Eclipse/BrachyVision™	SagiPlan® TPS with DICOM I/O, plan templates, BED evaluation & image fusion
Remote service / connectivity	SmartConnect™ encrypted remote monitoring (HIPAA / FIPS 140-2)	24/7 global support network; remote QA reporting & source-exchange logistics
Applicator portfolio	Compatible with Varian & third-party HDR applicators; 30-channel capacity	Extensive intracavitary, interstitial & skin range, MR-safe options, Mick® library integrated in TPS/afterloader
Regulatory & safety standards	IEC 60601-2-17, ICRP codes, NRC (USA) compliance	CE-marked; TG-43-equivalent dose formalism for both isotopes

Table 12 Comparison of the main suppliers of the HDR Brachy-IORT technology

3.2.4. DOSIMETRY

Coverage

Electron

The electron beam deposits 20 Gy of radiation out to the depth where the dose falls to 90 % of its maximum [20]. To protect underlying organs, the cone is paired with a beveled steel/PMMA housing and a 3 mm aluminum/lead disc placed beneath the treatment site. This eliminates any forward-leaking radiation with 6 - 8 MeV electrons and the disc in place, both the heart and the lung receive essentially zero dose at 6 MeV and over 99 % of the dose is stopped at 10 MeV [21].

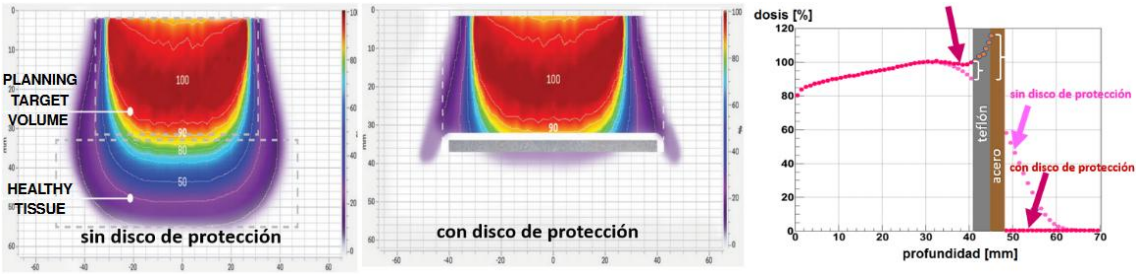


Fig. 14 Dose distribution maps and depth-dose curves in IOeRT: without a protective disc (left), the electron beam penetrates beyond the target into healthy tissues; with a shielding disc (center), the beam is stopped effectively. The depth-dose graph (right) shows how the disc drastically reduces dose transmission beyond the target volume. [12]

Because of this built-in shielding, mobile electron units require only minimal floor-level protection, making them highly practical for operating-room use

As the LIAC HWL curves illustrate *(Fig. 6)*, an electron IOERT field can be prescribed so that 20 Gy reaches the 90 %-isodose depth (d_{90}), about 9 mm at 4 MeV, 16 mm at 6 MeV, 23 mm at 8 MeV, 30 mm at 10 MeV and 37 mm at 12 MeV. This steep fall-off, combined with the depth-dose control seen in the graph, lets clinicians choose the lowest energy that fully encompasses the tumour bed while sparing tissue beyond the shielding disc.

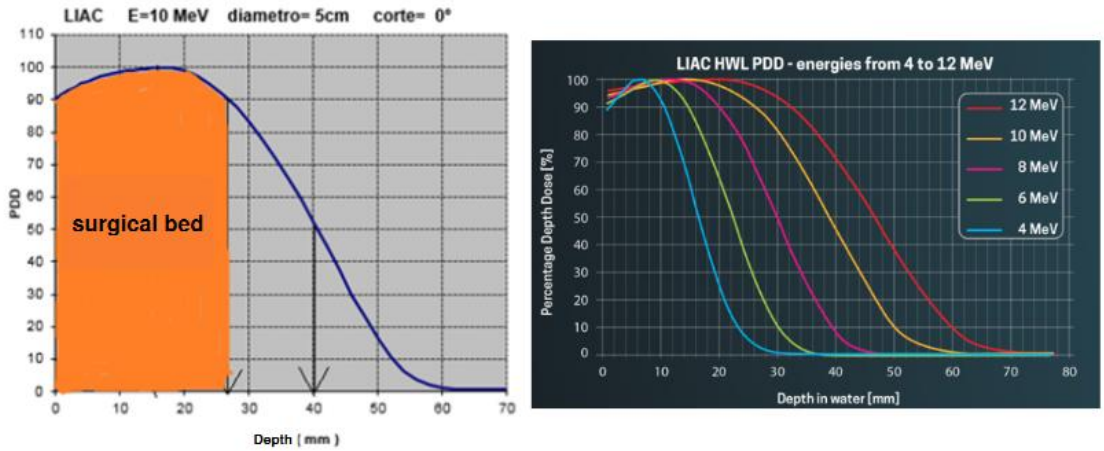


Fig. 15 Depth-dose profiles in IOeRT: the left graph shows how a 10 MeV electron beam covers the surgical bed with a uniform high dose up to the desired depth. The right graph compares different energies, illustrating how higher-energy beams penetrate deeper, allowing precise matching of dose to tumour. [11,12]

Low voltage

The output of the miniaturized X-ray tube is about 2 Gy min^{-1} at 1 cm in wàter, so a typical breast prescription of 20 Gy at the applicator surface takes 25 - 40 min to deliver. The applicator bathes the first 1 cm of tissue with a uniform shell: 20 Gy at the surface softens to 5 - 7 Gy at 10 mm and less than 1 Gy beyond 20 mm [22]. Because the miniature source sits inside the cavity, room scatter is extremely low, so simple mobile 0.5mm Pb drapes keep staff exposure less than 10 µSv per case and no permanent bunker is required [23].

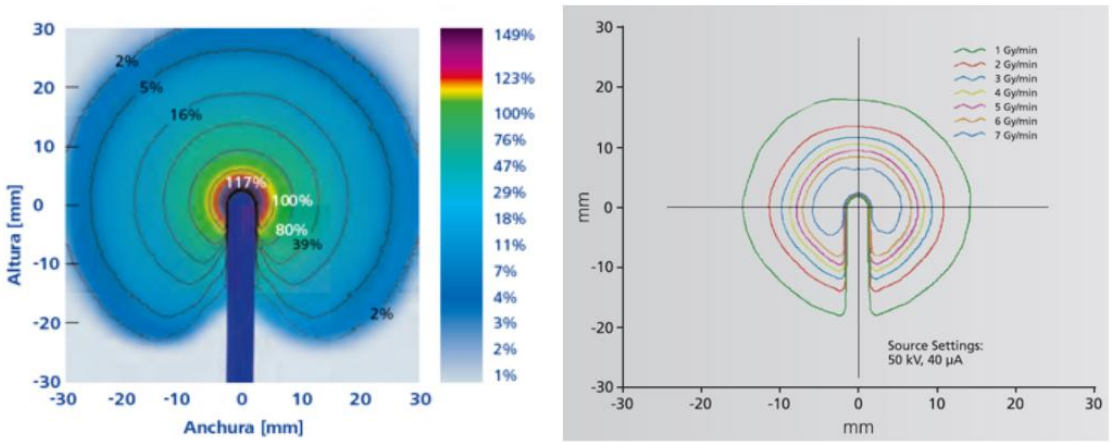


Fig. 16 Dose distribution patterns for low-kV IORT. The left image shows the characteristic steep radial dose fall-off around the applicator tip, with rapid reduction beyond the target zone. The right image displays isodose curves at different dose rates. [12]

HDR Brachytherapy

In CT-guided HDR brachytherapy IORT, a thin balloon or a multi-channel catheter is placed directly into the surgical cavity and its position is verified with a CT scan. This approach ensures that at least 98 % of the planned treatment volume (PTV) receives the prescribed 12.5 Gy dose at 10 mm depth, meaning almost the entire target gets full treatment. By using multiple channels (multilumen) instead of a single dwell position, the uniformity of the dose distribution improves dramatically.[24]

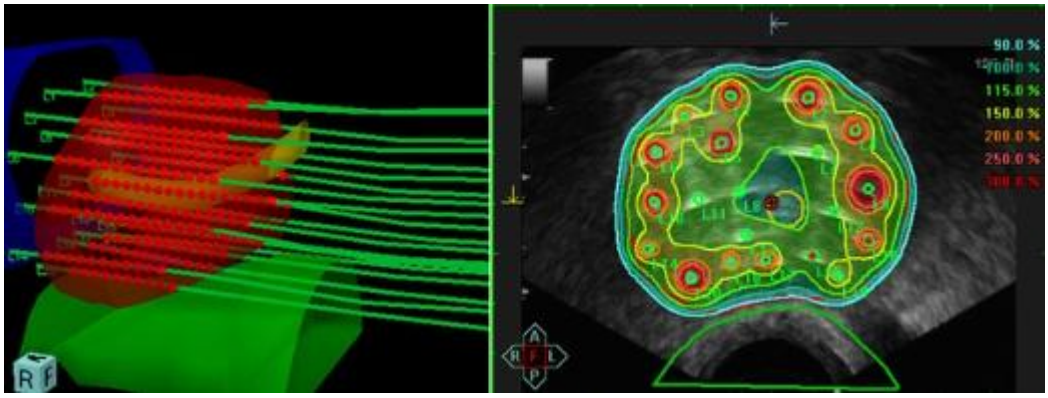


Fig.17 HDR brachytherapy intraoperative Planning. The left image shows the 3D arrangement of multiple catheter channels and planned dwell positions for dose delivery. The right image displays the dose distribution on a CT slice, with isodose curves illustrating how dwell times are adjusted.

Integral dose

Electron
In IOeRT, without a disc, 12 MeV beams can deposit up to 9.9 Gy in the closest lung voxel, but a properly aligned Al/Pb disc cuts heart and lung maxima to less than 0.1 Gy at 6 MeV and by more than 90 % at 10 - 12 MeV [25]. The shallow penetration means contralateral breast, thyroid and marrow receive less than 0.5 % of the prescription.

Low Voltage
When using a 50 kV IORT system with a 30 - 35 mm spherical applicator, the full prescription dose, typically 20 Gy, is confined almost entirely within a 3 - 4 cm diameter sphere around the applicator tip. Monte Carlo simulations and film dosimetry further demonstrate a steep dose fall-off of approximately 5 - 7 Gy at 1 cm depth and below 1 Gy beyond 2 cm [26]. As a result, critical structures, such as ribs, heart, lungs or contralateral breast, located more than 2 cm from the treatment cavity consistently receive ≤ 0.5 Gy, making the total integral dose to organs at risk negligible compared with any standard external-beam radiotherapy course.

HDR Brachytherapy
In CT-guided HDR balloon IORT, a small radioactive source inside a fluid-filled balloon emits gamma rays in nearly all directions, covering a wider area than low-energy X-rays but still with limited scatter. In a study of 60 patients receiving amounts of 34 Gy delivered in ten separate 3.4 Gy fractions, the average dose to the whole heart in left-sided treatments was only 2.4 ± 0.9 Gy, and fewer than 1 percent of heart voxels received 10 Gy or more. Likewise, the portion of the treated lung receiving at least 20 Gy stayed between 3 % and 5 %. Compared with a conventional whole-breast external-beam regimen, this represents roughly a ten-fold reduction in integral dose to non-target tissues, although it does deliver more spill-over than a 50 kV IORT system.[27]

Radiobiology

Electron
Electron IOERT is delivered at aproximately 10 Gy min^{-1} In electron IOERT, the entire therapeutic dose is delivered in under two minutes. Because the beam is on for such a short time, there's no opportunity for cells to start their repair processes while the radiation is being applied. In radiobiology terms, this means you're effectively giving a single, high-energy treatment all at once, rather than spreading it out.

Low voltage

Low-energy (50 kV) X-rays deposit energy more densely along their paths, about 10 keV per micrometer. Treatments are delivered at a moderate pace (0.3–2 Gy per minute) over 20–40 minutes. This slower dose delivery gives healthy cells a chance to repair minor damage as it occurs, while the tumor cells, stressed by reduced oxygen levels immediately after surgical removal, accumulate complex, irreparable DNA breaks.

HDR Brachytherapy

In HDR ^{192}Ir brachy-IORT, the radioactive source does not stay in one spot but steps through a series of positions inside the treatment cavity, pausing briefly at each one. Although the source itself emits a very high dose rate, over 7 Gy per minute, the actual dose delivered to any tiny volume of tissue (a “voxel”) comes in small bursts of about 0.5–1 Gy each time the source stops nearby. Over the full 15–25-minute treatment, these micro-bursts add up to the prescribed high single-fraction dose.

3.3. Financial analysis

The listed prices give only a rough idea of what hospitals will actually pay, as the true cost depends on many local factors. Actual expenses vary with import duties, taxes, exchange rates, and the hospital's bargaining power. Service contracts, room shielding, energy use, and staff training add country-specific operational costs. Additionally, the choice between purchase, lease, or public–private financing models further affects the real cost per treatment.

3.3.1. Acquisition costs

Electron

Item	Approximate Cost (€)
Accelerator (unit + console)	700,000 – 900,000
Accessories (PMMA cones, Al/Pb shielding disc)	80,000 – 120,000
Advanced TPS Software	15,000 – 30,000
QA Kit (phantoms + detectors)	20,000 – 50,000
Image Integration (portable X-ray)	50,000 – 100,000
Operating Room Adaptation (mobile shielding, alarms)	50,000 – 150,000
Total cost	**915.000 – 1.350.000**

Low Voltage

Item / Concept	Approximate Cost (€)
Accelerator (unit + console) • INTRABEAM X-ray source and control console. • SMART stand (with AutoDrape and AutoBalance functions) for positioning. • Basic set of SMART Spherical Applicators (4-6 sizes). • Spherical Sizer Set (for intraoperative sizing). • Radiance™ planning/simulation software module. • Initial on-site installation, factory acceptance testing, and basic user training.	511,000
Total Cost	**511 000**

HDR Brachytherapy

Item	Approximate Cost (€)
Core Bravos Afterloader Unit • Mobile afterloader cart • Ir-192 source drive mechanism • Treatment console • Basic dosimetry tools • Factory-level acceptance testing.	350,000 – 450,000
Mobile Shielded Case	30,000 – 50,000
QA Phantom & Accessory Set: • small water-equivalent phantom, • film or diode holders, • basic ion-chamber positioning inserts	10,000 – 15,000
Single-Use Balloon Applicator Set	1,000 – 1,500
Multilumen Catheter Set	1,500 – 2,000
Portable Local Shielding Panels	25,000 – 40,000
Total costs	**417,000 – 558,500**

3.3.2. Maintanance & operating costs

Maintenance Item	Approximate Cost annually (€)		
	Electron IOERT	**Low-kV (50KV)**	**HDR ^{192}Ir**
Service Contract	70,000 – 100,000	50,000 – 80,000	30,000 – 40,000
Energy consumption (300 interventions and 0,15€/kWh)	45	24	6
Software / security updates & licences	5,000 – 8,000	2,000 – 4,000	2,000 – 3,000
Shielding-disc replacement (Al/Pb)	2,000 – 5,000	–	–
Replacement of PMMA cones	1,000 – 2,000	–	–
^{192}Ir source (4 replacements / yr)	–	–	60,000 – 72,000
Source disposal (empty capsule return)	–	–	4,000 – 6,000
Balloon applicators	–	–	20,000
In-vivo detectors / dosimeters	1,000 – 2,000	1,000 – 2,000	2,000 – 3,000
Oncologist-radiotherapist	YES	YES	YES
Medical-physicist	YES	YES	YES
OR nurse	YES	YES	YES
Radiation technician	NO	NO	YES
Image Techinician	NO	NO	YES
TOTAL anual expense	**79,045 – 117,045 ***	**53.000 – 86,024 ***	**118,000 – 144,006 ***

*It does not include the staff cost because it is extremly variable, only if it is required.

Hospitals typically finance high-cost technologies like IORT through amortization over 7 to 10 years, based on the equipment's cost and expected lifespan. They spread the total amount into annual payments, adding interest if using leasing or loans. Ongoing costs like maintenance, insurance, and software updates are also factored in. The choice between direct purchase or leasing depends on available budget and local tax benefits.

3.4. Market Analysis

The global Intraoperative radiation therapy (IORT) market was valued at $48 million in 2020 and is projected to reach $66 million by 2025, growing at a CAGR of 6.4%. This growth is driven by the rising incidence of cancer, technological advancements, and the benefits of IORT over conventional radiotherapy. [39]

3.4.1. Drivers

One of the primary drivers of market expansion is the increasing global prevalence of cancer. For instance, in 2020, the U.S. reported 276,480 new cases of invasive breast cancer, while worldwide cancer cases are expected to rise from 17 million in 2018 to 27.5 million by 2040 (IARC). The advantages of IORT, such as precision, shorter treatment duration, and reduced side effects, are accelerating its adoption. However, the market faces challenges, including a shortage of trained professionals and concerns about radiation exposure risks for both patients and medical staff.[39]

3.4.2. Opportunity

Opportunities for growth lie in the expanding applications of IORT. Clinical trials are exploring its use in pancreatic cancer (IntraOp Medical, 2019) and brain metastases (Carl Zeiss Meditec, 2018). Additionally, technological innovations, such as portable systems and AI-assisted treatment planning, are expected to enhance market penetration.

3.4.3. Market overview

In the market, electron IORT holds the largest share among technologies, favored for its efficiency and dose homogeneity. By application, breast cancer leads due to high success rates and demand for non-invasive treatments. Geographically, North America holds the largest market share, supported by high healthcare spending and early adoption of advanced therapies. Meanwhile, the Asia-Pacific region is expected to grow the fastest, driven by rising cancer incidence, aging populations, and improving healthcare infrastructure.

Key players in the IORT market include ZEISS Group, Elekta AB, and Varian Medical Systems. Recent developments include Elekta's launch of the Geneva gynecological applicator (2020) and Varian's acquisition of Cancer Treatment Services International (2019) to expand its oncology solutions.

Despite its potential, the market faces hurdles such as high costs and regulatory challenges. However, with ongoing research, strategic collaborations, and increasing demand for precision oncology, the IORT market is poised for steady growth. Future trends may include AI integration for enhanced treatment planning and expansion into emerging markets through public-private partnerships.[39]

3.5. Design of an IORT operating room

The diagram shows a shielding layout for an operating room that hosts a mobile electron accelerator. The floor plan is divided into three protective zones. Zone A, outlined by the large red circle, is the beam area directly around the treatment table and must stop the highest level of scatter. For that reason its ceiling carries 6mm of steel plate topped with 8cm of barite-loaded concrete and a 12cm wall of barite concrete. Zone B surrounds the beam area and the ceiling carries the same steel plate plus 10cm of barite concrete and a 10cm wall of barite concrete, while Zone C covers adjacent corridors and the ceilings have the same steel plate plus 4cm centimetres of barite concrete and a 6cm wall of barite concrete.
The accelerator table sits inside Zone A. The control console is positioned just outside the shielded wall so staff can operate the unit without being exposed. Three fixed area-dosimetry stations, marked in green, continuously monitor radiation levels throughout the suite.
At Hospital Clinic, the team decided to reinforce both the walls and the ceiling with extra concrete so they would not have to wheel heavy lead screens in and out for every case. This permanent structural shielding keeps the workflow smooth and ensures that neighbouring rooms remain fully protected. [12]

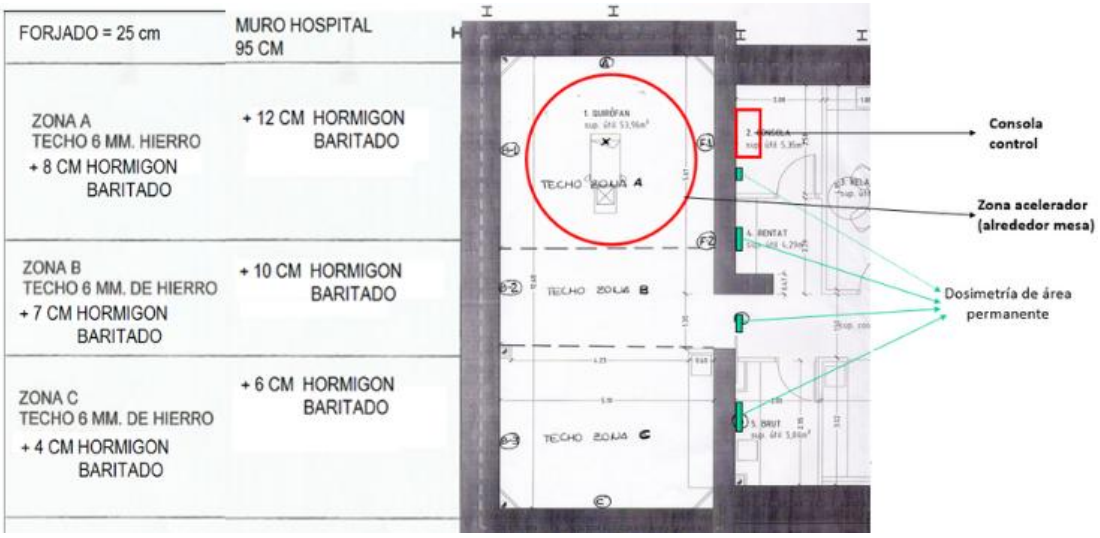


Fig. 18 Shielding layout for the IOeRT operating room of Hospital Clinic de Barcelona [12]

Radiation-safety regulations set maximum permitted doses (MPD) to protect workers and the general public.

Radiation Dose Limits at Work (MPD)	
Classification	**Annual Dose (mSv)**
General Population	1
Whole Body (5-Year Average)	100
Whole Body (1 Year)	50
Extremities	500
Eye Lens	150

Table 13 Information on màximum permitted dose (MPD).

3.5.1. Parts of an IOeRT room [12]

Fig 10 IOeRT Operating room of Hospital Clinic de Barcelona.

The diferent parts of a OR IOeRT room

1. **Lead-lined modular wall panels:** 3–5 mm Pb-equivalent attenuates the primary beam and leakage radiation.
2. **Shielded suspended ceiling:** Lead sheets above the grid/luminaires confine upward-scattered radiation.
3. **Baryte-concrete or conductive vinyl floor:** Final layer of shielding for downward radiation; prevents transmission to the level below
4. **Labyrinth-type ventilation grilles:** Internal bends block direct beam line-of-sight while maintaining HEPA airflow and over-pressure
5. **Control / interlock wall panel:** Key enable, emergency stop, and interlocks so the beam can fire only when the room is closed and empty.
6. **Embedded monitor & remote console link:** Allows LINAC control from outside; housing itself is lead-lined.
7. **Mobile IOeRT accelerator**

3.5.2. Improvements in IOeRT rooms

Real-Time Environmental & Radiation Safety

A unified IoT dashboard will stream temperature, CO_2, pressure, particle counts, room dose rate and staff badge doses in real time, with instant alerts and auto-LINAC shutdown on any breach. This safeguards patients and personnel, stabilizes environmental conditions, and embeds *"always-on"* regulatory compliance. Automated logs and predictive maintenance cut manual checks and downtime, boosting throughput and reinforcing a culture of safety.

3.6. IMRT VS IORT

3.6.1. Clinical overview

Long-term studies that followed patients for five to eight years show no meaningful difference in overall survival or in how often the cancer comes back near the surgery site. Whether the boost is given immediately in the operating room with IORT or later in several outpatient sessions with IMRT, local control remains above 95 % and five-year survival sits at essentially 100 %. [28]

Where the two methods separate is in the short-term side-effects and in how much stray dose the rest of the body sees. Because IORT releases its entire boost dose in a single hit that is physically confined to a 3 – 4cm sphere, tissues farther away, like heart, lungs, opposite breast, bone marrow, pick up only a few tenths of a gray, amounts that are considered negligible. Patients therefore leave the operating room with very little skin reddening or swelling, and the rate of acute reactions recorded immediately after the boost is markedly lower than with IMRT.

IMRT, by contrast, spreads the same boost over five to eight sessions delivered from several beam angles. This fractionated schedule is gentle on deep organs, but the multiple entry paths create a low radiation bath that the whole breast, a slice of lung, and sometimes the heart inevitably receive. The doses are small, on the order of a couple of gray, but large enough to bump up the incidence of temporary skin irritation and fatigue during the treatment weeks.

A single-dose IOeRT session adds only about 18 minutes of radiation work to the 60 minutes surgery, so the entire procedure is finished in 78 minutes. When IOeRT is used as a boost, the operating-room time remains short but a brief 15-day hypofractionated external-beam course is still required, bringing the total to roughly 527 minutes. By contrast, a conventional external radiotherapy cycle takes about 30 daily sessions, adding more than 900 minutes of machine time and several weeks of hospital visits.

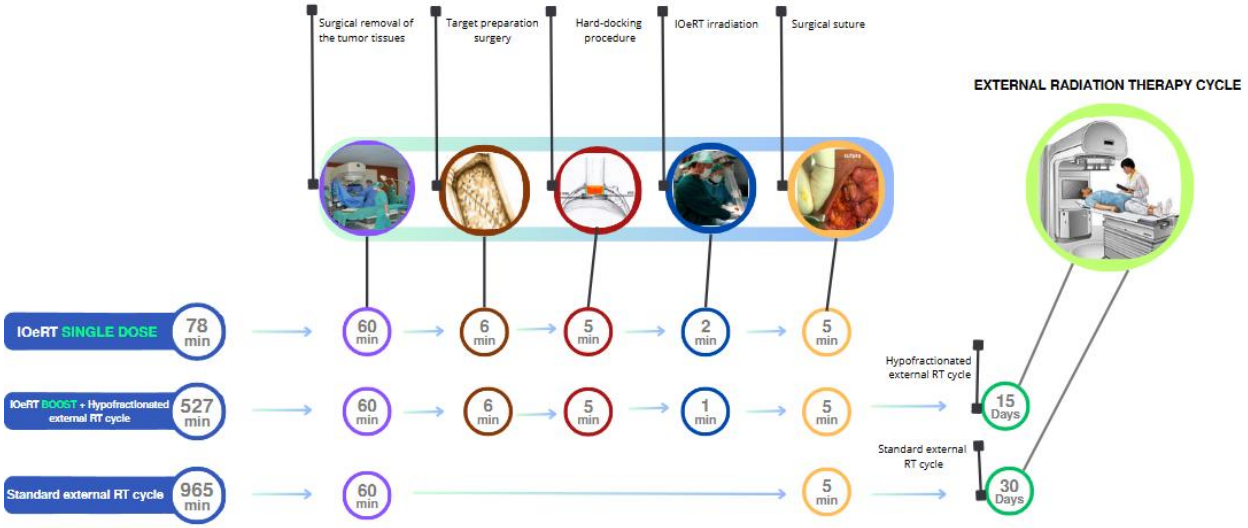


Fig. 11 Comparison of treatment workflows.[13]

Once healing and routine whole-breast irradiation are complete, both groups even out. Late effects such as fibrosis (firmness of breast tissue), tiny skin blood-vessel changes, arm swelling, or lung scarring are rare and occur at statistically the same rates. Modern shielding discs for electron IORT and careful source planning for HDR-balloon IORT, plus daily image guidance for IMRT, keep the heart and lung doses so low that measurable cardiac or pulmonary problems have not diverged between the techniques after a decade of follow-up.

3.6.2. Technical overview

IORT delivers its boost from inside the surgical cavity and therefore achieves its conformity through physics rather than beam modulation.
With a 30 - 35 mm low-kV spherical applicator the prescription is 20 Gy at the surface, the dose is already 5 - 7 Gy at 1 cm and less than 1 Gy beyond 2 cm [22,23]. Electron IOERT, using 6 - 12 MeV beams through flat or beveled cones, deposits 21 Gy to the 90 % isodose at depths of 1.6 cm (6 MeV) to 3.5 cm (12 MeV); an Al/Pb disc placed beneath the cavity reduces forward leakage so heart and lung receive ≤0.1 Gy at 6 MeV and >90 % less dose at 10 - 12 MeV [20,21]. HDR ^{192}Ir balloon or multilumen catheters cover ≥98 % of the planning target with 12.5 Gy at 10 mm and dose drops by roughly 10 % with every additional mm beyond the balloon edge. [24]

IMRT, planned on postoperative CT/MRI, employs 5 - 7 dynamic fields or VMAT arcs so that ≥95 % of the boost volume gets the prescription (e.g., 16 Gy over 5–8 fractions). The modulated beams inevitably create a low-level scatter bath with contralateral-breast mean dose ~2–3 Gy, ipsilateral-lung V_5 Gy ~20 % and heart mean ~2 Gy for left-sided cases. An integral dose roughly one order of magnitude higher than 50 kV IORT yet still lower than a full external course. [29]

3.6.3. Financial overview

IORT delivers its boost intra-operatively, so the entire radiation episode is folded into the surgical workflow. Once the surgeon excises the tumour and confirms margins, the radiation oncologist and physicist position either a low-kV spherical applicator, an electron cone or an HDR balloon/catheter set directly in the cavity, deliver a single 10–20 Gy dose, remove the applicator and close the wound, all under the same anaesthetic.
IMRT, by contrast, is an external-beam boost that begins four-to-six weeks after surgery; the patient returns for CT simulation, treatment planning and daily image-guided sessions, typically receiving 8 - 16 Gy split into 5 to 8 fractions over 2 weeks. This difference in timing drives the logistical footprint.
IORT adds roughly thirty minutes to the operating-room schedule and requires the simultaneous presence of the surgical, anaesthesia and radiation teams, but it eliminates the need for any postoperative radiotherapy visits. IMRT uses no additional OR time yet ties up the linear accelerator for 15–60 minutes per fraction and obliges the patient to multiple outpatient appointments, each staffed by therapists, a physicist on call and a radiation oncologist for weekly review. The economic profile mirrors these workflows.
To sum up, IORT concentrates expenditure in the operating theatre and in single-use applicators but minimises downstream clinic utilisation, whereas IMRT relies on existing high-cost LINAC infrastructure, spreads staffing and machine hours over many short appointments, and incurs higher cumulative running costs despite negligible impact on the initial surgery.

3.7. Future prospects

3.7.1. Future Market

Intra-operative radiotherapy is gradually moving from a niche technique to a recognised complementary modality in cancer treatment [30]. Worldwide sales of IORT systems are increasing, largely driven by their use in breast cancer, soft-tissue sarcoma, locally advanced rectal and pancreatic tumours and selected brain metàstasis [30]. At present, mobile electron linear accelerators that deliver beams of 6 to 12 MeV dominate the field because they combine versatility, relatively modest shielding requirements and a favourable cost-benefit ratio compared with fixed bunker installations [30].

3.7.2. IORT State-of-the-Art

Several technical trends are shaping the next generation of IORT. Image-guided procedures that couple cone-beam computed tomography or kilovoltage fluoroscopy with the applicator now allow surgeons and physicists to confirm target coverage and spare sensitive organs before a single pulse is delivered [31]. Mini-linacs that incorporate built-in, self-shielded vaults are small enough to operate inside standard operating rooms, opening IORT to centres that previously lacked space or funds for dedicated suites [31]. Adaptive planning assisted by artificial intelligence promises to shorten the workflow and trim the safety margins that compensate for positioning uncertainty [31]. Meanwhile, surgeons are beginning to print patient-specific applicators and use on-table dosimetry inserts, allowing real-time verification of dose while the wound is still open [31].
Electron beams will remain the workhorse of intra-operative radiotherapy, but their delivery is evolving. Ultra-high-dose-rate or “FLASH” IORT, defined by dose rates above 40 gray per second, has produced lower normal-tissue toxicity in multiple animal models and has already entered early-phase clinical testing for superficial disease [32][33]. At the same time, very-high-energy electrons in the range of 50 to 100 MeV are under development [33]. Because they can traverse deeper anatomy while still benefiting from the FLASH effect, they may extend IORT to retroperitoneal or paravertebral targets that today require conventional external beams.[33]

3.7.3. Next generation IORT

Proton intra-operative radiotherapy offers a tantalising theoretical advantage. The Bragg peak confines the highest dose to the last millimetres of the beam path, potentially sparing distal healthy tissue even more than electrons [34]. The obstacle is engineering rather than physics. Current accelerators and gantries are too large and expensive to share space with anaesthesia teams, sterile instruments and imaging devices [34][35]. Research groups are therefore focusing on compact superconducting cyclotrons that mount directly on a lightweight gantry and on sterilised nozzle assemblies that can be wheeled into the field.[34][35]

Heavy ions such as carbon provide an even higher relative biological effectiveness and a sharper distal edge than protons, which makes them attractive against radio-resistant tumors [36]. Unfortunately, the synchrotrons required to accelerate those ions cost hundreds of millions of euros and currently exist in only a handful of countries. Unless tabletop laser-plasma accelerators or other compact sources become clinically reliable, heavy-ion IORT will remain a remote prospect. [36]

By the end of the decade, compact proton rooms and the first feasibility studies of very-high-energy electron beams should appear in leading oncology centres. In the early-to-mid 2030s, fully integrated surgical robots, adaptive planning driven by artificial intelligence and hybrid imaging-irradiation systems may enable real-time, margin-controlled treatments for complex pelvic and abdominal tumours.[31][34][35]

4. Discussion

Feature	Electron IORT (IOeRT)	Low-kV IORT	HDR Brachy-IORT	IMRT
Clinical applications	Breast Cancer, Pancreatic Cancer, Colorectal Cancer, Gynecological Cancer, Head and Neck Cancer and Sarcomas	Breast Cancer, Pancreatic Cancer, Colorectal Cancer, Gynecological Cancer, Head and Neck Cancer and Sarcomas	Breast Cancer, Pancreatic Cancer, Colorectal Cancer, Gynecological Cancer, Head and Neck Cancer and Sarcomas	Widely applicable to any post-operative boost volume; standard for organs where IORT not feasible
Technology complexity	Mobile mini-linac, vacuum waveguide, bending magnet	Miniature 50 kV X-ray tube, self-shielded head	Remote afterloader, stepping ^{192}Ir source, CT-based plan	Full hospital linac, MLC, on-board imaging, treatment-planning system
Shielding requirements	Lead-aluminium disc under field, 1–2 mm Pb mobile panels, reinforced floor	Usually none; 0.5–2 mm Pb drapes or screens for staff	Mobile lead walls or HDR bunker.	Permanently shielded vault
Typical workflow time	Adds 18 min to surgery (beam-on ≤ 2 min)	Adds 45 min to surgery (beam-on ≤40 min)	Adds 30 min to surgery (beam-on 10 - 20 min)	5–8 outpatient fractions (boost) or 15–30 fractions. Each visit 15–20 min
Main suppliers	SIT Sordina (NOVAC & LIAC), IntraOp (Mobetron).	ZEISS (Intrabeam), Xoft (Axxent)	Varian (Bravos), Elekta (Flexitron), Eckert & Ziegler	Varian, Elekta, Accuray, Siemens, RefleXion
Integral dose	Shielded tail dose < 0.5 Gy beyond 3 cm	≤ 0.5 Gy beyond 2 cm	heart mean ≈ 2 Gy in left breast cases	Low-level scatter to contralateral tissues
Acquisition cost	915,000€ - 1,350,000€	511,000€	417,000€ - 558,500€	3,000,000€
Annual maintenance + operating cost	79,045€ - 117,045€	53,000€ - 86,024€	118,000€ - 144,006€	200.000€
Staff per case	Surgeon, radiation oncologist, medical physicist, OR nurse, RT technologist	Surgeon, radiation oncologist, medical physicist, OR nurse.	Surgeon, radiation oncologist, physicist, dosimetrist, OR nurse, afterloader operator	Radiation oncologist, physicist, 2 radiation therapists for every fraction
Dose coverage	Flat 90 % plateau to selectable depth.	Steep fall-off: 20 Gy 5–7 Gy at 1 cm < 1 Gy at 2 cm	Dwell optimisation smooths hotspots	Multiple fields create low-dose bath
Treatment course length	Single session	Single session	Single session	1–6 weeks depending on fractionation
Typical patient convenience	No extra RT visits if single-dose; 1-week EBRT if boost	No extra RT visits. Longest intra-op time	No extra RT visits. Postoperative catheter removal	Multiple hospital visits.

Each intra-operative radiotherapy modality strikes a different balance of technical complexity, logistics and cost. Electron IOeRT delivers a uniform dose with very short beam times, but it requires local shielding (disc and panels) and a high capital outlay. Low-kV systems are the easiest to install and rarely need structural shielding, yet they lengthen the operation because of their slower dose rate. HDR brachytherapy offers the greatest ability to sculpt the dose through multiple source positions, although it brings the added complexity of a remote afterloader and the recurring expense of ^{192}Ir source replacements. IMRT is the most versatile option outside the operating room, but it demands the highest-cost infrastructure and extends treatment over many outpatient fractions. From the patient's perspective, all three intra-operative techniques condense radiation into a single session, whereas IMRT requires several weeks of visits. Regarding whole-body exposure, low-kV and electron methods spare healthy tissues the most, HDR follows, and IMRT produces the broadest low-dose bath

5. Conclusion

Choosing an intra-operative radiotherapy platform cannot hinge on technology alone, but it must align with the clinical, economic and even architectural realities of each institution.
A university hospital with an established radiation-oncology department, a dedicated physics team and enough operating room for mobile equipment will obtain the greatest benefit from an electron system. Electrons provide the best mix of uniform depth coverage, robust multi-centre clinical evidence and anatomical versatility while keeping acquisition and maintenance costs at a moderate level.
In contrast, a local hospital or private centre with standard operating rooms and limited capacity for structural upgrades is likely to profit more from a low-kilovoltage unit. Installation is virtually plug-and-play, radiation protection can be achieved with simple lead curtains, but dose-delivery times are longer and the range of clinical indications is narrower.
When it is essential to sculpt the dose in irregular cavities, as in pelvic recurrences or head-and-neck tumors, HDR IORT brachytherapy becomes the preferred choice. It calls for a more complex workflow and budget planning for regular ^{192}Ir source exchanges, yet its dosimetric flexibility surpasses any other modality.
Finally, centres that already have a shielded vault and a modern LINAC may find it most cost-effective to continue using conventional IMRT for post-operative boost volumes. The technology benefits from decades of refinement, provided the multidisciplinary team accepts the logistics of multiple outpatient fractions.

Beyond these core considerations several emerging factors will influence future purchasing decisions:

Sustainability
A single-session IORT course eliminates the carbon footprint of dozens of patient journeys and linear-accelerator warm-up cycles.

Workforce resilience
Shortages of radiotherapy technologists make modalities that need fewer fractions more attractive.

Patient
Patient-reported outcomes are becoming central to policy and reimbursement, and current data suggest that intra-operative techniques often score higher on convenience and quality-of-life metrics than multi-week external schedules.

To sum up, the optimal choice depends on aligning hardware with workload, architectural realities, maintenance budgets and strategic goals.

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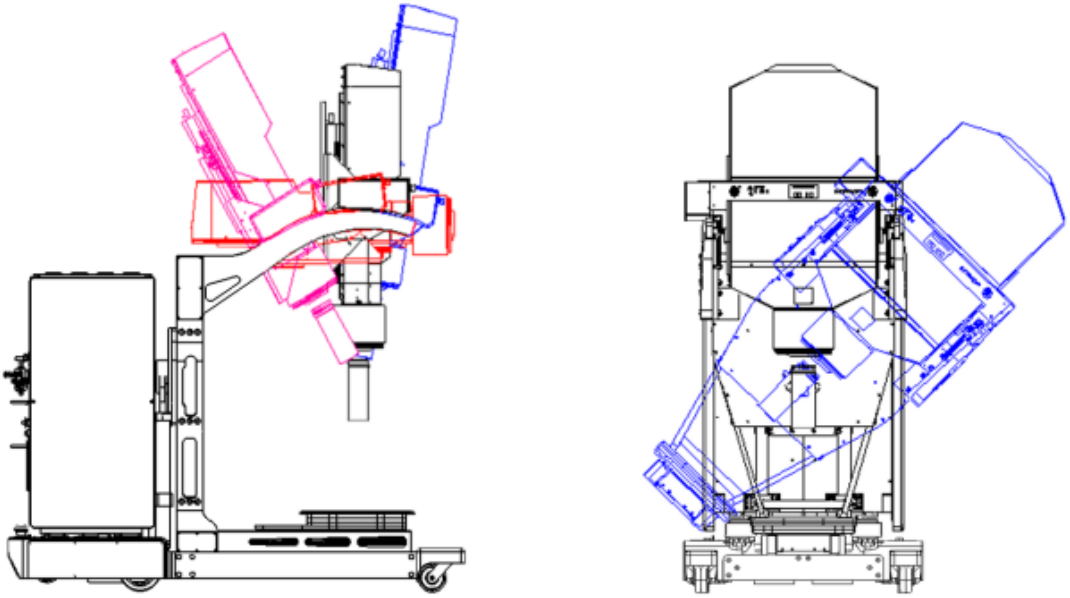
7. Appendix

Appendix A: Schemes of the technical configuration of IORT technologies

MOBETRON



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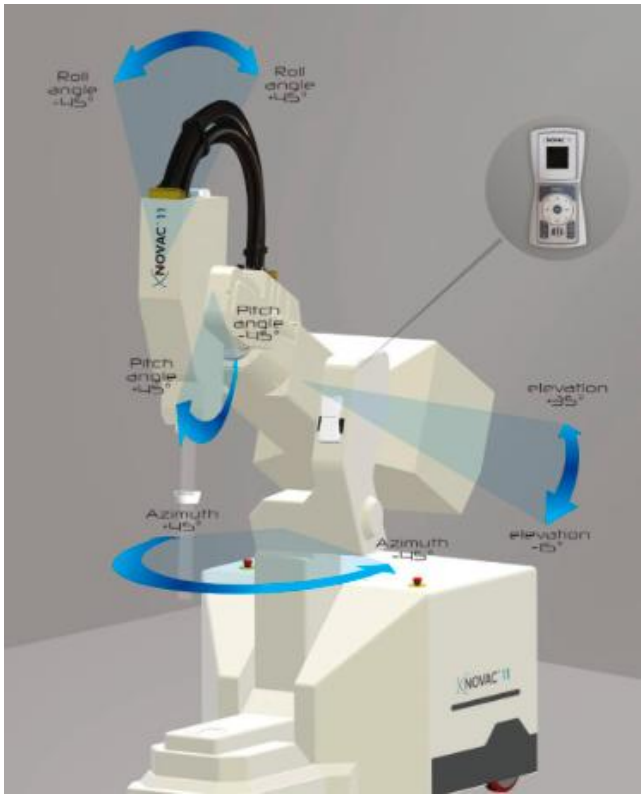

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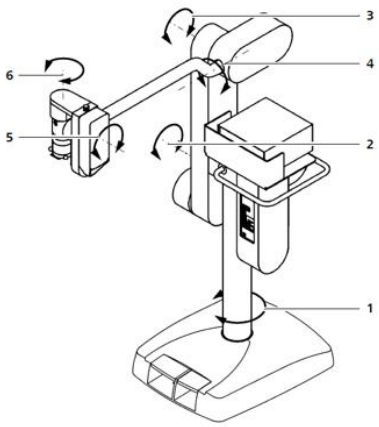

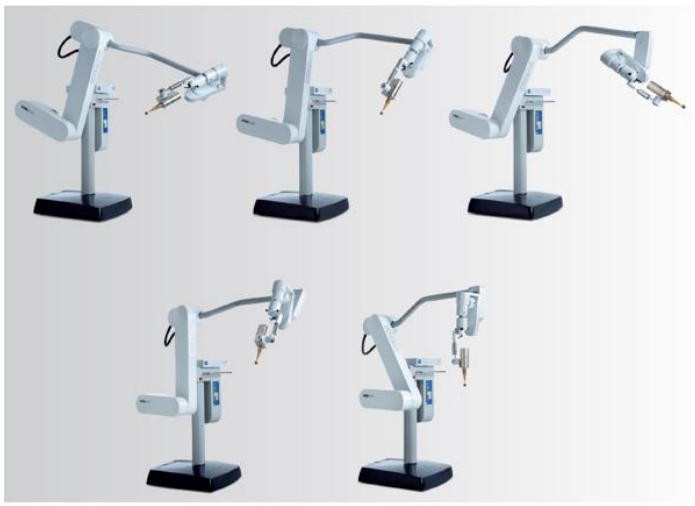

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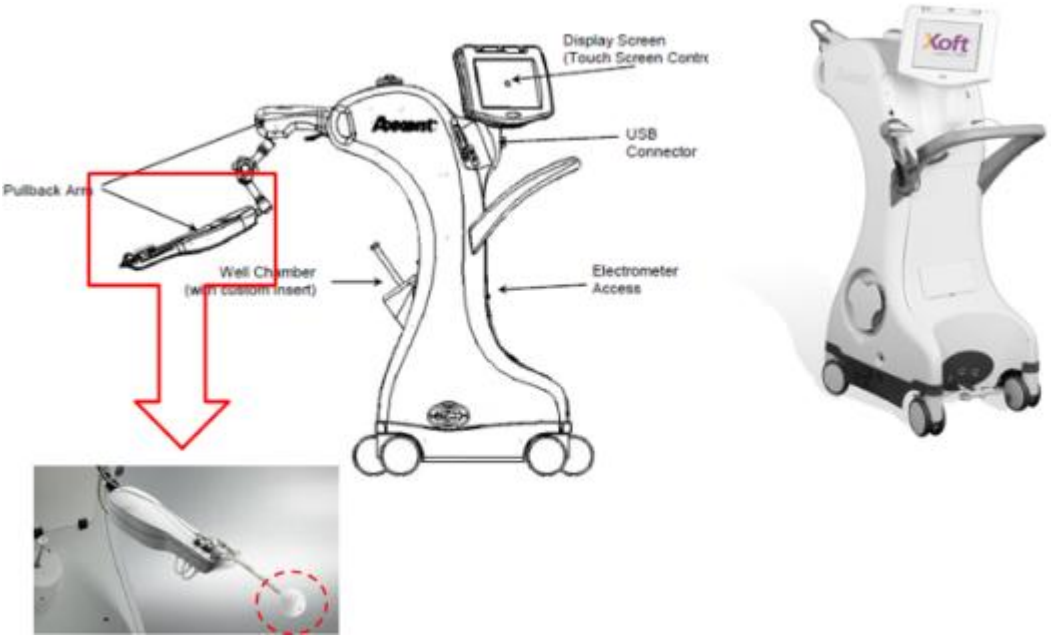
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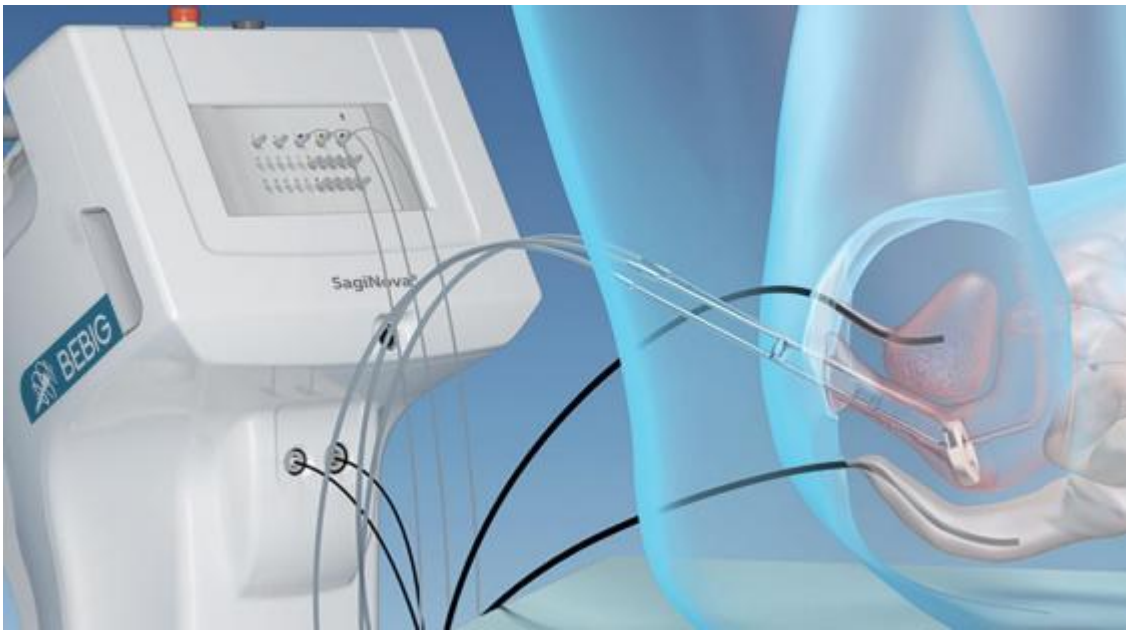
(Touch Screen Contr
USB
Connector
Pullback Arm
Well Chamber
(with custom insert)
Electrometer
Access
Xoft

BEBIG


BEBIG
SagiNova

Appendix B: Multicancer application of IOeRT [15]

District / Site	Indication (Stage)	Key Institution or Reference	Main Results	Remarks / Reported IOeRT Effects
PANCREAS	Unresectable	MGH (1)	2-yr OS 16 % (survivors > 5 yr)	IORT (applicator + beam) plus Charlson index > 3 and chemotherapy improved OS
	Borderline resectable	MCR (2)	LC 84 %; 3-yr OS 40 % vs 0 % without IOeRT	Median survival 23 mo; no R1/R2 resection advantage without IOeRT
	Resectable	HGUM (3)	5-yr LC 18 %	-
	Unresectable or borderline-resectable	MGH (4)	Median OS 35.8 mo	Neoadjuvant CRT + IOeRT improved survival; no added toxicity
ESOPHAGO-GASTRIC	Stage I and III	HGUM (5)	5-yr LC 85 %	Favourable effect of IOeRT in stage II and III
GASTRIC	Resectable	Meta-analysis HGUM (6)	IOeRT improved LC	Any stage: IOeRT promoted local control
RECTAL	cT2–4 N+	HGUM (8)	5-yr LC 97 %	IOeRT safe in risk-adapted treatment
	Primary and recurrent	Systematic review (7)	IOeRT improved LC and OS	Toxicity increment by IOeRT low
	Unresectable R2	MCR and CHU (10)	5-yr LRR 31.9 %, DFS 57 %, OS 65 %	IOeRT and preop RT improve LC
	Recurrent	MCR and CHU (11)	IOeRT advantage in pR1 and R2 resection	-
	pT4/N1–2	Multivariate analysis (12)	5-yr OS 89.7 %, LC 69.0 %, DFS –	No increase in acute and long-term complications
PROSTATE	Metastatic D1 and D2	Saitama Cancer (13)	5-yr OS 75 %/52 %	In D2 IOeRT significantly cancer-specific survival
RENAL	Recurrent / primary resectable	US-Europe	5-yr OS 37 % (vs 55 % without)	Factors affect renal bed involvement, sarcomatoid features and IOeRT dose
PEDIATRIC	Ewing / rhabdomyosarcoma	Pooled-European (15)	5-yr 70 %/74 %, EFS 68 %	R1 and recurrent influence outcome
	Neuroblastoma + sarcoma	Heidelberg Univ (16)	1/18 local recurrences	6 clinical significant late toxicity
SARCOMAS	Primary extremity soft-tissue	Multicentric pooled analysis (17)	10-yr LC 85 %, LTC 76 %, DFS 81 %	IOeRT boosted LC with low toxicity
	Retroperitoneal	Heidelberg Univ (18)	5-yr LRC 27 %, LC	Delayed intraperitoneal recurrence
	Retroperitoneal	MCR (19)	5-yr OS 60 %	92 % v 46 % with R1 (alone = 0.3)
	Retroperitoneal	Boston Univ (20)	5-yr OS 64 % for liposarcoma	IOeRT + adj. EBRT improved survival
	Retroperitoneal	Univ Freiburg (21)	5-yr OS 52 %	In pts < 65 yrs and R2 resection advantages
	Extremity soft-tissue	Pooled-European (22)	10-yr OS 82 %	In-field LC promoted by IOeRT dose > 12.5 Gy
	Osteosarcoma	MCR (23)	10-yr OS 82 %, LC 73 %, OS	R1 resection = favourable
OLIGO-RECURRENCES	Gynaec, GI, soft-tissue, head & neck	Univ of Navarre (25)	5-yr LC 37 %, LRC 67 %, DMFS 31 %, OS 66 %	EBRT + IOeRT escalation improves survival; gross macroscopic disease significant for LC

Table 14 Applications of IOeRT in càncer [15]

Abbreviations and Definitions of Table 7

- **MGH** = Massachusetts General Hospital
- **HCMU** = Hospital of China Medical University
- **MCR** = Mayo Clinic Rochester
- **CHE** = Catharina Hospital Eindhoven
- **LC** = Local Control
- **LRC** = Loco-Regional Control
- **OS** = Overall Survival
- **DMFS** = Distant Metastasis-Free Survival
- **m** = months
- **y** = years
- **pts** = patients
- **(p)** = primary locally advanced disease
- **(r)** = recurrent disease
- **St** = stage
- **IMRT** = Intensity-Modulated Radiotherapy
- **IOeRT** = Intra-Operative Electron Radiotherapy
- **R0** = complete resection (no residual tumour)
- **R1** = microscopic residual tumour
- **R2** = macroscopic residual tumour
- **C** = centre
- **S** = surgery
- **CT** = chemotherapy
- **CRT** = chemoradiotherapy
- **RT** = radiotherapy
- **EBRT** = external-beam radiotherapy
- **SR** = survival rate
- **STS** = soft-tissue sarcoma
- **D1** = cancer spread to regional lymph nodes only
- **D2** = cancer spread to distant lymph nodes and/or bones or organs
- **HGUM** = Hospital General Universitario Gregorio Marañón
- **cT2–4 N+** = clinical stage T2–4 with nodal involvement
- **pT4N0/T1–4N+** = pathologically advanced stage involving other organs/structures or metastatic pelvic nodes

Since 2016, the National Comprehensive Cancer Network (NCCN) has recommended intra-operative electron radiotherapy (IOeRT) for the treatment of:

- Soft-tissue sarcoma of the extremity, trunk, head-and-neck, and retroperitoneal or intra-abdominal locations
- Rectal cancer that is resectable with very close or positive margins, especially T4 or recurrent tumours
- Colon cancer that is locally unresectable, particularly T4 or recurrent cases
- Unresectable or locally recurrent pancreatic adenocarcinoma
- Recurrent cervical cancerñ
- Recurrent endometrial cancer
- Uterine sarcoma with radiologically isolated vaginal or pelvic recurrence
- Bladder cancer (stage IV A) in patients who show a complete response to chemotherapy or chemoradiotherapy
- Malignant pleural mesothelioma (stage I–III) that is medically operable with residual disease

Appendix C: Project Management timeline

Gantt Diagram

In this timeline, the Gantt diagram, we see how the main tasks of this project were managed.

ID	Task description	FEBRUARY				MARCH				APRIL				MAY				JUNE			
		WK1	WK2	WK3	WK4	WK1	WK2	WK3	WK4	WK1	WK2	WK3	WK4	WK1	WK2	WK3	WK4	WK1	WK2	WK3	WK4
1	Project defintion with Dr. Biete																				
2	Review scientific research																				
3	Clinical analysis																				
4	Visit to Hospital Clinic																				
5	Technical analysis																				
7	Financial analysis																				
8	Visit to ICO																				
9	Discussion																				
10	Deliver																				
11	Presentation																				
12	Writing the report																				